"EVALUATION OF *JEEVANTHYADI GHRITA MATRA BASTI* ON CHEMO-RADIATION INDUCED ADVERSE EVENTS IN CANCER PATIENTS"

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For the award of the degree of

Doctor of Philosophy

In Agadatantra

Under the Faculty of Ayurveda

By

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LIST OF ABBREVIATIONS USED

CCRT	:	Concurrent Chemoradiation Therapy
CCRT+MB	:	Concurrent Chemoradiation Therapy & *Jeevanthyadi Ghrita matra Basti*
JG	:	*Jeevanthyadi Ghrita*
JGMB	:	*Jeevanthyadi Ghrita matra Basti*
KCTRI	:	Karnataka Cancer Therapy and Research Institute.
QOL	:	Quality of Life
EORTC	:	European Organization for Research and Treatment of Cancer
H&N	:	Head & Neck Cancer Subjects
CX	:	Cervical Cancer
OES	:	Oesophagus Cancer
ECOG-PS	:	Eastern Cooperative Oncology Group Performance Status
ASU-DTL	:	Ayurveda Siddha Unani –Drug Testing Laboratory
GC-MS	:	Gas Chromatography and Mass Spectrometry
HPTLC	:	High-performance thin layer chromatography
LC-M	:	Liquid chromatography-mass spectrometry
TNF	:	Tumour Necrosis Factor

COX	:	Cyclooxygenase
PGE	:	Prostaglandins
Gy	:	Gray Units used for radiation
%	:	Percentage
±	:	Plus-Minus Sign
Q.S	:	Quantity Sufficient
Sl. No	:	Serial Number
S.E	:	Standard Error
S.D	:	Standard Deviation

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1.1 ABSTRACT

Introduction: Despite of known efficacy of Concurrent chemoradiation therapy [CCRT], one can understand that concurrent chemoradiation therapy will also lead to local and systemic acute toxicities that will negatively affect quality of life. Increasing evidences suggests scope of alternate medicine in cancer care. Indeed, it is only when we perform some pragmatic like studies, we can offer practicable and scientifically acceptable solutions.

Aim and Objective: In particularly this proposed thesis aims to determine the improvement in quality of life in different domains and amelioration of CCRT induced adverse effects among patients who receive *Jeevanthyadi ghrita matra basti* along with concurrent chemoradiation against the patient who only receive concurrent chemoradiation therapy.

Materials and Methodology: Ingredients of *Jeevanthyadi Ghrita* [JG] were procured from GMP certified pharmacies and natural habitat. Ghrita/ghee prepared by traditional fermentation process was procured. Prepared JG was subjected to analysis of standard ghee parameters, Qualitative and Quantitative phytochemical tests. HPTLC, GC-MS and LC-MS analysis of prepared JG for identifying active principles.

Clinical trial was ethically cleared, registered in Clinical Trail registry of India (CTRI) and conducted at Karnataka Cancer Therapy Research Institute Hubballi, Karnataka. Both Control group (CCRT, n=70) and Trail group [CCRT+MB, n=70] received Concurrent Chemoradiation therapy with weekly Cisplatin (40mg/m^2) and Radiation fractions based on type of cancer (25-35#). Trail group additionally

received *Jeevanthyadi ghrita Matra basti* for three consecutive days just before every chemotherapy cycle for six weeks. All the subjects were assessed for Primary outcome i,e Quality of Life using EORTC-QLQ-30 core questionnaire as a tool along with supplement scales of respective cancers (H&N-43, CX-24 and OES-18) every week. Secondary outcomes were assessed at three time points (Before, Mid and Post Trial) namely Adverse effects (assessed through CTCAE version 5), Safety parameter through CBC, Liver function test, serum urea and creatinine. Performance status was assessed by ECOG-PS scale.

Results and Observations: Analysis of all the ingredients of the JG showed values and characteristic features as per API. Quantitative phytochemical screening of JG showed presence of Alkaloids and terpenoid. HPTLC of JG showed 7 peaks and 10 peaks at 256 and 366 nm respectively. While the GC-MS showed presence of 17 peaks and LC-MS showed presence of more than 60 compounds out of which 40 were identified and forwarded for preliminary network pharmacology.

A total of 257 subjects were screened, out of which 218 were eligible based on inclusion criteria. Among them 140 consented for the study and each arm had 70 subjects (38 Head and Neck, 22 Cervical and 10 Esophagus Cancer subjects each).

Quality of life was significantly different ($p<0.05$) between CCRT and CCRT+MB group subjects. CCRT+MB had better mean scores in domains of Physical, Role, Social, Emotional, Cognitive Functions and in symptoms like nausea, vomiting, pain, dyspnoea, insomnia, constipation, diarrhoea and financial difficulty. Similar was the status in all strata i.e head and neck, cervix and oesophagus cancer subjects.

In Head and Neck subjects, symptoms score (H&N-43) was significantly different ($p<0.001$) in majority of symptoms expect dry mouth, sticky saliva, cough and pain opening mouth between CCRT and CCRT+MB group. In cervical cancer subjects, there was significant difference in symptoms score (CX-24) between the groups. In oesophageal cancer subjects, symptoms score (OES-18) showed no significant difference between the groups, however the mean scores were comparatively better in CCRT+MB group.

There were totally 40 symptoms noted in entire study. Independent 't' test showed significant difference [ranging from $p<0.001$ – $p<0.05$] in symptoms grading in 13 major symptoms induced by CCRT at 5^{th} week in CCRT and CCRT+MB. Independent 't' test showed significant difference [$p<0.001$] in both CCRT and CCRT+MB groups in 11 symptoms like Tastelessness, burning sensation in oral cavity/mouth, burning micturition, fatigue, Cough, Mucositis, Sticky saliva, Dry mouth, Oral Ulcers, Skin Discoloration and skin peeling. Here the difference noted was that in CCRT group there was considerable percentage of subjects suffering from grade 3 toxicities while the same was not evident in CCRT+MB group.

Significant difference was observed in Performance status [$p<0.001$, baseline to post-trial], in compliance and cancellation of Chemotherapy cycles, Adverse events like Number of IPD/Hospitalizations, Blood transfusions and Morphine prescriptions for pain was significantly different between CCRT and CCRT+MB group. Another major finding was loss of weight, which was significant in CCRT group when compared to CCRT+MB group. This was predominantly seen in Head and Neck cancer subjects and not so significant in cervical and esophagus cancer subjects.

There was no significant difference in safety parameters like Complete blood count, Liver function test, serum urea and creatinine in both CCRT and CCRT+MB groups.

Discussion: Amelioration of adverse effects and improvement in quality of life could be attributed to Alkaloids, terpenoids, mono unsaturated fatty acids, poly unsaturated fatty acids, Docosahexaenoic acid and different phytochemicals that are present in the prepared *Jeevanthyadi Ghrita*. These are known to downplay inflammation and bring immunomodulation. Given that short chain fatty acids are known to function in the colon as a nutrition quotient, the method of delivery of JG as *matra basti* may have also helped with another action to improve physical and psychological symptoms. Overall, the drug and mode of administration has shown effect in alleviating constipation and loss of appetite that could have helped in compliance of advised CCRT since these two symptoms have negative impact on weight and quality of life. Preliminary network pharmacology also corroborated with the above findings as the active phytochemicals in JG showed to have a considerable action on genes that regulate nausea, appetite loss, constipation weight loss etc.

Conclusion: *Jeevanthyadi Ghrita* can improve quality of life and ameliorate adverse effects of Concurrent chemoradiation therapy in cancer subjects receiving it. Tangentially it showed better compliance to CCRT and preventing weight loss.

Key Words: *Jeevanthaydi Ghrita*; *Matra Basti*; Concurrent Chemoradiation therapy; Adverse effects; Alternate medicine; *Ayurveda*.

1.2 INTRODUCTION

Cancer is becoming the leading cause of morbidity and mortality. In 2022, Worldwide 19.3 million new cancer cases and 10 million deaths due to cancer were reported.[1] It was also noteworthy that in 2018 approximately half of the new cases and more than half of the cancer deaths were in Asia[2]. The incidence of this condition is expected to rise from 1.1 million in 2015 to over 1·7 million annually by 2035 in India, mostly due to changes in lifestyle and population aging. India being not an exception with high mortality rate with 68% of the annual incidence.[3] As much as 26% of deaths during the most productive years (ages 30-70) are caused by one of the four major NCDs.[4]

In India there is interstate variability among types of cancer incidence. However, overall, Lung, head & neck cancers in males and Breast and cervix cancers in females were noted in higher incidence. A study estimated that the disability – adjusted life years (DALY's) due to cancer can rise up to 11.4% by the year 2025.[5]

The four main approaches used in conventional cancer management are surgery, radiation therapy, chemotherapy, and biologic therapy. Concurrent Chemoradiation therapy (CCRT) happens to be the primary line of management in cancers of Head and Neck, oesophageal, lung and cervix. This CCRT comes with known range of adverse effects which ranges from nausea, vomiting, mucositis to myelosuppression, fatigue, cachexia and compromising quality of life.[6]

According to Bese N. S. et al., about 50% of patients have a delay in chemotherapy or radiation therapy due to toxicity. Unintentional radiation therapy extensions are linked to markedly lower rates of locoregional control and survival.

Daniel J. G et al study showed 48.9% of patients not receiving their planned number of chemotherapy doses due to adverse effects. The prevalence of acute toxicities was higher in the CCRT group (n =612) than in the RT group (n =523), according to a meta-analysis of nine studies (1991-2014) comprising 1135 patients. There was no evidence of publication bias (t=0.13, P=0.903), and the RR value was 2.34 (95% CI:1.90–2.90, P <0.001).[7]

Chemotherapy or CCRT induced side effects are most distressing during treatment and addressed with anti-emetics and steroids with its own limitations.[8] These therapeutic barriers need to be overcome for better continuum of planned therapy.[9] Current trend in integrated oncology of India lauds about role of ethnic/Traditional or alternative medicines in cancer management as a palliative care if not parallel to conventional.[10] In India there is no well-developed Integrated system for cancer management. In India its reported that approximately 24-39% of people use or follow Traditional medicine for cancer and majorly *Ayurveda*, while in China its about 75-80%. There are few sporadic studies and center that have published and practice integration. [11]

A meta-analytic study shows *Ayurveda* formulations (herbal and herbo-mineral) were tried in improving quality of life and addressing conventional therapy induced side-effects. Studies conducted on ginger and honey in chemotherapy and radiation induced nausea and mucositis respectively have shown positive trends.[12]

Ayurveda, an ancient Indian system of healthcare defines both preventive and curative aspects for healthy lifestyle. Cancer and cancer therapy induced side effects are not an exception for this. In ayurveda, contextual references for anticipating, preventing, exacerbations and treatment for *visha* (toxin) induced aliments have been

well prescribed.[13,14] In such situations *ghrita* (cow ghee) is said to be of paramount importance since it can sustain Oja (~immunological balance) and do *Prana raksha* (lifesaving).[15] Among various *ghrita* preparations mentioned in Ayurveda, *Jeevanthyadi ghrita*[16] referenced in *Rajayakshma adhikara* has an edge since it is indicated in *dhatu kshaya* (tissue debilitation) which sooner or later is seen in cancer patients or during cancer therapies. Hence, *Jeevanthyadi Ghrita* was considered for evaluation of quality of life and amelioration of adverse effects in cancer patients during Concurrent Chemoradiation regimen.

1.3 BACKGROUND

Cancer is a condition or disorder caused when cells in body grow uncontrollably and spread to different parts of it. Unlike normal cells cancer cells are different by many ways. They are different because they are devoid of process of apoptosis, hide away from immune cells, able trick down new blood vessels for its successful survival, growth and spread. These qualities make this disorder a challenge in diagnosis, treatment, maintenance and surveillance. Several etiologies have been identified but the substrate remains in the DNA damage and tumor suppressor genes are altered.[17]

Cancer therapies are efficiently evolving; however, its complex pathology demands more. There are many types of therapies like surgery, chemotherapy, radiation therapy, immunotherapy, targeted therapy and hormonal therapy. In most of the situation a combination of therapies is used for treatment.[18] Among these Concurrent chemoradiation therapy is predominantly understood as standard line of treatment for many locally advanced cancers of cervix, esophagus, lung, head and neck.[19]

When Radiation therapy is combined with chemotherapeutic agents it is called as concurrent therapy. Chemotherapy aids to radiation in one or more ways. It can work as, radiosensitizer, destructing radio-resistant clones and potentially preventing metastases by its systemic action.[20] National Cancer Institute has advocated and raised alertness on use of Concurrent chemoradiation therapy as a standard care in few Cancers for better outcomes like improved survival rates and decreased loco-regional

re-occurrence. In India, presently few studies and trials have shown the better efficacy of CCRT when compared to either chemotherapy or radiation alone.[21]

Despite of the credible and undeniable outcomes of CCRT with varying regimens or protocol adherence, including different chemotherapeutic drugs there are still high rates of systemic, local, acute and delayed toxicities which raise the concern.[22] Combining two therapies have cumulative effect, leading to acute toxicity of normal tissue. Acute toxicities like mucositis, dermatitis, nausea, vomiting, diarrhea, esophagitis, myelosuppression, depression, cachexia, fatigue, pain and occasional renal impairment are common, which vary according to the chemotherapeutic agent used in different cancers or regimen. These events though being acceptable, but at times can be distressing leading to unplanned delay of CCRT and hospitalizations, which reflects later as loco-regional spread, negative survival rates, and compromised quality of life (QoL).[23]

The rate of toxicities and type of toxicities seen in each type cancer differ due to the irradiated area and chemotherapeutic agent used. Here are few studies indicating the incidence of adverse effects in individual cancers. Meta-analytical study which included 41 definitive CCRT studies for comparing weekly(n=14) and three weekly cisplatin (n=25) regimen in Head and neck cancer, showed equal efficacy over survival outcomes. Toxicities produced by three weekly cisplatin were more severe then weekly, but still among weekly group 4 studies reported neutropenia, nausea, nephrotoxicity, anemia, febrile neutropenia of grade 3-4. Mucositis/stomatitis and skin toxicity was reported by 7-8 studies indicating incidence of toxicity irrespective of regimen adopted. 122 patients with histologically confirmed squamous cell carcinoma of the head and neck (nasopharynx, oropharynx, larynx,

hypopharynx, and oral cavity) receiving chemoradiation were included in another retrospective study that was carried out between 2007 and 2009 in order to evaluate the compliance, tolerability, and clinical outcomes of weekly cisplatin (40 mg/m2). The following conditions were associated with grade 3/4 toxicity: mouth/neck discomfort (17%), dysphagia (15%), dermatitis (41%), mucositis (33%), neutropenia (2%), and renal impairment 3%. For the purpose of symptom management, 53% of patients needed at least one hospital stay. An further observation was that 68% of patients were able to finish six treatment regimens.[26]

Systematic analysis of CCRT in cervical cancer conducted in India at 12 institutes between 2006-2008 deliberated importance of CCRT in cervical cancer than radiation alone as advised by National Cancer Institute. Study also briefed on toxicities saying that there are obvious adverse effects experienced during CCRT which include parametrial fibrosis followed by hematological, Gastrointestinal disturbances, renal complications and skin reactions, but the data was not accurately ascertained.[27]

A study conducted to analyze the effect of toxicities on survival period in esophageal patients receiving CCRT showed that irrespective of dose, type of chemotherapy 50% of patients experienced leukopenia, 33% developed grade 3 anemia, and 23% patients developed grade 3 thrombocytopenia. Also, the paper suggested that there was no significant correlation between CCRT and age, addictions, tumor load, and pretreatment blood indices.[28]

Few other studies of Pan Xin Bin etal2017, Zhang L et al 2022 and Tsan YH et al 2021 indicate that this treatment induced symptoms have negative effect on different domains of quality-of-life scales (assessed by EORTC-QLQ30 and FACT

scores) and treatment outcomes in long term.[29,30,31,32] Timely managing these toxicities is of prime importance since it can affect the treatment course and the outcome of the patient in his physical, mental and social wellbeing.[33]

There are treatment modalities available to counter these side effects however they have their own limitations and mat be barrier in themselves. Hence therapy induced side effects management in evolving clinical research. Personalized medicine and risk identification of toxic drugs is increasing and addressed by changes in dose, early intervention, or use of alternative therapies.[34] Clinical trials, which comprise safety and clinical efficacy evaluations, ought to be carried out with scientific rigor. Adjuvant therapy and remission therapy using AYUSH modalities, the advantages of such approaches in the form of customized medicine, and the enhancement of quality of life ought to be the main areas of focus.[35]

There are increasing evidence of Alternative therapies like natural products that are being used to counter chemotherapy or chemoradiation therapy induced side effects. They are believed to be acting by alleviating inflammation, infection, improving gut microflora or through rich anti-oxidant properties. A study showed that Complementary and alternative medicine when used along with cancer therapy help in reducing side effects and stress.[36] They are opinion about using natural products either as dietary supplements or as prophylactically as therapeutic protocols to prevent CCRT induced side effects.[37]

Recently there are evidences stating that cow ghee prepared in a traditional way has higher percentage of docosahexaenoic acid and omega 3 long chain polyunsaturated fatty acid which are believed to modulate immune regulators like cytokines and proinflammatory markers. Another study conducted by Thatte U et al

2015 et al showed that *Basti karma* helps immune modulation and regulation of proinflammatory markers and cytokines. Similarly, Nakanekar A et al 2023 documented two different Basti composition in Covid -19 patients based on Ayurveda fundamentals of *Santarpana and Apatarpana* etiologies. This study showed the comprehensive effect of *Basti karma* based on ingredients of the drugs used, and still able to modulate the immune system towards physiological plane.[38,39]

Without the doubt, one can understand that concurrent chemoradiation therapy will lead to local and systemic acute toxicities that will negatively affect quality of life. This warrants for the newer approaches to combat these toxicities. Increasing evidences suggests scope of alternate medicine in cancer care. Indeed, it is only when we perform some pragmatic like studies, we can offer practicable and scientifically acceptable solutions. In particularly this proposed thesis aims to determine the improvement in quality of life in different domains among patients who receive *Jeevanthyadi ghrita matra basti* along with concurrent chemoradiation against the patient who only receive concurrent chemoradiation therapy.

2. AIM & OBJECTIVES AND HYPOTHESIS

Primary objective

To evaluate the effect of *Jeevanthyadi Ghrita matra basti* on quality of life in patients receiving concurrent chemo-radiation therapy.

Secondary Objective

To evaluate the effect of *Jeevanthyadi Ghrita matra basti* in ameliorating the side effects of concurrent chemo-radiation therapy.

Hypothesis

Research Hypothesis: *Jeevanthyadi ghrita* can improve the quality of life and has ameliorating effect on adverse events experienced during concurrent chemoradiation therapy in cancer patients.

Null Hypothesis: *Jeevanthyadi ghrita* has no effect on improving quality of life and ameliorating effect on adverse events experienced during concurrent chemoradiation therapy in cancer patients

3. REVIEW OF LITERATURE

CONCURRENT CHEMORADIATION THERAPY (CCRT).

When Radiation therapy is combined with chemotherapeutic agents it is called as concurrent chemoradiation therapy. Presently, Concurrent Chemoradiation therapy is widely adopted line of treatment for solid tumors like Gastro-intestinal, Genito-urinary, Gynecological, Lung, Head and neck malignancies. CCRT is well established in few cancers as definitive treatment and is area of investigation for combined therapy with new modalities like targeted and immunotherapies.

Initially this therapy was considered as spatial cooperation where by radiation helps in loco-regional way and chemotherapy taking care of distant micro metastases. However, later it was understood that Chemotherapy aids to radiation in one or more ways. It can work as, radiosensitizer, destructing radio-resistant clones and potentially preventing metastases by its systemic action. In CCRT the chemotherapeutic drugs are chosen where they can provide feasibility to enhance radiation dose and allow normal cells to be less affected than tumor cells. Moreover, such a modality allows beneficial effect by overcoming resistance phenomenon, but the infield cooperation of these two modalities can cause synergistic toxicity of each treatment. [40,41,42]

Overall, the CCRT acts by three ways firstly by Temporal Modulation where the phenomenon of 4R is followed. In this, the fractionized radiation modulates the cells Repair, repopulation, reoxygenation and redistribution. Here the second therapy mainly the chemotherapeutic agents like cisplatin or nucleoside analogs such as gemcitabine are given to inhibit the repair mechanism of cells, leading to tumor shrinkage. Secondly, Biological cooperation which means a strategy to delay the

tumor growth or targeting to kill the cells by combing radiation with drugs like mitomycin C that target hypoxic tumor cells. Thirdly, Cytotoxic enhancement, here the cells are killed by inducing or modulating the intracellular damage along with irradiation by using drugs like 5FU. [43]

National Cancer Institute has advocated and raised alertness on use of Concurrent chemoradiation therapy as a standard care in few solid cancers for better outcomes like improved survival rates and decreased loco-regional re-occurrence. In India, presently few studies and trials have shown the better efficacy of CCRT when compared to either chemotherapy or radiation alone. In CCRT the optimal radiation dose depends on size and location of primary tumors, local and distant spread. CCRT can reduce the risk of distant metastasis and improve survival outcomes compared to chemotherapy or radiation alone.[44]

RADIATION THERAPY

Radiation therapy is one among the three well-established and effective cancer therapy delivered with a curative intent. Radiation is used in cancer therapy since 1898. Radiation therapy uses ionizing radiations like X-rays, gamma rays and high energy electrons to kill the cancer cells. The ions of radiations while passing through the cell deposits energy into the cells of the tissues and then damage the cells by different mechanisms. These ionizing radiations damage the genetic material especially the Deoxyribonucleic acid (DNA) structure, by inducing Double strand DNA breaks. It happens primarily by release of electrons form atoms and molecules that lead to DNA break. Secondly the generating reactive oxygen species (ROS) oxidize lipids and proteins, which also induce indirect damage to DNA by deaminated

adducted bases. Collectively these mechanisms lead to induced cell death and mitotic failure. [45,46]

Radiation dose is measured in Gray (Gy) and is defined as 'absorption of one joule of energy/kilogram of matter [tissue or water]. The higher the energy, deeper it can penetrate. The Radiation doses depends on the tumor volume, histopathology and location involved.[47]

Radiation therapy is delivered majorly in three ways. Firstly, External Radiation or External Beam radiation therapy [EBRT]. It involves a machine that directs high energy rays onto the body into the tumor. Beams of the radiation are shaped and directed to match the size and location of the tumor to minimize damage to surrounding healthy tissues. Used especially for Head& neck, Lung, prostate, cervical cancers.

Secondly. Internal radiation therapy involves placing a radioactive source inside or near the tumor. This can be done in different ways, such as

Brachytherapy: implanting small radioactive seeds or pellets into the tumor or nearby tissue. This delivers a high dose of radiation to a small area, sparing the normal tissues around it. Brachytherapy can be used for prostate, cervical, endometrial, vaginal, and breast cancers.

Thirdly, Systemic radiation therapy: swallowing or injecting a radioactive substance that travels through the blood and targets the cancer cells. This can be used for thyroid cancer or bone metastases.[48,49]

However, in general the amount of radiation dose selected for Head & neck, Cervix and esophagus are as follows

Table No 1. Type of Cancer and Radiation dose advised

Sl no	Cancer type	Radiation Dose Range (Gray unit)	Fractions
1.	Head and Neck [50]	60 – 70 Gy	33-35
2.	Lung[51]	50 – 80 Gy	30-35
3.	Esophagus[52]	50 – 70 Gy	28-30
4.	Cervix[53]	45 – 50 Gy	25-28

CHEMOTHERAPY

Chemotherapy is often referred to drugs or medicines used to treat any systemic infection or malignancy. In cancer management the chemotherapy drug has no clear differentiation of tumor and normal cells due to which the untoward toxicities arise. There are various chemotherapeutic agents and that are classified as follows[54]

1. Phase non-specific
    a. Alkylating Agents – eg, Cyclophosphamide
    b. Platinum Analogues – eg, Carboplatin, Cispaltin
2. Phase -specific or cell specific
    a. Anti-metabolite – eg, 5-Flurouracil, Hydroxycarbamide
    b. Taxane – eg, Paclitaxel, Docetaxel
    c. Vinca Alkaloids – Vincristin and Vinblastin.
3. Hormones and Antihormone – eg, Tamoxifen
4. Miscellaneous
    a. Immunological agents – eg. Ipilimumab.

CISPLATIN

Cisplatin is a phase non-specific platinum anti-neoplastic agent. This platinum compound counters with number of macromolecules. Cisplatin specifically binds to N-7 position of guanine and adenine in undamaged DNA. Tumor growth is inhibited by attacking DNA strands by cross linking the guanine bases and making them incapable to uncoil and separate so that cell cannot divide further. Cisplatin is active in both well oxygenated and hypoxic cells making it potential candidate.[55]

Cisplatin is called and used as radiosensitizer in CCRT. Radiation to tumor site leads to generation free radicals and generation of intermediate toxic platinum intermediates that are readily taken up by cells, which increase the cell killing. Radiation also causes DNA damage which is repairable and here the cisplatin inhibits this process through its free electron scavenging property. Finally, these two mechanisms lead to cell cycle arrest and pave way for apoptosis.[56] Cisplatin is indicated in Head & Neck, Breast, Ovarian, Bladder, Brian and Lung cancers.[57]

Toxicities that arise form chemoradiation have complex molecular mechanisms. Acute symptoms are now considered as Toxicity Syndromes instead of single complaint. Since the concept of chemotherapy effecting rapidly dividing epithelial cells leading to gastrointestinal disturbances and/or radiation causing local dermatitis etc is not complete sequel, but the toxic effects of CCRT are also seen to distant normal tissues through the orchestra of systemic, interorgan signaling and immune system via proteins in blood. These proteins can be interleukins, cytokines, chemokines and endogenous molecular patterns released due to death of tumor cells or normal cells driven to apoptosis or necrosis

This happens through phases namely Initiation phase, which causes cellular damage to rapidly dividing cells, induced by CCRT leading to oxidative stress and enforcement of innate immunity to act swiftly via interleukins. Secondly, Upregulation or activation of different signaling mechanisms through cytokines leading to inflammation developed during initial hours of radiation therapy and systemic chemotherapy. Thirdly signal amplifications through intracellular and intercellular signaling loops causing cascading effect. Finally, in case of breeched mucosal layer and inflammatory process becomes the reason for bacterial colonization and ulceration. This biological pathway is so intricate that even behavioral toxicities are exacerbated in the form of depression, fatigue and cachexia. [58]

CONCEPT OF *VISHA AND VIRUDHA DRAVYA*.

***VISHA GUNA AND KARMA*: QUALITIES OF POISON AND MODE OF ACTION**

रूक्षमुष्णं तथा तीक्ष्णं सूक्ष्ममाशुव्यवायि च ॥१९॥ विकाशि विशदं चैव लघ्वपाकि च तत् स्मृतम्।

तद्रौक्ष्यात् कोपयेद्वायुमौष्ण्यात् पित्तं सशोणितम् ॥२०॥ मतिं च मोहयेत्तैक्ष्ण्यान्मर्मबन्धान् छिनत्ति च।

शरीरावयवान् सौक्ष्म्यात् प्रविशेद्विकरोति च ॥२१॥ आशुत्वादाशु तद्धन्ति व्यवायात् प्रकृतिं भजेत्।

क्षपयेच्च विकाशित्वाद्दोषान्धातून्मलानपि ॥२२॥ वैशद्यादतिरिच्येत दुश्चिकित्स्यं च लाघवात्।

दुर्हरं चाविपाकित्वात्तस्मात् क्लेशयते चिरम् ॥२३॥

Acharya Sushruta and *Charaka* listed ten comparable *gunas of visha*; the only difference is that *Sushruta* listed *apaaki*, whereas Charaka listed *anirdeshya rasa*. When one of these 10 *gunas* is fully present in a *visha dravya*, that poison/substance

is referred to as *mahavisha*. When one of these *gunas* is present in fewer amounts or with fewer than ten *gunas*, that poison/substance is referred to as an *upavisha*. By adding *apaki* and *Avyaktarasa* (instead of anirdeshya rasa), Acharya *Vagbhata* has credited eleven *gunas* to a *visha dravya*. Sharngadhara described some other *gunas of visha dravya*, such as *chhedi, madavaha, jivitahara, and yogavahi*..

All *gunas*, which are related to *visha*, have some effect on *dosha, dhatu*, and mala. *Visha* is erratic and does not stay still in one location because of *Laghu guna* (*anavasthitatva*). Therefore, it prevents the interaction that is required to treat the *guna* between the *visha* and the administered *bheshaja*. The vitiation of *rakta dhatu* is caused by the infiltration of the body's *sukshma srotas* by the *visha dravya's sukshma guna*. *Ruksha guna* causes the body's *soshana* by vitiating the *vata* dosha.

The concept known as *samanya-vishesha siddhanta* causes vitiation of *Kapha* due to *avayaktarasatva* of *visha*, an analogous *guna* assigned to *Kapha* and *jala*. Additionally, because of its *avyaktarasa, visha* becomes *yogavahi* and bonds with the *annarasa*, vitiating the food. Similar to how a drop of oil spreads across water the moment it touches it, *ashu and vyavayi gunas* cause *visha* to disperse quickly throughout the body. *Dalhana* states that while *visha* travels rapidly throughout the body, it is not discharged from either *urdhvamarga* or *adhomarga* while discussing *vyavayi guna. Agnimahabhuta's* attribute, *tikshna guna*, has an impact on *marma*. It causes putrefaction, burning feeling, and discomfort of the body's components. *Vishada guna* is a clear *guna* that can perform *vibhajana* and remove obstacles in its path, assisting *Visha* in passing through all doshas and dhatus that cause their vitiation. Because *visha* causes vitiation of all three doshas, treating it is exceedingly difficult. *Vikasi guna* causes the dhatus to become loose (*dhatushaithilya*), breaking

the bonds that bind the different dhatus together and causing inappropriate functioning. A *visha dravya's* activity is determined by the strength of the guna it possesses. For example, *ruksha guna* dominance will cause *vata* to become vitiated; *sukshma guna* will cause *rakta dhatu* to become vitiated relative to others; and *tikshna guna* will cause impairment to three *marmas* of the body, namely *shira, hridaya*, and *basti*, resulting in *murchha, sanyasa*, and other *marmaghata* symptom. *Laghu guna* makes the *visha durupakrama and dushchikitsya while sukshma* does the *vata kopana*. Vishada is said to be *asakta gati* dosha making the *visha* uncontrollable. *Vikasi and aashu* makes the *visha pranagna and ashu hanti* respectively therefore making it *krichrasadya* to treat *visha*.[59,60,61,62,63]

At the same time *Acharaya sushruta* also tell that if the *visha* [poison] happens to be in *amashaya* [before getting digestion or not yet distributed into body] the presents symptoms as following.

When *visha* enters the ***amashaya*** along with food or alone it causes symptoms namely *moorcha* (giddiness), *vamanam* (vomiting), *atisara* (losse stools), *adhmana* (flautulence), *daha* (burning sensation), *vepathu* (tremors) and *indriya vikara* (disruption in the working of sense organs).[64]

And if *visha* resides in ***pakwashaya*** [post absorption and under distribution process] the presents signs and symptoms like *daha* (burning sensation), *atisara* (loose stools), *trishna* (excessive thirst), *indriyavaikrtam* (disruption in the working of sense organs), *atopa*(gurgling sounds), *panduta* (pallor), and *karshya* (emaciation).[65]

VIRUDHA DRAVYA AND SHAHIR SAMSKARNA:

[Incompatible medicine and optimization of body for future insults]

Virudha Definition:

देहधातुप्रत्यनीकभूतानि द्रव्याणि देहधातुभिर्विरोधमापद्यन्ते; परस्परगुणविरुद्धानि कानिचित्, कानिचित् संयोगात्, संस्कारादपराणि, देशकालमात्रादिभिश्चापराणि, तथा स्वभावादपराणि॥८१॥

Substances that are in opposition to *deha-dhatus* exhibit *virodha*, or antipathy, towards them. This antagonistic relationship could be based on natural composition or on characteristics, combination, processing, place, time, dose, etc.[66]

यत् किञ्चिद्दोषमास्राव्य न निर्हरति कायतः| आहारजातं तत् सर्वमहितायोपपद्यते॥८५

Everything about the (medication or) food that vitiates the dosha but doesn't get rid of it is *viruddha*.[67]

TREATMENT OF *VIRUDHA*

एषां खल्वपरेषां च **वैरोधिकनिमित्तानां व्याधीनामिमे भावाः प्रतिकारा भवन्ति**| तद्यथा- वमनं विरेचनं च, तद्विरोधिनां च द्रव्याणां संशमनार्थमुपयोगः, तथाविधैश्च द्रव्यैः **पूर्वमभिसंस्कारः शरीरस्येति**॥१०४॥

भवतश्चात्र- विरुद्धाशनजान् रोगान् प्रतिहन्ति विवेचनम्| वमनं शमनं चैव पूर्वं वा हितसेवनम्॥१०५॥

सात्म्यतोऽल्पतया वाऽपि दीप्ताग्नेस्तरुणस्य च| **स्निग्धव्यायामबलिनां विरुद्धं वितथं भवेत्**॥१०६॥

Acharaya also advise that for any such *visha* [poison/*virudha ahara*] one can be prepared by optimizing the body physiology to counter the future insult to the body. Or else using wholesome foods and *Sneha* [especially *ghrita*/lipids] regularly will not cause much adverse effects of incompatible food or treatment. [68]

IMPORTANCE OF GHRITA IN VISHA CONDITIONS.

नाघृतं स्रंसनं शस्तं प्रलेपो भोज्यमौषधम्|

सर्वेषु सर्वावस्थेषु विषेषु न घृतोपमम्||६९||

विद्यते भेषजं किञ्चिद्विशेषात् प्रबलेऽनिले|

There is no medicine equivalent to *ghrita* in poisonous conditions at any phases in any form like *lepa* [ointment form], *bhojana* [with food], *oushadhi* [as medicine]. *Ghrita* has strength to control the vitiated *vata* in *visha* conditons. [69]

***GHRITA* : QUALITIES AND INDICATIONS**

1. वातपित्तप्रकृत यो वातपित्तविकारिणः| चक्षुःकामाः क्षताः क्षीणा वृद्धा बालास्तथाऽबलाः||४१||
   आयुःप्रकर्षकामाश्च बलवर्णस्वरार्थिनः| पुष्टिकामाः प्रजाकामाः सौकुमार्यार्थिनश्च ये||४२||
   दीप्त्योजःस्मृतिमेधाग्निबुद्धीन्द्रियबलार्थिनः| पिबेयुः सर्पिरार्ताश्च दाहशस्त्रविषाग्निभिः||४३||

2. स्मृतिबुद्ध्यग्निशुक्रौजःकफमेदोविवर्धनम्। वातपित्तविषोन्मादशोषालक्ष्मीज्वरापहम् ॥२३१॥
   सर्वस्नेहोत्तमंशीतंमधुरंरसपाकयोः सहस्रवीर्यंविधिभिर्घृतंकर्मसहस्रकृत्॥२३२॥
   मदापस्मारमूर्च्छायशोषोन्मादगरज्वरान् योनिकर्णशिरःशूलंघृतंजीर्णमपोहति॥२३३॥
   सर्पींष्यजाविमहिषीक्षीरवत्स्वानिनिर्दिशेत्।

Acharya charaka strongly advocated and considered *Ghrita* [ghee] as the best source to keep the body healthy which can promote good eye sight, wound healing, immunity, healthy progeny, good vitality, strength of sense organs, and improve complexion, voice, nourishment, digestive power, memory intelligence.

It is specifically indicated for people with *Vata-pitta prakruti* and those suffering from *Vata-pitta* disorders like burning sensation in body or in-situ and poisonous conditions [even *acharya sushruta*]. Ghee is said to possess the qualities like *seeta* in potency, *madhura rasa* and *vipaka*, and can increase the availability of drugs .[70,71]

Similarly, *Acharya Vagabhata* and has also extended the effects of *ghrita* in tumorous growths, sinuses, ulcers and worm infestations.[72]

IMPORTANCE OF MEDICATED *GHRITA*

जीर्णज्वरेषु तु सर्वेष्वेव सर्पिषः पानं प्रशस्यते **यथास्वौषधसिद्धस्य;**

सर्पिर्हि स्नेहाद्वातं शमयति, संस्कारात् कफं, शैत्यात् पित्तमूष्माणं च;

तस्माज्जीर्णज्वरेषु सर्वेष्वेव सर्पिर्हितमुदकमिवाग्निप्लुष्टेषु द्रव्येष्विति॥३७॥

भवन्ति चात्र- यथा प्रज्वलितं वेश्म परिषिञ्चन्ति वारिणा| नराः शान्तिमभिप्रेत्य तथा जीर्णज्वरे घृतम्॥३८॥

स्नेहाद्वातं शमयति, शैत्यात् पित्तं नियच्छति| घृतं तुल्यगुणं दोषं संस्कारात्तु जयेत् कफम्॥३९॥

नान्यः स्नेहस्तथा कश्चित् **संस्कारमनुवर्तते**| यथा सर्पिरतः सर्पिः सर्वस्नेहोत्तमं मतम्॥४०॥

In the context of Chronic fever treatment, the *Acharya Charaka* says that *Ghrita* has quality of *Sanskaro hi gunantaradhanam* which means it imbibes the values of material/drugs added to it and delivers the effect along with its own potency which can be said as synergistic effect. [73]

JEEVANTHAYDI GHRITA [JG]

Jeevanthyadi ghrita is explained in the context of *Rajayakshma chikthsa* by acharya *Charaka*[74] and *Vagabhata in Astanga hrudaya*.[75]

Jeevanthyadi ghrita is polyherbal lipid based pharmacological agent indicated for *Rajayakshma*. Ayurveda explains *Rajayakshama* as a disorder [Debilitating disorder] which presents a cluster of symptoms namely *Aruchi* [Anorexia] *Angamarda* [Myalgia], *Kasa* [Cough], *Swasa* [Dyspnea], *Jwara* [Fever], *katiparshwa shula* [Lowback ache], *Amsa shula* [pain in shoulder region] and *swara bheda* [dysphonia or hoarseness of voice] and few others. This can develop through four different etiopathogenesis namely *Ayatha bala aarmbha* [over excretion], *vegaavrodha* [suppression of natural urges], *dhatukshaya* [depletion of body tissues] and *vishamashana* [irregular dietary habits].[76]

The ingredients of *Jeevanthyadi ghrita* are predominantly *Madhura Tiktka rasa, Singdha laghu guna, sheeta virya* and *Madhura vipaka*. Most of the *dravya's* are having *deepana, pachana, Daha and trushna shamaka, raktadoshara, kshayahara, kasaswasa hara, brihmana, vrushya*, and above all *rasayana* in nature [table no 2]. Several recent in-vitro and pre-clinical studies researches on the individual drugs of the *Jeevanthaydi ghrita* have shown to possess considerable immunomodulatory, anti-inflammatory, analgesic, anti-proliferative, free radical scavenging, anti-oxidant, anti-tumor, hepatoprotective, nephroprotective, cytoprotective and myeloprotective activities [table no 3].

Table no. 2. Ayurveda Pharmacological properties of Individual drugs of *Jeevanthyadi Ghrita*

Sl n	Drug	Rasa	Guna	Virya	Vipaka	Karma
1.	*Jeevanti*	*Madhura*	*Snigdha*	*Sheeta*	*Madhura*	*Rasayana, Balakaraka, grahi, Mamsa vardhaka* Vrusya*, Brihmana[!].*
2.	*Yasthimadhu*	*Madhura*	*Guru, Snigdha*	*Sheeta*	*Madhura*	*Shukrala, Kshayahara[‡#], Balakaraka, Kantya, Glani trushna hara[#*], Visha[#‡] & Chardi hara[#+], Raktashaamaka[#], Shwasa & Shirashoola[!], Ruchikaarka[*]*
3.	*Draksha*	*Madhura, Kashaya[#] Amla[*]*	*Sara, Guru Snigdha[#‡]*	*Sheeta*	*Madhura*	*Bruhmana[!+], vrushya, swaravardhaka, Kshaya[‡] Daha[!‡], Mutravikarahara Ruchikaraka[*!] Jawargna[‡*] Raktavikarhara[#], Balya[!], Trishnahara [!#] and Kasa[!] Panduhara[!], Kamala[+], Shosha[+], Mutrakrichra[+]*
4.	*Kutaja*	*Katu*	*Ruksha laghu*	*Sheeta*	*Katu*	*Sangrahi, Jwarahara*
5.	*Pushkaramula*	*Katu,tikta*		*Ushna*	*Katu*	*Swasa[#!] jwarahara[*#], Pandu[*],Parswashulahara[#!], Adhamanahara[‡], arcuhi[#]*
6.	*Sati*	*Tikta, Katu[#!] Kashaya[#]*	*Tikshna, grahi Laghu[*#!]*	*Ushna Sheeta[+]*	*Katu*	*Ruchiprada[*], Kasahara[#!‡] Shulahara[#!], Hikka[#] , Grahani[+],Jwaranashni[*#+]Mukhamalahar[#!], Raktadoshgna*,*
7.	*Pippali*	*Katu Tikta[*] Madhura[+]*	*Snigdha Ruksha[#] Guru[+]*	*Anushna Sheeta[‡] Ushan [*!]*	*Madhura*	*Rasayan[#!+], Vrushya[*+#], Dipana[*#!+‡], Pachana[#] Shwasahara[*+], Gulma[+!] Kshayahara[*], Hrudya[#+] Jwarahara[*#+‡], Udara[#+], Ruchikaraka[#], Pleeha[#+]*
8.	*Kantakari*	*Katu Tikta*	*Laghu*	*Ushna*	--	*Deepana[*#] , pachana[#+] Shwaskasa[*#!+‡], aruchi Jwarahara[*#!+‡], peenasa[*#!] hrudroga[#+‡], bhedana[*] parshwashula[#+] krimi[#+]*

9.	*Gokshura*	*Madhura*		*Sheeta*	*Madhura*	*Brihama*[*ǂ], *Balakara*[#], *Vrushya*[#ǂ], *Deepana, Vidahanaska*[*], *hrudya*[#!+], *Mutrakricha*[*#!ǂ], *Jwara*[!] *Prameha*[*#ǂ], *Shulaahra*[ǂ]
10.	*Bala*	*Madhura Tikta*[*]	*Snigdha, Grahi*	*Sheeta*	*Madhura*	*Balakaraka*[ǂ], *Shukrala*[*ǂ!] *Kshat nashaka*[+ǂ], *Brihamna*[!] *Ojavardhaka*[ǂ,]
11.	*Nilothpala*	*Atiswadu*[*] *Tikta* Madhura*[!+ ǂ] *kashaya*[ǂ]	*Guru ruksha*[#]	*Sheeta*	--	*Raktapittahara**[ϕ] *dahaahara*[ϕ]** *chardihara* pippasahara* ruchya* dehavrudhiakara**
12.	*Bhumyamalaki*	*Kashaya madhura Tikta*[ǂ]		*Sheet*	---	*Dahashaman**[ǂ] *prameha*[!] *trishnahara*[#+] *mutraroga*[*] *Kshatakshayahara*[+] *panduhara*[!+] *kamalahara*[!] *Trushnahara*[+#] *Raktavikara*[ǂ]
13.	*Trayamana*	*Tikta Kashaya*[#ǂ] *Madhura*[*]	*Sara*	*Sheeta*[*] *Ushan*[ǂ]		*Vishahara*[*#], *Shulahara*[#+ǂ], *Jwara*[*+ǂ] *trishnahara*[*] *chardihara*[*] *bramahara*[*#] *gulma*[*#ǂ]
14.	*Duralabha*	*Madhura tikta Kashaya*[#!ǂ]	*Sara Laghu*	*Sheeta*	*Madhura*	*Bramahara # Raktadoshahara*[#!ǂ]

Note: Following table is the compilation from following texts books of *Ayurveda* known as *Nighantu's,* which describe the properties of drugs in *Ayurveda* fundamentals of pharmacology. All the properties are compiled and any additional properties explained other than *Bhavaprakash Nighantu*[77] have been given a superscript for referencing.

** -- Raja Nighantu*[78]
 # -- Kaideva Nighantu[79]
! -- Priya Nighantu[80]
+ -- Madanphala Nighantu[81]
ǂ -- Dhavantara Nighantu[82]
ϕ -- Shodala Nighantu[83]

Table no.3. Recent Pharmacological activities of Individual drugs of *Jeevanthyadi Ghrita*

Sl	Drug	Recent activities
1.	*Jeevanti* (*Leptadenia reticulata* Wight and Am.)	Aqueous extract of Jeevanti showed immunomodulatory effect in mice. Terpenoids named amyrin acetate has shown to mitigate NF-KB activation and enhance GSH levels in immunosuppressed mice. In another study it has shown analgesic activity and the ethyl acetate extract downplayed proinflammatory cytokines like IL-2, IL-6 and TNF-alpha. [84,85]
2.	*Yasthimadhu* (*Glycyrrhiza glabra* linn)	It has been demonstrated that phospholipase A2 is blocked by glycyrrhizin, and prostaglandin and cyclooxygenase are inhibited by glycyrrhizic acid. It has been demonstrated that the flavonoids and terpenoids found in yasthimadhu inhibit the growth of inflammation-related disorders by downregulating TNF-a, MMPs, PGE2, and oxidative stress. Aqueous extract of Glycyrrhiza glabra could also elicit it's mode of action was through increasing norepinephrine and dopamine in brain and not due to serotonin.[86,87,88]
3.	*Draksha* (*Vitis vinifera* Linn.)	On blood-brain barrier cultured vascular endothelial cells, Vitis vinifera was also assessed as a natural grape compound for leptin receptor expression and defense against cytokine-induced oxidative and inflammatory damage. It has been noted that it can control the expression of the leptin gene, which is disrupted in chronic inflammation through the NF-κB, IL-1β, and TNF-α pathway. Analgesic activity was demonstrated by observing the normalised molecular proteins like mRNA and nuclear factor erythroid-2 [Nrf-2] in dorsal root ganglion and spinal cord of rats, which are main factors for noci-reception. Anti-neuropathic effect and improved

		body weight of rats indicated that subchronic administration of drug can act by preventing neural damage and control chronic pain. [89,90]
4.	*Kutaja* (*Holerrhena antidysentrica* Wall.)	Methanolic extract of Holarrhena anti-dysentrica leaves was tested for analgesic effect in swiss albino rats by tail immersion and hot plate method. At three different doses also the drug could elicit analgesic effect uptill 60th minute of study and was statistically comparable with standard drug pentazocine.[91]
5.	*Pushkaramula (Inula racemosa* Hook.F.)	Extract from Inula racemose and Alantolactone, a sesquiterpene lactone present in Inula species, have demonstrated anti-inflammatory effect by preventing the formation of NO from lipopolysaccharide (LPS)-induced prostagladin E2, TNF-alpha, iNOS, and COX-2. Aqueous root extract of inula racemose showed anti-inflammatory and analgesic activity which was dose dependent and at 400 mg/kg it was comparable with standard drug indomethacin.[92,93]
6.	*Sati (Hedychium spicatum* Ham.Ex Smith.)	Aqueous and ethanolic extract of Hedychium spicatum could show protective activity against histamine induced gastric ulceration in guinea pig, Anti-inflammatory activity against carrageenan induced paw edema in rats which was greatest at 3rd hour of experimentation. Immuno-modulatory effect was demonstrated by inducing abdominal sepsis through E.*coli* at different doses. Decreased mortality and increased phagocytic index was seen at dose of 500 mg/kg dose in comparison to control groups. Same extract could also significantly reverse the cyclophosphamide induced myleosuppression (increased WBC and RBC) at 200 mg 500 mg/kg. Methanolic extract of Hedychium spicatum demonstrated adaptogenic activity which was evaluated by anoxia stress tolerance test.[94,95]

7.	*Pippali (Piper longum* Linn.)	Piperine's anti-inflammatory and antioxidant qualities were examined after it was isolated from Piper longum using a series of extraction solvent systems. The molecular pathway was determined by evaluating both attributes using the following techniques. By preventing nuclear factor-κB (NF-κB) from being activated in endothelial cells and subsequently blocking TNF-α-induced production of cell adhesion molecules such as Intercellular Adhesion molecule 1 (ICAM-1), piperine demonstrated its anti-inflammatory properties. The ability of piperine to prevent gamma radiation-induced lung tissue inflammation in rats. Piperine was given to Sprague Dawley rats six weeks prior to the radiation test. Tumor necrosis factor alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) were among the inflammatory markers measured in the rats' serum, and the results showed that the levels were well within normal range. Following pretreatment with piperine, radiation exposure restored almost normal levels of antioxidant enzymes, including GSH, GPx, and CAT. [96,97]
8.	*Kantakari (Solanum surattense* Burm. F.)	Analgesic activity of alcoholic and petroleum ether extract of Kantkari (*Solanum xanthocarpum* schard & wendl) was evaluated after doing phytochemical screening. Analgesic activity was tested using Eddy's hot plate method and acute toxicity was also evaluated. Extract could increase the reaction time to pain even at second hour of experiment upto 9.45 sec which was comparable with standard durg Pentazocin of 11.66 seconds.[98]
9.	*Gokshura (Tribulus terrestris* Linn.)	Human peripheral blood mononuclear cells were used to assess the immuno-modulatory effects of Tribulus terrestris (80% steroidal extract) in rats and in vitro. Between treatment and control rats, the extract did not

		reveal any differences in the total or differential counts. The outcomes of the IL-6 and TNF-α testing were also similar. When tests of the anti-oxidant activity were conducted using enzymes such as GSH and malonaldehyde (MDA), the extract was able to lower MDA and raise GSH levels.[99]
10.	*Bala (Sida cordifolia* Linn.)	A number of Sida cordifolia organic extracts were assessed for their anti-inflammatory qualities using molecular markers like prostaglandins (PGs, PGE2, PGD2, and PGF2) and thromboxane A2 (TXA2). Anti-inflammatory activities of S Cordifolia may be present even at the lowest dose of 10 µg/ml. Activity of PGE2 and PGD2 was reduced in a dose-dependent manner. Aqueous extract of Sida cordifolia root was assessed for acute toxicity test followed by nephro-protective activity induced by gentamycin and cisplatin. S cordifolia (400/kg) could significantly counter the nephrotoxicity by controlling the renal markers namely serum urea (75.32 mg/dl), creatinine (1.98 mg/dl), BUN (34.5 mg/dl) in comparison with cisplatin group serum urea (153.36 mg/dl), creatinine (5.04 mg/dl), BUN (80.4.5 mg/dl). At same time the drug had also shown raised anti-oxidant enzyme levels of SOD and CAT, which indicates its protective mechanism.[100,101]
11.	*Nilothpala (Nymphaea nouchali* Burm.F.)	Methanolic extract of *Nymphea nouchali* was tested for Anti-nociceptive (tail immersion & acetic acid writing methods) and Anti-depressant activity (hole cross and open field tests) at 200 mg/kg and 400 mg/kg. N nouchali showed dose dependent and significant effect over pain upto 67.75% (400 mg/kg) which was comparable with standard drug diclofenac sodium 78 %.[102]

12.	*Bhumyamalaki* (*Phylanthus amarus* Schum & Thonb.)	Ethanolic extract of *Phyllantus amarus* roots was evaluated for understanding anti-inflammatory activity on molecular pathway using U937 macrophages. On Alamar blue test the extract showed cell viability of greater than 90% in U937 macrophages. For understanding proinflammatory players TNF-α and IL-1β were studied and extract showed IC50 of 16.12 and 7.13 μg/mL, respectively against standard dexamethasone. Paralleled study to understand mRNA expression of TNF-α and IL-1β was done with qRT-PCR, which showed that on dose dependent manner the extract (15 μg/mL viz lowest) could inhibit the up regulation of genes caused by LPS upto 35 folds. Similarly PGE2 and COX-2 were less produced and gene expression was inhibited (259 folds) at 30 μg/mL. LPS caused phosphorylation of MAP Kinase signalling and this was also suppressed in pre-treated marcophages with P.amarus extract at significance of $p<0.001$, to confirm this mode of action through NF-κB genes responsible for them were studied and the showed well regulation. Even MyD88 and TLR4 protein expression were not expressed by pretreatment of extract at dose of 30.[103]
13.	*Trayamana* (*Gentian Kurroo* Royle.)	Among different extractive forms, methanolic extract of *Gentiana kurroo* Royle (MGK) was more effective in immunomodulation when challenged by carrageenan induced paw edema in wistar rats, Humoral antibody response and delayed type of Hypersensitivity in Balb/C mice [with Sheep Red Blood Cells and cyclophosphamide (50mg/kg)]. MGK was able to suppress both cell mediated (65.27 % and 75%) and humoral immunity (57.57% and 54.05%) indicating its potentiality as anti-inflammatory and immunosuppressant. They also showed the dose-dependent reaction of the molecular route

		through Lipopolysaccharide (LPS)-stimulated macrophages using Raw264.7 cells in an in vitro inflammatory model. In this model, MGK showed a reduction in the expression of NF-Kappa B in mice peritoneal macrophages, which is the primary transcription factor for the pro-inflammatory mediators, as well as the release of pro-inflammatory mediators including NO, TNF-α, and IL-6.[104,105]
14.	*Duralabha (Fagonia cretica* Linn.)	Liver enzymes did not rise when comparing the ethanolic extract of Fagonia indica to the toxicity control group, suggesting that oral administration prevented the liver harm. Furthermore, compared to the control group, which had 78% damage to its DNA, the extract had 17% less damage [according to the TUNEL assay]. It also showed the capacity to downregulate TLR-4 and TLR-9 genes, which are connected to pro-inflammatory markers like IL-6, TNF-Alpha, TGF-β, and Il-1B as well as innate immunity. [106]

MATRA BASTI

Basti is the main therapeutic procedure in *Panchakarma* therapy (mediated enema). The instrument known as the *Basti yantra*, is composed of animal urinary bladder or Basti, is what gives rise to the term *Basti. Basti* is typically applied through the rectum, though it can also be applied through the urethra. Despite being used in a general sense, the name "*Basti*" refers to all types of *bastis*, including *Shiro, Niruha, Anuvasana, Uttar*, and others. It seems that *Chakrapani* and *Jejjata's* interpretation of the *Charaka's* description of *Basti* is unique to *Niruha Basti*.[107,108]

Definition of *Basti*:-

Definition:

नाभिप्रदेशं कटिपार्श्वकुक्षिं गत्वा शकृत् दोषचयं विलोड्य ॥

संस्नेह कायं सपुरीष दोषः सम्यक् सुखेनैति च यःस बस्तिः॥

The term "*basti*" refers to the therapy that moves through the *Kati, Parshva, Kukshi, and Nabhipradesha*, churning up and dissolving the *Purisha* along with all other *Doshas* there and easily eliminating them when the body has been nourished (oleated).[109]

Classification of Basti

They are classified according to the drug's potency, substance quality, and anticipated mode of action. It can therefore be categorized as follows

Pharmaceutical Classification (According to drugs used):

1. *Niruha Basti:*

   The main ingredient in *Niruha Basti is Kashaya* (Decoction), which is frequently made with *Kashaya, Madhu, Saindhava, Sneha, and Kalka*. Other synonyms for it are *Kashaya Basti* and *Asthapana Basti. Niruha Basti* is the name of the *Basti* that, due to its effectiveness, purges the body of its vitiated *Dosha* and increases bodily vigor.

2. *Basti Anuvasana*:

   Only Sneha is used in *Anuvasana Basti*. This type is separated into the following categories based on the amount of oil provided:

   - *Sneha Basti*: ¼ of the total number of *Niruha*, or 6 *Pala*.
   - *Anuvasana Basti*: ½ of *Sneha Basti, or 3 Pala*, in quantity.
   - ***Matra Basti*: ½ to the *Anuvasana Basti* amount, or 1½ Pala**.

   According to the numbers of *Basti* to be used [110]

1. *Karma Basti* (30 Basti's)
   a. 18 *Anuvasana Basti* and 12 *Niruha basti* are administered.
2. *Kala Basti (16 Basti's*)
   a. 10 *Anuvasana* and 6 *Niruha Basti* are administered.
3. *Yoga Basti (8 Basti's*)
   a. 5 *Anuvasana* and 3 *Niruha Basti* are administered.

   According to Pharmacological Action [111]

   a. Acharaya Sushrta mentions *Shodhana, Lekhana, Brimhana Shukra vriddhikara basti's* etc.
   b. Acharaya Charaka mentions *Vataghna, Krimighna Basti* etc.
   c. Acharaya Vagabhta mentions *Utkleshana, Doshahara, Shamana Basti*.

MATRA BASTI

Anuvasana Basti is classified into three categories based on how the dosage is administered. These three are called *Anuvasana, Sneha, and Matra basti*. The reason *Matra Basti* is called so is because, in comparison to *Sneha Basti,* relatively little *Sneha* (Hruswa Matra) is utilized in it. The dosage of *Matra Basti* is equal to the dosage of *Hruswa Matra of Snehapana,* according to *Acharya sushruta* and *Vagbhata*.[112,113]

Indications and Dose of Matra Basti

कर्मव्यायामभाराध्वया(पा)नस्त्रीकर्षितेषु च|

दुर्बले वातभग्ने [१] च मात्राबस्तिः सदा मतः॥५२॥

यथेष्टाहारचेष्टस्य सर्वकालं निरत्ययः|

ह्रस्वायाः स्नेहमात्राया मात्राबस्तिः समो भवेत्॥५३॥

बल्यं सुखोपचर्यं च सुखं सृष्टपुरीषकृत्|

स्नेहमात्राविधानं हि बृंहणं वातरोगनुत्॥५४॥

Acharya Charaka states that *Matra Basti* is always appropriate for people who are malnourished as a result of excessive labour, physical activity, moving heavy objects, traveling by car, traveling during wartime, and indulging in women when they are incapacitated or suffering from *Vata* diseases. Regular administration of *Matra Basti* is advisable, and it can be given at any time of year.[114]

Dose of *Matra Basti*.

The recommended minimal dosage of *Sneha* for *Anuvasana Basti* is also the same for *Matra Basti. Hrusva Matra* is the term for this dose, which is metabolized in two hours, or two *Yama*, however the amount needed to be metabolized in two *Yama* is not stated. Another work states that for *Anuvasana Basti*, the maximum dose is 6 *Pala* of *Sneha*, the moderate dose is 3 Pala of *Sneha*, and the smallest dose is 1½ Pala of *Sneha*. In line with this, Sushruta has also stated. As a result, 1½ Pala is the dosage for *Matra Basti*. Speaking about *Matra Basti, Chakrapani* stated that *Anuvasana Basti* has three *Pala* of *Sneha, Matra Basti* has one and a half *Pala of Sneha*, and *Sneha Basti* has six *Pala* of *Sneha*. Based on the aforementioned references, the recommended dosage of *Matra Basti* is 1½ Pala of *Sneha*, or roughly 60 millilitres.

Basti procedure: Before administration.

The patient should not consume too much *Snigdha* or too much *Ruksha Ahara*. Because *Mada and Murcha* are caused by the excessive *Snigdha Ahara*. Depletion of *Bala* and *Varna* results from an excess of *Ruksha Ahara*. Consequently, the patient should be instructed to follow an *alpa sneha*-containing diet.[115]

***Matra Basti Pratyagamana* time.**

Matra Basti's Pratyagamana Kala typically lasts three *Yama*, or nine hours. If the substance stays in the body, there is no harm. Due to the fact that *Sneha's* dosage is so small, it can be readily absorbed by the body and remains there. The *Sneha Basti* is thought to be something that should stay inside the body. *Basti* substance cannot have the intended impact if it returns considerably sooner.[116]

Signs of *Samyak Yoga of Matra Basti*

Since *Samyak Yoga Lakshana* of Sneha *Basti* is a kind of *Sneha Basti*, it should be interpreted as *Samyak Yoga Lakshana of Matra Basti*. The return of *Sneha* with the faecal matter in a satisfactory evacuation, the optimum functionality of *Rakta, Mamsa*, etc., *Dhatu* and sense organs, sound sleep, a lighter body, increased strength, and control over the natural urges are all examples of *Samyak Anuvasana's Lakshana.*[117].

Complications of *Sneha Basti*

Although it is claimed that using *Matra Basti* does not usually result in serious complications, *Sneha avrodha* caused by *Vata, Pitta, or Kapha*, as well as excess *Mala* or food when given to a person on an empty stomach, can occasionally cause complications. There are the six circumstances that could lead to difficulties when using *Sneha Basti*.[118]

4. JUSTIFICTAION

Visha guna and *karma* when compared with Chemoradiation's mode of action and their anticipated adverse/side effects [as mentioned in review of literature], they both have an approximation in features of *pakwashayagata visha lakshana*.

Similarly in accordance to this, if one sees Concurrent Chemo-radiation therapy as *Virrudha Aushadhi* [incompatible drug to body] which can cause disturbances in body's physiology then one can co-relate to the concept of *Viruddha*. In such a scenario, *Shahrir samkskarna* [preventive care] can be understood as prophylactic care to prevent or to avoid the future insults to the body.

On the other hand, the CCRT induced symptoms like mucositis, dysphagia and pain lead to malnutrition and cachexia. This phase of conventional pathology may share common understanding for *dhatu kshaya janya Rajayaksham* based on symptoms like *aruchi, kasa, amsa shula, parswashula, swara bheda* etc.

Considering all the three possible *nidana* and intricate *samprapti*/pathology of the CCRT induced adverse effects/events/toxicities, it may be understood as *Vyavayi, Vikashi, Tikshana and Ushna guna* of Chemoradiation therapy leading to dysregulation of *Vata (ruksha, laghu, sukshma and khara guna*), *Pitta dosha (sneha, drava and sara guna*) and *kapha kshaya (snigdha, slakshanm and sthira guna*). Due to vitiation of these *guna's* there will be *Vidagdatha* of *anna rasa* that sooner or later leads to *vikruti* in dhatus namely *rasa, rakta and mamsa*. Due to this the *prenan karma of rasa, Jeevan karma of rakta and lepana karma of mamsa* gets altered and cause cascading effect on other dhatus until *Oja* becomes weak.

To anchor such situation of *dhatu kshaya* incurred due to *visha or viruddha, ghrita* has been told as primordial medicament due to *ojakara guna*. Among *ghrita, samskaarit ghrita* are better hence *Jeevanthyadi ghrita* is chosen since the *samprapti* of *dhatu kshaya* can also be addressed.

Hence the *Jeevanthyadi Ghrita* which is told in *Rajayaksham adhikara* [Debilitating disease] by Acharya's was chosen as medicine in the form of *matra basti* [retention lipid enema] as a mode of *sharir samskara* to prevent the concurrent chemotherapy induced adverse effects.

5. MATERIALS AND METHODS

The study was conducted in two phases

1. Preparation of *Jeevanthyadi ghrita* at KLE Ayurveda Pharmacy (GMP Certified) Belagavi, Karnataka, India.
    a. Raw drugs collection, authentication and analysis.
    b. Collection of ghee prepared in traditional method.
    c. Preparation of *Jeevanthyai ghrita* as per classical method.
    d. Analysis of *Jeevanthyadi ghrita*.
2. Clinical Study conducted at Karnataka Cancer Therapy and Research Institute (KCTRI) Hubballi, Karnataka, India.
    a. Study was accepted by Institutional Ethics Committee (KAHER/EC/ 19-20/290619005), then registered in Clinical Trials Registry-India (CTRI/2021/03/032043), and conducted in accordance with the principles of Good Clinical Practice.

PART I

5.1: PREPARATION OF JEEVANTHYADI GHRITA

Raw Materials.

1. As mentioned in Table no 4, 11 out of 14 raw drugs were provided by GMP certified Dabur India Ltd (Dabur Pharma), New Delhi as goodwill gesture towards research. After receiving the raw materials, they were for tested for Preliminary Physico-chemical and Phytochemical standards as per API and they were found be in Standard range.
2. *Traayamana* (*Gentian Kurroo* Royle) was procured from Nainithal [High Altitude Medicinal Plant Garden and research centre Uttarakand] and from its natural habitat Jammu near Shiv Koddi place. These were then authenticated at National Institute of Traditional Medicine – Indian Council of Medical Research [NITM-ICMR] [Herbarium number RMRC-1677] Belgaum.
3. *Kantakari* [*Solanum surattense* Burm. F.] and *Duralabha* [*Fagonia cretica* Linn.] were procured from KLE Ayurveda Pharmacy, Belagavi, Karnataka, India.
4. *Ghrita*/ghee was prepared by traditional fermentation process was obtained from a farm located in Kushalnagar, Madikeri District, Karnataka, India. The milk used to make *ghrita* was obtained from a native breed of cow known as the Hallikar cow (Image no. 6), which was reared in the same farm.

Table No.4. *Jeevanthyadi Ghrita* ingredients[16]

Slno	Drug	Latin name	Part	Source
1.	*Jeevanti*	*Leptadenia reticulata* Wight and Am.	Whole Plant	Dabur Pharma
2.	*Yasthimadhu*	*Glycyrrhiza glabra* linn	Root	Dabur Pharma
3.	*Draksha*	*Vitis vinifera* Linn.	Fruit	Dabur Pharma
4.	*Kutaja*	*Holerrhena antidysentrica* Wall.	Stem bark	Dabur Pharma
5.	*Pushkaramula*	*Inula racemosa* Hook.F.	Root	Dabur Pharma
6.	*Sati*	*Hedychium spicatum* Ham.Ex Smith.	Rhizome	Dabur Pharma
7.	*Pippali*	*Piper longum* Linn.	Fruit	Dabur Pharma
8.	*Kantakari*	*Solanum surattense* Burm. F.	Root	KLE Pharma
9.	*Gokshura*	*Tribulus terrestris* Linn.	Fruit	Dabur Pharma
10.	*Bala*	*Sida cordifolia* Linn.	Root	Dabur Pharma
11.	*Nilothpala*	*Nymphaea nouchali* Burm.F.	Flower	Dabur Pharma
12.	*Bhumyamalaki*	*Phylanthus amarus* Schum & Thonb.	Whole plant	Dabur Pharma
13.	*Trayamana*	*Gentian Kurroo* Royle.	Rhizome	Natural habitat
14.	*Duralabha*	*Fagonia cretica* Linn.	Whole plant	KLE Pharma
15.	Cow Ghee	*Hallikar Breed*	Ghee	

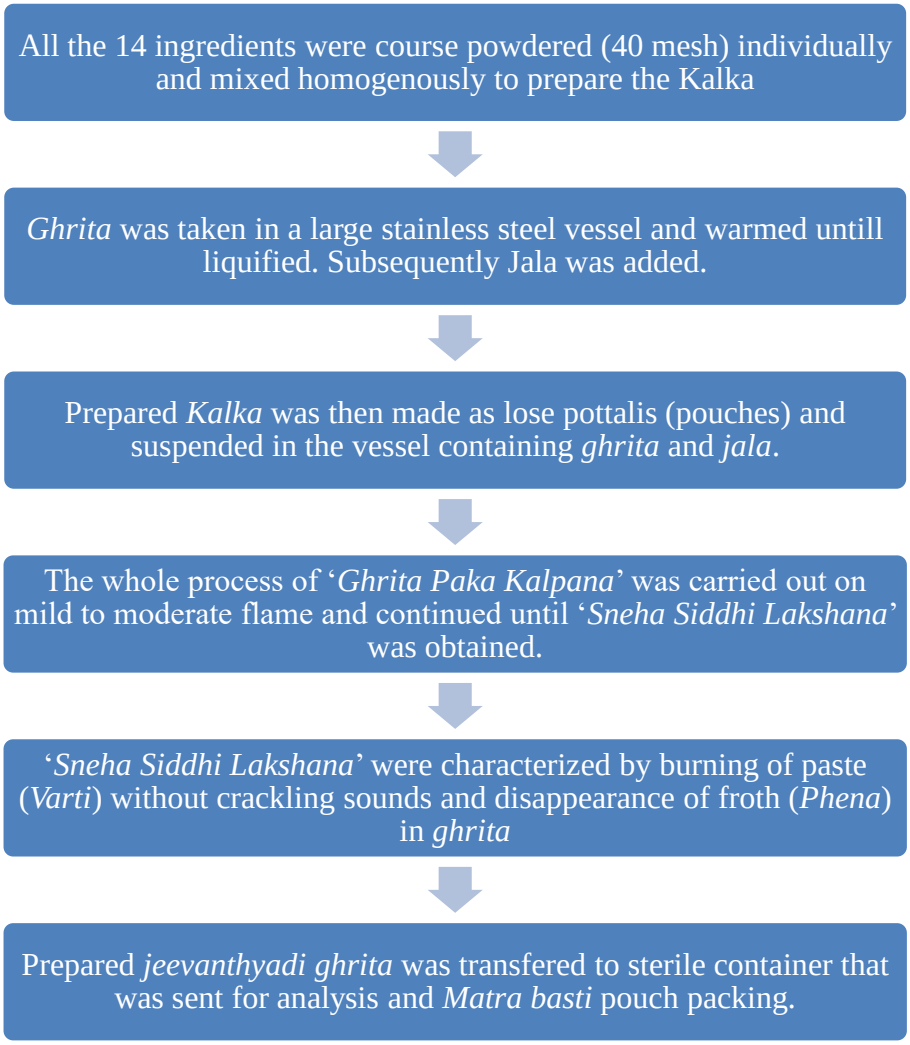
***Jeevanthyadi Ghrita* Preparation:**

Standard operating procedure mentioned for *Ghrita Kalpana* in the *Ayurveda* Formulary of India[119] was followed to prepare the *Jeevanthyadi ghrita*.

Table No.5. Ratio and amount of *Ghrita, Kalka Dravya* and *Jala* taken to prepare *Jeevanthyadi ghrita*.

S.no	Particular	Ratio to be taken as classical method	Taken for preparation
1.	*Ghrita* (Ghee)	1 part	78 liters
2.	*Kalka* (paste of 14 drugs)	¼ part of Ghrita	19.5 kilograms
3.	*Jala* (Water)	4 parts of water	312 liters

Image No.1. Flow Chart of SOP and Preparation of *Jeevanthyadi Ghrita*



***Jeevanthyadi Ghrita* Preparation Gist**

1. *Ghrita* Preparation started on 20-09-2021 and ended on 22-09-2021.
2. *Ghrita* Taken for Preparation: 78 liters
3. *Ghrita* obtained after processing: 73 liters
4. Processed *Ghrita* was made as Basti Packets: 1475 packets/pouches of ~55 ml each.

Images of Raw drugs and *Jeevanthyadi ghrita* preparation.

Image No.2 Ingredients of *Jeevanthyadi Ghrita.*

Image no.3 Place of collection of drugs *Trayamana*.

Image no.4. Shade drying of raw drugs *of Jeevnathyadi ghrita*

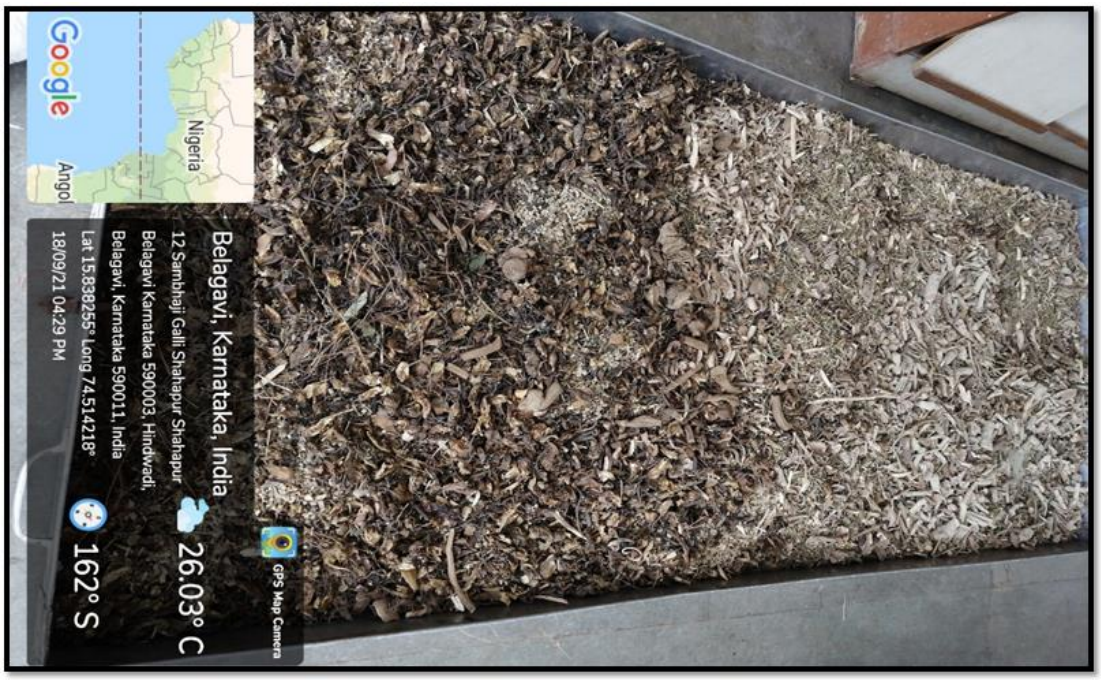


Image no.5: Raw drug processing to *Kalka churna* consistency.

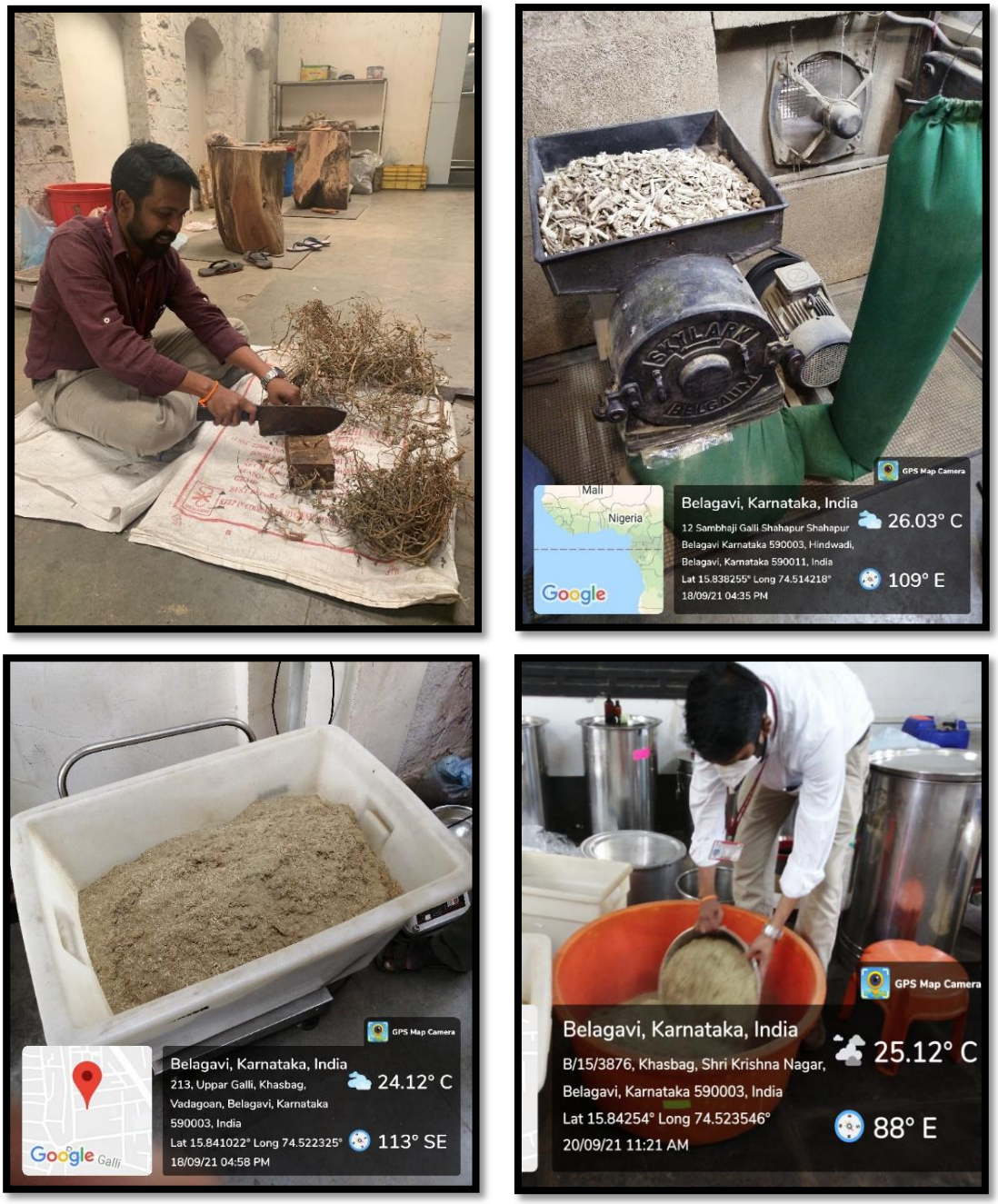


Image no.6 Hallikar cow rearing in same farm and traditionally prepared ghee.

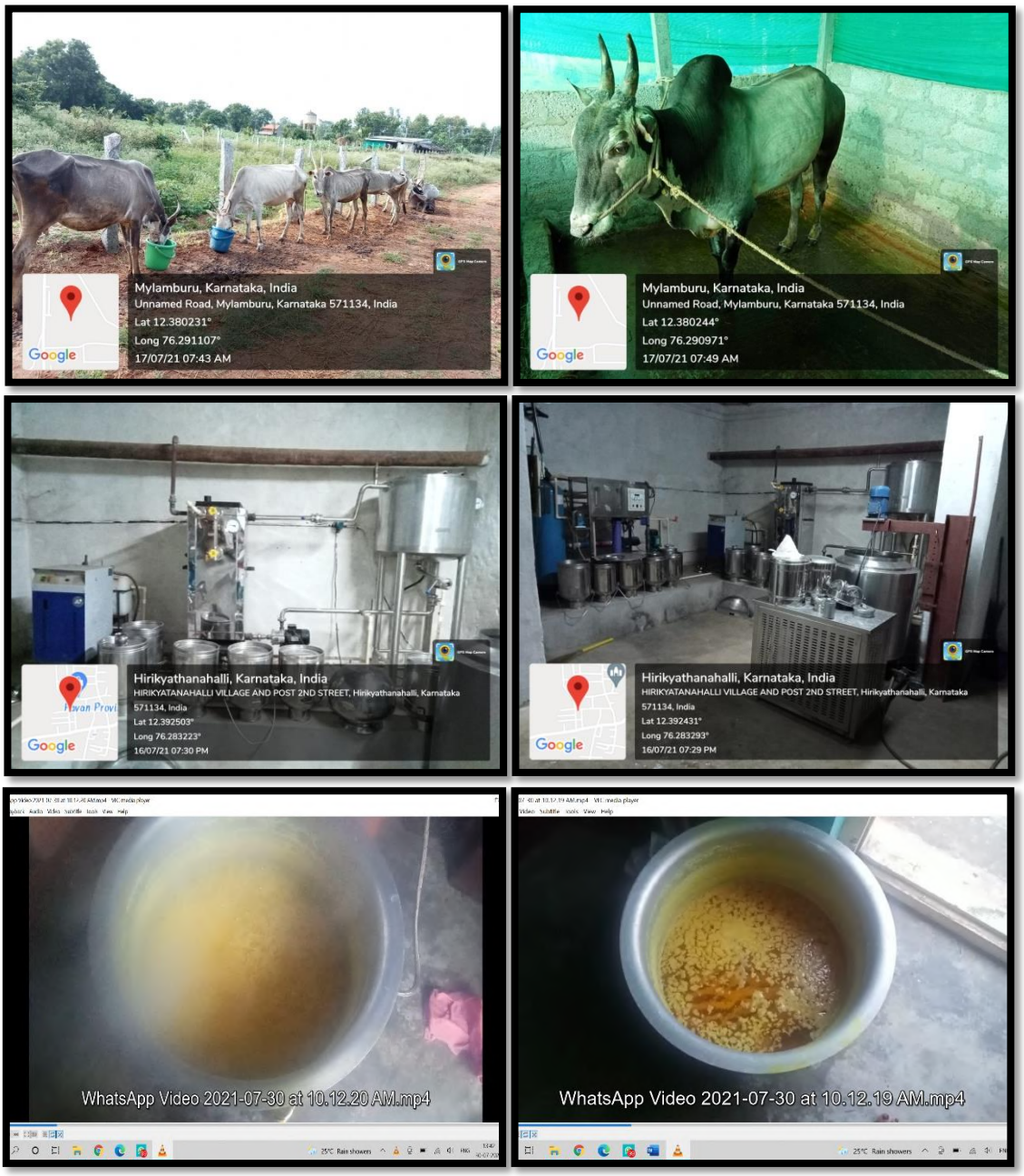


Image no.7 Initiation of *Jeevanthyadi Ghrita* preparation.

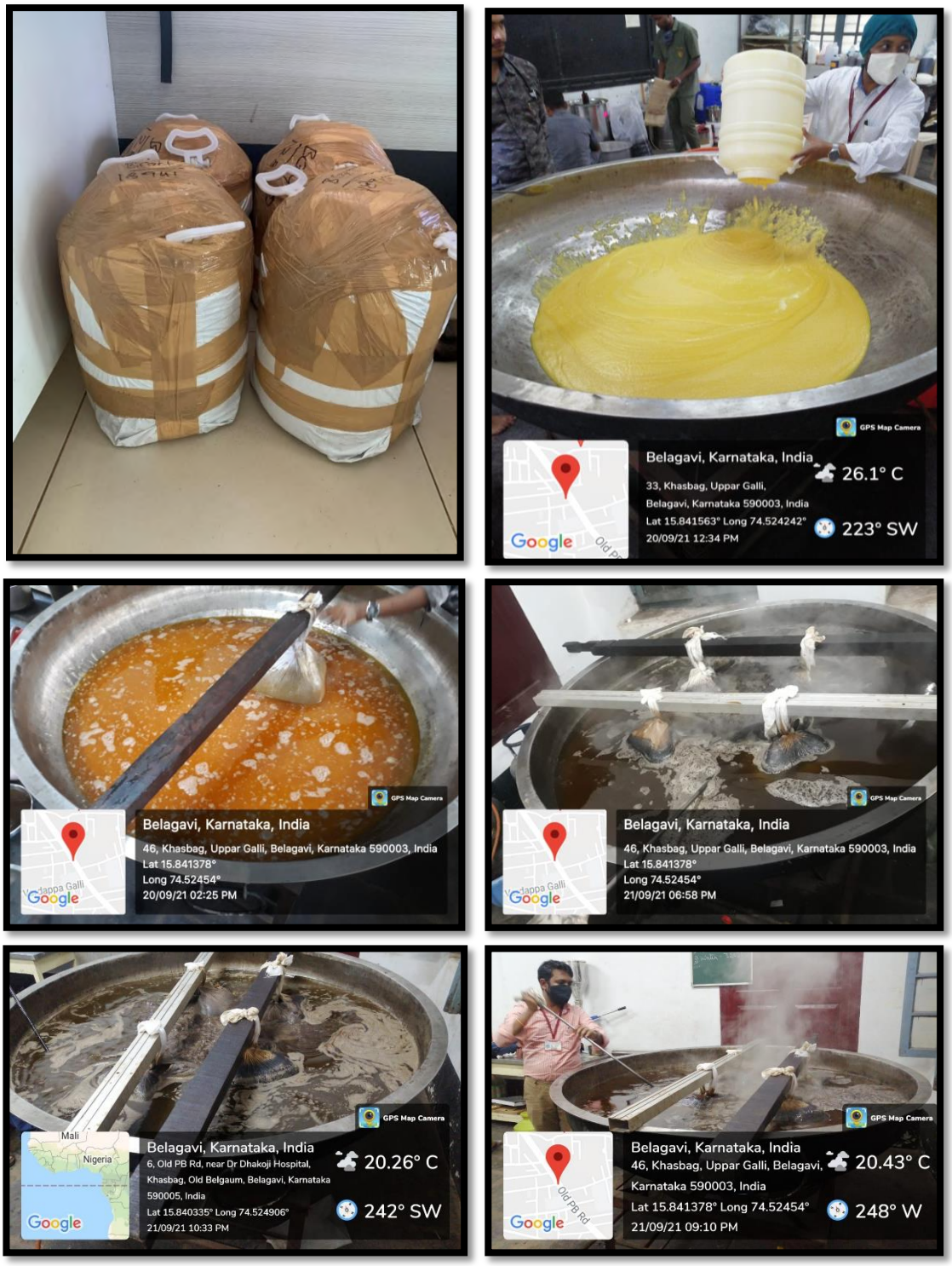


Image No.8 *Sneha siddhi lakshan* achieved during preparation.

Images no.9 Prepared *Jeevanthyadi ghrita* and packing into Basti pouch

5.2 ANALYSIS OF RAW MATERIALS AND PREPARED *JEEVANTHYADI GHRITA*

1. Raw Drugs provided by GMP certified DABUR PHARMA LIMITED, New Delhi [11 drugs as mentioned in earlier report], *Duralabha* [*Fagonia cretica* Linn.] and *Kantakari* [*Solanum surattense* Burm. F] procured from GMP certified KLE Ayurveda Pharmacy, *Trayamana* (*Gentian Kurroo* Royle) collected from natural habitat were tested for **Macroscopic, Preliminary Physico-chemical and Phytochemical standards** at KAHER's Shri B. M. K. Ayurveda Mahavidyalaya's, Central Research Facility's (CRF) *Ayurveda Siddha Unani* –Drug Testing Laboratory (ASU-DTL), approved by AYUSH Department Government of Karnataka. as per API and they were found be in Standard range. [120]
2. Traditionally prepared plain *ghirta* and prepared *Jeevanthyadi Ghrita* samples were tested for Ghee parameters at ESSAR Laboratories (Government of India Approved AGMARK Laboratory, ISO 9000:2015 certified and NABL Accredited), Hubballi, Karnataka, India and at KAHER's Shri B. M. K. Ayurveda Mahavidyalaya's, Central Research Facility's (CRF) *Ayurveda Siddha Unani* –Drug Testing Laboratory (ASU-DTL), approved by AYUSH Department Government of Karnataka.
3. Prepared *Jeevanthyadi Ghrita* samples were also subjected for the presence, quantification of phytochemicals, **High-performance thin layer chromatography (HPTLC)** and **Gas chromatography–mass spectrometry (GC–MS)** at CARe KERALAM Confederation for Ayurvedic Renaissance Keralam Ltd A joint venture of Ayurvedic Entrepreneurs & KINFRA Govt. of Kerala, supported by Dept of AYUSH, Govt. of India [Test report number:

CKL/22/ T376]. **Liquid chromatography-mass spectrometry (LC-MS)** at BIOCYTE Research and Development (BIRD), Sangli, Maharashtra for standardization.

4. Network pharmacology methodology: Based on the presence of phytochemicals/active principles/metabolites found through GC-MS and LC-MS, preliminary network pharmacology was derived to understand probable mode of action of drug. [121]
    a. Preparation of phytochemical dataset: Dataset was prepared by removing duplicate entries and verifying the chemical details of each phytochemical in the PubChem database to create a unique collection of phytochemicals. Second, SWISS ADME was used to obtain the ADME parameters of the phytochemicals.
    b. Candidate protein targets of phytochemicals: The BindingDB database is used to retrieve phytochemicals' putative human protein targets. The UniProt database is used to translate the target names into UniProt IDs in order to make further analysis easier.
    c. Symptoms related genes: Target gene information was gathered using databases such as Drug Bank, ChEMBL, DisGeNET, and GeneCards Human Protein Atlas platforms. Venny ver. 2.1, an online tool for constructing Venn diagrams, was then used to see where the chosen compounds and the illness target overlapped.
    d. Protein-Protein Interaction (PPI), Pathway analysis and enrichment were obtained using databases like STRING, KEGG.
    e. Network analysis: A "Compound-Target-Pathway" was created by further importing an enriched route linked to the target sick genes into

Cytoscape. Using nodes representing diseases, targets, and related pathways, the network linkages of the components in the target protein pathway were constructed.

HPTLC METHOD

Instrumentation

The apparatus used was a CAMAG HPTLC system with a LINOMAT 5 applicator that had a 100 µl syringe, a CAMAG TLC scanner, and winCATS software.

Chemicals and solvents

Every chemical utilized was an analytical reagent grade, and every solvent was of the chromatography grade.

Preparation of samples

Ghrita was filtered after being dissolved in 100 cc of HPTLC-grade methanol. For the HPTLC investigation, this solution served as a test solution.

Chromatographic conditions

A 60 F 254 HPTLC plate (E. MERCK KGaA) with a precoated 5.0 × 10.0 cm silica gel was used for the HPTLC procedure. There was no pre-washing or plate alteration. Using a 100 µl syringe-equipped CAMAG Linomat applicator, the sample solution was applied to the plate in bands (Table 1). 150 nl/s was the steady application rate. The mobile phase—TOLUENE: ETHYL ACETATE: HEXANE (6:3:1 v/v/v)—was maintained in an automated development chamber with the sample-loaded plate. Using the winCATS-equipped CAMAG TLC scanner-17019, densitometric scanning was carried out. The photographs were taken in white light at wavelengths of 254 nm (short UV) and 366 nm (long UV), with the bands displayed

using the CAMAG visualizer (Table 2). UV-active chemicals suffer fluorescence quenching when subjected to short-wave UV radiation at a wavelength of 254 nm, making them appear as black spots on a brilliant background. On the other hand, substances that absorb UV light at 366 nm will show up as bright spots on a black backdrop. Details of the calibration, detection and Integration parameter are attached in annexure.

GAS CHROMATOGRAPHY AND MASS SPECTROMETRY

Instrument Model - A 7890 A GC with 5975C and a triple axis detector was the equipment utilized.

Column - DB 5MS 30 m x 0.250mm Diameter x 0.25 Micro Meter Thickness

Preparation of Sample: Unsaponifiable matter was removed from approx. 5g sample, reconstituted in 1mL GC grade Methanol, filtered

Method: A split ratio of 10:1 was used to inject 2 µL of the material for analysis. The carrier gas, helium gas (99.9995%), was employed at a flow rate of 1 mL/min. With an ionization energy of 70 eV, the study was carried out in the electron impact (EI) mode. A constant temperature of 280°C was maintained for the injector. The program for temperature control in column ovens is

Table.no.6 GC-MS Column program parameters.

Oven	Rate °C/min	Value °C/min	Hold Time
Initial		40	2
Ramp 1	7	150	10
Ramp 2	5	280	5

After comparing the observed spectrum configurations with those of the mass spectral database (NIST -08 spectrum DATA), the compounds were identified.

LIQUID CHROMATOGRAPHY & MASS SPECTROMETRY

Liquid Chromatograph Make: Waters, USA **Model:** 1525µ Binary Pump

Mass Spectrometer Make: Waters, USA **Model:** Xevo G2-XS QTof

Column: Accucore C18, 50 x 4.6, 5µ Particle size from ThermoScientific.

Capillary Voltage: 3.0KV

Collision Energy: 20V

Ramp Collision Energy: 30-90V

Source Temp: 150^{o}C

Desolvation Temp: 450^{o}C

Cone gas: 50L/Hr

Desolvation Gas Flow: 800L/Hr

Processing Software: MassLynx V4.1

Mobile Phase-A: 0.1% Formic acid in water

Mobile Phase-B: Acetonitrile

Diluent: Methanol and Tetrahydrofuran

Sample Preparation: About 10mg of sample is dissolved in 1ml of THF and diluted to 10mL with methanol. Filtered and injected.

Injection Volume: 10uL

Table no. 7 Details of Gradient Programme of LC-MS

Time	Flow	%A	%B
Initial	0.500	95.0	5.0
1.00	0.500	95.0	5.0
6.00	0.500	50.0	50.0
12.00	0.500	5.0	95.0
17.00	0.500	5.0	95.0
18.00	0.500	95.0	5.0
20.00	0.500	95.0	5.0

PART II

5.3 CLINICAL STUDY

ETHICAL CONSIDERATIONS

Institutional Ethics Committee approval: Obtained. Approval taken for the study protocol, written informed consent document including participant information sheet.

Informed Consent: Prior to conducting any study-related procedures, each participant provided informed written consent in the format required (i.e. physical examination, laboratory screening or any other investigational technique). Complete study details were provided to the participants, including with a language-specific explanation of any potential hazards or discomforts. Additionally, participants were made aware of their freedom to withdraw from the study at any moment and without explanation.

TRIAL DESIGN:

Randomized open labelled control study

PARTICIPANTS:

DIAGNOSTIC CRITERIA

Histopathological and radiologically diagnosed primary cancer patients of Cervix, Lung, Oesophagus, Head and Neck of stage II, III, IV.

INCLUSION CRITERIA

1. Consented patients who are advised for Concurrent Chemo-Radiation therapy protocol of KCTRI.
2. Age $\geq$ 30 years and $\leq$ 70 years

3. ECOG ≤ 2
4. Eligible for *Matrabasti*.
5. Acceptable Baseline Hematological and biochemical parameters. (Hb > 8mg/dl, WBC > 4*109/ml, Platelet > 150*109 /ml, Urea ≤40 mg/dl, Creatinine ≤ 1.5 mg/dl, Total bilirubin ≤ 1mg/dl, SGOT and SGPT ≤ 50 IU/ml)

EXCLUSION CRITERIA

1. Unfit for Concurrent Chemo-Radiation therapy
2. K/C/O Ischemic Heart Disease, Thyroid.
3. Haemorrhoids.
4. Acute Diarrhoea
6. Second cancers.
7. Concomitant major illness requiring long term medication.

WITHDRAWAL CRITERIA

1. Any serious adverse events requiring major interventions.
2. Any time during course of intervention patient developing *Ayogya Lakshana* (adverse events) for continuing *matra basti.*
3. Any untoward event where in investigator feels continuation of trail may jeopardise the health state of the patient.
4. If subject wishes to discontinue the study.

RESCUE MEDICATION

As the study was being conducted in IPD setup of Tertiary oncology center patient were managed as per conventional protocol.

SITE OF STUDY:

Karnataka Cancer Therapy and Research Centre, Hubballi, Karnataka.

INTERVENTIONS:

CONTROL GROUP: Received standard conventional care of Concurrent Chemo-Radiation Therapy (weekly Inj Cisplatin (5-6 cycle) at a dose of 40-70 mg/m2 and radiation at a dose of 45-70 Gy in 25-35 fractions).

TRAIL GROUP: Along with standard conventional care of Concurrent Chemo-Radiation Therapy (weekly Inj Cisplatin (5-6 cycle) at a dose of 40-70 mg/m2 and radiation at a dose of 45-70 Gy in 28-35 fractions), trail group patient received *Jeevanthyadi Ghrita matra basti* at dose of 50 ml, for three days, before every chemotherapy dose.

Table no 8. Study plan execution and Outcome parameter assessment days

Study plan	Outcome measures and Intervention	EORTC-QLC 30 & Supplements	ECOG	CBC	LFT	RFT
Pre-treatment		√	√	√	√	√
Day 1-3	JGMB					
Day 4-8	1st CT + RT					
Day 9-11	JGMB	√				
Day 12- 16	2nd CT + RT					
Day 17-19	JGMB					
Day 19th		√	√	√	√	√
Day 20-24	3rd CT + RT					
Day 25-27	JGMB	√				
Day 28-32	4th CT + RT					
Day 33-35	JGMB	√				
Day 36-40	5th CT + RT					
Day 41-43	JGMB	√				
Day 44-48	6th CT + RT					
Day 49		√	√	√	√	√
Note: JGMB- *Jeevanthyadi Ghrita Matra basti*, CT- chemotherapy, RT - Radiation therapy.						

OUTCOMES

PRIMARY OUTCOME MEASURES AND ASSESSMENT TOOLS.

1. Quality of life assessed with EORTC-QLQ 30 (permission obtained), and respective supplements namely H&N-43, CX-24 and OES-18. [EORTC-QLQ-30 tool has First six domains for functional assessment where higher score represents a "**better**" level of functioning and next nine domains are **Symptoms** that can be experienced due to therapy during treatment, where higher the score represents a "**worse**" level of symptoms/problem. Similarly in Supplements higher score of symptoms is worse level of symptom.]

SECONDARY OUTCOME MEASURES ASSESSMENT TOOLS.

1. Amelioration of adverse events as assessed by Common terminology criteria adverse events (CTCAE) version 5 was used.
2. Safety profile done as per KCTRI protocol [Complete blood Count, Serum Creatinine, Serum Urea, SGOT, SGPT, ALP and Total Bilirubin, Total protein]
3. Performance Status assessed by scale of Eastern Cooperative Oncology Group (ECOG).

SAMPLE SIZE

Sample size considerations, as this was a proof-of-concept study that aimed to evaluate effect of *Jeevanthyadi ghrita matra basti* in cancer patients, a sample size '**n' of 70** participants had been considered as adequate after going through the literature and study site foot fall. The sample size was calculated by using below mentioned formula

$$n = \frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 (p_1 q_1 + p_2 q_2)}{(p_1 - p_2)^2}$$

Where, $Z_{1-\alpha/2}$ = 1.96 at 5% α error (α=0.05)

$Z_{1-\beta}$= 0.84 at 80 %, Power of the test (β=80)

Based on review of literature of toxicity changes

% of toxicity changes from baseline to last follow up P1=65%

% of toxicity changes from baseline to last follow up P2=40 %

Estimated risk difference =d = P1-P2= 25%

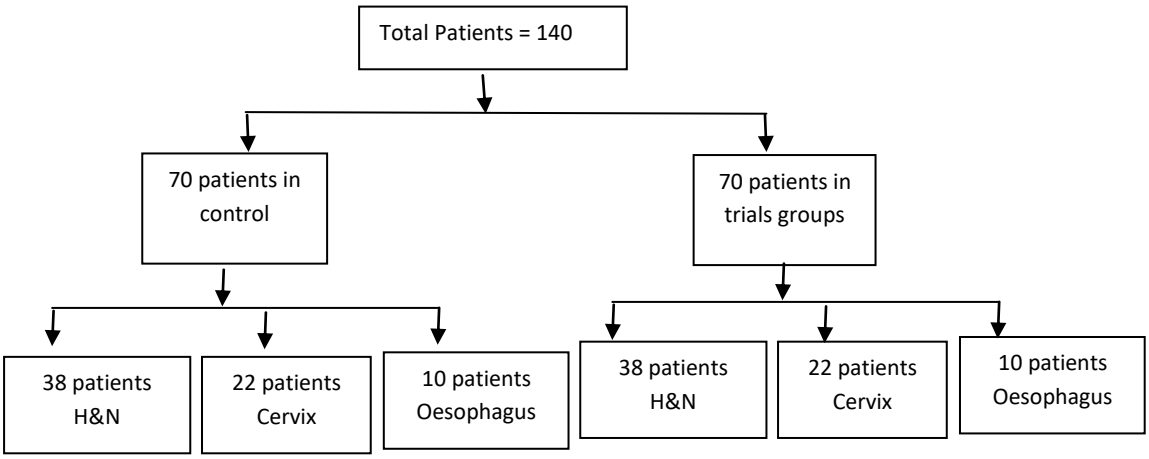
$n = 63$ per group, which minimum required sample size per group. Accounting drops out cases as 10%, then the calculated sample size was = 70 for each group. Hence, required sample 70 has been taken per group, which leads to total sample size for the study = 70 x 2 = 140.

RANDOMIZATION

Sample Selection

The patients were enrolled as per inclusion criteria and then randomly divided into CCRT group and CCRT+MB Group. Patients were selected by envelope method of randomization for the treatment stated as:

Image no 10. Randomization and Allocation of consented cancer subjects



ALLOCATION CONCEALMENT MECHANISM & IMPLEMENTATION

Radiation oncology consultants directed the eligible patients to the investigator after considering the inclusion and exclusion criteria. Patients were selected by envelope method of randomization for the treatment stated in the above flow chart. A total of 140 envelope were prepared for the patients of Head and Neck (38 for each control and trial groups), Cervix (22 for each control and trial group) and Oesphagus (10 for each control and trial group) cancer patients.

BLINDING

Participant blinding was followed**.**

STATISTICAL METHODS

Those subjects **completed minimum of 4 cycles of CCRT and 4 weeks of *Jeevanthyadi Ghrita matra basti*** were considered for statistical analysis.

IBM, SPSS (Statistical Package for the Social Sciences) version 22 was used for analyzing the collected data and statistical significance was set at 5% level ($p<0.05$).

For Basic data demographic and distribution of subject's Descriptive statistics (%, mean, SD etc),

Primary outcome

1. For Quality-of-life and symptoms score (supplements) score Parametric tests like one-way Annova test, and Independent 't' test

Secondary outcomes

1. For Adverse events/side effects: One-way Annova, Independent t Test and and Pearson co-relation coefficient test was applied.
1. For Safety parameter (Complete Blood count, Liver function test and Serum creatinine and serum urea): One-way Annova test & Independent 't' test was applied.
2. For ECOG: Descriptive statistics (%, mean, SD etc), Independent 't' test was applied.

6. RESULTS AND OBSERVATIONS

Results are mentioned in two parts

1. **6.1 Quality control and Drug Analysis of *Jeevanthaydi Ghrita***
    1. Macroscopic, Physico-chemical and phytochemical Analysis of 14 raw drugs of *Jeevanthyadi ghrita*.
    2. Basic and FSSAI standards of plain ghrita and prepared *Jeevanthyadi ghrita*
    3. Phytochemical quantification, HPTLC, GC-MS and LC-MS analysis of plain *ghrita* and prepared *Jeevanthyadi ghrita*
    4. Preliminary Network pharmacology of *Jeevanthyadi ghrita* in CCRT induced side effects.
2. **6.2 Clinical study results**
    1. Consort flow
    2. Basic Demographic data and Test for Homogeneity of group.
    3. Primary outcomes: Quality of life and symptom scores.
    4. Secondary outcomes: Adverse effects, Safety profile (CBC, LFT, Serum Creatinine, Serum Urea), Performance status (ECOG).
    5. CCRT compliance and adverse events like cancellation, IPD/Hospital admissions, Blood transfusion and morphine prescriptions, weight loss.
3. **6.3 Observations.**

6.1 Quality control and Analysis of Ingredients and *Jeevanthayadi Ghrita*

Analysis of all the ingredients of the *Jeevanthyadi ghrita* [JG] showed characteristic macroscopic features [table no 9] and Normal range of values of preliminary physico-chemical parameters [table no 10]. Qualitative phytochemical screening showed presence of sugars, flavonoids, tannins, alkaloids, steroids and saponins [table no 11] which were in consensus as per API. Quantitative phytochemical screening of JG showed presence of Alkaloids and terpenoid [table no 13]. HPTLC of *JG* showed 7 peaks and 10 peaks at 256 and 366 nm respectively [table no 14 and image no 11-13]. While the GC-MS showed presence of 17 peaks [table no 15 and image 14] [active compounds and fatty acids] and LC-MS showed presence of more than 60 compounds out of which 40 [table no 17] were identified and forwarded for preliminary network pharmacology [table no 16 & 18 respectively and image number 15-17]. Basic parameters of ghee were as per AGMARK standards [table no 12].

Table no 9. Macroscopic characters of Ingredients of *Jeevanthyadi Ghrita*.

S no	Drug	Part	Colour	Odour	Taste
1.	*Jeevanti*	Stem	Dull yellow	Odourless	Bitter
2.	*Yasthimadhu*	Root	Yellowish Brown	Faint Character	Sweetish
3.	*Draksha*	Fruit	Dark Brown	Pleasant	Sweetish
4.	*Kutaja*	Stem Bark	Buff to Brownish	Odourless	Acrid & Bitter
5.	*Pushkaramula*	Root	External brown Internal Yellowish	Bitter and Camphoraceous	Aromatic and Camphoraceous
6.	*Sati*	Rhizome	Dark brown	Camphoraceous	Bitter
7.	*Pippali*	Fruit	Greenish black	Aromatic	Pungent
8.	*Kantakari*	Root	Yellowish green	Not distinct	Bitter
9.	*Gokshura*	Fruit	Light yellow	Characteristic	Slight Astringent
10.	*Bala*	Root&Stem	Brownish	Not specific	Not specific
11.	*Nilothpala*	Flower	Brownish	Characteristic	Not specific
12.	*Bhumyamalaki*	W.Plant	Greenish brown	Indistinct	Slightly Bitter
13.	*Trayamana*	Rhizome	Dark brown with yellow patches	Characteristic Aromatic	Bitter
14.	*Duralabha*	W.Plant	Brownish green	Characteristic	Bitter

Table no 10. Physicochemical Analysis of the *Jeevanthyadi ghrita* ingredients

Sl no	Drug	Foreign Matter in %	Ash Value in %	Acid Insoluble value in %	Water soluble extract in %	Alcohol soluble extract in %
1.	*Jeevanti*	Nil	6.280	1.483	5.834	1.916
2.	*Yasthimadhu*	Nil	7.157	1.590	22.231	11.460
3.	*Draksha*	Nil	1.890	0.146	82.982	33.492
4.	*Kutaja*	Nil	6.552	0.880	15.933	22.187
5.	*Pushkaramula*	Nil	4.886	0.345	25.824	14.342
6.	*Sati*	Nil	7.870	1.377	9.101	7.824
7.	*Pippali*	Nil	6.611	0.388	43.027	9.258
8.	*Kantakari*	Nil	6.875	0.913	6.088	2.291
9.	*Gokshura*	Nil	13.667	1.702	16.772	7.509
10.	*Bala*	Nil	1.588	0.962	12.340	3.354
11.	*Nilothpala*	Nil	12.964	3.326	29.002	7.077
12.	*Bhumyamalaki*	Nil	6.372	0.910	15.077	4.760
13.	*Trayamana*	Nil	6.450	1.772	31.588	29.531
14.	*Duralabha*	Nil	9.081	0.397	24.072	6.712
Note: According to the Indian Ayurvedic Pharmacopeia, all of the values fall within the range.						

Table no 11. Qualitative Phytochemical screening of Ingredients *Jeevanthyadi ghrita.*

Sl no	Drug Name/Test Name	*Jeevanthi*		*Yasthimadhu*		*Draksha*		*Kutaja*		*Pushakarmula*		*Sati*		*Pippali*	
		WE	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**
1.	Carbohydrate	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2.	Monosaccharaides	+	--	+	+	--	--	+	+	+	+	+	--	--	+
3.	Reducing Sugar	+	--	+	+	+	+	+	--	+	+	+	--	+	+
4.	Pentose sugar	--	--	--	--	--	--	--	--	--	--	--	--	+	--
5.	Hexose Sugar	--	--	--	--	--	--	--	+	--	--	--	--	--	--
6.	Protein	--	--	+	--	--	--	--	+	--	--	--	+	--	--
7.	Amino acid	--	--	+	--	--	--	--	+	--	--	--	+	--	--
8.	Steroids	+	+	--	+	--	--	--	--	--	--	--	+	--	--
9.	Cardiac Glycosides	--	--	--	--	--	--	--	--	+	--	--	--	+	+
10.	Saponins	+	--	+	--	+	+	+	--	--	--	+	--	--	
11.	Alkaloids	--	--	--	+	--	--	--	--	--	+	--	--	--	+
12.	Flavonoids	+	--	+	--	--	--	+	--	+	+	--	--	+	+
13.	Tannins	--	--	+	+	+	+	+	+	+	+	+	--	+	+

Sl no	Drug Name/Test Name	*Gokshur*		*Bala*		*Nilothpala*		*Bhumayamlaki*		*Kantakari*		*Durlabha*		*Trayamana*	
		WE	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**	**WE**	**AE**
1.	Carbohydrate	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2.	Monosaccharaides	+	--	+	+	+	+	+	+	+	--	+	--	+	--
3.	Reducing Sugar	+	--	--	--	+	--	--	+	+	+	+	--	--	--
4.	Pentose sugar	--	--	--	--	--	--	--	--	--	--	--	--	--	--
5.	Hexose Sugar	--	--	--	--	+	--	+	--	--	--	--	--	--	--
6.	Protein	+	--	--	--	--	--	+	--	--	--	--	--	--	--
7.	Amino acid	+	--	--	--	--	--	+	--	--	--	--	--	--	--
8.	Steroids	+	+	+	+	+	+	--	--	--	+	+	+	--	--
9.	Cardiac Glycosides	--	--	--	--	--	--	--	--	--	--	--	--	--	--
10.	Saponins	+	--	+	--	+	--	--	+	+	--	+	--	+	+
11.	Alkaloids	--	+	--	+	--	--	--	--	--	--	--	--	--	+
12.	Flavonoids	+	+	+	--	+	+	--	+	+	+	+	--	+	+
13.	Tannins	+	+	+	+	+	+	+	+	+	--	+	--	+	--
Note: WE- Water Extract and AE- Alcoholic extract, + Present. – Absent.															

Table no 12. Ghee parameters for Plain *ghrita* and *Jeevanthyadi Ghrita*

Sl no	Parameter	Plain *Ghrita*	*Jeevanthyadi Ghrita*	AGMARK Specifications
1.	Baudouin test	Negative	Negative	Negative
2.	Butro-Refractometer @ 40C	41.6	42.2	40-43
3.	Reichert Meissel Value	25.6	26.5	Min 24
4.	Polenske Value	1.40	1.36	1.0- 2.0
5.	Moisture Content	0.32 %	0.30	0.3-0.5
6.	Free Fatty acid (as oleic)	1.14 %	1.24	2.8 Max
7.	Colour	7.50	7.90	10
8.	Saturated Fat	65.5 %	67.5 %	-
9.	MUFA	17.6 %	18.2 %	-
10.	PUFA	2.80 %	2.50 %	-
11.	DHA	0.04 %	0.03 %	-
12.	Milk Fat	99.2 %	99.26 %	99-99.5
13.	Cholesterol	0.18 %	0.20 %	0.5 Max
14.	pH	5.3	5.8	-
15.	Iodine Value	34.01	33.09	25-38
16.	Saponification value	223	221.5	205-235
17.	Acid value	1.8	2.08	-

MUFA=Mono unsaturated fatty acids, PUFA=Poly unsaturated fatty acids, DHA=Docosahexaenoic acid

Table no 13. Phytochemical Screening and Quantification of *Jeevanthyadi ghrita*.

Sl no	Parameter	Result	Method/Test Used	Value	Method used
1.	Alkaloids	**Present**	Dragendroff's reagent test	0.32 %	Experimental Phyto pharmacognosy
2.	Flavonoids	Absent	Shinoda test	---	CKL/ANL/UV-OO3
3.	Glycosides	Absent	Picric acid test	---	Not Done
4.	Phenols	Absent	Folin ciocalteu reagent	---	CKL/ANL/UV-OO2
5.	Saponins	Absent	Foam test	---	Standardization of Botanicals
6.	Tannins	Absent	Lead Acetate test	---	CCRAS 40.3
7.	Terpenoids	**Present**	Salkowski reaction test	---	--
8.	Steroid	Absent	Salkowski reaction test	---	--
These analyses were done at CARe Keralam, Kerala. Here the *Jeevanthyadi Ghrita* has shown presence of **Alkaloids and Terpenoids**. May be the other active parameters are below detectable limit.					

Table no 14. HPTLC of *Jeevanthyadi Ghrita* and Rf values (254 nm and 366 nm)

Sl.no	254 nm Rf	% of Compound	366 nm Rf	% of Compound
1.	**0.01**	11.76	**0.01**	7.76
2.	**0.04**	4.09	**0.07**	6.52
3.	**0.19**	8.32	**0.21**	14.14
4.	**0.36**	8.01	**0.29**	4.74
5.	**0.57**	10.71	**0.36**	13.70
6.	**0.67**	17.88	**0.39**	3.28
7.	**0.73**	39.32	**0.42**	7.63
8.			**0.56**	13.69
9.			**0.59**	3.59
10.			**0.74**	9.67

Image no 11. Chromatogram after derivatization of *Jeevanthyadi Ghrita* (A.254nm, B.366 nm and C. Day light)

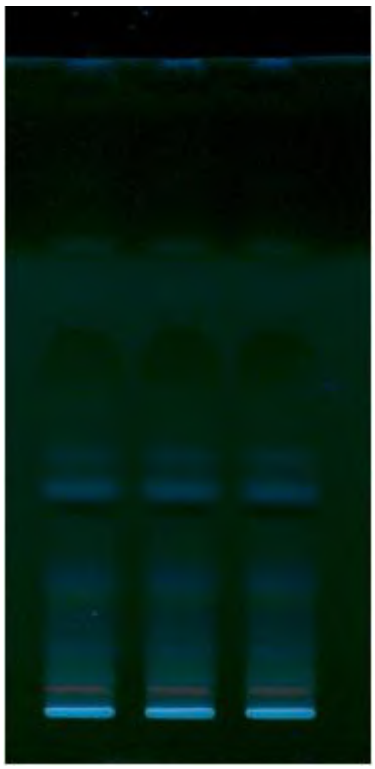
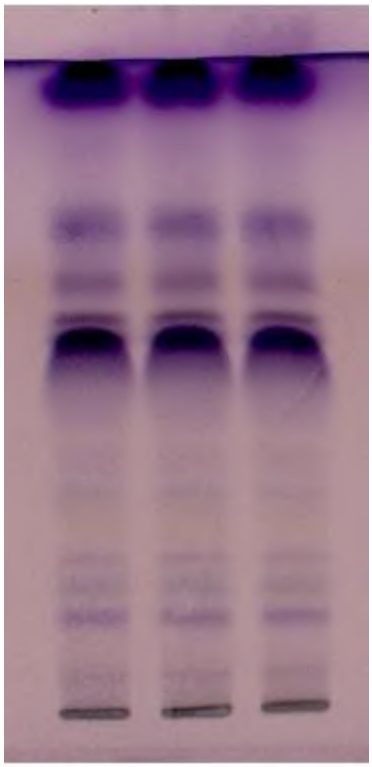
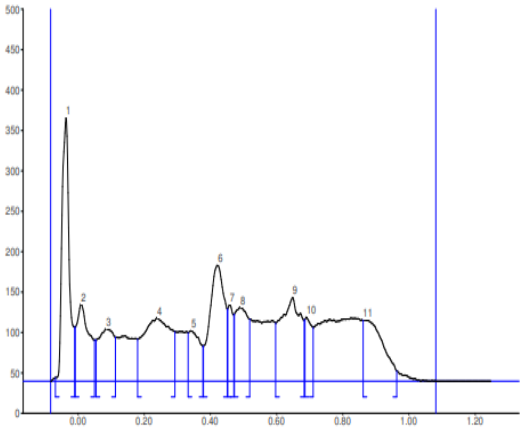
A. 256 nm	B.366 nm	C.Daylight
		

Image no 12. HPTLC chromatogram at 366nm of *Jeevanthyadi Ghrita*



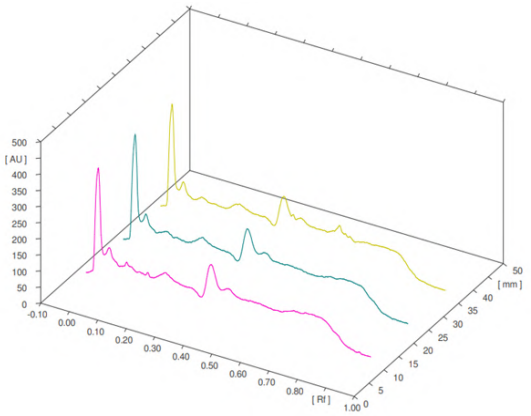


Image no 13. HPTLC chromatogram at 254 nm of *Jeevanthyadi Ghrita*.

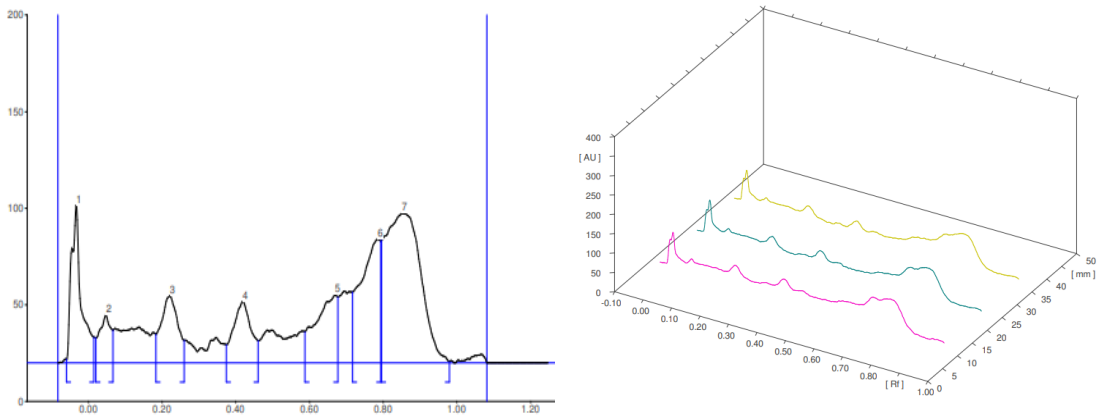


Image no 14. GC-MS spectra of *Jeevanthyadi Ghrita.*

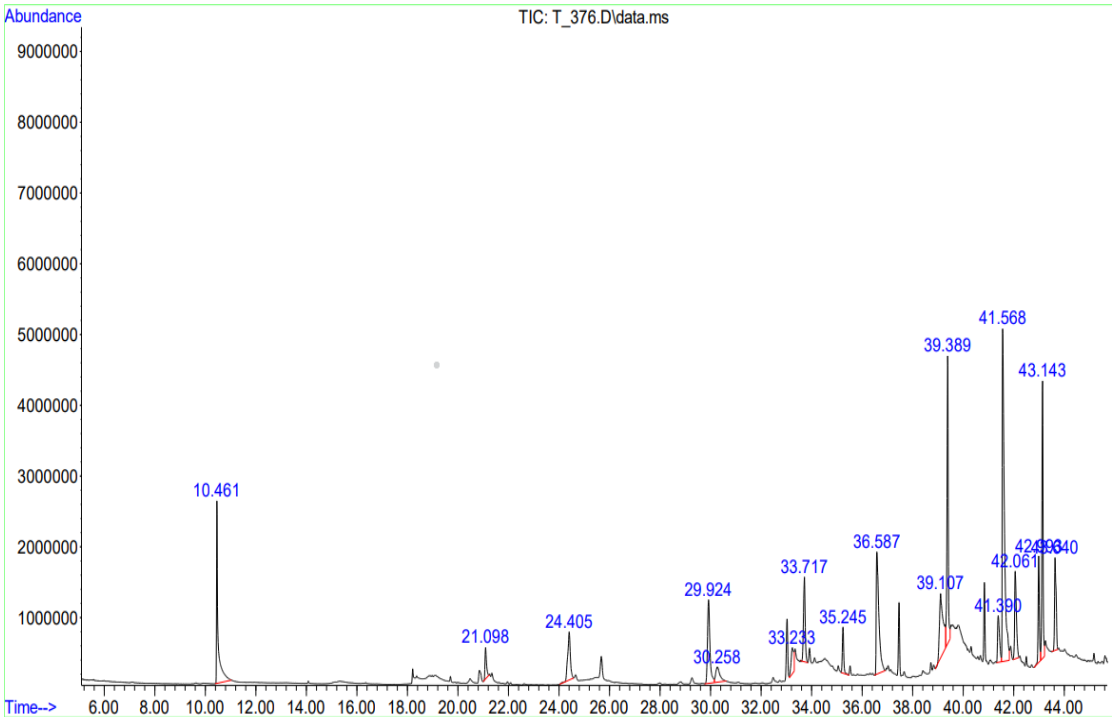


Table no 15. List of compounds identified through GC-MS in *Jeevanthyadi ghrita*

Sl. No	Name	Retention time	AUC
1	2-Ethylhexanol	10.46	7.882
2	N,N-Dimethyldodecylamine	21.09	1.318
3	Lauric acid	24.40	3.717
4	2-Pentadecanone	29.92	5.862
5	N,N-Dimethyltetradecylamine	30.25	1.824
6	Tetradecanoic acid	33.23	2.060
7	Ethyl myristate	33.71	4.031
8	(2E)-3,7,11,15-Tetramethyl-2-hexadecene	35.24	1.840
9	1-Hexadecanol	36.58	9.309
10	n-Hexadecanoic acid	39.10	6.615
11	Hexadecanoic acid, ethyl ester	39.38	10.651
12	1-Hexadecanol, 3,7,11,15-tetramethyl	41.39	2.680
13	1-Octadecanol	41.56	20.438
14	Phytol	42.06	4.524
15	9,12-Octadecadienoic acid	42.99	3.712
16	Ethyl Oleate	43.14	9.334
17	Octadecanoic acid, ethyl ester	43.64	4.203

Table no 16. Common gene targets identified to act on CCRT induced adverse effects by compounds identified in *Jeevanthyadi ghrita* through GC-MC.

Sl no	Symptoms	Number of Bio-active compounds	Number of targets	Common Targets
1.	Anorexia	14	107	PTGS2, PTGES, HTR2A, KDR, **EGFR**.
2.	Anxiety	15	378	SLC6A4, DRD2, CNR1, NR3C1.
3.	Cachexia	15	74	EGFR, **PPARG, PPARA**, VDR, PDE4B.
4.	Constipation	15	127	GPBAR1, CHRM3, SLC6A4, PGR.
5.	Depression	15	265	CYP19A1, SLC6A4, DRD2, MAPK1.
6.	Gastrointestinal mucositis	15	46	MAPK1, **EGFR**, PLA2G1B.
7.	Nausea	15	108	ESR1, UGT2B7, DRD2, CNR1, SLC6A4.
8.	Oral Mucositis	13	22	ESR1, **PPARG**.
9.	Pain	15	655	DRD2, PGR, MAPK1, SLC6A4, NR3C1.
10.	Urinary Incontinence	11	25	ADRA1A, MAPK1, HTR2A.

Table no 17. List of compounds identified through LC-MS in *Jeevanthyadi ghrita*

Sl. No	Name
1.	Palmitic Acid
2.	Nonadecanoic acid
3.	Sparfloxacin
4.	Sesamin
5.	2-Hydroxy-3-(phosphonooxy)propyl myristate
6.	Taxifolin
7.	Perseitol
8.	Elaidic Acid
9.	Trihydroxychalcone
10.	Apigenin
11.	Chrysin
12.	Kaempferide
13.	12(13)Ep-9-KODE
14.	Isosungucine
15.	Mulberroside A
16.	Neoandrographolide
17.	(2S,3R,5R,10R,13R,14S,17S)-2,3,14-trihydroxy-10,13-dimethyl-17-[(2R,3R)-2,3,6-trihydroxy-6-methylheptan-2-yl]-2,3,4,5,9,11,12,15,16,17-decahydro-1H-cyclopenta[a]phenanthren-6-one
18.	(5R)-5-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)decan-3-one
19.	Sachaliside
20.	1-({[3-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-methyl-4-oxo-4H-chromen-7-yl]oxy}acetyl)-L-prolyl-D-leucylglycinamide
21.	Ustin
22.	Portentol
23.	2-(hydroxymethyl)-6-[4-[(2S,3S)-3-(hydroxymethyl)-5-[(E)-3-hydroxyprop-1-enyl]-7-methoxy-2,3-dihydro-1-benzofuran-2-yl]-2-methoxyphenoxy]oxane-3,4,5-triol
24.	Methyl (Z)-5-[(1R,4aR,8aR)-5,5,8a-trimethyl-2-methylidene-3,4,4a,6,7,8-hexahydro-1H-naphthalen-1-yl]-3-(acetyloxymethyl)pent-2-enoate

25.	4-(2,7-Dihydroxy-6-methylheptan-2-yl)-3-hydroxybenzoic acid
26.	[4a,7-dihydroxy-7-methyl-1-[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-1,5,6,7a-tetrahydrocyclopenta[c]pyran-5-yl] (E)-3-(4-methoxyphenyl) prop-2-enoate
27.	1-Tridecanoyl-sn-glycero-3-phosphocholine
28.	Deoxycholic acid 3-glucuronide
29.	NCGC00384939-01_C28H38O8_Methyl 3-acetoxy-16-hydroxy-4,4,8,12,16-pentamethyl-15,17,19-trioxoandrost-11-ene-14-carboxylate
30.	[(4E)-7-acetyloxy-6-hydroxy-2-methyl-10-oxo-2,3,6,7,8,9-hexahydrooxecin-3-yl] (E)-but-2-enoate
31.	[5-Acetyloxy-3-(hydroxymethyl)-2-oxo-6-propan-2-ylcyclohex-3-en-1-yl] 3-methylbutanoate
32.	(4aR,5S)-9,9a-dihydroxy-3,4a,5-trimethyl-5,6,7,8,8a,9-hexahydro-4H-benzo[f][1]benzofuran-2-one
33.	4-Hydroxy-5-(1,2,3-trihydroxy-3-phenylpropyl)oxolan-2-one
34.	methyl3-[(1E,3E)-3,5-dimethylhepta-1,3-dienyl]-8-hydroxy-6a,8-dimethyl-6-oxo-9,9a-dihydrofuro[2,3-h]isochromene-9-carboxylate
35.	5-[(Z)-12-(3,5-dihydroxyphenyl)dodec-8-enyl]benzene-1,3-diol
36.	4-(3-Hydroxybutyl)phenyl beta-D-glucopyranoside
37.	NCGC00347421-02_C35H54O10_Olean-12-ene-23,28-dioic acid, 16-hydroxy-3-(beta-D-xylopyranosyloxy)-, (3beta,5xi,9xi,16alpha)-
38.	5-Hydroxy-7-[4-hydroxy-2-methoxy-3-(3-methylbut-2-enyl)phenyl]-2,2-dimethyl-7,8-dihydropyrano[3,2-g]chromen-6-one
39.	Miriquidic acid
40.	Splendoline

Table no 18. Common gene targets identified to act on CCRT induced adverse effects by compounds identified in *Jeevanthyadi ghrita* through LC-MC.

Sl no	Symptoms	No of Bio-active compounds	No of targets	Common Targets
1.	Nausea vomiting	6	257	ABCB1, ACE,CYP1A1, KIT, NR1I2
2.	Loss of appetite	2	243	ARG1, **EGFR**
3.	Constipation	11	424	ACE, ACHE, CSNK2A1, FABP4, KIT, **MMP1**, SI, SNCA, TRPV1, TTR
4.	Diarrhoea	9	633	ABCB1, ABCG2, CDK5R1, **CYP1A2**, **EGFR**, KIT, LPAR2, LPAR3, **MMP9**, NR1I2, **PIK3CG**, SI, SNCA, TOP1, TOP2A, TRPV1, TTR,
5.	Dysphonia	2	78	AR TTR
6.	Increased salivation	4	33	CA12, **EGFR**
7.	Urinary urgency	1	35	SNCA
8.	Insomnia	3	70	AHR, PSIP1, SNCA
9.	Anxiety	13	1048	ABCB1, ACE, ACHE, ADORA1, NT5E, ADORA2A, AKR1C3, ALOX15, SNCA,AR, ATP1A2, ATP1A3, **CYP1A1**, **CYP1A2**, ESR2, GLO1, TRPC5, GSK3B, IGF1R, LPAR2, MAOA, MAOB, MKNK1, **MMP12**, **MMP2, MMP9**, NR1I2, NR5A1, TRPV1.

Image no 15: LC-MS spectra of *Jeevanthyadi Ghrita*

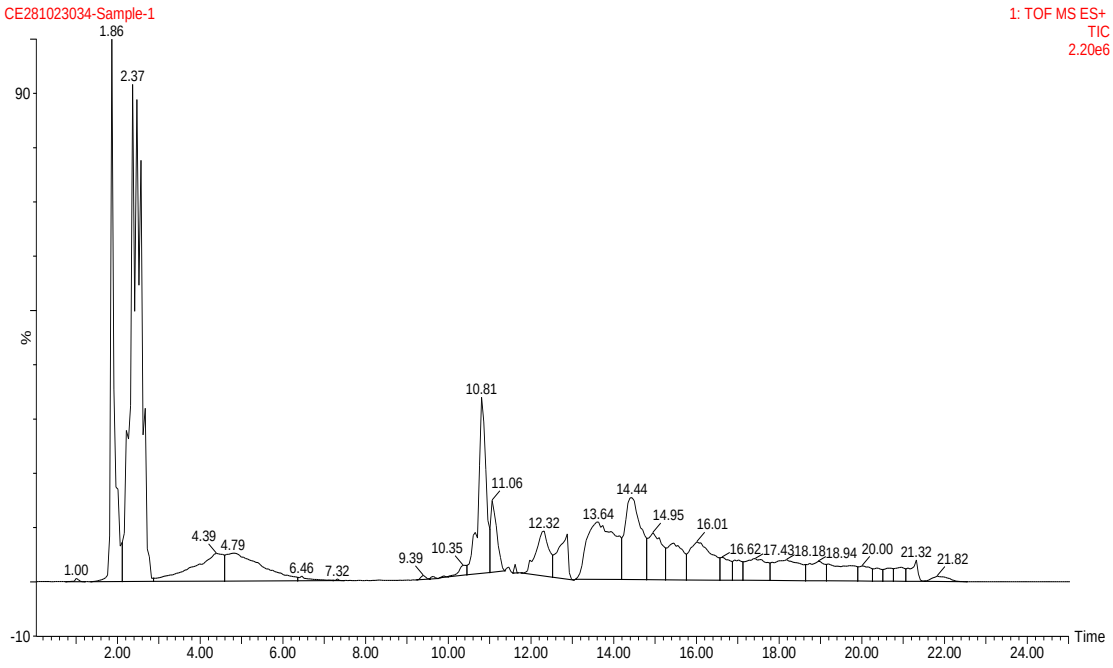


Image no 16. Network Construction of *Jeevanthyadi Ghrita* in CCRT Induced Adverse effects.

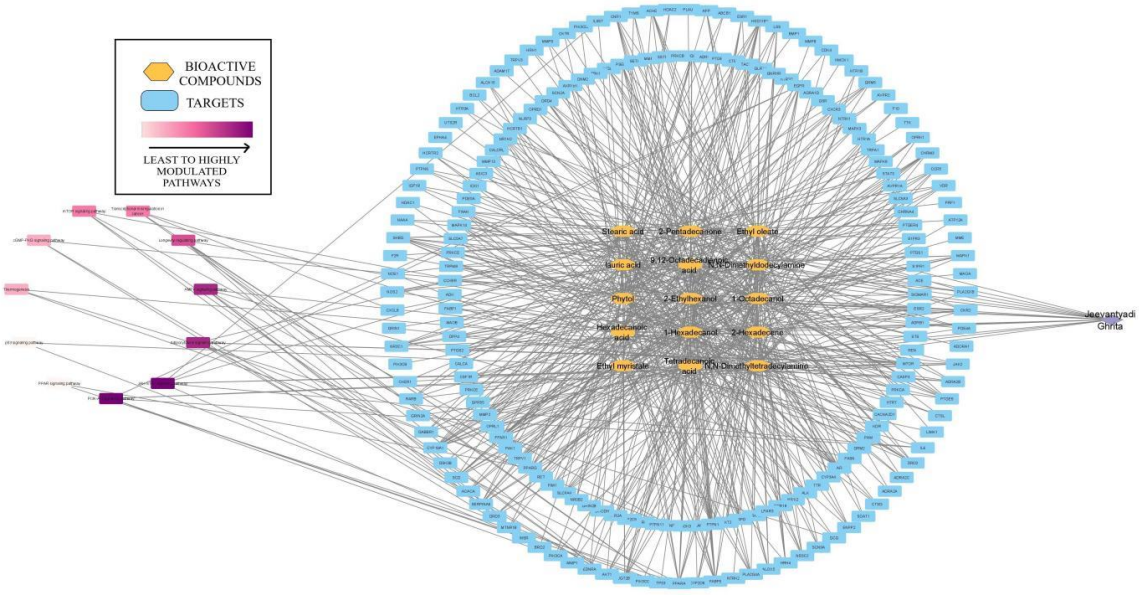


Image no 17. Top 13 hub gene of *Jeevanthyadi Ghrita* in CCRT Induced adverse effects.

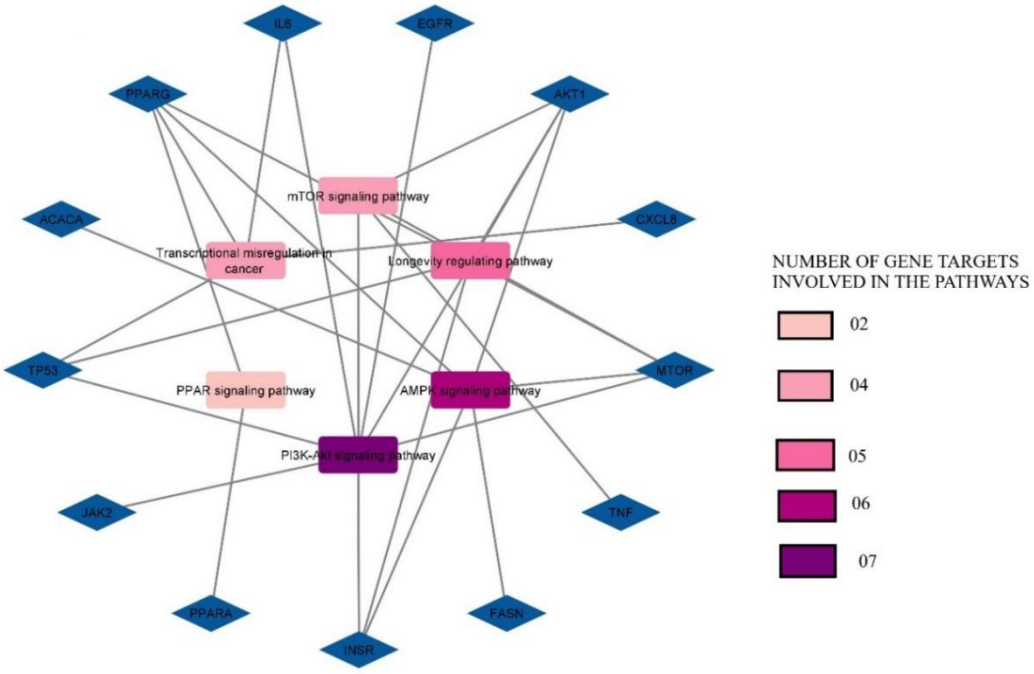
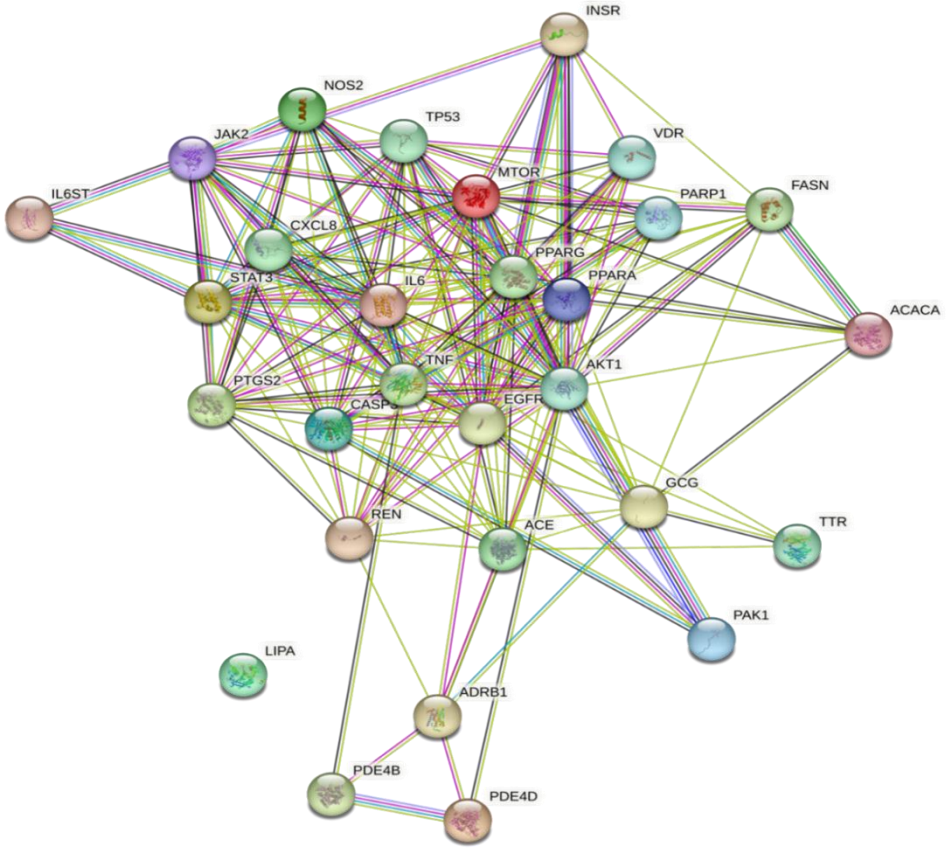
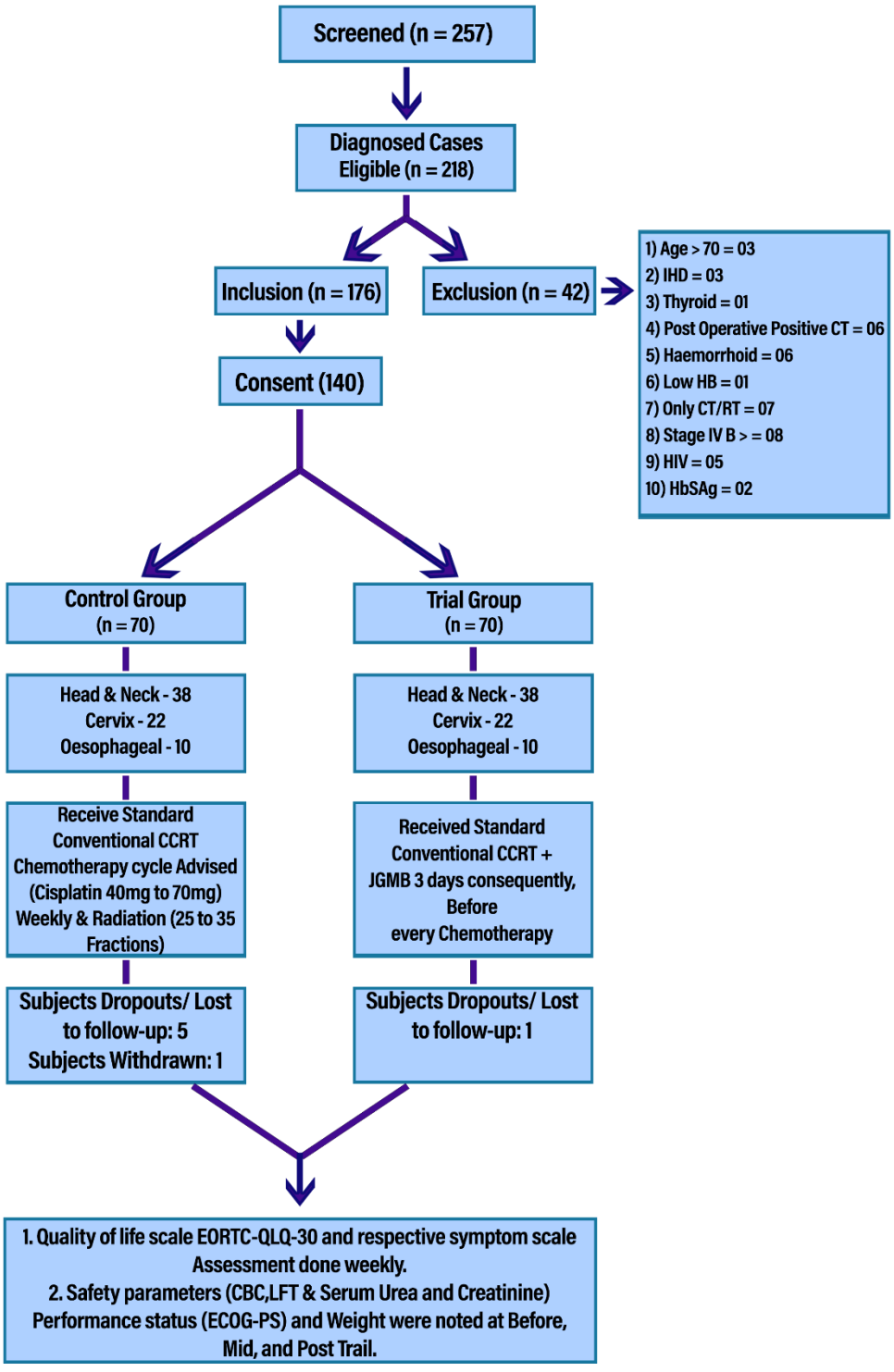


Image no 18. Protein-protein interaction network of *Jeevanthyadi Ghrita* in CCRT Induced cachexia.



6.2 Clinical Study

6.2.1 CONSORT FLOW



6.2.2. Basic Demography and Baseline parameters

Demographic and baseline parameters were analysed by **Independent 't' test** for homogeneity in all the parameters that could confound the outcomes. All the factors like Age, Gender, Diagnosis [Head & Neck, Cervix and Oesophageal cancer], Histopathology, Weight, Advised chemotherapy cycles, Radiation fractions, ECOG-PS, Blood counts, Biochemistry and Quality of life score (EORTC-QLQ-30) and respective symptom score (H&N-43, CX-24, Oes-18) showed 'p value > 0.05' indicating that both **Control group** i.e Concurrent Chemoradiation therapy [CCRT] and **Trial group** i.e Concurrent Chemoradiation Therapy and *Jeevanthyadi ghrita Matrabasti* [CCRT+MB] **were similar** in all aspects [table no 30 & ECOG table no 29]. Only the stage of cancer showed significant difference ($p<0.03^*$) between both the groups. It was observed that only in stage IIB, the subjects were distributed more in CCRT+MB[n=11] than CCRT [n=1] [table no 22].

Table no 19. Distribution of Cancer Subjects based on Diagnosis

Sl No	Cancer Type	CCRT (n=70)	CCRT+MB (n=70)
1	Head & Neck	38	38
2	Cervix	22	22
3	Oesophagus	10	10
	Total	70	70

Table no 20. Gender wise distribution of Cancer Subjects

Sl N	Cancer type	Male	Female	Total
CCRT				
1.	Head & Neck	30	8	38
2.	Cervix	-	22	22
3.	Oesophagus	4	6	10
CCRT+MB				
1.	Head & Neck	36	2	38
2.	Cervix	--	22	22
3.	Oesophagus	4	6	10

Table no 21. Site wise distribution of Head & Neck Cancer subjects

Sl No	Cancer type	CCRT [n=38]	CCRT+MB [n=38]
1.	Tongue	6	5
2.	Larynx/Cricoid	7	6
3.	Buccal Cavity	11	11
4.	Pharynx	12	14
5.	Palate/Mandible/Maxilla	2	2
	Total	38	38

Table no 22. Stage wise Distribution of Diagnosed Cancer Subjects

Sl No	Cancer Stage	CCRT [n=70]		CCRT+MB [n=70]	
		n	%	n	%
1.	II	9	12.9	7	10
2.	IIB	1	1.4	11	15.7
3.	III	35	50.0	26	37.1
4.	IIIB	10	14.3	7	10
5.	IVA	15	21.4	19	27.1
	Total	70	100	70	100

Table no 23. Stage wise Distribution of Head & Neck Cancer Subjects

Sl No	Head & Neck Cancer Stage	CCRT [n=38]		CCRT+MB [n=38]	
		n	%	n	%
1.	II	3	7.9	3	7.9
2.	IIB	0	0.0	1	2.6
3.	III	21	55.3	15	39.5
4.	IIIB	00	0.0	1	2.6
5.	IVA	14	36.8	18	47.4
	Total	38	100	38	100

Table no 24. Stage wise Distribution of Cervical Cancer Subjects

Sl No	Cervical Cancer Stage	CCRT [n=22]		CCRT+MB [n=22]	
		n	%	n	%
1.	II	6	27.3	2	9.1
2.	IIB	1	4.5	10	45.5
3.	III	5	22.7	3	13.6
4.	IIIB	10	45.5	6	27.3
5.	IVA	0	0.0	1	4.5
	Total	22	100	22	100

Table no 25. Stage wise Distribution of Oesophagus Cancer Subjects

Sl No	Oesophagus Cancer Stage	CCRT [n=10]		CCRT+MB [n=10]	
		n	%	n	%
1.	II	0	0	2	20
2.	IIB	0	0	0	0
3.	III	9	90	8	80
4.	IIIB	0	0	0	0
5.	IVA	1	10	0	0
	Total	10	100	10	100

Table no 26. Distribution of Subjects as per Age group.

Sl No	Age in year	CCRT [n=70]		CCRT+MB [n=70]	
		n	%	n	%
1.	30-40	9	12.8	9	12.8
2.	41-50	16	22.8	15	21.5
3.	51-60	25	25.8	35	50.0
4.	61-70	20	28.6	11	15.7
Total		70	100	70	100

Table no 27. Chemotherapy Cycles advised at Baseline in CCRT and CCRT+MB

Sl No	Chemotherapy cycles Advised [Cisplatin 40mg to 70mg Weekly]	CCRT		CCRT+MB	
		n	**%**	**n**	**%**
1.	4 Cycles	0	0	2	2.9
2.	5 Cycles	35	50	47	67.1
3.	6 Cycles	35	50	21	30.0
Total		70	100	70	100

Table no 28. Radiation Dose and Fractions advised at start of CCRT

Sl No	Radiation Dose (Gy)and Fractions (#) Advised	CCRT		CCRT+MB	
		n	**%**	**n**	**%**
1.	45Gy / 25#	11	15.7	8	11.4
2.	50.4Gy / 28#	14	20.0	16	22.9
3.	60Gy / 30#	17	24.3	21	30.0
4.	70Gy / 33#	26	37.1	25	35.7
5.	70Gy / 35#	2	2.9	0	0.0
Total		70	100	70	100

Table No 29. Distribution of Performance status (ECOG-PS scale) of subjects at Baseline

ECOG score	CCRT (n=70)		CCRT+MB (n=70)		p value
	n	%	n	%	
0	29	41.4	21	30	0.365
1	38	54.3	45	64.3	
2	3	4.3	4	5.70	
*p<0.05, Pearson chi square test. There was no difference in Physical Performance status (ECOG-PS) in CCRT and CCRT+MB group.					

Table no 30. Pearson Chi Square Test of different factors at Baseline for Homogeneity

Sl no	Parameters	CCRT	CCRT + MB	p Value
1.	Age in years (Mean ± SD)	54 ± 10	52 ± 9	0.732
2.	Gender	Male - 34 Female - 36	Male - 40 Female - 30	0.310
3.	Head & Neck cancer subjects (H&N)	38	38	0.734
4.	Cervix cancer subjects (Cx)	22	22	0.229
5.	Esophagus cancer subjects (Oes)	10	10	0.606
6.	Histopathology of cell	PDSCC-2 MDSCC-38 WDSCC-29 ASCC -1	PDSCC-1 MDSCC-38 WDSCC-29 ASCC -2	0.881
7.	Stagewise	II-9 IIB-1 III-35 IIIB-10 IVA-15	II-7 IIB-11 III-26 IIIB-7 IVA-19	0.030*
8.	Weight (kilograms)(Mean ± SD)	51.54 ±11.05	50.75 ± 10.49	0.716
9.	Chemotherapy cycles advised (Weekly Inj Cisplatin 40mg/m^2)	4 cycle - 00 5 cycle - 35 6 cycle - 35	4 cycle - 02 5 cycle - 47 6 cycle - 21	0.570
10.	Radiation Fractions (#) advised (H&N: 33-35, Cx: 25-28, Oes: 28-30)	25#- 11 28#- 14 30#- 17 33#- 26 35#- 02	25# - 08 28# - 16 30# - 21 33# - 25 35# - 00	0.930
*p<0.05, PDSCC-Poorly Differentiated Squamous cell carcinoma, MDSCC-Moderately Differentiated Squamous cell carcinoma, WDSCC- Well Differentiated Squamous cell carcinoma, ASCC- Adenosquamous cell carcinoma.				

Table no 31. Baseline Complete Blood Count, Liver Function Test, Serum Creatinine and Serum Urea.

Sl No	Haematology & Biochemistry	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	p Value
1.	Hb	12.15 ± 1.8	12.02 ±1.7	0.32
2.	WBC	7769.14 ± 2756.1	7823.29 ± 2157.7	0.08
3.	RBC	4.21 ± 0.5	4.27 ± 0.7	0.05
4.	Platelet	2.89 ± 0.9	2.79 ± 0.8	0.42
5.	Neutrophil	63.87 ± 9.6	65.52 ± 9.9	0.86
6.	Lymphocyte	29.59 ± 8.7	28.30 ± 8.9	0.97
7.	Monocytes	6.41 ± 3.8	6.59 ± 8.4	0.79
8.	Basophil	0.39 ± 0.3	0.38 ± 0.1	0.52
9.	Urea	24.97 ± 7.2	24.01 ± 6.1	0.53
10.	Creatinine	0.96 ± 0.2	0.95 ± 0.2	0.68
11.	Total Bilirubin	0.77 ± 0.1	0.81 ± 0.2	0.83
12.	Direct Bilirubin	0.32 ± 0.1	0.33 ± 0.1	0.73
13.	T. Protein	7.06 ± 0.5	7.07 ± 0.4	0.17
14.	Albumin	3.81 ± 0.5	3.95 ± 0.7	0.57
15.	SGOT /AST	28.17 ± 8.6	28.63 ± 8.1	0.62
16.	SGPT /ALT	25.14 ± 7.1	27.06 ± 7.7	0.99
17.	Alkaline Phosphatase	153.89 ± 57.8	160.73 ± 49.4	0.27

*$p<0.05$, Pearson chi square test showed that there was no significant difference observed in Complete Blood count, LFT, Serum Urea and Creatinine between CCRT and CCRT+MB group at baseline indicating similar status between groups.

Table no 32. Baseline Quality of life score of All subjects (EORTC QLQ-30)

Sl No	Quality of Life EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	p Value
1	Global Health function	88.53 ± 9.8	87.14 ± 12.5	0.11
2	Physical Function	93.62 ± 8.9	93.71 ± 7.7	0.84
3	Role function	91.55 ± 12.3	90.48 ± 14.3	0.05
4	Emotional function	83.94 ± 11.7	82.14 ± 11.1	0.48
5	Cognitive function	97.83 ± 5.6	96.43 ± 6.89	0.10
6	Social function	80.68 ± 12.9	80.24 ±11.8	0.38
7	Fatigue score	16.91± 15.6	16.19 ± 14.4	0.50
8	Nausea & Vomiting	4.11 ± 8.7	4.05 ±10.1	0.84
9	Pain score	18.36 ± 15.4	20.00 ±14.6	0.97
10	Dyspnoea	4.35 ± 12.6	7.14 ± 14.9	0.02*
11	Insomnia	17.39 ± 21.0	18.10 ± 25.1	0.28
12	Appetite	9.18 ± 16.0	8.57 ± 15.7	0.75
13	Constipation	5.80 ± 15.0	8.57 ± 18.5	0.07
14	Diarrhoea	0.00 ± 00	0.00 ± 0.0	--
15	Financial difficulty	24.15 ± 17.0	23.81 ± 16.1	0.83

*$p<0.05$, Pearson chi square test showed that there was no significant difference observed in functional domains and symptoms scores between CCRT and CCRT+MB group except for Dyspnoea complaint. However, the number of subjects experiencing Dyspnoea complaints were low.

Note: EORTC-QLQ-30 tool has First six domains for functional assessment where higher score represents a "**better**" level of functioning and next nine domains are **Symptoms** that can be experienced due to therapy during treatment, where higher the score represents a "**worse**" level of symptoms/problem.

Table no 33. Baseline Symptom scores of Head & Neck Cancer Subjects (EORTC-H&N-43)

Sl No	H&N Supplement Score (HN43)	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	p Value
1.	Pain in the mouth	12.50 ± 7.6	12.28 ± 7.6	0.873
2.	Swallowing	13.38 ± 8.9	12.06 ± 9.0	0.843
3.	Problem with teeth	7.60 ± 8.2	7.02 ± 6.5	0.292
4.	Dry mouth and sticky saliva	1.75 ± 6.4	1.32 ± 4.5	0.464
5.	Problem with senses	0.88 ± 3.7	0.44 ± 2.7	0.244
6.	Speech	5.44 ± 8.4	2.98 ± 9.2	0.468
7.	Body Image	3.51 ± 9.7	3.51 ± 10.3	0.919
8.	Social Eating	9.21 ± 8.4	6.80 ± 9.2	0.609
9.	Shoulder Problem	2.63 ± 8.2	1.75 ± 6.4	0.301
10.	Skin Problems	0.00 ± 0.0	0.00 ± 0.0	--
11.	Fear of Progression	2.19 ± 5.7	3.51 ± 8.8	0.097
12.	Problem Opening Mouth	4.39 ± 11.4	2.63 ± 9.1	0.138
13.	Cough	5.26 ± 12.3	3.51 ± 12.9	0.293
14.	Social Contact	2.63 ± 11.9	0.88 ± 5.4	0.096
15.	Swelling in Neck	0.88 ± 5.4	0.00 ± 0.0	0.043*
16.	Weight loss	0.88 ± 5.4	1.75 ± 7.5	0.244
17.	Wound Healing Problem	0.88 ± 5.4	3.51 ± 16.9	0.067
18.	Peripheral Neuropathy	1.75 ± 7.5	1.75 ± 7.5	1.000

*$p<0.05$, Pearson chi square test showed that there was no significant difference observed among Head & neck symptoms between CCRT and CCRT+MB group except for swelling in neck complaint. However, the number of subjects experiencing this complaint were low.

Table no 34. Baseline Symptom scores of Cervical Cancer subjects (EORTC-CX-24).

Sl No	Cervix Supplement score (CX-24)	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	p Value
1.	Symptom Score	10.10 ± 7.4	14.60 ± 4.8	0.02*
2.	Body Image Score	4.76 ± 9.0	3.54 ± 9.3	0.721
3.	Lymphoedema	0.00 ± 0.0	0.00 ± 0.0	--
4.	Peripheral Neuropathy	3.17 ± 10.0	9.09 ± 15.1	0.002*
5.	Menopausal symptoms	7.94 ± 14.55	18.18 ± 16.99	0.011*
*p<0.05, Pearson chi square test showed that there was significant difference observed among cervical cancer symptoms between CCRT and CCRT+MB group except in body image score, indicating some degree of difference in complaints.				

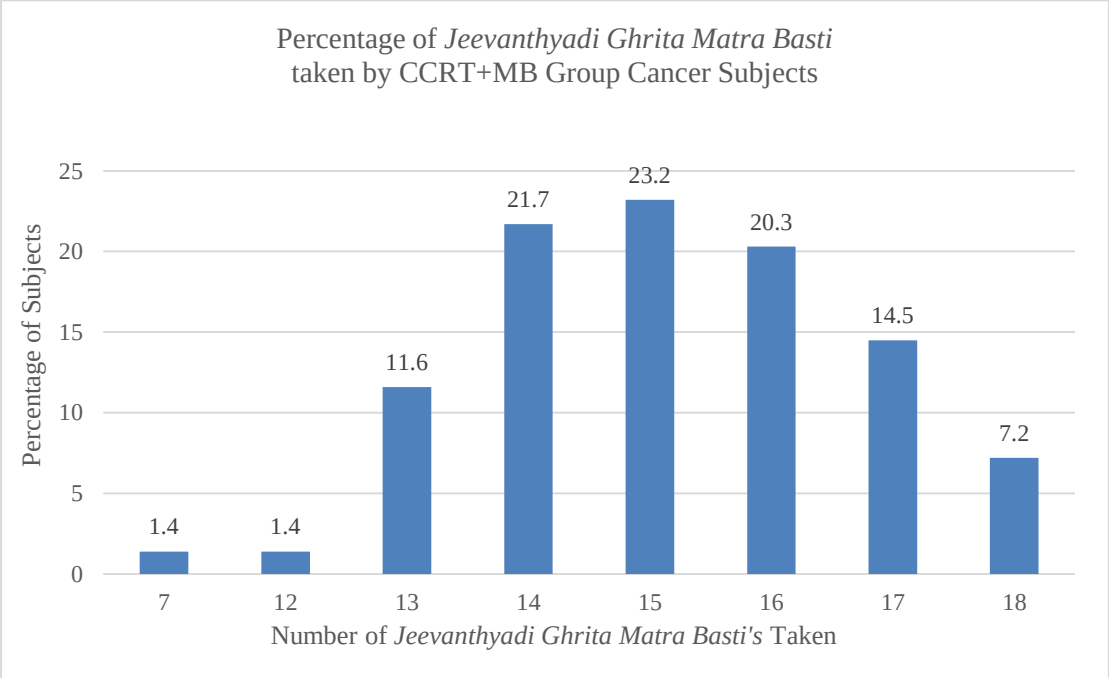
Table no 35. Baseline Symptom scores of Oesophagus Cancer Subjects (EORTC-OES-18)

Sl No	Oesophagus Supplement Score (Oes-18)	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	p Value
1.	Dysphagia	34.44 ± 19.9	31.11 ±16.4	0.414
2.	Eating	30.00 ± 11.2	32.50 ±15.9	0.652
3.	Pain	28.89 ± 10.7	30.00 ± 17.4	0.566
4.	Reflux	21.67 ± 15.8	18.33 ±21.4	0.726
5.	Trouble Swallowing	33.33 ± 22.2	50.00 ±32.3	0.090
6.	Choked when swallowing	46.67 ± 17.2	46.67 ±17.2	1.000
7.	Dry mouth	6.67 ± 14.0	0.00 ±0.0	0.001*
8.	Trouble with Taste	3.33 ± 10.5	6.67 ±14.0	0.232
9.	Trouble with cough	3.33 ± 10.5	10.00 ±22.5	0.081
10.	Trouble Talking	3.33 ± 10.5	3.33 ± 10.5	1.000
*p<0.05, Pearson chi square test showed that there was no significant difference observed among oesophageal cancer symptoms between CCRT and CCRT+MB group except for Dry mouth (p<0.001) which was present in CCRT group.				

Table no 36. Number & Percentage of *Jeevanthyadi Ghrita Matra Basti's* received by CCRT+MB Group Cancer subjects.

Sl No	Number of Jeevanthyadi Ghrita Matra Basti's Taken	CCRT+MB	
		n	%
1.	7	1	1.4
2.	12	1	1.4
3.	13	8	11.6
4.	14	15	21.7
5.	15	16	23.2
6.	16	14	20.3
7.	17	10	14.5
8.	18	5	7.2
Total		**70**	**100**

Graph no 1. Number & Percentage of JGMB taken by CCRT+MB subjects



6.2.3. Primary Outcomes: Quality of Life and symptom scores.

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core30 (EORTC-QLQ-C30) and supplements scales of Head & Neck [H&N-43], Cervix [CX-24] and Oesphagus [OES-18] were adopted as a tool for weekly Quality-of-life [QoL] assessment on the day of every Chemotherapy for 5/6 weeks. The collected data was analyzed by Annova and Independent 't' test.

Quality of Life score was compared between Baseline and 5^{th} week in all subjects of both the groups [table no 37] and separately for Head & Neck [table no 38], Cervical [table no 40.] and Oesophageal subjects [table no 42]. Similarly, the cancer specific supplement scales were also assessed between 1^{st} week and 5^{th} week with Head & Neck [H&N-43] [table no 39. and image no 20], Cervix [CX-24] [table no 41 and image no 21] and Oesophagus [OES-28] [table no 42 and image no 22].

Annova test showed significant difference [$p<0.001$] in in functional domains and symptom scores over the time in CCRT group. While there was no significant difference [$p>0.05$] in **Physical, Role, Social, Emotional, Cognitive functions** and Symptoms namely **Dyspnoea, Insomnia, Appetite, Constipation and financial difficulty** in CCRT+ MB group indicating the role of *Jeevanthaydi ghrita* in sustaining quality of life and amelioration of CCRT induced side effects [Table no 37 and Image no 19]

Independent 't' test showed significant difference [$p<0.05$] in scores between CCRT and CCRT+MB groups in Domains like **Physical, Social, Emotional, Cognitive functions and symptoms namely Nausea Vomiting, Pain,**

Dyspnoea, Insomnia, Constipation, Diarrhoea and financial difficulty. There was no significant difference observed on parameters like **Global health function, role function, Fatigue and appetite score** however the mean score values of these parameters were better in CCRT+MB group when compared to CCRT group. [Table no 37]

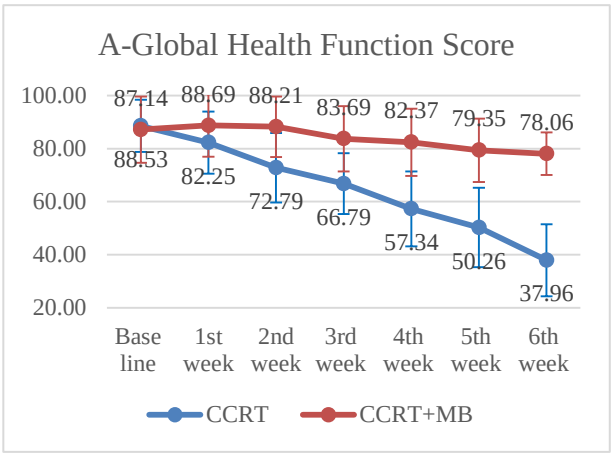
Table no 37. Quality of life (EORTC-QLQ-30) Mean score, Annova and Independent t Test of all subjects at 5th week.

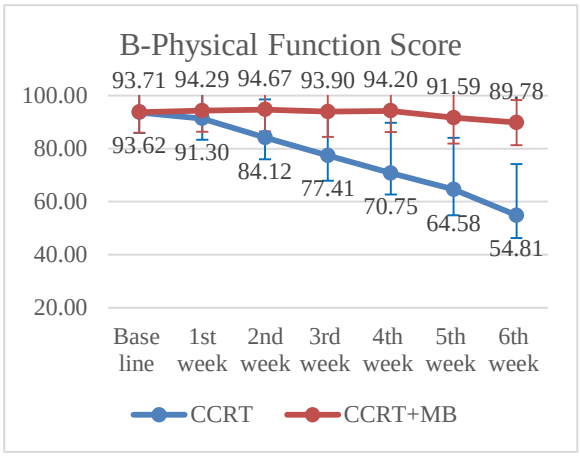
Sl No	EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	Annova		t Test
				CCRT	CCRT+MB	
1	Global Health function	50.26 ± 14.92	79.35 ± 11.92	0.001*	0.001*	0.19
2	Physical Function	64.58 ± 19.44	91.59 ± 9.75	0.001*	0.07	**0.001***
3	Role function	64.06 ± 21.25	89.13 ± 13.95	0.001*	0.6	0.14
4	Emotional function	45.83 ± 21.77	88.29 ± 10.63	0.001*	0.001*	**0.001***
5	Cognitive function	79.95 ± 14.90	96.62 ± 7.33	0.001*	0.88	**0.01***
6	Social function	55.47 ± 18.79	82.13 ± 11.90	0.001*	0.32	**0.001***
7	Fatigue score	65.80 ± 17.63	22.06 ± 16.45	0.001*	0.02*	0.92
8	Nausea & Vomiting	33.07 ± 18.90	10.39 ± 12.16	0.001*	0.01*	**0.045***
9	Pain score	54.95 ± 23.88	18.12 ± 14.78	0.001*	0.001*	**0.001***
10	Dyspnoea	9.90 ± 16.46	2.42 ± 10.41	0.01*	0.09	**0.001***
11	Insomnia	54.17 ± 26.89	10.63 ± 15.65	0.001*	0.13	**0.001***
12	Appetite	53.13 ± 19.44	14.98 ± 20.24	0.001*	0.32	0.64
13	Constipation	42.71 ± 34.87	5.80 ± 12.73	0.001*	0.88	**0.001***
14	Diarrhoea	19.27 ± 30.17	6.76 ± 16.74	0.001*	0.001*	**0.001***
15	Financial difficulty	47.40 ± 20.41	21.26 ± 17.12	0.001*	0.96	**0.045***

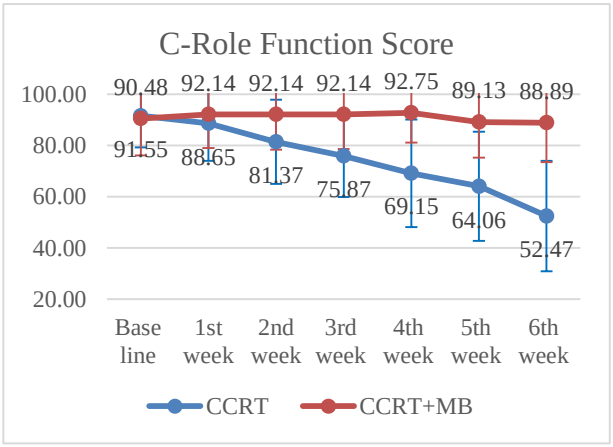
*$p < 0.05$.

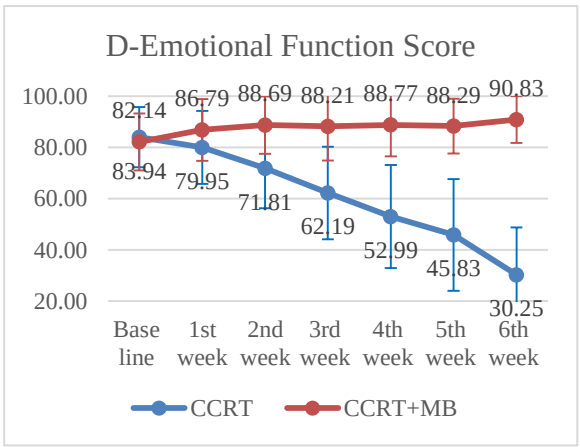
Following are the graphical representation of Weekly Quality-of-life score (QLQ-30) expressed as Mean±SD. **Graph no 2**.A- Global Health Function, B-Physical function, C-Role function, D-Emotional Function, E-Cognitive Function, F-Social Function, G-Fatigue score, H- Nausea & Vomiting, I-Pain score , J-Dyspnoea, K-Insomnia, L-Appetite, M-Constipation, N-Diarrhoea, O-Financial Difficulty.

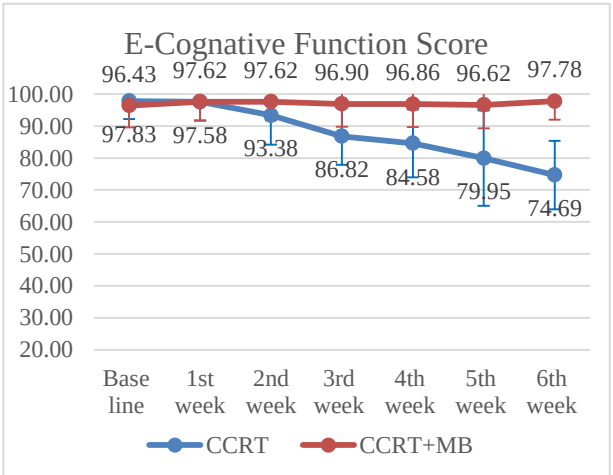
Graph no 2. Weekly Quality-of-life score of All cancer subjects

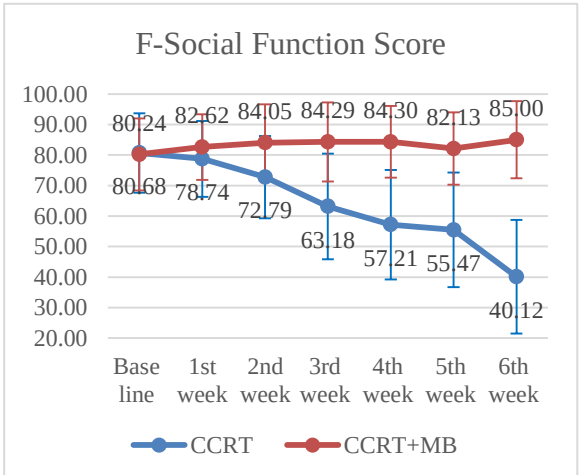


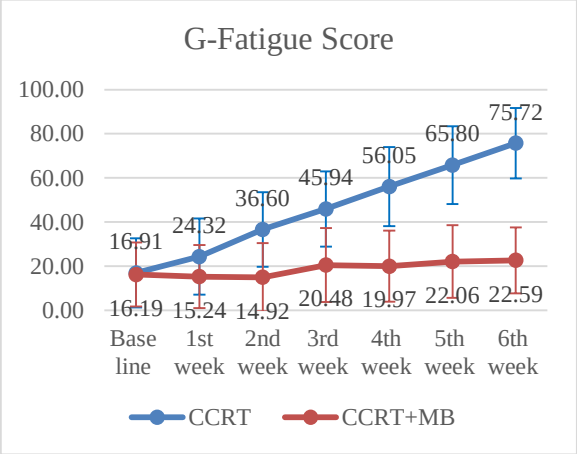


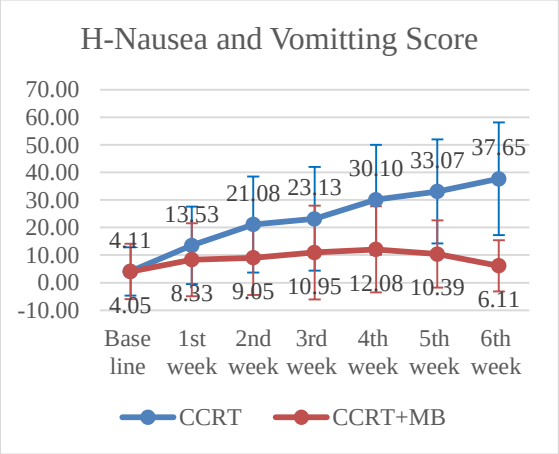


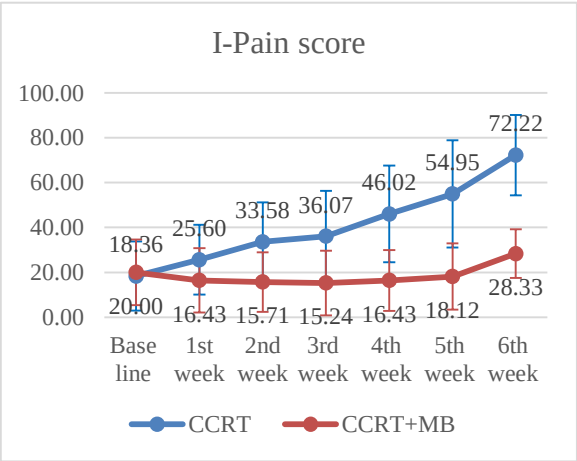


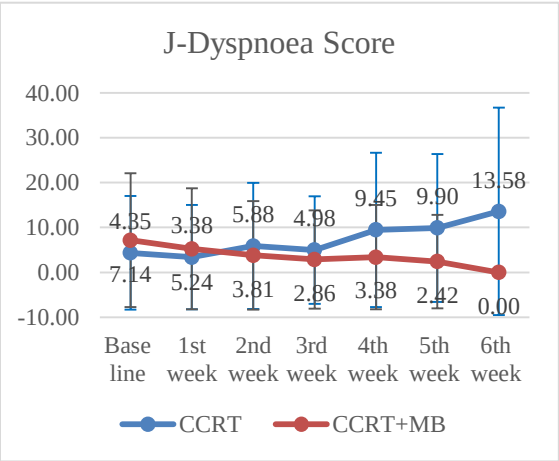


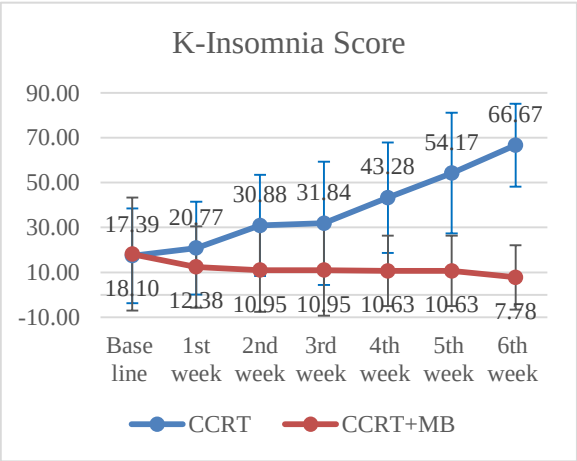



G-Fatigue Score
100.00
80.00
60.00
40.00
20.00
0.00
16.91
24.32
36.60
45.94
56.05
65.80
75.72
16.19
15.24
14.92
20.48
19.97
22.06
22.59
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


H-Nausea and Vomitting Score
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
-10.00
4.11
13.53
21.08
23.13
30.10
33.07
37.65
4.05
8.33
9.05
10.95
12.08
10.39
6.11
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


I-Pain score
100.00
80.00
60.00
40.00
20.00
0.00
18.36
25.60
33.58
36.07
46.02
54.95
72.22
20.00
16.43
15.71
15.24
16.43
18.12
28.33
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


J-Dyspnoea Score
40.00
30.00
20.00
10.00
0.00
-10.00
4.35
3.38
5.88
4.98
9.45
9.90
13.58
7.14
5.24
3.81
2.86
3.38
2.42
0.00
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


K-Insomnia Score
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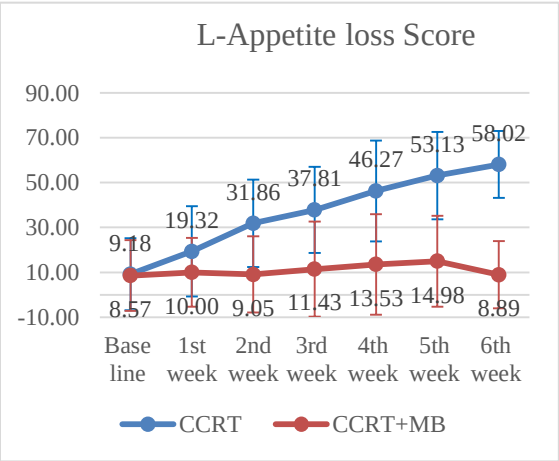
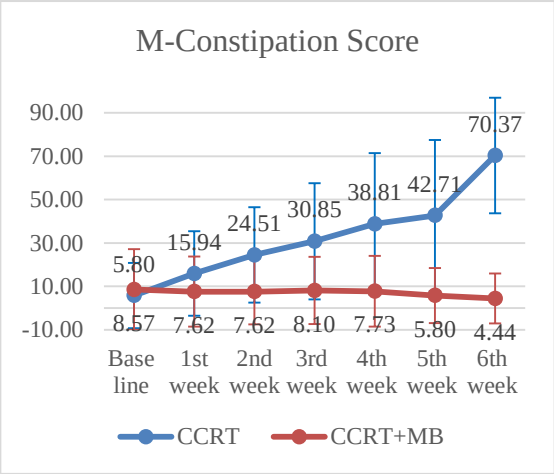
70.00
50.00
30.00
10.00
-10.00
17.39
20.77
30.88
31.84
43.28
54.17
66.67
18.10
12.38
10.95
10.95
10.63
10.63
7.78
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


L-Appetite loss Score
90.00
70.00
50.00
30.00
10.00
-10.00
9.18
19.32
31.86
37.81
46.27
53.13
58.02
8.57
10.00
9.05
11.43
13.53
14.98
8.89
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


M-Constipation Score
90.00
70.00
50.00
30.00
10.00
-10.00
5.80
15.94
24.51
30.85
38.81
42.71
70.37
8.57
7.62
7.62
8.10
7.73
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Base line
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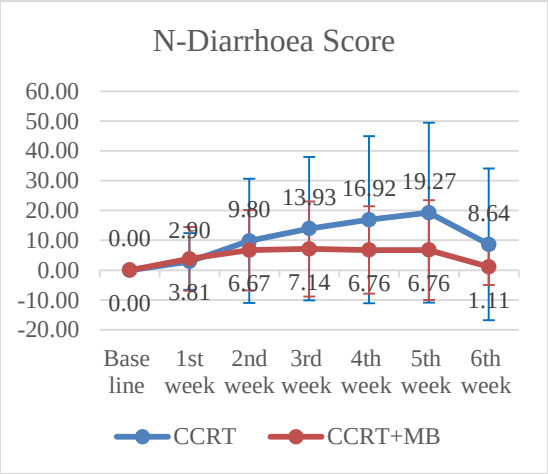
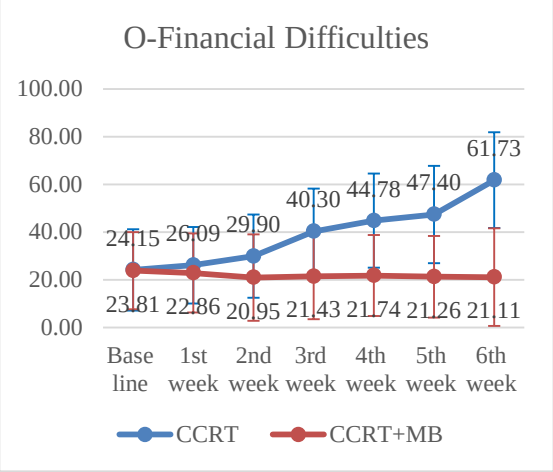
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


N-Diarrhoea Score
60.00
50.00
40.00
30.00
20.00
10.00
0.00
-10.00
-20.00
0.00
2.80
9.80
13.93
16.92
19.27
8.64
0.00
3.81
6.67
7.14
6.76
6.76
1.11
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


O-Financial Difficulties
100.00
80.00
60.00
40.00
20.00
0.00
24.15
26.09
29.90
40.30
44.78
47.40
61.73
23.81
22.86
20.95
21.43
21.74
21.26
21.11
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

Head and Neck Cancer Subjects

Quality of Life of Head and Neck cancer subjects

Annova test showed significant difference [p<0.001] in in functional domains and symptom scores in CCRT group subjects. While in CCRT+MB group there was **no significant difference** [p>0.05] in scores of **Physical, Role, Social, Cognitive functions** and Symptoms namely**, Fatigue, Nausea & Vomiting, Pain, Dyspnoea, Insomnia, Appetite, Constipation, Diarrhoea and financial difficulty** group indicating the role of *Jeevanthaydi ghrita* in sustaining quality of life and amelioration of CCRT induced side effects in Head and Neck cancer subjects.

Independent 't' test showed significant difference [p<0.05] in scores between CCRT and CCRT+MB groups in Domains like **Physical, Emotional, Cognitive functions and symptoms namely Dyspnoea and Appetite** indicating effect of *Jeevanthaydi ghrita* in these parameters**.** There was no significant difference observed in rest of the parameters however the mean score values of these parameters were better in CCRT+MB group when compared to CCRT group. [table no 38]

Symptom score of Head and Neck Cancer [H&N43].

Annova test showed significant difference [p<0.001] in scores over the time in all the symptoms of CCRT group subjects and in majority of symptoms in CCRT+MB group. While there was **no significant difference** [p>0.05] in score of symptoms namely **shoulder pain, social contact, swelling in neck, weight loss, wound healing problem and peripheral neuropathy** indicating the role of *Jeevanthaydi ghrita* in sustaining quality of life and amelioration of CCRT induced

side effects in Head and Neck cancer subjects. However, the mean score values of Pain, swallowing, tooth problem, Dry mouth, sticky saliva, problem with senses, speech, body image and social eating, cough and opening of mouth in CCRT+MB group were on lower side in comparison with CCRT group. [table no 39. and Images no 20]

Independent 't' test showed significant difference [$p<0.001$] in scores between CCRT and CCRT+MB groups in majority of symptoms. However, there was no significant difference observed in swallowing, Dry mouth, sticky saliva, Pain opening mouth and cough. Followingly are the graphs of weekly scores of symptoms and percentage of subjects that experienced them in CCRT and CCRT+MB group [**Graph no 3.**A Pain in the mouth, B-Swallowing, C-Problem with teeth, D- Dry mouth & sticky saliva, E-Problem with senses, F-Speech, G-Body Image, H-Social Eating, I- Shoulder Problem, J- Skin Problems, K- Fear of Progression, L- Problem with opening mouth, M- Cough, N- Social Contact, O- Swelling in Neck, P- Weight loss, Q- Wound Healing Problem, R- Peripheral Neuropathy.]

Table no 38. Quality of life (EORTC-QLQ-30) Mean score, Annova and Independent t Test of Head and Neck subjects at 5th week.

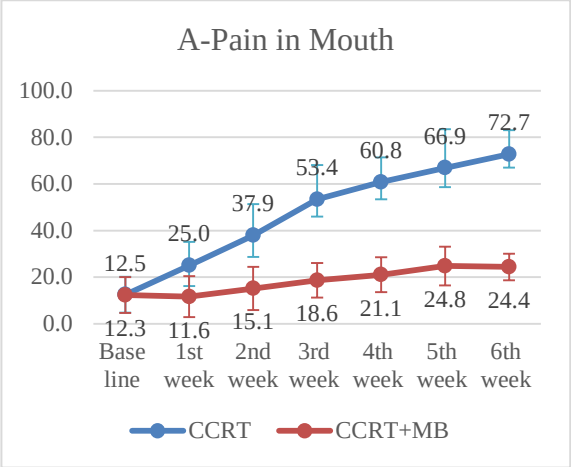
Sl No	EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	Annova		t Test
				CCRT	CCRT+MB	
1	Global Health function	44.21 ±12.57	79.17 ± 9.24	0.001*	0.001*	0.101
2	Physical Function	60.37 ± 18.72	93.51 ± 7.98	0.001*	0.15	**0.001***
3	Role function	58.33 ± 20.12	89.47 ± 15.22	0.001*	0.84	0.293
4	Emotional function	38.43 ± 17.40	89.69 ± 9.96	0.001*	0.04*	**0.022***
5	Cognitive function	77.31 ± 10.66	96.05 ± 8.16	0.001*	0.3	**0.015***
6	Social function	50.46 ± 17.13	83.33 ± 13.97	0.001*	0.44	0.590
7	Fatigue	70.37 ± 15.49	17.54 ± 14.76	0.001*	0.48	0.705
8	Nausea & Vomiting	30.56 ± 15.17	7.89 ± 8.43	0.001*	0.07	0.119
9	Pain score	66.20 ± 20.11	21.93 ± 12.91	0.001*	0.25	0.096
10	Dyspnoea	11.11 ± 17.82	0.88 ± 5.41	0.02*	0.02*	**0.000***
11	Insomnia	62.96 ± 26.16	9.65 ± 15.32	0.001*	0.1	0.131
12	Appetite	51.85 ± 20.23	9.65 ± 15.32	0.001*	0.94	**0.008***
13	Constipation	69.44 ± 14.64	6.14 ± 13.10	0.001*	0.5	0.519
14	Diarrhoea	0.00 ± 0.00	0.00 ± 0.00	0.39	0.46	---
15	Financial difficulty	50.93 ± 20.29	18.42 ± 18.50	0.001*	0.92	0.516
*$p < 0.05$.						

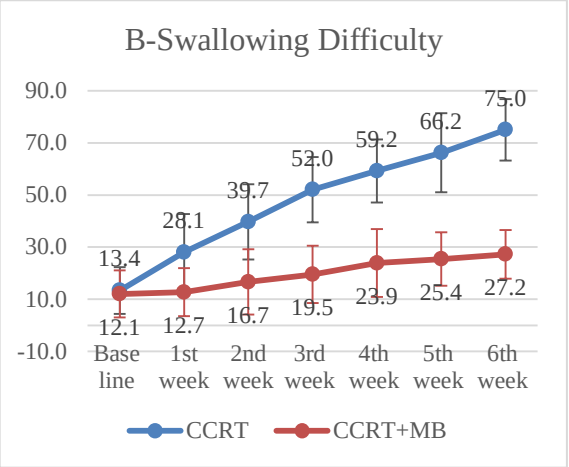
Table no 39. Comparison of Post trail (5th week) Head and Neck symptom score (H&N-43)

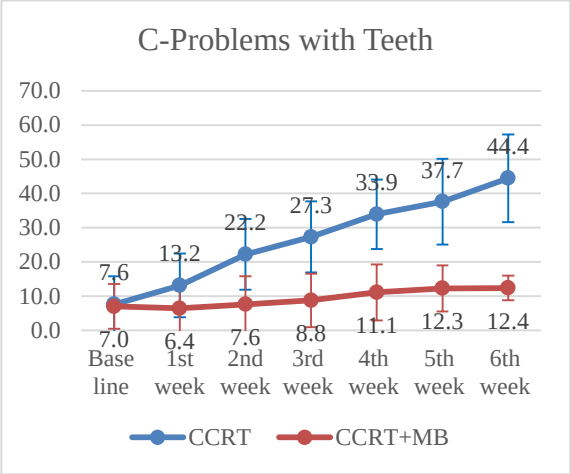
Sl No	EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	Annova		t Test
				CCRT	CCRT+MB	
1.	Pain in the mouth	66.90 ± 16.61	24.78 ± 8.33	0.001*	0.001*	**0.030***
2.	Swallowing	66.20 ± 15.16	25.44 ± 10.24	0.001*	0.001*	0.142
3.	Problem with teeth	37.65 ± 12.54	12.28 ± 6.73	0.001*	0.001*	**0.001***
4.	Dry mouth & sticky saliva	82.87 ± 15.68	35.53 ± 11.08	0.001*	0.001*	0.402
5.	Problem with senses	45.37 ± 13.58	16.67 ± 8.66	0.001*	0.001*	**0.001***
6.	Speech	54.26 ± 18.73	9.30 ± 10.91	0.001*	0.01*	**0.005***
7.	Body Image	54.63 ± 17.08	6.73 ± 7.09	0.001*	0.01*	**0.001***
8.	Social Eating	60.19 ± 14.92	17.32 ± 10.14	0.001*	0.001*	**0.005***
9.	Shoulder Problem	25.46 ± 18.47	2.63 ± 6.16	0.001*	0.27	**0.001***
10.	Skin Problems	50.00 ± 18.31	14.33 ± 8.13	0.001*	0.001*	**0.002***
11.	Fear of Progression	48.61 ± 19.67	8.77 ± 11.45	0.001*	0.001*	**0.043***
12.	POM	60.19 ± 15.57	7.02 ± 13.77	0.001*	0.001*	0.681
13.	Cough	50.00 ± 27.02	16.67 ± 21.57	0.001*	0.001*	0.150
14.	Social Contact	55.56 ± 26.43	3.51 ± 10.37	0.001*	0.78	**0.001***
15.	Swelling in Neck	1.85 ± 7.74	0.00 ± 0.00	0.78	0.46	**0.002***
16.	Weight loss	43.52 ± 22.28	1.75 ± 7.54	0.001*	0.2	**0.001***
17.	WHP	15.74 ± 20.29	1.75 ± 7.54	0.001*	0.67	**0.001***
18.	Peripheral Neuropathy	39.81 ± 23.66	2.63 ± 9.11	0.001*	0.47	**0.001***

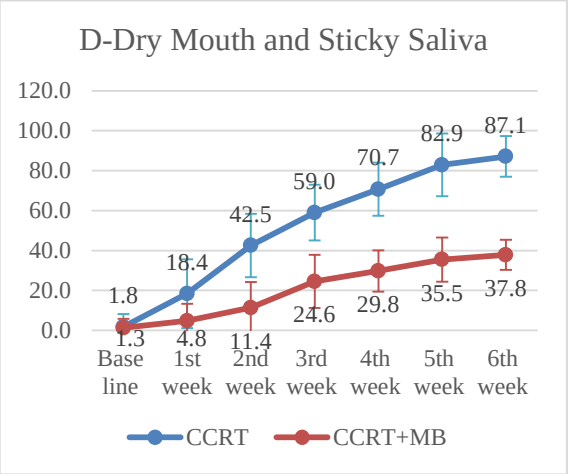
*p < 0.05. POM- Problem opening mouth, WHP- Wound Healing problem.

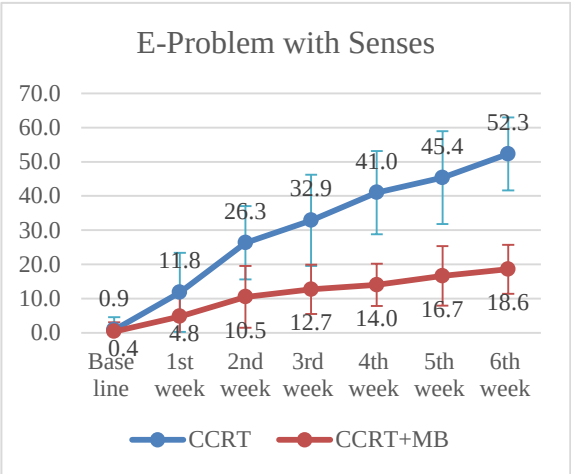
Graph No 3. Weekly symptoms score (%) in Head and Neck Subjects

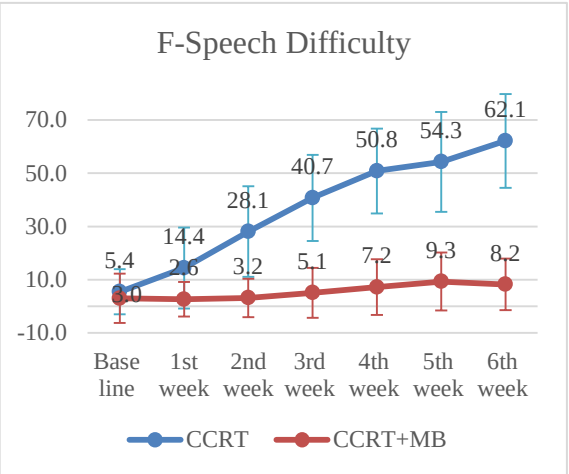


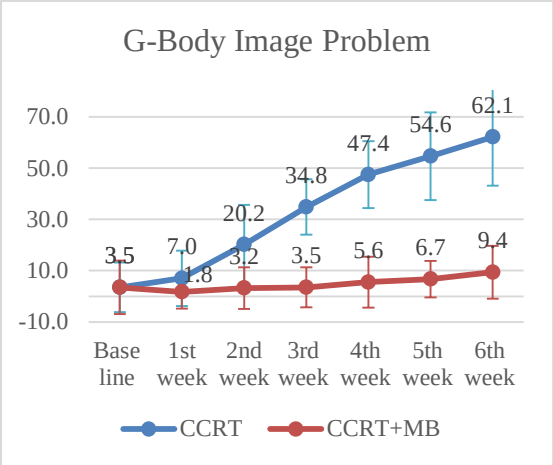


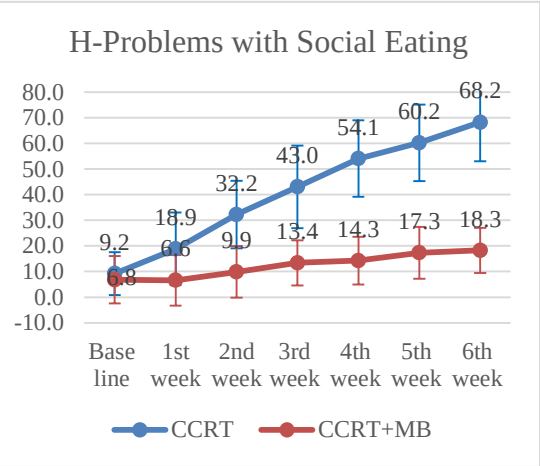


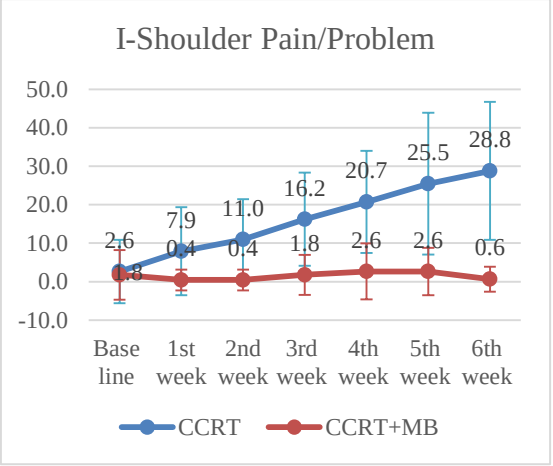


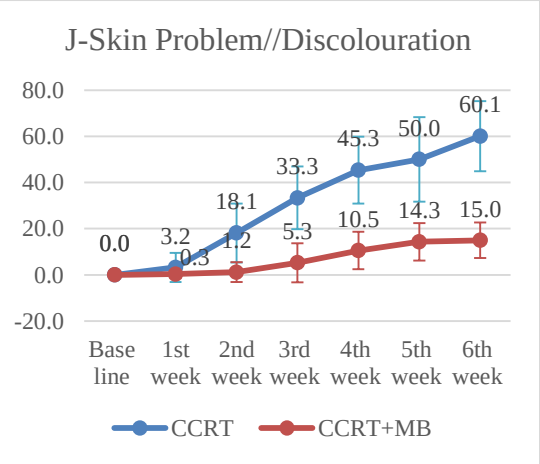


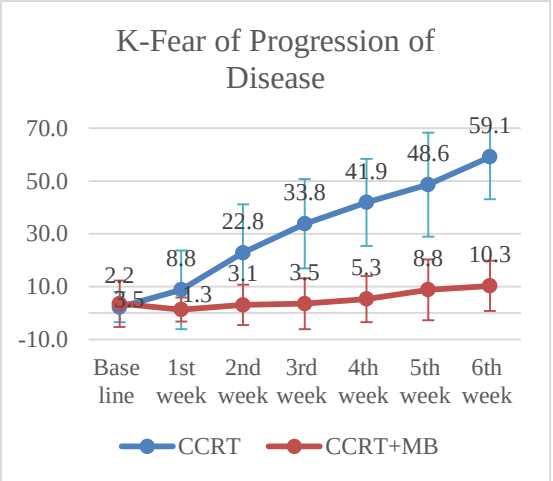


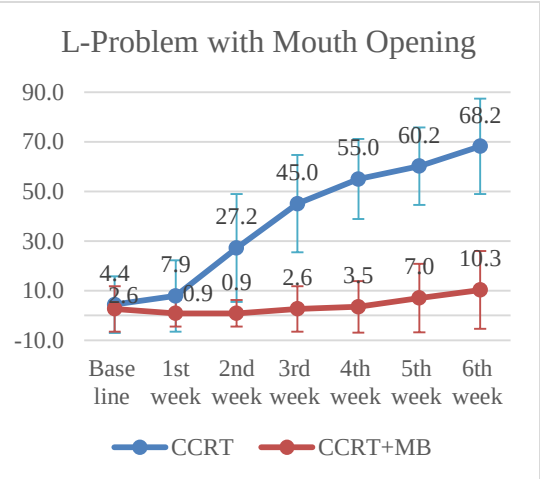

G-Body Image Problem
70.0
50.0
30.0
10.0
-10.0
3.5
7.0
20.2
34.8
47.4
54.6
62.1
1.8
3.2
3.5
5.6
6.7
9.4
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

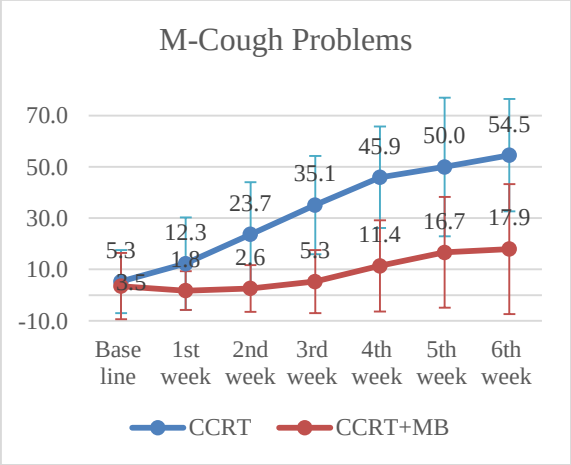

H-Problems with Social Eating
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
9.2
18.9
32.2
43.0
54.1
60.2
68.2
6.8
6.6
9.9
13.4
14.3
17.3
18.3
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

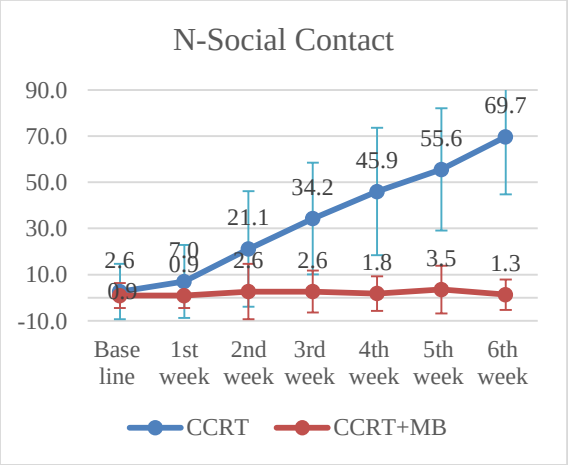

I-Shoulder Pain/Problem
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
2.6
7.9
11.0
16.2
20.7
25.5
28.8
0.4
0.4
1.8
2.6
2.6
0.6
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

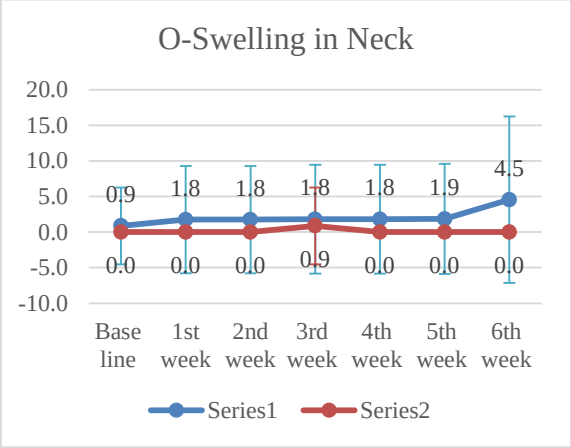

J-Skin Problem//Discolouration
80.0
60.0
40.0
20.0
0.0
-20.0
0.0
3.2
18.1
33.3
45.3
50.0
60.1
0.3
1.2
5.3
10.5
14.3
15.0
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

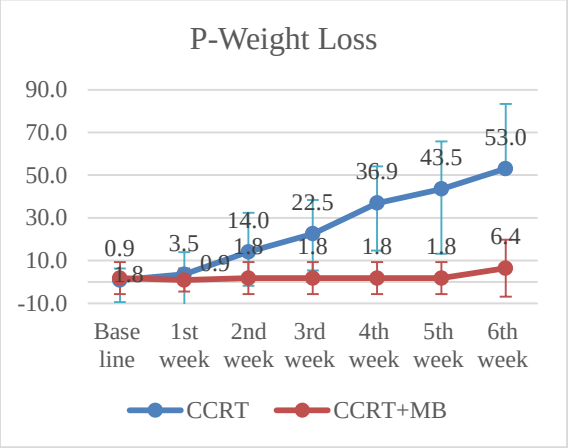

K-Fear of Progression of Disease
70.0
50.0
30.0
10.0
-10.0
2.2
8.8
22.8
33.8
41.9
48.6
59.1
1.3
3.1
3.5
5.3
8.8
10.3
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

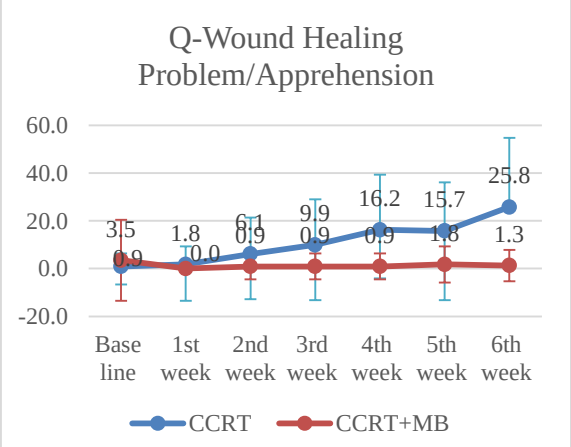

L-Problem with Mouth Opening
90.0
70.0
50.0
30.0
10.0
-10.0
4.4
7.9
27.2
45.0
55.0
60.2
68.2
0.9
2.6
3.5
7.0
10.3
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

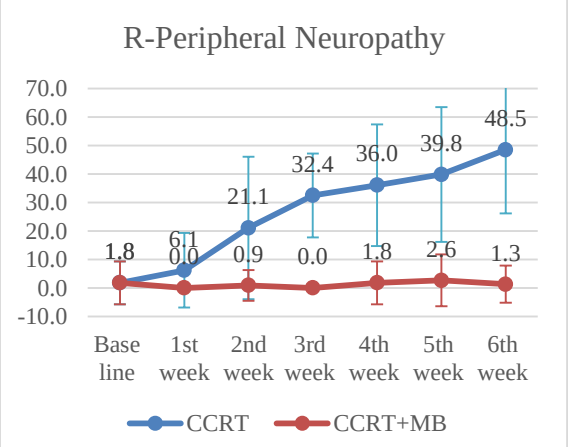

M-Cough Problems
70.0
50.0
30.0
10.0
-10.0
5.3
12.3
23.7
35.1
45.9
50.0
54.5
5.3
1.8
2.6
5.3
11.4
16.7
17.9
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


N-Social Contact
90.0
70.0
50.0
30.0
10.0
-10.0
2.6
7.0
21.1
34.2
45.9
55.6
69.7
0.9
0.9
2.6
2.6
1.8
3.5
1.3
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


O-Swelling in Neck
20.0
15.0
10.0
5.0
0.0
-5.0
-10.0
0.9
1.8
1.8
1.8
1.8
1.9
4.5
0.0
0.0
0.0
0.9
0.0
0.0
0.0
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
Series1
Series2


P-Weight Loss
90.0
70.0
50.0
30.0
10.0
-10.0
0.9
3.5
14.0
22.5
36.9
43.5
53.0
1.8
0.9
1.8
1.8
1.8
1.8
6.4
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


Q-Wound Healing Problem/Apprehension
60.0
40.0
20.0
0.0
-20.0
3.5
1.8
6.1
9.9
16.2
15.7
25.8
0.9
0.0
0.9
0.9
0.9
1.8
1.3
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB


R-Peripheral Neuropathy
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
1.8
6.1
21.1
32.4
36.0
39.8
48.5
0.0
0.9
0.0
1.8
2.6
1.3
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRT+MB

CERVICAL CANCER SUBJECTS

Quality of Life of Cervical cancer subjects

Annova test showed significant difference [p<0.001] in scores over the time in all the domain and symptoms in CCRT group subjects. While there was **no significant difference [p>0.05] in CCRT+MB group** in all domains and symptoms, except for Diarrhoea [0.001] group indicating the role of *Jeevanthaydi ghrita* in sustaining quality of life and amelioration of CCRT induced side effects in Cervical cancer subjects. There was significant difference [p<0.001] observed between 5^{th} week symptom score of Pain [9.1] and Constipation [0.0] when compared to baseline pain score [19.7] and constipation [6.1] which is lowered indicating role of *jeevanthyadi ghrita* in these symptoms.

Independent 't' test showed significant difference [p<0.05] in scores between CCRT and CCRT+MB groups in all domains and symptoms except for Fatigue, Appetite and Diarrhoea. However, the mean score values of these parameters were better in CCRT+MB group [Fatigue (22.7), Appetite (18.2) and Diarrhoea (21.2)] in comparison to CCRT group [Fatigue (59.8), Appetite (55.6) and Diarrhoea (55.6)]. [table no 40]

Symptom score of Cervical Cancer [CX-24].

Annova test showed significant difference [p<0.001] in symptom score, body image score over the time in CCRT group and no difference in case of Lymphedema, Peripheral neuropathy and Menopausal symptoms. In CCRT+MB group there was significant difference [p<0.001] in symptom score, Lymphedema, Peripheral neuropathy and Menopausal symptoms scores over the time, expect Body image

score [p>0.88]. The difference observed in CCRT+MB was in positive magnitude as the scores were lower than the baseline values respectively. [Table no 41].

Independent 't' test showed significant difference [p<0.05] in scores between CCRT and CCRT+MB groups in all scale namely symptom score, body image, Peripheral neuropathy and menopausal symptoms. However, the mean score values CCRT+MB group [Symptom score (5.23), Peripheral Neuropathy (0.00), Menopause symptoms (0.00)] when compared to CCRT Group [Symptom score (29.1), Peripheral Neuropathy (12.7), Menopause symptoms (17.46)]. Followingly are the graphs of weekly scores of symptoms and percentage of subjects that experienced them in CCRT and CCRT+MB group [**Graph no 4**. A Symptom score, B- Body image C-Peripheral neuropathy, D- menopausal symptoms]

Table no 40. Quality of life (EORTC-QLQ-30) Mean score, Annova and Independent t Test of Cervical cancer subjects at 5th week.

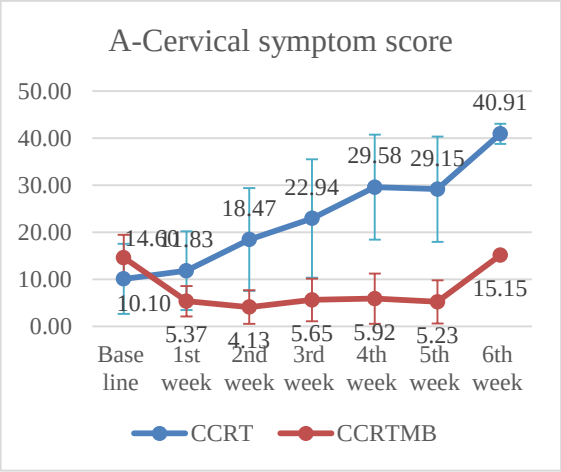
Sl No	EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	Annova CCRT	Annova CCRT+MB	p Value
1	Global Health function	57.94 ± 15.92	84.85 ± 11.68	0.001*	0.72	**0.028***
2	Physical Function	70.16 ± 20.29	93.94 ± 7.67	0.001*	0.88	**0.000***
3	Role function	73.02 ± 22.03	92.42 ± 9.93	0.003*	0.34	**0.014***
4	Emotional function	53.97 ± 26.04	89.39 ± 9.68	0.001*	0.1	**0.000***
5	Cognitive function	83.33 ± 21.73	97.73 ± 5.85	0.001*	0.43	0.084
6	Social function	62.70 ± 20.35	81.82 ± 8.77	0.001*	0.75	**0.000***
7	Fatigue score	59.79 ± 21.22	22.73 ± 15.13	0.001*	0.16	0.069
8	Nausea & Vomiting	38.89 ± 24.34	9.85 ± 9.84	0.001*	0.06	**0.007***
9	Pain score	38.89 ± 22.57	9.09 ± 13.34	0.001*	0.01	**0.022***
10	Dyspnoea	7.94 ± 14.55	0.00 ± 0.00	0.847	0.21	**0.000***
11	Insomnia	41.27 ± 23.34	10.61 ± 15.89	0.003*	0.65	**0.01***
12	Appetite	55.56 ± 19.25	18.18 ± 24.62	0.001*	0.24	0.093
13	Constipation	1.59 ± 7.27	0.00 ± 0.00	0.041*	0.001*	**0.037***
14	Diarrhoea	55.56 ± 26.53	21.21 ± 24.22	0.001*	0.001*	0.788
15	Financial difficulty	42.86 ± 21.46	22.73 ± 15.89	0.004*	0.80	0.166

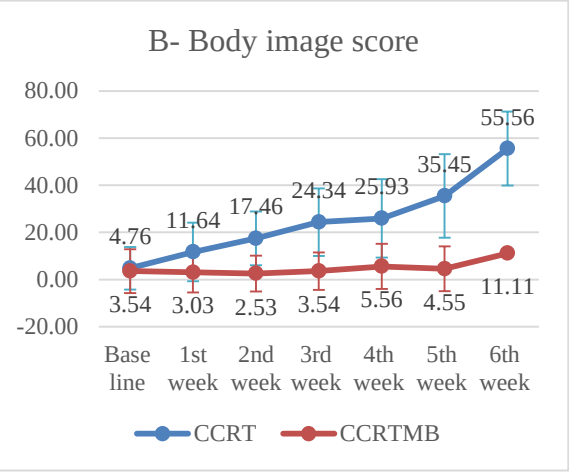
*$p < 0.05$.

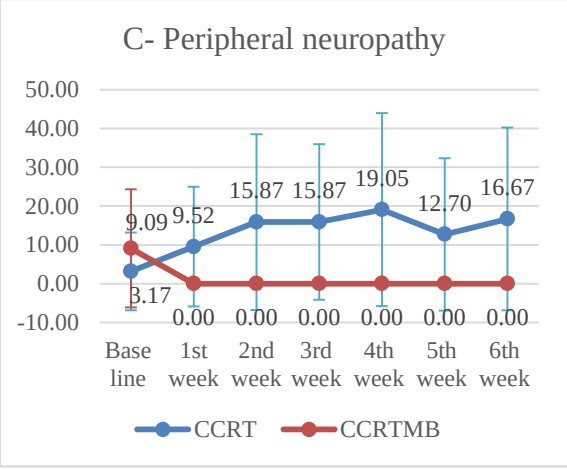
Table no 41. Comparison of Post Trail (5th week) cervical cancer symptom scores (Cx-24)

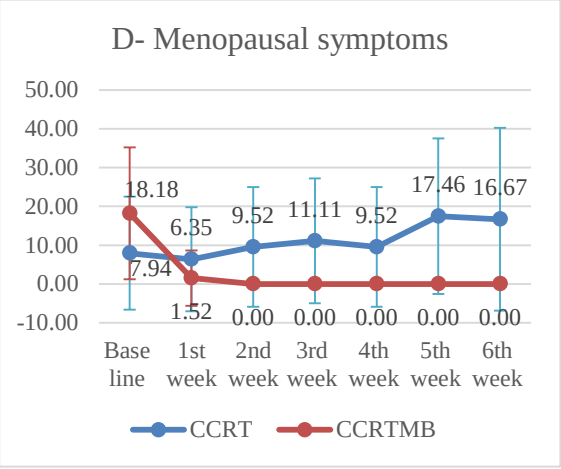
Sl No	EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	Annova CCRT	Annova CCRT+MB	t Test
1.	Symptom Score	29.15 ±11.19	5.23 ± 4.60	0.001*	0.001*	**0.001***
2.	Body Image Score	35.45 ± 17.78	4.55 ± 9.49	0.001*	0.88	**0.033***
3.	Lymphoedema	0.00 ±0.00	0.00 ± 0.00	0.3	--	--
4.	Peripheral Neuropathy	12.70 ±19.65	0.00 ± 0.00	0.18	0.001*	**0.001***
5.	Menopausal Symptoms	17.46 ±20.05	0.00 ± 0.00	0.39	0.001*	**0.001***
. *p < 0.05.						

Graph no 4. Weekly symptoms score (%) in Cervical cancer subjects









OESOPHAGUS CANCER SUBJECTS

Quality of Life of Oesophageal cancer subjects

Annova test showed significant difference [$p<0.05$] in scores over the time in Global health, Emotional, Cognitive, Fatigue, Nausea Vomiting, Pain, Appetite and Financial difficulty in CCRT group subjects. While in CCRT+MB group there was no significant difference [$p>0.05$] in all domain and symptoms except Global Health[$p<0.01$], Physical function [$p<0.04$] and pain score [$p<0.03$] indicating the role of *Jeevanthaydi ghrita* in sustaining quality of life and amelioration of CCRT induced side effects in oesophagus cancer subjects. [Table No 42]

Independent 't' test showed no significant difference [$p>0.05$] in scores between CCRT and CCRT+MB groups in all domains and symptoms except Cognitive function [$p<0.002$] and Diarrhoea symptoms [$p<0.001$]. However, the mean score values of different function and symptoms in CCRT+MB were better in comparison to CCRT Group. [Table No 42]

Symptom score of Oesophageal Cancer Subjects [OES-18].

Annova test showed significant difference [$p<0.01$] in symptom scores over the time expect for swallowing difficulty, Dry mouth and Pain in CCRT group. While in the CCRT+MB group there was no significant difference [$p>0.05$] in symptom scores expect dry mouth [$p>0.01$] and Trouble Talking [$p<0.02$] indicating the role of *Jeevanthaydi ghrita* in amelioration of CCRT induced side effects in oesophagus cancer subjects. [table 43]

Independent ‘t’ test showed no significant difference [p>0.05] in scores between CCRT and CCRT+MB groups in symptoms scales. Followingly are the graphs of weekly scores of symptoms and percentage of subjects that experienced them in CCRT and CCRT+MB group [**Graph no 5**. A- Dysphagia Score, B-Trouble Swallowing Saliva, C- Choked when swallowing, D- Eating Score, E- Dry Mouth, F-Trouble with Taste, G- Trouble with cough, H- Trouble Talking, I- Reflux Score, J-Pain Score].

Table no 42. Quality of life (EORTC-QLQ-30) Mean score, Annova and Independent t Test of oesophageal cancer subjects at 5th week.

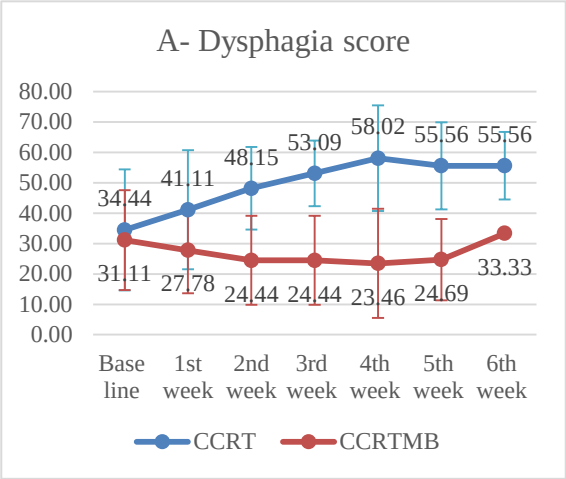
Sl No	EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	Annova CCRT	Annova CCRT+MB	t Test
1	Global Health function	58.33 ± 8.33	66.67 ± 13.82	0.001*	0.01*	0.591
2	Physical Function	69.52 ± 17.58	77.78 ± 10.54	0.13	0.04*	0.249
3	Role function	66.67 ± 16.67	79.63 ± 13.89	0.23	0.09	0.696
4	Emotional function	59.52 ± 13.11	79.63 ± 12.58	0.01*	0.99	0.949
5	Cognitive function	83.33 ± 0.00	96.30 ± 7.35	0.001*	0.22	**0.002***
6	Social function	59.52 ± 16.27	77.78 ± 8.33	0.14	0.97	0.082
7	Fatigue score	60.32 ± 8.74	39.51 ± 15.82	0.001*	0.06	0.222
8	Nausea & Vomiting	28.57 ± 15.85	22.22 ± 22.05	0.01*	0.94	0.674
9	Pain score	45.24 ± 12.60	24.07 ± 16.90	0.02*	0.03*	0.321
10	Dyspnoea	9.52 ± 16.27	14.81 ± 24.22	0.59	0.94	0.254
11	Insomnia	47.62 ± 26.23	14.81 ± 17.57	0.19	0.97	0.195
12	Appetite	52.38 ± 17.82	29.63 ± 20.03	0.001*	0.17	0.577
13	Constipation	28.57 ± 29.99	18.52 ± 17.57	0.35	0.98	0.111
14	Diarrhoea	9.52 ± 16.27	0.00 ± 0.00	0.65	0.55	**0.001***
15	Financial difficulty	42.86 ± 16.27	29.63 ± 11.11	0.03*	0.78	0.102

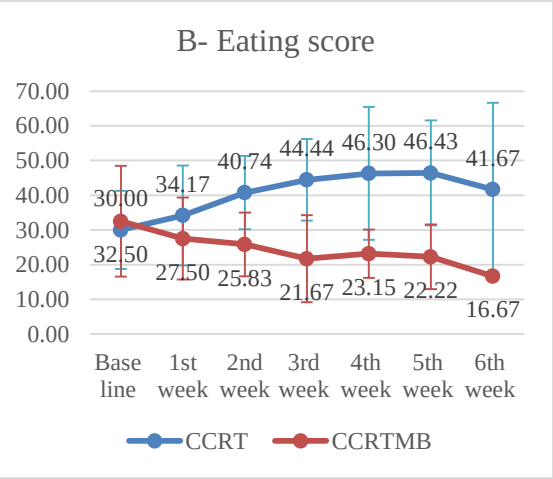
*$p < 0.05$.

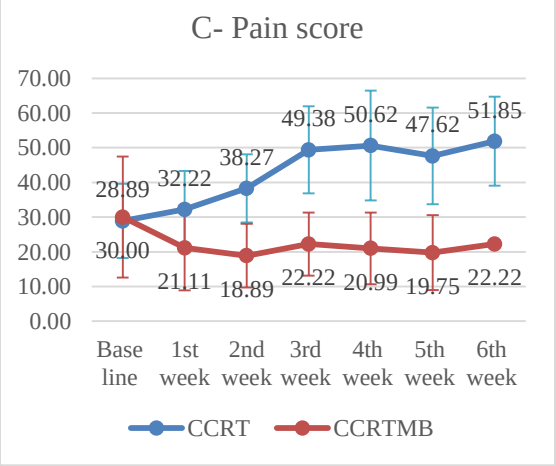
Table no 43. Comparison of Post Trail (5th week) Oesopgaeal cancer symptom scores (Oes-18)

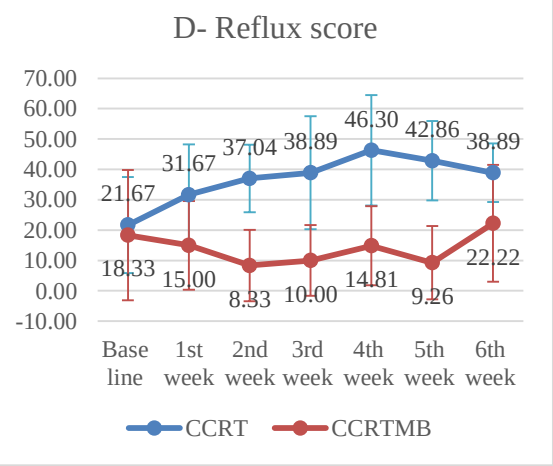
Sl No	EORTC-QLQ-30	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	Annova		t Test
				CCRT	CCRT+MB	
1.	Dysphagia	55.56 ± 14.34	24.69 ± 13.35	0.03*	0.86	0.491
2.	Eating	46.43 ± 15.11	22.22 ± 9.32	0.04*	0.58	0.565
3.	Pain	47.62 ± 13.93	19.75 ± 10.80	0.16	0.63	0.321
4.	Reflux	42.86 ± 13.11	9.26 ± 12.11	0.001*	0.25	0.833
5.	Trouble Swallowing	33.33 ± 19.25	11.11 ± 16.67	0.14	0.24	0.375
6.	Choked when swallowing	42.86 ± 16.27	29.63 ± 11.11	0.001*	0.45	0.102
7.	Dry mouth	61.90 ± 23.00	3.70 ± 11.11	0.26	0.001*	0.120
8.	Trouble with Taste	57.14 ±2 5.20	11.11 ± 16.67	0.69	0.02*	0.239
9.	Trouble with cough	33.33 ± 19.25	22.22 ± 28.87	0.001*	0.52	0.050
10.	Trouble Talking	9.52 ± 16.27	3.70 ± 11.11	0.001*	0.52	0.102
. *p < 0.05.						

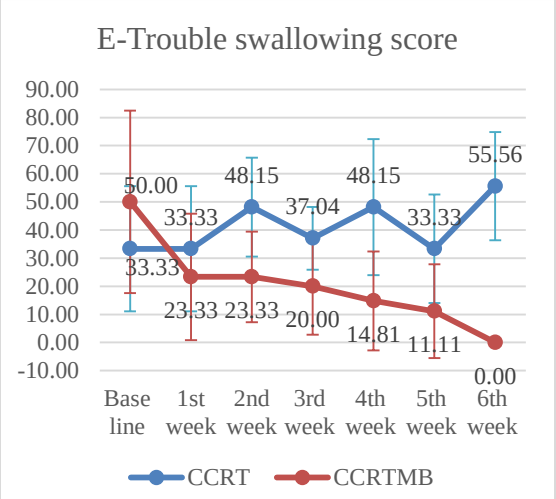
Graph no 5. Weekly symptoms score (%) in Oesophageal cancer subjects

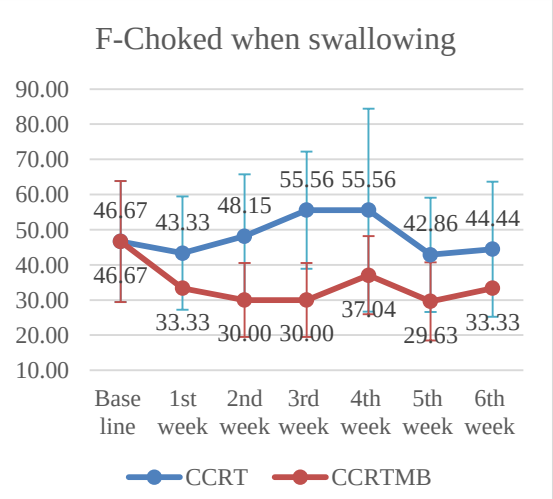


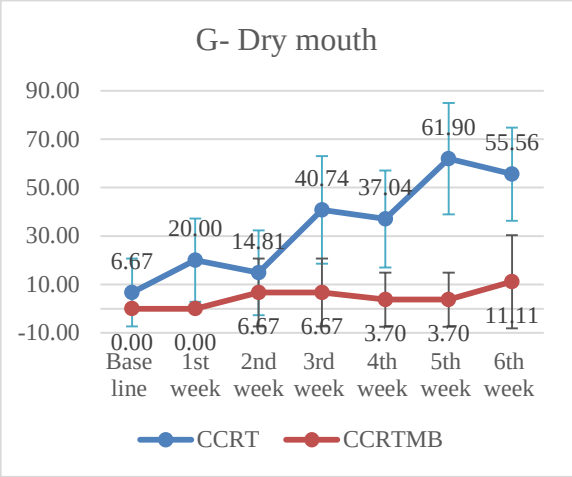


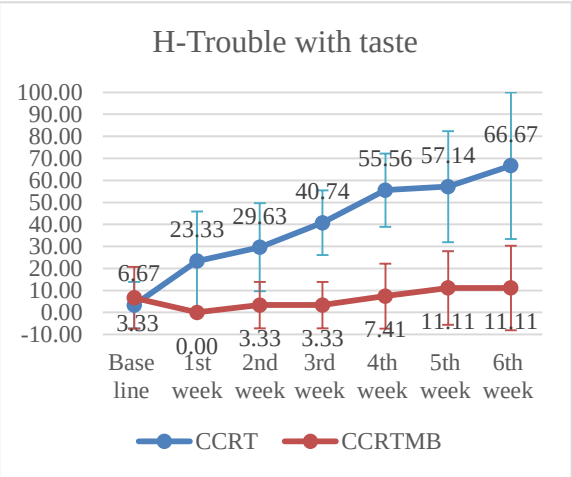


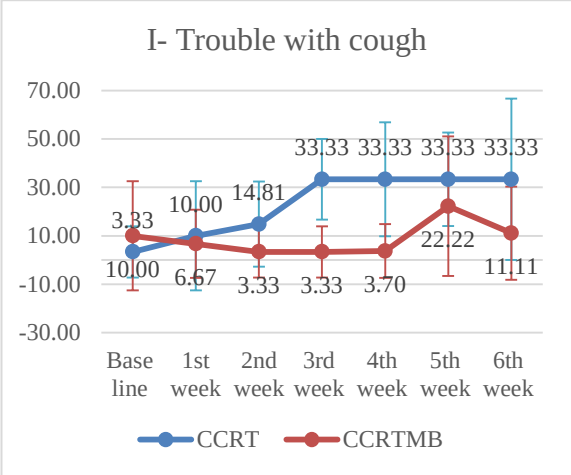


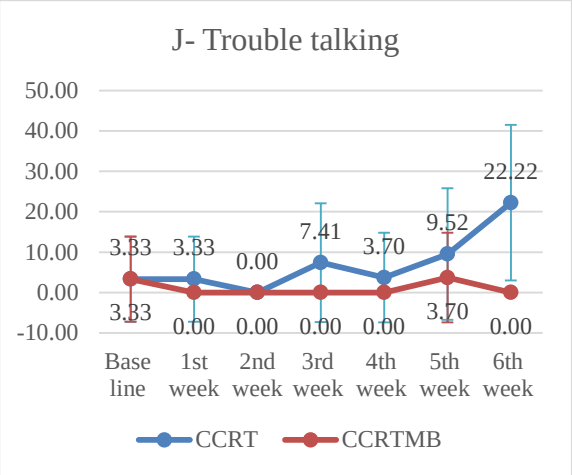





G- Dry mouth
90.00
70.00
50.00
30.00
10.00
-10.00
6.67
20.00
14.81
40.74
37.04
61.90
55.56
0.00
0.00
6.67
6.67
3.70
3.70
11.11
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRTMB


H-Trouble with taste
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
-10.00
6.67
23.33
29.63
40.74
55.56
57.14
66.67
3.33
0.00
3.33
3.33
7.41
11.11
11.11
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRTMB


I- Trouble with cough
70.00
50.00
30.00
10.00
-10.00
-30.00
3.33
10.00
14.81
33.33
33.33
33.33
33.33
10.00
6.67
3.33
3.33
3.70
22.22
11.11
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRTMB


J- Trouble talking
50.00
40.00
30.00
20.00
10.00
0.00
-10.00
3.33
3.33
0.00
7.41
3.70
9.52
22.22
3.33
0.00
0.00
0.00
0.00
3.70
0.00
Base line
1st week
2nd week
3rd week
4th week
5th week
6th week
CCRT
CCRTMB

6.2.4. Concurrent Chemoradiation Therapy Induced side effects and their amelioration

There were totally 40 symptoms noted in entire study [table no 44.]. Independent 't' test showed significant difference [ranging from $p<0.001$ – $p<0.05$] in symptoms grading in 13 major symptoms induced by CCRT at 5^{th} week in CCRT and CCRT+MB. In CCRT group symptoms like Loss of appetite [$p<0.001$], Nausea [$p<0.001$], Constipation [$p<0.001$], Diarrhoea [$p<0.001$], Dysphagia [$p<0.001$], Choking [$p<0.001$], Urinary Urgency [$p<0.02$], Sleep disturbed [$p<0.001$], Pain in throat or oral cavity [$p<0.001$], Restricted mouth opening [$p<0.001$], Change in Voice [$p<0.001$], Depression [$p<0.001$], Anxiety [$p<0.001$] showed significant difference while in CCRT+MB there was no significant difference [$p>0.05$] in above symptoms indicating effect of *Jeevanthyadi ghrita* in amelioration of side effects.

Independent 't' test showed significant difference [$p<0.001$] in both CCRT and CCRT+MB groups in 11 symptoms like Tastelessness, Burning Sensation In Oral Cavity/Mouth, Burning Micturition, Fatigue, Cough, Mucositis, Sticky Saliva, Dry Mouth, Oral Ulcers, Skin Discoloration and Skin Peeling. Here the difference noted was that in CCRT group there was considerable percentage of subjects suffering from grade 3 toxicities while the same was not evident in CCRT+MB group indicating that *Jeevanthadi ghrita* has a role in anchoring the symptoms from getting worsen or go to next grades. [table no 46]

In rest of the side effects like Vomiting, Abdominal discomfort, Bleeding per vagina, Low back ache, Bleeding per rectal, fever, dyspnea, Excessive salivation, Headache, Blurred vision, Numbness in limbs, giddiness, Peripheral neuropathy, wound discharge, Herpes, there was no significant difference observed in both the

groups. However, the number and percentage of subjects experiencing these symptoms were less in CCRT+MB in comparison to CCRT group. [table no 45]

There were two cases in CCRT group who suffered serious adverse effects one subject had radiation induced blurred vision and another subject had herpes infection. While one subject sustained a fracture [due to fall on the day of chemotherapy]. It was also noteworthy that Loss of appetite was ranking first in CCRT group [Annexure, weekly ranking of complaints] throughout the study for six weeks.

Table no 44. List of adverse effects noted during the study

Sl No	Signs and symptoms	Sl No	Signs and symptoms
	Gastro-intestinal symptoms		**Head and Neck local symptoms**
1.	Loss of Appetite	**22.**	Mucositis
2.	Nausea	**23.**	Sticky Saliva
3.	Vomiting	**24.**	Dry mouth
4.	Constipation	**25.**	Pain in Throat/ Buccal Cavity
5.	Loose Stools/Diarrhoea	**26.**	Oral ulcers
6.	Tastelessness	**27.**	Restricted mouth Opening
7.	Dysphagia	**28.**	Change in voice
8.	Choking	**29.**	Excessive Salivation
9.	Abdominal discomfort	**30.**	Blurred Vision
10.	Burning sensation in Chest /Anal verge	**31.**	Headache
	Genito-urinary symptoms		**Central nervous symptoms**
11.	Burning Micturition	**32.**	Depressive
12.	Urinary Urgency	**33.**	Anxiety
13.	White Discharge	**34.**	Numbness in Limbs
14.	Bleeding Per Vaginal	**35.**	Giddiness
15.	Low back ache	**36.**	Peripheral Neuropathy
	Systemic symptoms		**Skin signs**
16.	Weakness/ fatigue	**37.**	Skin discoloration
17.	Sleep disturbed	**38.**	Skin peeling
18.	Bleeding Per Rectal/oral	**39.**	Wound Discharge
19.	Fever	**40.**	Herpes
	Respiratory symptoms		
20.	Cough		
21.	Dyspnoea		

Table no 45. Number and Percentage of Subjects having adverse effects after 1st week and 5th week of trail.

Sl No	Signs and symptoms	1st Week				5th Week			
		CCRT		CCRT + MB		CCRT		CCRT + MB	
	Gastro-intestinal	**n=70**	**%**	**n=70**	**%**	**n=65**	**%**	**n=69**	**%**
1.	Loss of Appetite	30	42.9	21	30	64	98.4	23	33.3
2.	Nausea	29	41.4	18	25.7	55	84.62	16	23.2
3.	Vomiting	13	18.6	9	12.9	25	38.5	8	11.6
4.	Constipation	19	27.1	10	14.3	42	64.6	8	11.6
5.	Loose Stools/Diarrhoea	6	8.6	4	5.7	20	30.8	13	18.8
6.	Tastelessness	16	22.9	6	8.6	61	93.8	46	66.7
7.	Dysphagia	28	40	25	35.7	44	67.69	37	53.6
8.	Choking	11	15.7	8	11.4	43	66.2	9	13
9.	Abdominal discomfort	18	25.7	13	18.6	24	36.9	7	10.1
10.	Burning sensation	15	21.4	7	10	58	89.2	40	58
	Genito-urinary symptoms								
11.	Burning Micturition	2	2.9	7	10	19	29.2	11	15.9
12.	Urinary Urgency	2	2.9	1	1.4	15	23.1	3	4.3
13.	White Discharge	9	12.9	9	12.9	3	4.6	1	1.4
14.	Bleeding Per Vaginal	2	2.9	3	4.3	1	1.5	0	0
15.	Low back ache	9	12.9	14	20	12	18.5	4	5.8
	Systemic Symptoms								
16.	Weakness/ fatigue	27	38.6	14	20	64	98.5	30	43.5
17.	Sleep disturbed	19	27.1	17	24.3	58	89.2	6	8.7
18.	Bleeding PR/PO	0	0	2	2.9	0	0	0	0
19.	Fever	1	1.4	0	0	1	1.5	3	4.3
	Respiratory Symptoms								
20.	Cough	6	8.6	4	5.7	15	23.1	11	15.9
21.	Dyspnea	1	1.4	1	1.4	1	1.5	1	1.4

	Head & Neck local symptoms								
22.	Mucositis	8	11.4	1	1.4	39	60.0	29	42
23.	Sticky Saliva	16	22.9	6	8.6	48	73.8	29	42
24.	Dry mouth	14	20	7	10	50	76.9	35	50.7
25.	Pain in Throat/ Buccal Cavity	40	57.1	27	38.6	43	66.15	35	50.7
26.	Oral ulcers	0	0	2	2.9	39	60.0	8	11.6
27.	Restricted mouth Opening	2	2.9	0	0	34	52.3	6	8.7
28.	Change in voice	7	10	2	2.9	32	49.2	2	2.9
29.	Excessive Salivation	2	2.9	0	0	2	3.1	9	13
30.	Blurred Vision	0	0	0	0	1	1.5	0	0
31.	Headache	8	11.4	5	7.1	10	15.4	3	4.3
	Central nervous symptoms								
32.	Depressive	3	4.3	2	2.9	36	55.4	11	15.9
33.	Anxiety	6	8.6	6	8.6	50	76.9	15	21.7
34.	Numbness in Limbs	3	4.3	2	2.9	5	7.7	0	0
35.	Giddiness	2	2.9	0	0	2	3.1	1	1.4
36.	Peripheral Neuropathy	1	1.4	0	0	4	6.2	0	0
	Skin signs								
37.	Skin discoloration	0	0	0	0	37	56.9	20	29
38.	Skin peeling	1	1.4	0	0	37	56.9	6	8.7
39.	Wound Discharge	0	0	0	0	1	1.5	0	0
40.	Herpes	0	0	0	0	1	1.5	0	0

Table no 46. Grading, Number, Percentage and Independent 't' test of CCRT induced adverse effects/symptoms.

Sl no	Symptoms	Timeline of Assessment at 5th week							
		CCRT Group (n=65)				CCRT+MB Group (n=69)			
		Grade	n	%	p<0.05	Grade	n	%	p<0.05
1	Loss of Appetite	1	6	9.2	0.001*	1	17	24.6	0.753
		2	42	64.6		2	6	8.7	
		3	16	24.6		---	---	---	
2	Nausea	1	2	3.1	0.001*	1	9	13	0.753
		2	38	58.5		2	7	10.1	
		3	15	23.1		---	---	---	
3	Vomiting	1	8	12.3	0.154	1	7	10.1	0.424
		2	12	18.5		2	1	1.4	
		3	5	7.7		---	---	---	
4	Constipation	1	3	4.6	0.001*	1	7	10.1	0.671
		2	18	27.7		2	1	1.4	
		3	21	32.3		---	---	---	
5	Loose Stools /Diarrhoea	1	4	6.2	0.029*	1	7	10.1	0.241
		2	10	15.4		2	6	8.7	
		3	6	9.2		---	---	---	
6	Tastelessness	1	1	1.5	0.001*	1	33	47.8	0.001*
		2	42	64.6		2	13	18.8	
		3	18	27.7		---	---	---	
7	Dysphagia	1	4	6.2	0.001*	1	20	29	0.123
		2	16	24.6		2	14	20.3	
		3	22	33.8		3	3	4.3	
		4	2	3.1		---	---	---	
8	Choking	1	18	27.7	0.001*	1	9	13	0.844
		2	21	32.3		2	0	0	
		3	4	6.2		---	---	---	
9	Abdominal discomfort	1	0	0	0.150	1	3	4.3	0.433
		2	23	35.4		2	4	5.8	
		3	1	1.5		3	0	0	
10	Burning sensation in Mouth/Chest /Anal verge	1	3	4.6	0.001*	1	18	26.1	0.001*
		2	26	40		2	21	30.4	
		3	29	44.6		3	1	1.4	

Sl no	Symptoms	Timeline of Assessment 5th week							
		CCRT Group (n=65)				CCRT+MB Group (n=69)			
		Grade	n	%	p<0.05	Grade	n	%	p<0.05
11	Burning Micturition	1	6	9.2	0.001*	1	5	7.2	0.001*
		2	11	16.9		2	6	8.7	
		3	2	3.1		---	---	---	
12	Urinary Urgency	1	4	6.2	0.022*	1	1	1.4	0.271
		2	11	16.9		2	2	2.9	
13	White Discharge	1	2	3.1	0.433	1	1	1.4	0.047*
		2	1	1.5		---	---	---	
14	Bleeding Per Vaginal	1	0	0	0.428	1	0	0	0.362
		2	1	1.5		---	---	---	
15	Low back ache	1	5	7.7	0.573	1	3	4.3	0.124
		2	7	10.8		2	1	1.4	
16	Weakness/fatigue	1	5	7.7	0.001*	1	21	30.4	0.015*
		2	36	55.4		2	7	10.1	
		3	23	35.4		3	2	2.9	
17	Sleep disturbed	1	10	15.4	0.001*	1	4	5.8	0.283
		2	30	46.2		2	2	2.9	
		3	18	27.7		---	---	---	
18	Bleeding Per Rectal/Oral	1	0	0	0.428	1	0	0	0.275
19	Fever	1	1	1.5	0.536	1	3	4.3	0.543
20	Cough	1	2	3.1	0.001*	1	4	5.8	0.001*
		2	11	16.9		2	7	10.1	
		3	2	3.1		---	---	---	
21	Dyspnea	1	0	0	0.419	2	1	1.4	0.988
		2	0	0		---	---	---	
		3	1	1.5		---	---	---	
22	Mucositis	1	0	0	0.001*	1	23	33.3	0.001*
		2	14	21.5		2	6	8.7	
		3	25	38.5		---	---	---	
23	Sticky Saliva	1	0	0	0.001*	1	15	21.7	0.001*
		2	25	38.5		2	14	20.3	
		3	23	35.4		---	---	---	
24	Dry mouth	1	1	1.5	0.001*	1	21	30.4	0.001*
		2	21	32.3		2	14	20.3	
		3	28	43.1		---	---	---	

Sl no	Symptoms	Timeline of Assessment 5th week							
		CCRT Group (n=65)				CCRT+MB Group (n=69)			
		Grade	n	%	p<0.05	Grade	n	%	p<0.05
25	Pain in Throat/ Buccal Cavity/ Chest	1	2	3.1	0.001*	1	25	36.2	0.063
		2	21	32.3		2	10	14.5	
		3	20	30.8		---	---	---	
26	Oral ulcers	1	0	0	0.001*	1	7	10.1	0.001*
		2	21	32.3		2	1	1.4	
		3	18	27.7		---	---	---	
27	Restricted mouth Opening	1	0	0	0.001*	1	2	2.9	0.131
		2	24	36.9		2	4	5.8	
		3	10	15.4		---	---	---	
28	Change in voice	1	1	1.5	0.001*	1	2	2.9	0.770
		2	23	35.4		---	---	---	
		3	6	9.2		---	---	---	
		4	2	3.1		---	---	---	
29	Excessive Salivation	1	0	0	0.559	1	5	7.2	0.266
		2	2	3.1		2	4	5.8	
30	Headache	1	4	6.2	0.396	1	3	4.3	0.907
		2	6	9.2		2	--	--	
31	Blurred Vision	1	1	1.5	0.053	---	---	---	---
32	Depressive	1	7	10.8	0.001*	1	11	15.9	0.05
		2	27	41.5		2	0	0	
		3	2	3.1		---	---	---	
33	Anxiety	1	13	20	0.001*	1	12	17.4	0.413
		2	36	55.4		2	3	4.3	
		3	1	1.5		---	---	---	
34	Numbness in Limbs	1	0	0	0.210	1	---	---	0.726
		2	5	7.7		---	---	---	
35	Giddiness	1	0	0	0.752	1	0	0	0.670
		2	2	3.1		2	1	1.4	
36	Neuropathy	1	0	0	0.380	1	0	0	0.471
		2	3	4.6		---	---	---	
		3	1	1.5		---	---	---	
37	Skin discoloration	1	1	1.5	0.000*	1	16	23.2	0.000*
		2	17	26.2		2	4	5.8	
		3	19	29.2		---	---	---	
38	Skin peeling	1	4	6.2	0.000*	1	3	4.3	0.000*
		2	26	40		2	3	4.3	
		3	7	10.8		---	---	---	
39	Wound Discharge	1	1	1.5	0.053	---	---	---	---
40	Herpes/Infection	2	1	1.5	0.609	---	---	---	---

SAFETY PROFILE

Table no 47. Complete blood count and Biochemistry of CCRT group at different timeline

Sl. no	Time of Assessment	Baseline n=70		Mid Trail n=67		Post Trail n=62		F Value	P Valve
	Parameter	Mean	Std.D	Mean	Std.D	Mean	Std.D		
	Complete Blood Count								
1.	Hb	12.15	1.83	12.17	1.53	11.55	1.71	2.80	0.06
2.	WBC	7769	2756	5073	1963	4418	2250	38.33	0.001*
3.	RBC	4.21	0.53	4.11	0.65	3.90	0.67	4.15	0.02*
4.	Platelet	2.89	0.96	2.17	0.76	2.00	0.78	21.26	0.001*
5.	Neutrophil	63.87	9.65	74.16	7.46	69.63	11.61	19.51	0.001*
6.	Lymphocyte	29.59	8.77	18.81	6.63	21.55	8.82	32.58	0.001*
7.	Monocytes	6.41	3.84	7.07	2.58	8.09	4.40	3.46	0.03*
8.	Basophil	0.39	0.35	0.28	0.15	0.25	0.13	6.96	0.001*
	Renal Function Test								
9.	Urea	24.97	7.22	26.90	8.10	25.75	10.37	0.87	0.42
10.	Creatinine	0.96	0.22	0.99	0.20	0.95	0.24	0.63	0.54
	Liver Function Test								
11.	T. Bilirubin	0.77	0.18	0.82	0.21	0.83	0.21	1.97	0.14
12.	D. Bilirubin	0.32	0.10	0.34	0.13	0.36	0.11	2.26	0.11
13.	T. Protein	7.06	0.56	6.77	0.49	6.72	0.51	8.06	0.001*
14.	Albumin	3.81	0.55	3.69	0.43	3.67	0.44	1.64	0.20
15.	SGOT /AST	28.17	8.64	29.43	9.04	29.30	7.07	0.46	0.63
16.	SGPT /ALT	25.14	7.18	27.58	9.49	26.89	6.35	1.76	0.18
17.	ALP	153.89	57.86	159.11	46.72	155.8	49.15	0.17	0.84

Table no 48. Complete blood count and Biochemistry of CCRT+MB group at different timeline

Sl. no	Time of Assessment	Baseline n=70		Mid Trail n=70		Post Trail n=69		F Value	P Valve
	Parameter	**Mean**	**Std.D**	**Mean**	**Std.D**	**Mean**	**Std.D**		
	Complete Blood Count								
1.	Hb (gm/dl)	12.02	1.75	11.97	1.72	11.47	1.53	2.35	0.10
2.	WBC (cc/m)	7823	2158	5520	1975	4701	1727	47.41	0.001*
3.	RBC	4.27	0.74	4.12	0.60	3.97	0.59	3.63	0.03*
4.	Platelet	2.79	0.80	2.24	0.64	2.16	0.74	15.66	0.001*
5.	Neutrophil	65.52	9.91	73.88	8.48	71.63	9.84	14.73	0.001*
6.	Lymphocyte	28.30	8.98	19.51	7.86	20.77	9.93	19.66	0.001*
7.	Monocytes	6.59	8.47	6.43	2.33	7.22	2.54	0.43	0.65
8.	Basophil	0.38	0.17	0.28	0.15	0.27	0.16	9.72	0.001*
	Renal Function Test								
9.	Urea	24.01	6.18	24.24	5.44	26.44	11.24	1.93	0.15
10.	Creatinine	0.95	0.21	0.92	0.17	0.95	0.39	0.35	0.71
	Liver Function Test								
11.	T. Bilirubin	0.81	0.20	0.81	0.19	0.86	0.24	1.23	0.30
12.	D. Bilirubin	0.33	0.10	0.35	0.11	0.35	0.11	1.54	0.22
13.	T. Protein	7.07	0.48	6.93	0.50	6.76	0.44	7.46	0.001*
14.	Albumin	3.95	0.70	3.85	0.48	3.70	0.57	2.98	0.06
15.	SGOT /AST	28.63	8.17	29.66	7.09	29.65	7.74	0.42	0.66
16.	SGPT /ALT	27.06	7.77	25.59	5.87	26.19	6.96	0.80	0.45
17.	ALP	160.73	49.46	159.90	49.06	152.95	46.50	0.53	0.59

Table no 49. Comparison of Post trail Complete Blood Count, Liver Function Test, Serum Creatinine and Serum Urea between CCRT & CCRT+MB group at 5th week

Sl No	Haematology & Biochemistry	CCRT (Mean ± SD)	CCRT+MB (Mean ± SD)	p Value
1.	Hb	11.55 ± 1.7	11.47 ± 1.53	0.43
2.	WBC	4418 ± 2250	4701 ± 1727	0.18
3.	RBC	3.9 ± 0.67	3.97 ± 0.59	0.16
4.	Platelet	2 ± 0.78	2.16 ± 0.74	0.82
5.	Neutrophil	69.63 ± 11.61	71.63 ± 9.84	0.55
6.	Lymphocyte	21.55 ± 8.82	20.77 ± 9.93	0.55
7.	Monocytes	8.09 ± 4.40	7.22 ± 2.54	0.04
8.	Basophil	0.25 ± 0.13	0.27 ± 0.16	0.29
9.	Urea	25.75 ± 10.3	26.44 ± 11.24	0.77
10.	Creatinine	0.95 ± 0.24	0.95 ± 0.39	0.86
11.	Total Bilirubin	0.83 ± 0.21	0.86 ± 0.24	0.34
12.	Direct Bilirubin	0.36 ± 0.11	0.35 ± 0.11	0.90
13.	T. Protein	6.72 ± 0.51	6.76 ± 0.44	0.24
14.	Albumin	3.67 ± 0.44	3.7 ± 0.57	0.84
15.	SGOT /AST	29.3 ± 7.07	29.65 ± 7.74	0.25
16.	SGPT /ALT	26.89 ± 6.35	26.19 ± 6.96	0.54
17.	Alkaline Phosphatase	155.8 ± 49.15	152.95 ± 46.5	0.80

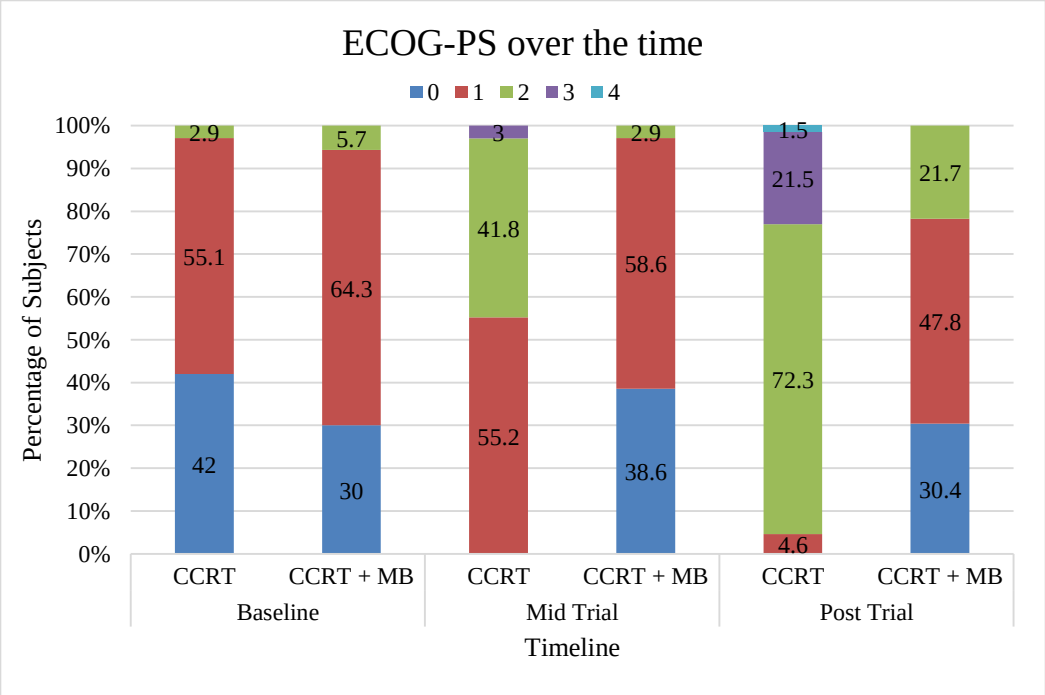
Annova test showed similar significant difference [$p<0.001$] in parameters like Total count, RBC, Platelet and Total Protein in both CCRT and CCRT+MB groups, while there was no significant [$p>0.05$] difference in other parameters of blood count, serum urea, serum creatinine and liver function test [Table no 48&47]. Independent 't' Test also showed no significant difference between both the groups at 5th week evaluation [Table no 49]. This deliberates that *Jeevanthyadi ghrita* has no negative effect on the blood, renal and liver profiles when administered along with concurrent chemoradiation therapy.

PERFORMANCE STATUS [ECOG-PS]

Table No 50. Distribution of subjects based on Performance status (ECOG-PS scale) of subjects at different timeline.

Time line	Group	ECOG scoring										p value
		0		1		2		3		4		
		n	%	n	%	n	%	n	%	n	%	
Base line	CCRT	29	42.0	38	55.1	3	2.9	0	0	0	0	0.365
	CCRT + MB	21	30.0	45	64.3	4	5.7	0	0	0	0	
Mid Trial	CCRT	0	0	37	55.2	28	41.8	2	3.0	0	0	0.001*
	CCRT + MB	27	38.6	41	58.6	2	2.9	0	0	0	0	
Post Trial	CCRT	0	0	3	4.6	47	72.3	14	21.5	1	1.5	0.001*
	CCRT + MB	21	30.4	33	47.8	15	21.7	0	0	0	0	
*p<0.05, Pearson chi square test. **Annova Test = F value: 45.2, p<0.003**												

Graph no 6. Percentage of Performance status of all subjects at Different timeline



Annova Test showed significant difference [p<0.003] between CCRT and CCRT+MB. Independent 't' showed significant difference [p<0.001] in Performance status between CCRT and CCRT+MB groups at mid trail and post-trial. At 5th week of trial, the percentage of subjects with performance status 2 was on higher in CCRT group [72.3] in comparison to CCRT+MB [21.7]. [table no 50]

6.2.5. Compliance of Concurrent Chemo-Radiation Therapy (CCRT)

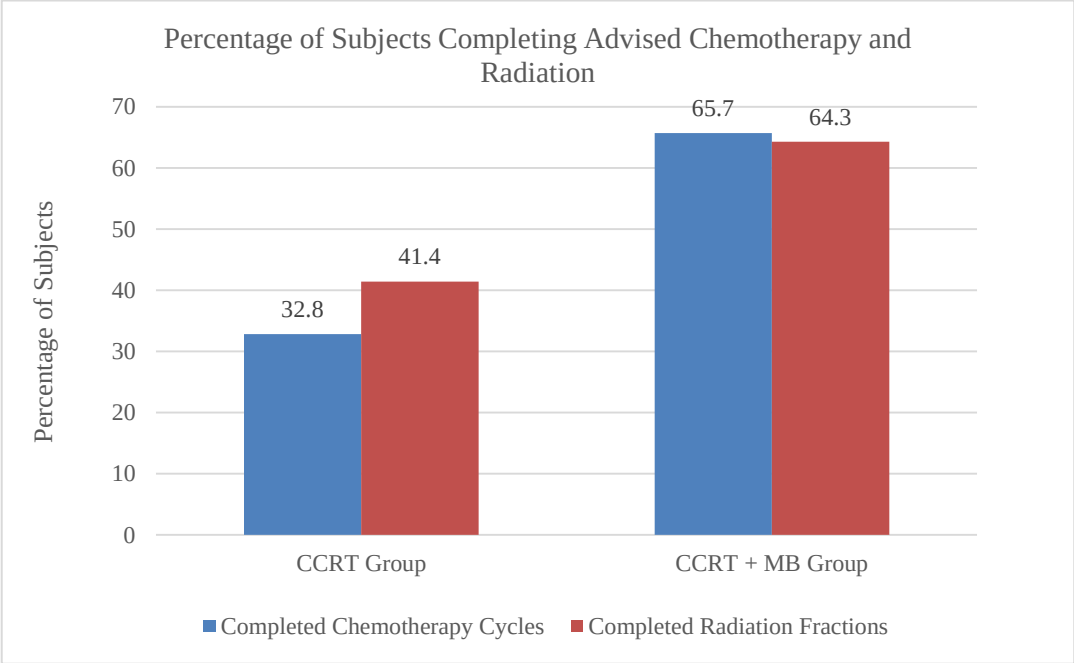
Pearson Chi-Square showed significant difference [p<0.003] in regards to compliance of chemotherapy cycles between CCRT and CCRT+MB group. In regards to Radiation therapy compliance there was no significant difference [p<0.433] observed between CCRT and CCRT+MB groups. Indicating role of J*eevanthyadi ghrita* in promoting compliance of advised therapy. [table no 51.]

Pearson corelation co-efficient test showed a considerable relationship [r= 0.349*] between *Jeevanthyadi ghrita matra basti* and compliance of chemotherapy [table no 54]

Table no 51. Compliance number & percentage of subjects to Concurrent Chemo-Radiation Therapy (CCRT).

Sl. No	Completed Therapy	CCRT		CCRT+MB		Pearson Chi-Square
		n	%	n	%	
1.	Chemotherapy Cycles	23	32.8	46	65.7	0.003*
2.	Radiation Fractions	29	41.4	45	64.3	0.433

Graph no 7. Percentage of Subjects completing Advised chemotherapy in both groups.



Cancellation of Concurrent Chemo-Radiation Therapy (CCRT)

Independent 't' Test showed significant difference in regards to cancellation of advised chemotherapy cycles [$p<0.001$] [table no 52.] and Radiation fractions [$p<0.014$] [table no 53] between CCRT and CCRT+MB group. Indicating role of *Jeevanthyadi ghrita* in promoting compliance of advised therapy.

Table no 52. Number & Percentage of Chemotherapy Cycles Cancelled in both groups

Sl No	Number of Chemotherapy cycle Cancelled	CCRT		CCRT+MB		Pearson Chi-Square
		n	%	n	%	
1.	1	20	28.6	18	25.7	0.001*
2.	2	14	20.0	6	8.6	
3.	3	11	15.7	0	0.0	
4.	4	2	2.9	0	0.0	
Total		**47**	67.2	**24**	43.3	

Graph no 8. Percentage of Chemotherapy cycles cancelled in both groups

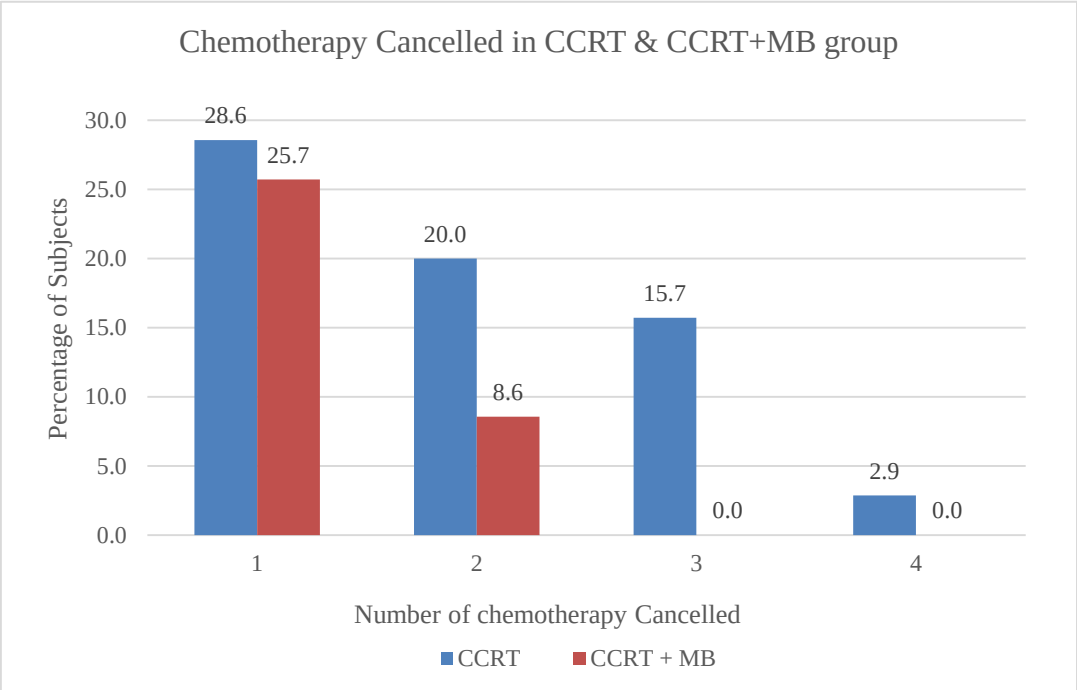


Table no 53. Number & Percentage of Radiation Fractions not received/ cancelled

Sl No	Number of Radiation Fractions Not Received/Cancelled	CCRT		CCRT+MB		Pearson Chi-Square
		n	%	n	%	
1.	1-5	32	45.7	23	32.9	0.014*
2.	6-10	06	8.6	01	1.4	
3.	11-15	01	1.4	01	1.4	
4.	16-20	02	2.9	00	0.0	
Total		**41**	**58.6**	**25**	**35.7**	

Graph no 9. Percentage of Radiation fractions cancelled in both groups

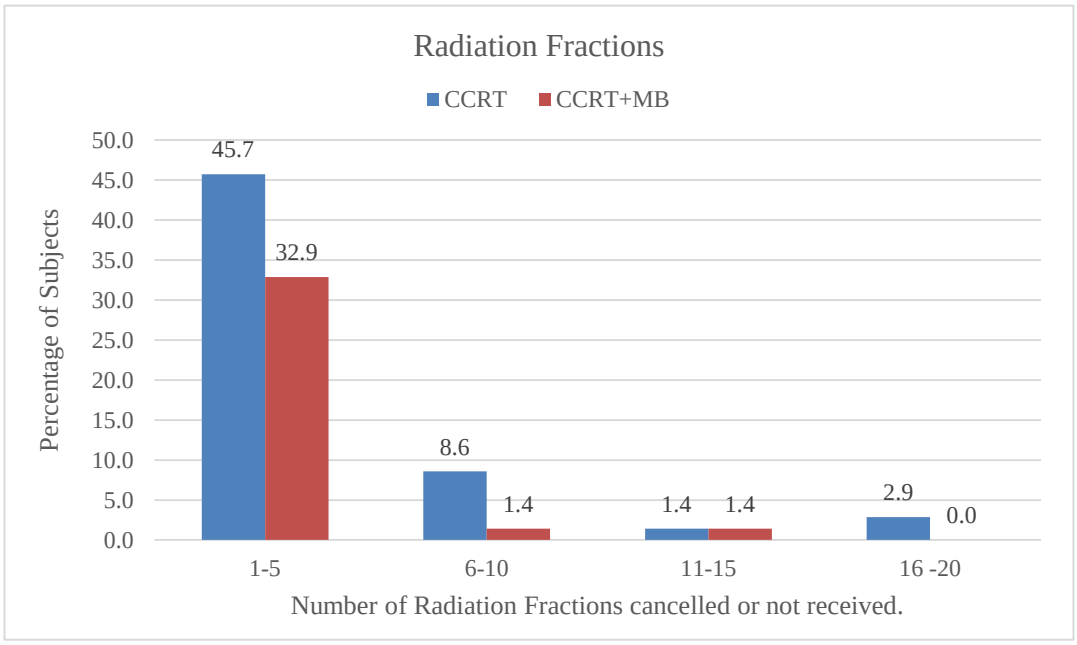


Table No 54. Correlation between *Matra Basti Taken* and CCRT Compliance

Pearson Correlation coefficient	Basti Taken
CT compliance	.349**
CT cancelled	-.423**
RT compliance	.198*
RT Cancelled	-.221**
** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).	

ADVERSE EVENTS DURING CONCURRENT CHEMORADIATION

Independent 't' Test showed significant difference [$p<0.001$] between CCRT group and CCRT+MB group in regards to incidence of Adverse events namely In-Patient/Hospital admissions [table no 56], Blood Transfusion [table no 57] and advising morphine for Pain management [table no 58] induced due to Concurrent chemo-radiation therapy. Following are the tabular and graphical presentation of these events [Graph no 10-12]

Table no 55. Number & Percentage of In-Patient Department (IPD)/Hospital admissions.

Sl.no	Event	Frequency	CCRT		CCRT+MB		Pearson Chi-Square
			n	%	n	%	
1	Number of IPDs	1	38	54.29	20	28.57	0.001*
		2	5	7.14	2	2.86	
		3	2	2.86	0	0.00	

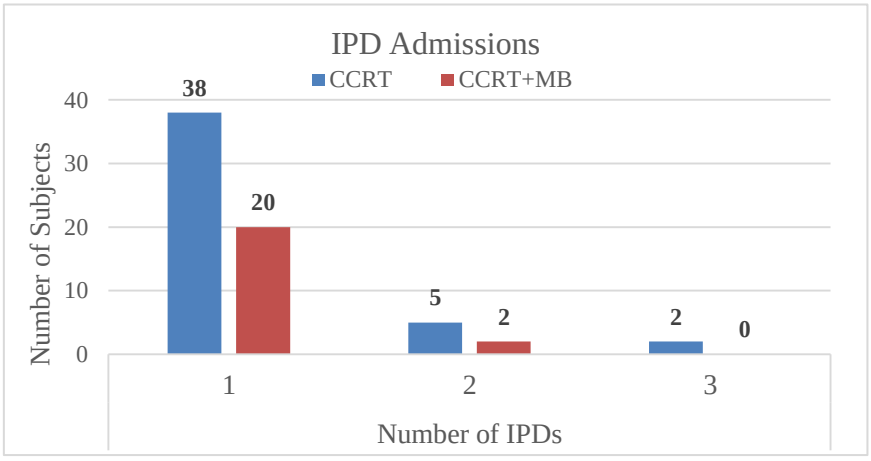
Table no 56. Number & Percentage of Blood Transfusions.

Sl.no	Event	Frequency	CCRT		CCRT+MB		Pearson Chi-Square
			n	%	n	%	
1	Blood Transfusions Underwent	1	18	25.71	12	17.14	0.001*
		2	14	20.00	1	1.43	
		3	4	5.71	0	0.00	
		4	1	1.43	0	0.00	

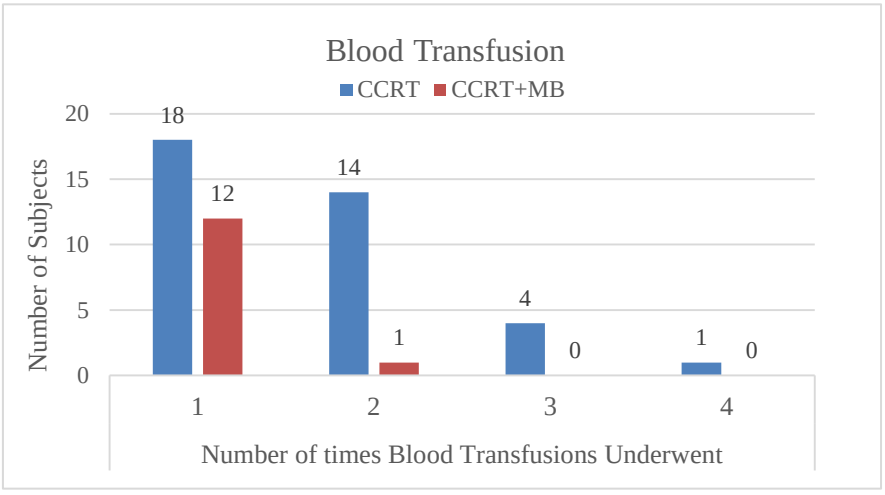
Table no 57. Number & Percentage of Morphine Tablets advised for Pain.

Sl.no	Event	Frequency	CCRT		CCRT+MB		Pearson Chi-Square
			n	%	n	%	
1	Advised Morphine Tablets	1	22	31.43	5	7.14	0.001*
		2	2	2.86	0	0.00	

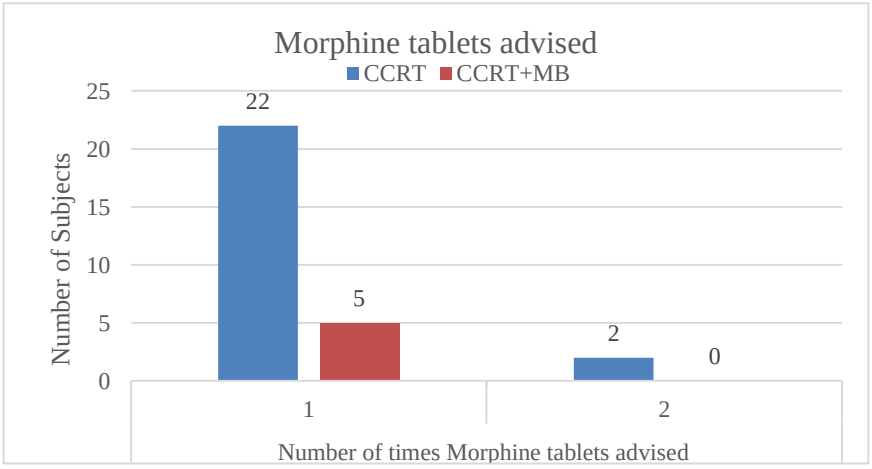
Graph no 10. Number of Subjects advised IPD/Hospital Admissions.



Graph no 11. Number of Subjects advised Blood Transfusions.



Graph no 12. Number of Subjects advised Morphine for Pain.



WEIGHT LOSS

Annova showed significant difference [p<0.02] in weight among cancer subjects of CCRT and CCRT+MB group [table no 58]. There was significant difference [p<0.003] between Baseline to post trial weight loss in CCRT group, while the same was not observed in CCRT+MB group [table no 59].

Annova showed significant difference [p<0.009] in weight among Head and Neck cancer subjects of CCRT and CCRT+MB group [table no 60]. There was significant difference [p<0.006] between Baseline to post trial weight loss in CCRT group, while the same was not observed in CCRT+MB group [table no 61.].

Annova Test showed no significance difference [p<0.05] in weight loss of Cervical [Table no 62 &63] and Esophagus cancer subjects [Table no 64 & 64].

WEIGHT OF CANCER SUBJECTS IN CCRT AND CCRT+MB GROUP

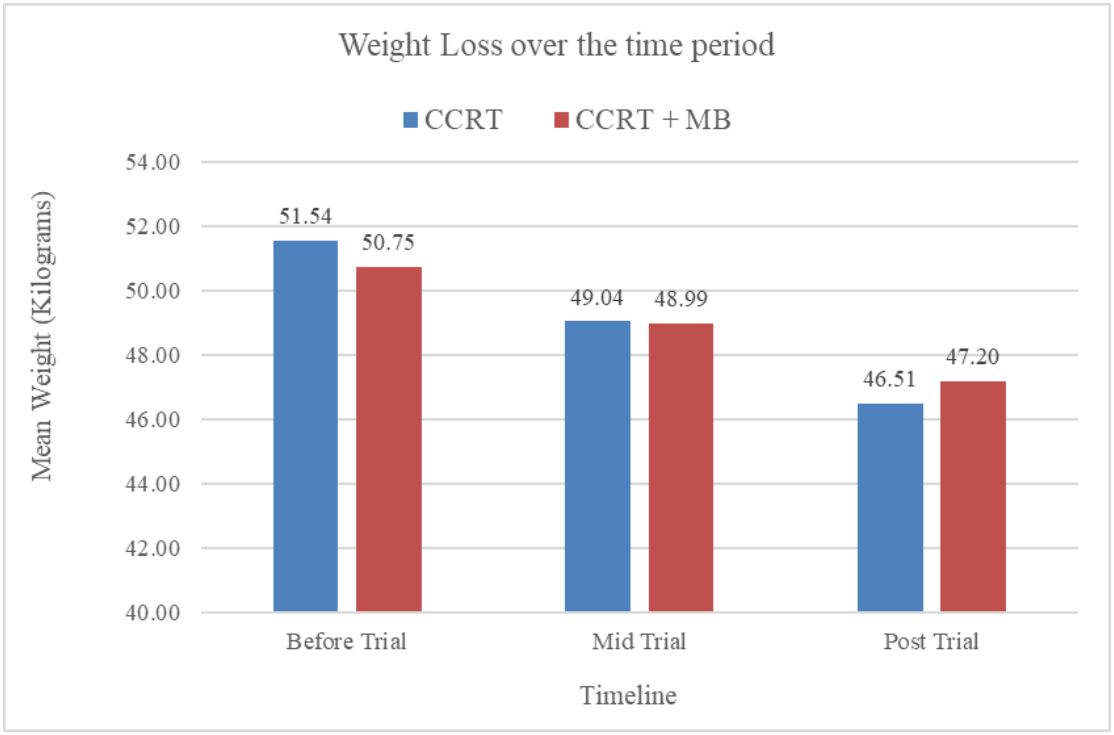
Table no 58. Weight at Different Timeline in CCRT & CCRT + MB Group.

Sl no	Timeline and significance level	CCRT			CCRT+MB		
		n	Mean	SD	n	Mean	SD
1.	Before Trial	70	51.54	11.06	70	50.75	10.50
2.	Mid Trial	68	49.04	10.82	70	48.99	10.25
3.	Post Trial	66	46.51	10.10	69	47.20	10.20
4.	F value	3.78			2.05		
5.	Annova p<0.05	**0.024***			0.13		

Table no 59. Comparison of Weight loss of Cancer Subjects at Different timeline.

Sl no	Time of Assessment Code		CCRT			CCRT+MB		
	From	To	Mean Difference	Std. Error	p Value	Mean Difference	Std. Error	p Value
1.	Baseline	Mid Trial	2.499	1.818	0.171	1.759	1.745	0.944
2.	**Baseline**	**Post Trial**	**5.035***	**1.832**	**0.007***	3.553	1.751	0.131
3.	Mid Trial	Post Trial	2.537	1.845	0.171	1.794	1.751	0.920
4.	p value		0.003*			0.009		
Post hoc test Bonnferri * The mean difference is significant at the 0.05 level.								

Graph no 13. Weight Loss over the time period in CCRT and CCRT+MB group



HEAD & NECK CANCER SUBJECTS

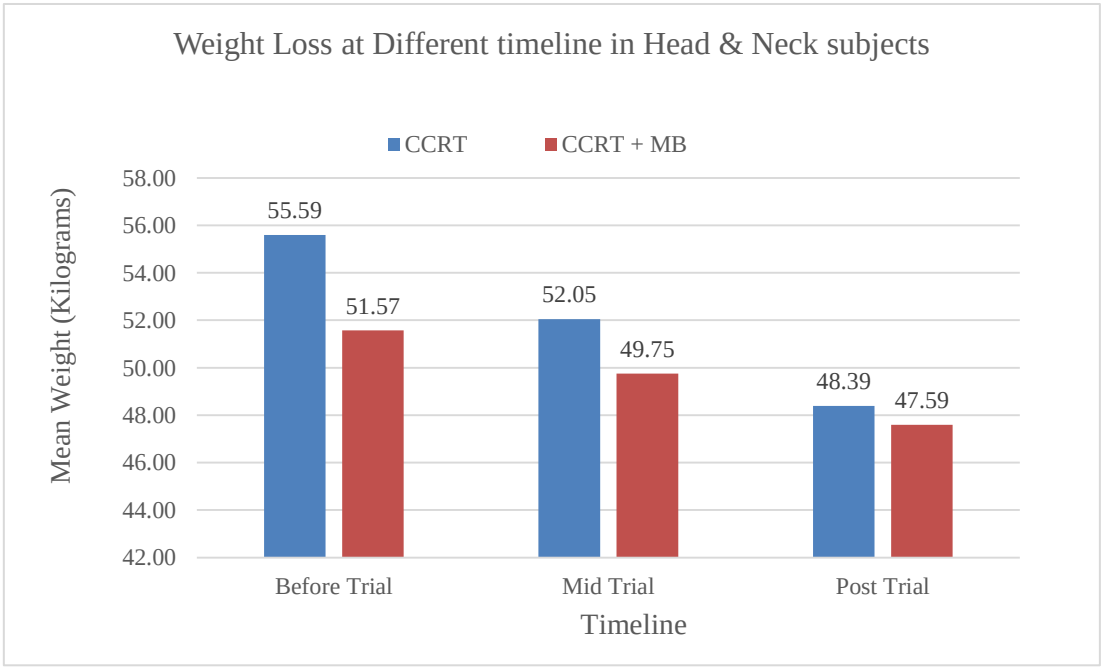
Table no 60. Weight (in Kilograms) of Head & Neck Cancer Subjects at Different Timeline.

Sl no	Timeline and significance level	CCRT			CCRT+MB		
		n	**Mean**	**SD**	**n**	**Mean**	**SD**
1.	Before Trial	38	55.59	10.21	38	51.57	8.92
2.	Mid Trial	38	52.05	9.95	38	49.75	8.67
3.	Post Trial	37	48.39	9.51	38	47.59	8.09
4.	F value	4.963			2.057		
5.	p<0.05	**0.009***			0.133		

Table no 61. Comparison of Weight loss of Head and Neck Cancer Subjects at Different Timeline.

Sl no	Time of Assessment Code		CCRT			CCRT+MB		
	From	To	Mean Difference	Std. Error	P Value	Mean Difference	Std. Error	p Value
1.	Baseline	Mid Trial	3.547	2.270	0.363	1.824	1.965	1.000
2.	Mid Trial	Post-Trial	3.653	2.285	0.338	2.158	1.965	0.824
3.	**Baseline**	**Post-Trial**	**7.200***	**2.285**	**0.006***	3.982	1.965	0.135
	* The mean difference is significant at the 0.05 level.							

Graph no 14. Weight Loss at Different timeline in Head & Neck subjects



CERVICAL CANCER SUBJECTS

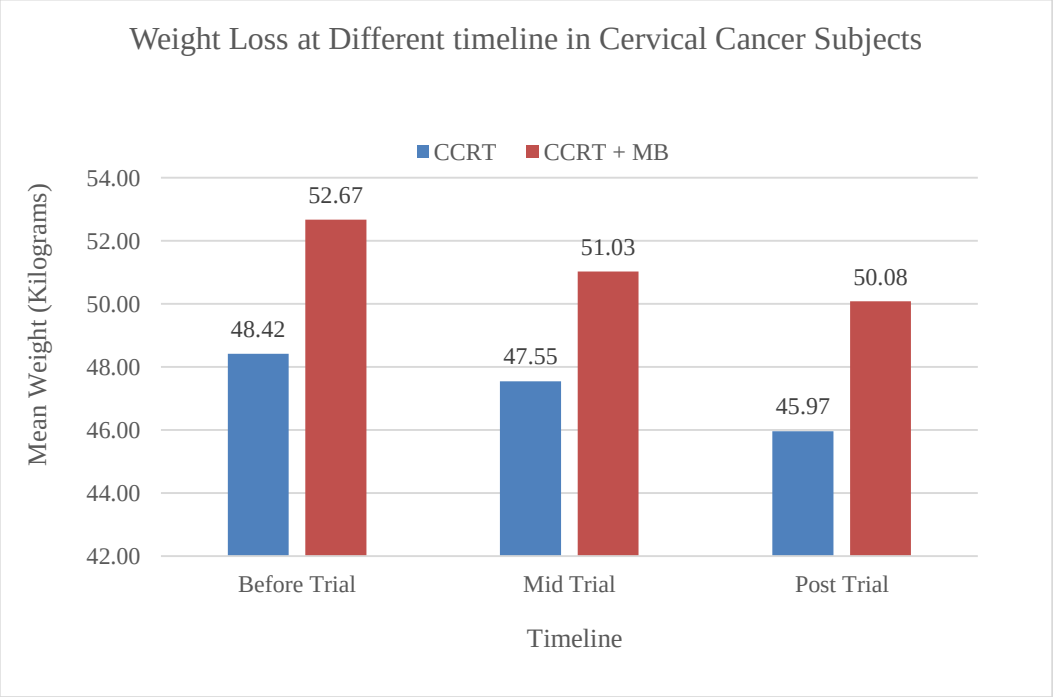
Table no 62. Weight (in Kilograms) of Cervical Cancer Subjects at Different Timeline.

Sl no	Timeline and significance level	CCRT			CCRT+MB		
		n	**Mean**	**SD**	**n**	**Mean**	**SD**
1.	Before Trial	22	48.42	9.77	22	52.67	12.76
2.	Mid Trial	21	47.55	9.91	22	51.03	12.78
3.	Post Trial	21	45.97	9.55	22	50.08	12.67
4.	F value	0.349			0233		
5.	P<0.05	0.707			0.793		

Table no 63. Comparison of Weight loss of Cervical Cancer Subjects at Different Timeline.

Sl no	Time of Assessment Code		CCRT			CCRT+MB		
	From	To	Mean Difference	Std. Error	p Value	Mean Difference	Std. Error	p Value
1.	Baseline	Mid Trial	0.875	2.973	1.000	1.641	3.841	1.000
2.	Mid Trial	Post-Trial	1.581	3.007	1.000	0.950	3.841	1.000
3.	**Baseline**	**Post-Trial**	2.456	2.973	1.000	2.591	3.841	1.000
	* The mean difference is significant at the 0.05 level.							

Graph no 15. Weight Loss at Different timeline in Cervical subjects



OESOPHAGUS CANCER SUBJECTS

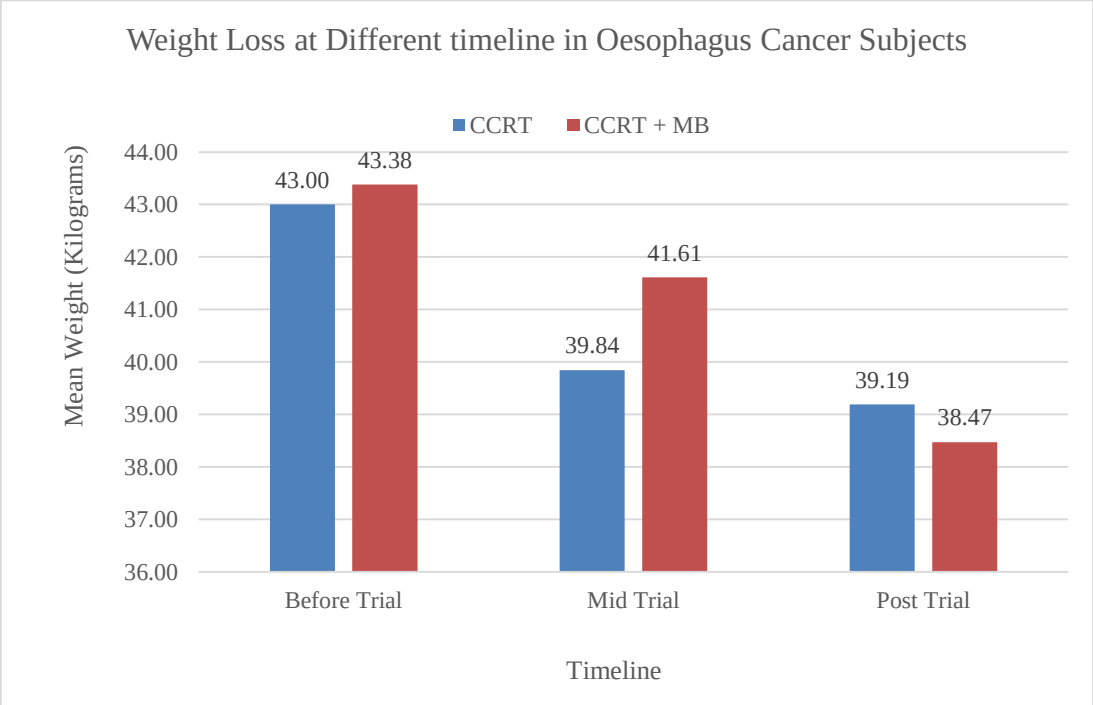
Table no 64. Weight (in Kilograms) of Esophagus Cancer Subjects at Different Timeline.

Sl no	Timeline and significance level	CCRT			CCRT+MB		
		n	Mean	SD	n	Mean	SD
1.	Before Trial	10	43.00	10.58	10	43.38	8.14
2.	Mid Trial	9	39.84	11.50	10	41.61	6.64
3.	Post Trial	8	39.19	11.91	9	38.47	7.20
4.	F value	0.304			1.075		
5.	P<0.05	0.741			0.356		

Table no 65. Comparison of Weight loss of Oesophagus Cancer Subjects at Different Timeline.

Sl no	Time of Assessment Code		CCRT			CCRT+MB		
	From	To	Mean Difference	Std. Error	p Value	Mean Difference	Std. Error	p Value
1.	Baseline	Mid Trial	3.156	5.187	1.000	1.770	3.290	1.000
2.	Mid Trial	Post Trial	0.657	5.485	1.000	3.143	3.380	1.000
3.	Baseline	Post Trial	3.813	5.355	1.000	4.913	3.380	0.474

Graph no 16. Weight Loss at Different timeline in Oesophagus subjects



6.3 OBSERVATIONS

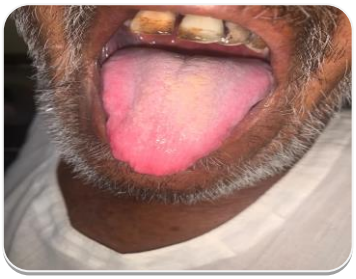
Notable observations in the trial are related to the adverse effects and events. There were significant differences in the gradings as mentioned earlier in the result section. Firstly, the images of the skin, mucositis and opening of mouth are being presented.

1. **Image no 19. Mucositis in CCRT and CCRT + MB Group.**

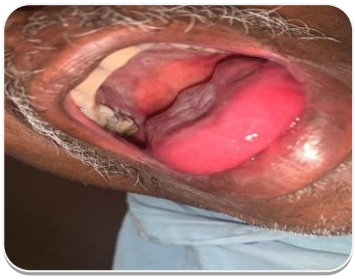
Garde 1 Mucositits in CCRT group

Garde 2 Mucositits in CCRT group

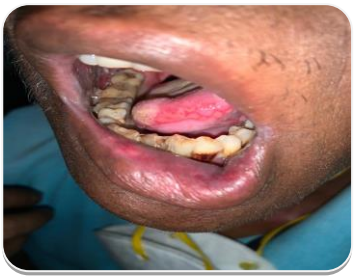
Garde 3 Mucositits in CCRT group



Normal in CCRT + MB group

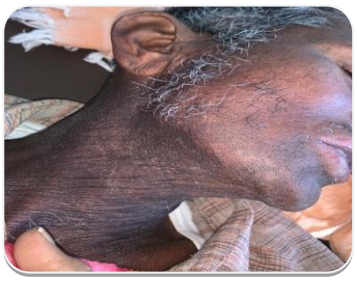


Garde 1 Mucositits in CCRT + MB group



Garde 2 Mucositits in CCRT + MB group

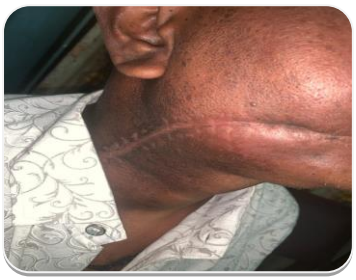
2. Image no 20. Skin Discoloration in CCRT & CCRT MB Group.



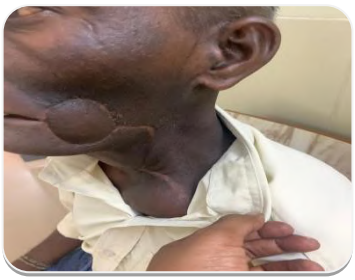
CCRT group

CCRT group

CCRT group



CCRT + MB group

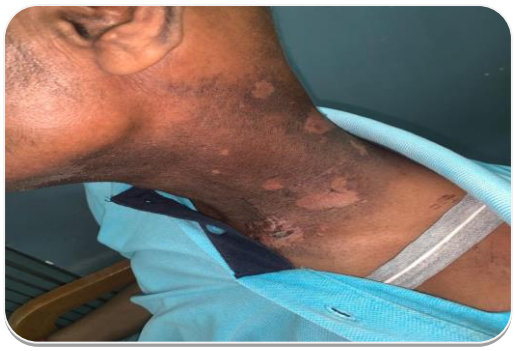


CCRT + MB group

CCRT + MB group

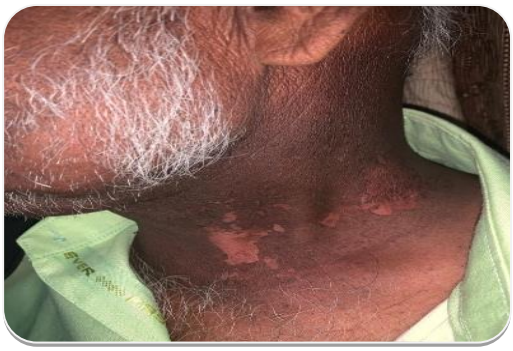
3. Image no 21. Skin Peeling in CCRT & CCRT MB Group.

Skin Peeling in CCRT group



Skin Peeling in CCRT group

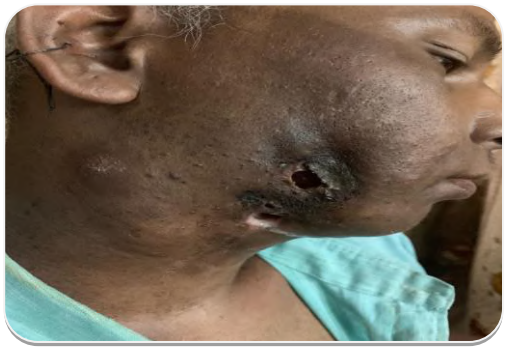
Skin Peeling in CCRT+MB group



Skin Peeling in CCRT+MB group

4. **Image no 22. Wound formation in CCRT group**

Wound formation in CCRT group



Wound Discharge in CCRT group

5. **Image no 23. Adverse event in CCRT group**

Radiation induced Blurred Vision in CCRT group

Another notable observation was that the Loss of appetite complaint was ranking top in CCRT group form 2nd week onwards [Annexure], which could have been one of the reason for significant weight loss in CCRT group.

Constipation and Insomnia was experienced more in CCRT group subjects in comparison to CCRT+MB group.

In case of Cervical cancer subjects the complaints of urinary urgency and loose stools due to proctitis were significantly less in CCRT+MB group in comparison to CCRT group.

7. DISCUSSION

Concurrent Chemoradiation therapy (CCRT) happens to be the primary line of management in cancers of Head and Neck, oesophageal, lung and cervix. Despite of its efficacy it heralds with range of adverse effects like nausea, vomiting, mucositis, fatigue, cachexia, reduced treatment compliance that are known to compromise quality of life. Hence, addressing these adverse effects still remains a challenging area. Integrated oncology has started to believe that Alternate medicines have a role in such scenario. In particularly this proposed thesis was aimed to determine the improvement in quality of life in different domains and amelioration of CCRT induced adverse effects among patients who receive *Jeevanthyadi ghrita matra basti* along with concurrent chemoradiation therapy against the patient who only receive concurrent chemoradiation therapy.

Jeevanthyadi ghrita matra basti [JG *matra basti*] has shown considerable effect in improving quality of life and amelioration of adverse effects of Concurrent Chemoradiation therapy in cancer subjects of Head and Neck, Cervix and Oesophagus. *Jeevanthyadi ghrita matra basti* showed significant difference in number of IPD/Hospitalizations, Blood transfusions, Morphine tablet prescriptions, Performance status (ECOG-PS) and Weight loss when compared to control group. In regards to safety parameters complete blood count, liver function test, serum urea and creatinine there was no significant difference between the groups indicating safety of *Jeevanthyadi ghrita matra basti*. *Jeevanthyadi ghrita* has shown presence of active biological compounds like Alkaloids and terpenoids on phytochemical quantification. LC-MS and GC-MS of *Jeevanthyadi ghrita* elucidated presence of active biological principles that have preliminarily shown to possess an undeniable role or action in

CCRT induced side effects like anorexia, depression, cachexia, mucositis, insomnia, cachexia etc.

Discussion on Drug analysis.

Jeevanthyadi ghrita has shown presence of different bioactive compounds like alkaloids and terpenoids. While, Qualitative analysis like water soluble and alcoholic soluble extracts of raw ingredients of the JG showed presence of active principles like Alkaloids, Tannins, Flavonoids, Steroids, Phenols and Sugars. *Jeevanthaydi Ghrita* analysis also showed to have normal range of Docosahexaenoic acid (DHA), Polyunsaturated fatty acids (PUFA) and Monounsaturated fatty acids (MUFA)

It has been demonstrated that alkaloids and terpenoids inhibit pro-inflammatory cytokines including IL-2, IL-6, and TNF-α and stop lipid peroxidation, which gives them anti-inflammatory, immunomodulatory, analgesic, anti-pyretic, and anti-cancerous effects. [122,123,124,125]

Similar to this, it is known that the components of ghee, such as PUFA, reduce prostaglandin levels and leukotriene production. Leukotrienes are inflammatory mediators that are produced by the arachidonic acid cascade. The traditional ayurvedic preparation of ghrita has a higher concentration of DHA, or omega-3 long-chain polyunsaturated fatty acids, which have been shown to prevent or reduce the risk of diseases like cancer, heart attacks, insulin resistance, and arthritis. At the same time, free fatty acids play a crucial role as a fuel source for colonocytes, which can correct nutritional deficiencies and colon pathology.[126,127,128]

GC-MS has shown presence of 17 compounds which are majorly fatty acids and LC-MS has shown nearly 66 compounds and among them 37 were identified through the library. In 2015, In order to comprehend the ancient Ayurvedic engineering involved in merging water-soluble ingredients to lipid-soluble mode without utilizing surfactants by HPTLC, Duraipandi S. et al. looked into Guggulu tiktaka ghrita. Their investigation made it clear that the biologically active chemicals had eluted in ghrita as a monophasic, oily liquid with no discernible layers. Whereas non-polar fractions did not show the presence of active biological components, the HPTLC run utilizing polar fractions did. It is obvious that they postulated that hydrophilic components would have been held in a nano vesicular form in lipids, which could regulate the medication delivery to targets.[129]

According to Pouton CW et al. (2000), a drug reservoir of this kind may result in a partition that stops drug precipitation and permits effective, passive [transcellular] drug absorption. Through lymphatic transport and supersaturation, or intestinal absorption, this can affect kinetics and increase bioavailability. These investigations contribute to the understanding that by altering their pharmacological formulation, even hydrophilic or water-soluble medications can be targeted for certain indications. According to these beliefs, the idea of using a same formulation in a variety of pharmacological dosage forms for the purpose of target drug delivery is explained by ayurveda.[130,131,132]

In regards to the identified compounds through LC-MS and GC-MS, an attempt was made to study the network pharmacology based on the clinical outcomes noted, which are discussed later in this chapter.

Discussion on Clinical Study Results – Quality of Life

Acute toxicities and symptoms brought on by CCRT are now regarded as toxicity syndromes rather than isolated complaints. Radiation causes local dermatitis and Chemotherapy acts on rapidly dividing epithelial cells, causing gastrointestinal disturbances, but the toxic effects of CCRT also extend to distant normal tissues through the immune system, systemic, and interorgan signaling via blood proteins. These proteins can be cytokines (TNF-α), interleukins (IL-6, IL-8), and a variety of other endogenous molecules such as prostaglandins that are generated when tumor cells die or when normal cells undergo necrosis or apoptosis.

This happens through phases namely Initiation phase, which causes cellular damage to rapidly dividing cells, induced by CCRT leading to oxidative stress and enforcement of innate immunity to act swiftly via interleukins. Secondly, Upregulation or activation of different signaling mechanisms through cytokines leading to inflammation that is developed during initial hours of radiation therapy and systemic chemotherapy. Thirdly signal amplifications through intracellular and intercellular signaling loops causing cascading effect. This biological pathway is so intricate that even behavioral toxicities are exacerbated in the form of depression, fatigue and cachexia along with commonly found toxicities like mucositis, pain, peripheral neuropathy etc. All these symptoms will have a negative impact on the quality of life during and after the therapy.[133]

The present study was in accordance with recent studies[134,135,136] indicating CCRT induced adverse effects can have a negative impact on quality-of-life [EORTC-QLQ-30]. At the end of 5th week of trail, in contrast, the subjects who received *JG matra basti* were able to show significant difference in quality-of-life

Functional score (Physical – 91.6, Role- 89.1, Emotional – 88.3 and Social – 82.1) when compared to CCRT group (Physical –64.6, Role- 64.1, Emotional – 45.8 and Social – 55.5). Global health score showed no significant difference between CCRT [50.3] and CCRT+MB (JG Matra Basti) [79.3] group but the mean score values were considerably wide. *JG matra basti* was able to ameliorate the symptoms (EORTC-QLQ-30) like Pain, Dyspnea, Insomnia, Appetite loss, constipation and Diarrhea in a significant manner. However, other symptoms [like Fatigue (22.1) and Appetite (15)] were comparably better in CCRT+MB group when compared to mean score values of CCRT group [Fatigue (65.8) and Appetite (53.1.)].

In case of Head and Neck cancer subjects the Quality of life (EORTC-QLQ-30) scores were significantly better in CCRT +MB group in comparison to CCRT except for Global health score. Though statistically insignificant there was difference in mean score of global health (79.2 in CCRT+MB and 44.2 in CCRT group).

There was significant difference in mean scores of Head and Neck specific symptoms (EORTC-H&N-43) between CCRT and CCRT+MB group. However, few symptoms like swallowing (CCRT-66.9 & CCRT+MB-24.8), Dry mouth and Sticky saliva (CCRT-82.9 & CCRT+MB-35.5), cough (CCRT-50 & CCRT+MB-16.7) and problem opening mouth (CCRT-60.2 & CCRT+MB-7) were statistically insignificant but the mean score values were lower in CCRT+MB in comparison to CCRT group.

In case of cervical cancer subjects the Quality of life (EORTC-QLQ-30) scores were significantly better in CCRT +MB group in comparison to CCRT. Symptoms like Appetite and Diarrhea showed insignificant difference statistically, however the mean score in CCRT (Fatigue- 59.8, Appetite-55.6 and Diarrhea-55.8) were differing in comparison to CCRT+MB (Fatigue-22.7, Appetite-18.2 and

Diarrhea-21.2). In case of Insomnia the *JG matra basti* was able improve sleep in CCRT+MB group (base line score 15.6 and 5^{th} week score - 10).

There was significant difference in mean scores of cervical cancer specific symptoms (EORTC-CX-24) between CCRT and CCRT+MB group. However, the symptoms related sexual heath were not documented and unanswered. In comparison to CCRT group the CCRT + MB showed better outcome in symptom score and menopausal score as it was able to bring them down.

In case of oesophageal cancer subjects the Quality of life (EORTC-QLQ-30) scores showed no significant difference between CCRT and CCRT +MB. While cognitive function and diarrhea symptom showed significant difference. Similarly, the oesophagus specific symptoms (EORTC-OES-18) score also showed no significant difference in all symptoms. However, few symptoms mean score value between CCRT (Pain-47.6, Reflux-42.9, Choking-42.9) and CCRT+MB (Pain-19.8, Reflux-9.3, Choking-29.6) was differing considerably. In Eating symptom, CCRT+MB (baseline – 32.5 and 5^{th} week-22.2) showed slight improvement in comparison to CCRT group (baseline – 30 and 5^{th} week-46.4).

Discussion on Adverse effects.

Adverse effects due to CCRT are common and in present study 40 symptoms were noted. Among them there was significant difference in 13 symptoms between CCRT group CCRT+MB group. These symptoms like Loss of appetite, Nausea, Pain, insomnia, dysphagia, urinary urgency, anxiety, depression and restricted mouth opening. While in another 11 symptoms there was difference in grading between

grade 2/3 in CCRT+MB and CCRT group. There are many studies in accordance to our finding of toxicity grading.[137,138,139,140]

Azizi A. et al, 2023 evaluated and proposed that there is need to improve quality of life among cervical cancers patients since few factors like appetite, pain, fatigue, insomnia and emotional function can viciously affect anxiety and depression.[141] There are evidences generated that Ayurveda oral interventions have been effective in improving the Quality of life in domains (like global, physical, emotional) and symptoms (like depression, anxiety, fatigue, sleep and appetite) in patients of breast cancer subjects.[142] Another study where Ashwagandha was administered at 2 grams every 8 hourly to breast cancer subjects undergoing Chemotherapy showed statistically significant in regards to fatigue and 7 domains out of 18 in EORTC-QLQ-30.[143]

In present study also the anxiety and depression showed no difference form baseline to last week. JG matra basti also ameliorated the complaints of appetite, insomnia and pain which indicate that *JG matra basti* might have its role in anchoring them. They say that Ayurveda herbal preparations have complex combinations that may be synergistic in action since they are being consumed by large populations over millennia, which in turn can be a clue to discover new biomarkers, possible mechanisms for prevention and treatment of chronic and acute stages. Adjuvant therapy and remission therapy using AYUSH modalities, the advantages of such approaches in the form of customized medicine, and the enhancement of quality of life ought to be the main areas of focus.[144]

In the present study there was significant difference [$p<0.01$] seen in the incidence of adverse events. Nearly 54.29% of subjects in CCRT and 28.57% in

CCRT+MB group required at least one-time In-Patient Department Admissions/Hospitalization for severe symptoms like cough, fatigue, low Hb, weakness etc. Present study is in consensus with previous studies which say that 36 to 60% of subjects who received CCRT required at least one time hospitalization.[145,146,147,148,149]

Similarly, the onetime blood transfusion percentage in CCRT group was 25.7 [18 units] and in CCRT+MB 17.1% [12 units] due to low hemoglobin (<8 gm/dl). While 20% of patients in CCRT required two-time blood transfusion and in CCRT+MB only 1.4%. There are evolving protocols and guidelines on lower range of blood transfusion requirement in CCRT induced chemotoxicities (8-10gm/dl). Present study also showed same trend as previous studies which documented approximately 22 to 38 % subjects required at least one time Blood transfusion due to chemoradiation toxicities. [150, 151]

Eventual pain due to CCRT induced mucositis and other inflammatory pathology is common from second week onwards. In present study the H&N and oesophagus subjects showed significant difference in Pain and swallowing difficulty between the CCRT and CCRT+MB group of subjects. The mean scores of pain in mouth (CCRT group: H&N-66.9, oesophagus-47.6 :: CCRT+MB: H&N-24.8, oesophagus-19.8) and swallowing difficulty (CCRT group: H&N-66.2, oesophagus-33.3 :: CCRT+MB: H&N-25.4, oesophagus-11.) are as mentioned. Also, there was difference in grading of these symptoms, Pain (CCRT group: Grade 3-20, Grade 2-21 and in CCRT+MB: Grade 2-20, Grade 1-25), Oral ulcers (CCRT group: Grade 3-18, Grade 2-20 and in CCRT+MB: Grade 2-1, Grade 1-7) and Mucositis (CCRT group: Grade 3-25, Grade 2-15 and in CCRT+MB: Grade 2-33, Grade 1-8.7). These numbers are reflected in the management of pain where all subjects were given non-steroidal

anti-inflammatory drugs as per CCRT protocol, despite which 34.29% of subjects in CCRT group and 7.14% in CCRT+MB group required morphine. Present study is again in consensus with recent findings which tell that 25-50% of subjects require opioids for the pain management during CCRT. This shows that there is an undeniable role of *Jeevanthaydi ghrita Matra basti* in alleviating pain and its pathology. By controlling pro-inflammatory cytokines, immunoglobulins, and T-cell functional characteristics, basti treatment modifies immunological responses. The levels of IFN-γ and IL-6 have been downregulated by basti treatment. Even 90 days after the start of treatment, the impact persisted in the case of IL-6. Also, after Basti therapy, a progressive decline in IL-8 levels was noted.[152,153,154] This could be the reason for *JG matra basti* to ameliorate toxicities.

Another major finding was the compliance to the advised weekly cisplatin chemotherapy cycles, which showed significant differences [$p<0.01$] between CCRT [completed-32.8 %] and CCRT+MB group [completed-65.7%]. In regards to the cancellation, all subjects got one cycle cancellation in both the group in equal proportion (CCRT-28.6% and CCRT+MB-25.75). However, when it came to cancelation of more than one cycle, CCRT group had more cancelations (2 cycles -20%, 3 cycles-15.7%, 4 cycles -2.9%) in comparison to CCRT+MB (2 cycles -8.6%, 3 & 4 cycles-0 %).

Pearson corelation coefficient [table no 54] showed positive relation between taking *basti* and compliance of chemotherapy ($r =0.349^{**}$) and a negative co-relation between cancelation and basti taken ($r = - 0.423^{**}$). These findings hint about a positive role of *JG matra basti* in compliance of CCRT regimen. Our findings corroborate and reiterate a study that showed [n=62] when complementary and Integrative medicine was given for at least 4 weeks can improve the adherence to

chemotherapy regimen (paclitaxel and carboplatin) when compared chemotherapy alone group. Similarly, another study evaluated integrated oncology in gynecological cancer subjects receiving taxnes [significant] and platinum-based chemotherapy regimens, which showed better adherence in subjects that received integrated oncology protocol. Also, it was noted that these subjects experienced lower incidence of peripheral neuropathy and pain.[155,156]

There was significant difference noted in weight loss [$p<0.02$*] between CCRT [5.05 kg] and CCRT+MB group [3.53 kg] at the end of trail. This difference [$p<0.006$] was still striking in Head and Neck Cancer subjects between CCRT [7.20 kg] and CCRT+MB [3.98 kg].

Significant difference [$p<0.003$] was also noted in Performance status (ECOG-PS). At the end of 5^{th} week majority of subjects in CCRT group were distributed in ECOG 2 [72.3%] and 3 [21.5%] while in case of CCRT+MB majority of subjects were in ECOG 1 [47.8%], 2 [21.7%] and ECOG 0 [30.4%]. *JG matra basti* was able to sustain the weight, performance status and prevent weigh loss. There are references saying Patient's nutritional condition is impacted by cancer and its numerous therapies due to changes in physiological and psychological processes. Poor nutrition can have a detrimental effect on one's performance and quality of life.[157]

Unionized and lipid-soluble ingredients included in basti medication are easily absorbed from the stomach. Basti treatment may work as a stimulant for both the entire body and the gastrointestinal tract. Serotonin, enteroglucagon, and vasoactive intestinal polypeptide (VIP), which stimulate the dopaminergic neural system, are examples of regulatory peptides produced in the colon.[158] *Ayurveda* medicated *ghritas*

have low molecular weight SCFA (short chain fatty acids) formed due to the alkaline nature of paste of herbal drugs and liquid media during preparations. These SCFA are understood as a pivotal in the form of fuel source for colonocytes, particularly in distal colon. SCFA are readily absorbed and believed to play an important role as a protective effect for distal colon and has nutritional value.[159,160]

There was no significant difference observed in safety parameters between CCRT and CCRT + MB group in regards to Complete blood count, liver function test and serum urea and creatinine at 5th week of trail. This indicates that integration of *JG matra basti* along with conventional CCRT can be safe in terms of above parameters. Additionally, if one sees the percentage of blood transfusions there was difference in CCRT and CCRT+MB group as mentioned earlier and **overall, the CCRT group received 37 units and CCRT+MB 13 units of blood transfusions**. This hints that there is an undeniable role of *JG matra basti* in preventing hematological toxicity or thrombocytopenia.

Discussion on preliminary network pharmacology of *Jeevanthyadi Ghrita*.

Overall, the present study showed significant result in quality of life, weight, performance status and symptoms like loss of appetite, constipation, nausea vomiting, pain, depression, anxiety and urinary urgency. GC-MS and LC-MS results have shown presence of active biological compounds. These active compounds have been worked on network pharmacology to elucidate the probable role in following symptoms

While screening for **Nausea and vomiting** following common genes were identified ABCB1, ACE, CYP1A1, KIT, NR1I2 where the phytochemicals present in

Jeevanthyadi ghrita may target the or be responsible preventing for nausea vomiting, The Response to xenobiotic stimulation gene ontology pathway appears to be implicated. Two closely similar liver-enriched nuclear hormone receptors that were initially identified as xenobiotic receptors are the constitutive androstane receptor (CAR) and the pregnane X receptor (PXR). In addition to controlling the transcription of enzymes and transporters involved in drug metabolism, they also coordinate energy metabolism and immunological responses in response to xenobiotic exposure-induced stressors.[161] By influencing this route, *Jeevanthyadi Ghrita* may be beneficial in cases of nausea and vomiting. Pregnane X receptor (PXR) and constitutive androstane receptor (CAR) both regulate drug-induced stress, thus *Jeevanthyadi ghrita* may help reduce feelings of nausea and vomiting by accommodating the stress.

Similarly, the common targets obtained for **Loss of appetite** include ARG1 and EGFR gene. It is well known that ARG 1 controls L-arginine, which controls the dysregulated immune system. ARG1 can mediate dysregulated inflammation, immunosuppression, fibrosis, and the immune system evading cancer cells. It can also control the bioavailability of L-arginine. The intricate physiological metabolism of L-arginine is essential for immune cell responsiveness. Neutrophils release ARG1, a crucial component in controlling immunological responses, when there is inflammation.[162,163]

The EGFR gene play a role in the inflammatory process. An increase in inflammatory cytokines causes changes in the regulation of hunger, such as an imbalance in amino acids, which facilitates the passage of free tryptophan over the blood-brain barrier. A hyper serotoninergic condition that is prone to decreased

hunger is produced by this. *Jeevanthyadi Ghrita* may be helpful in loss of appetite by regulating these genes.[164]

The common genes identified for c**onstipation** include ACE, ACHE, CSNK2A1. Colic motility in the gastrointestinal tract is influenced by ACh. Increased gastrointestinal motility is a result of higher levels of ACh, People may be more prone to constipation due to a decline in cholinergic function.[165,166] CSNK2A1 gene is involved in a number of biological functions, such as circadian rhythm, apoptosis, and cell cycle regulation. Many GI illnesses can be caused by circadian disruption, which can also affect barrier function and, potentially, stomach motility.[167] Consequently, *Jeevanthyadi Ghrita* may be able to alleviate constipation by acting on these genes.

The common genes identified for **diarrhea** are ABCB1, ABCG2, LPAR2, LPAR3 gene**.** Diarrhea brought on by Afatinib is linked to SNP ABCB1 2677 T(A)/T(A). indicating that there is a considerable increase in the incidence of diarrhea in people with ABCB1 polymorphisms more likely than those who carry the G gene to experience grade 3 diarrhea.[168,169] When it comes to the LPAR2 and LPAR3 gene, lysophosphatidic acid receptor agonists block enterotoxins-mediated fluid secretion in mice, suggesting that dietary supplements based on LPA may be used as an adjuvant treatment for diarrhea. Lysophosphatidic acid also stimulates NHE3 in the small intestine via lysophosphatidic acid receptor 5 on Na+-absorptive cells. Therefore, Jeevanthyadi Ghrita may act on these genes to help with diarrhea.[170]

When it comes to **anxiety,** the catabolic process of dopamine is the involved GO pathway. There is evidence to suggest that dopamine regulates anxiety in a number of brain regions. The mesolimbic, mesocortical, and nigrostriatal dopaminergic systems have all been implicated in anxiety, according to some

research. Anxiety is mediated by both dopamine D1 and D2 receptor pathways.[171] Therefore, by influencing this pathway, *Jeevanthyadi Ghrita* may be beneficial in treating anxiety.

For i**nsomnia** the common gene identified is AHR gene. A few genetic variants in the AHR-signaling pathway, which includes AHRR and CLOCK, may help lower the likelihood of developing insomnia. The AHR-signaling pathway may modify the risk of insomnia by interacting with recognized regulators of sleep-wake cycles.[172] Jeevanthyadi *Ghrita* may act on this gene to help with insomnia.

Between 40 and 80 percent of cancer patients will at some time throughout chemotherapy and radiation therapy suffer from malnutrition as a result of anorexia. A mere 5% **loss in body weight** has the potential to indicate declines in treatment responsiveness, survival, quality of life, and cachexia. Anorexia and weight loss were found to be lessened when IL-6 and IL-1 biological activity in the brain were pharmacologically disrupted. Not only that, but Ghrelin, Leptin, Glucagon-like peptide, lactase enzyme, and serotonin all play a part in suppressing hunger, as does TNF alpha Growth Differentiation Factor, etc. The most effective nutrition management technique is to change what you eat and drink. Choose soft, well-combined, and moist foods from every food group. Verifying oral ingestion's safety is also crucial. promoting double swallows and talking after ingestion. But what about silvery taste, dry mouth, nausea, vomiting, and mucositis? There is still no word on whether they would heed the advice.[173,174]

GS-MS analysis of *Jeevanthyadi Ghrita* showed 17 active compounds, among them 7 compounds could show anti-cachexic activity through 29 targets in 74 different combinations. Results indicated that the Janus kinase and Signal Transducer

and Activator of Transcription (JAK-STAT signaling pathway), PI3K-Akt signaling pathway were highly interactive including PPAR pathway.

The JAK-STAT pathway is a signaling cascade that transmits extracellular signals from cytokines and growth factors to the nucleus, where it regulates gene expression. This pathway is involved in various cellular processes, including cell proliferation, differentiation, apoptosis, and immune response. In cachexia, the JAK-STAT pathway is dysregulated, leading to the promotion of muscle wasting and systemic inflammation. Several pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), are upregulated in cachexia. These cytokines activate the JAK-STAT pathway and contribute to muscle protein degradation and inhibition of muscle protein synthesis.[175,176]

Maximum target genes are seen interacting with PI3K-Akt signaling pathway, which is involved in muscle cell proliferation. mTOR signaling pathway in collaboration with PI3K-Akt signaling pathway play an important role in muscle protein synthesis which is affected in cancer induced cachexia. Several factors contribute to the dysregulation of this pathway in cachexia, including pro-inflammatory cytokines, tumor-derived factors, and altered nutrient availability. Tumor-derived factors such as myostatin and activin, which are elevated in cachexia, can also suppress the PI3K-AKT pathway and promote muscle wasting. These factors inhibit Akt phosphorylation and downstream targets involved in protein synthesis and muscle growth.[177]

Similarly, Peroxisome proliferator-activated receptors (PPARs) belong to nuclear receptor superfamily which help in cellular and metabolic processes. PPAR regulate the genetic expression and transcription mechanism of metabolism, cell

proliferation and differentiation. It is also associated with inflammation and other pathologies that lead to type 2 diabetes, atherosclerosis and cancer. There are basically three isoforms of PPAR namely, α, δ, and γ.[178] Among them PPARG is expressed abundantly in adipose tissue and considerably in skeletal muscle, lung, heart, liver, ovary and placenta. PPARG is responsible for regulation of homeostasis of whole-body glucose level and enhancing insulin sensitivity which translates as energy regulator. Its currently being explored in context of cancer and lipid metabolism. PPARG activation is known to cause anti-inflammatory effect by inhibiting IL-6 and other pro-inflammatory markers through the regulation of NF-κB signaling and STAT3 pathway. Recent in-vivo study explored the mechanism of cancer cachexia in mice by using Alpinetin [a plant flavonoid] which reported that activation of PPARG lead to attenuation of phosphorylation's of NF-κB and STAT3 and preventing muscle atrophy. PPARG has also been understood for inhibiting malignant cells through different pathway which can contribute to prevent cachexia.[179] Plain *Ghrita*/Ghee, if prepared through traditional fermentation method has shown possess higher value of Docosahexaenoic acid [DHA] and conjugated linoleic acid (CLD).[180] DHA is a well-known endogenous PPARG ligand and proven for anti-inflammatory activity[181]. CLD acts like a natural ligand for PPARG. CLD activates PPRAG and negatively regulates pro-inflammatory markers like TNFα at mRNA level and IL-6 at protein level. CLD have also shown to possess higher affinity to PPARG than compared to the octadecadienoate parent compounds.[182,183,184,185] In view of exploring natural dietary supplements as new therapeutic agents, *Jeevanthyadi ghirta* may be a potential candidate since most of the active principles like DHA, CLD, apigenin, Neoandrographolide and many others are present.

Discussion on Ayurveda understanding.

As per Ayurveda understanding, CCRT may act like visha and viruddha oushadi. Any samprapti that leads to Dhatu kshaya may be considered as substratum of Rajayaksham. Rajayakshma disease is defined by Ayurveda *as* dehaushadha kshayakrute kshayatatsambhavaat ca sa, which refers to any condition that depletes body tissues and diminishes by mass or by function. In a same vein, rasaadi shoshanaat shosho - it is believed that in such diseases, there would be a depletion of Rasa dhatu, which will influence uttarottara dhatu poshana and eventually cause the depletion of all body tissues. The pathophysiological mechanism primarily involves the vitiation of the Vata dosha, which in turn causes the vitiation of the Pitta and Kapha doshas and modifies their gati and Agni maandhya.

In the event that *Ruksha, Laghu, Khara guna of Vaata, Vidagda guna* of *Pitta* cause the *Rasa dhatu* to be depleted, then the *sneha guna in Mamsa* is lost and *Lepan*a *karma* too. This leads to the emaciation (depletion) of tissues that can be associated with cachexia, namely *dravyataha, gunataha, and karmataha kshaya* of *Rasa Rakta* and *mamsa dhatu*.

Chemotherapy agent like cisplatin is known to effect enteric nervous system (ENS) (ENS helps in generating myogenic activity and aid contractile activity which is affected during chemotherapy) and cause gastrointestinal dysfunction like nausea etc.[186] This can be corelated to vata avorodha and *agni mandhya. Jeevanthyadi Matra basti* has shown to bring in this *Vata anulomana* action, correct constipation and improve *Agni* [digestion] as seen in the present study.

This action of *basti* can then improve or normalize the *dhatu upachaya* process. Once the *Dhatu upachaya* is established the *Rasa, rakta and Mamsa dhatu* is stablised which has reflected in subjects. *Prenana* of *mana* [psychological optimization] was seen through less frequency of Anxiety and depression, *Jeevan karma* of *rakta* was noticed by reduced number of Blood transfusion and *Mamsa dhatu karma* by weight loss prevention, in CCRT+MB group. Similarly, the hoarseness of voice that is *rasa kashaya lakshana* was seen in only 2 subjects CCRT+MB group in comparison to CCRT group which had 30 subjects.

Overall, its known that signaling mechanisms controlling cell division, proliferation, and death have been linked to *vata dosha*. Movements of molecules, cells, nutrients, and waste products are likewise regulated by vata dosha (preliminary network pharmacology of *Jeevanthyadi Ghrita* showed regulation genes like JAK-STAT, PI3K-Akt and PPAR pathways). Transformational functions including energy creation, metabolism, immune maintenance, and digestion are under the purview of the *Pitta Dosha. Pitta Dosha* is linked, at the cellular level, to the functions of hormones, growth factors, enzymes, and the processes necessary for maintaining basal metabolism and energy balance dosha (preliminary network pharmacology of Jeevanthyadi Ghrita showed few genes controlling IL-6 and TNF-α that are inflammatory markers). The kapha dosha regulates body mass, shape, and flexibility. At the cellular level, *Kapha Dosha* may be linked to anabolic processes (such as the production of macromolecules) and the coordination of gene and protein function. (Protein Protein Interaction showed that *Jeevanthaydi ghrita* can prevent weight loss.)[187]

There are encouragements and evidences tracing up saying that *Ayurveda* may not be substitute to conventional therapies but has potential to be supportive and palliative care in coherence to conventional therapies. This study can be an evidence-based document to strengthen the dialogue of safety concern and efficacy note of Traditional medicines especially Indian system of medicine Ayurveda. However, the study sample was moderate and can be evaluated in larger population.

8. SUMMARY

Concurrent Chemoradiation therapy (CCRT) happens to be the primary line of management in cancers of Head and Neck, oesophageal, lung and cervix. Pan Xin Bin etal2017, Zhang L et al 2022 and Tsan YH et al 2021 indicate that this treatment induced symptoms have negative effect on different domains of quality-of-life scales (assessed by EORTC-QLQ30 and FACT scores) and treatment outcomes in long term. Timely managing these toxicities is of prime importance since it can affect the treatment course and the outcome of the patient in his physical, mental and social wellbeing

Considering the CCRT induced adverse effects/events/toxicities as *visha* and *virudha aushadhi lakshan*a and eventual pathology of *rajayakshma* and decreased *oja*. *Jeevanthyadi Ghrita* told in *Rajayaksham adhikara* [Debilitating disease] by Acharya's was chosen as medicine in the form of *matra basti* [retention lipid enema] as a mode of to prevent the concurrent chemotherapy induced adverse effects.

Jeevanthyadi ghrita was prepared with traditionally prepared *ghrita* of Hallikar cow breed after preliminary phytochemical and physicochemical analysis of raw drugs. Standard operating procedure as mention in the Ayurveda Formulary of India was followed to prepare the *Jeevanthyadi ghrita*. *Jeevanthyaid ghrita* was packed in 55 ml ready to give *matra basti* pouches for ease of administration during the clinical trial.

Prepared *Jeevanthyadi ghrita* was subjected to analyze basic ghee parameters, quantification of phytochemicals, High-performance thin layer chromatography (HPTLC), Gas chromatography–mass spectrometry (GC–MS), Liquid

chromatography-mass spectrometry (LC-MS) for standardization. Then identified active compounds form GC-MS and LC-MS were subjected to preliminary network pharmacology for understanding any role in CCRT induced adverse effects like nausea vomiting, loss of appetite etc.

Analysis of all the ingredients of the *Jeevanthyadi ghrita* showed characteristic macroscopic features. Normal range of values of preliminary physico-chemical parameters and Qualitative phytochemical screening showed presence of sugars, flavonoids, tannins, alkaloids, steroids and saponins which were in consensus as per API. Quantitative phytochemical screening of *Jeevanthyadi ghrita* showed presence of Alkaloids and terpenoid. HPTLC of *Jeevanthyadi ghrita* showed 7 peaks and 10 peaks at 256 and 366 nm respectively. While the GC-MS showed presence of 17 peaks [active compounds and fatty acids] and LC-MS showed presence of more than 60 compounds out of which 40 were identified and forwarded for preliminary network pharmacology. Basic parameters of ghee were as per AGMARK standards.

Clinical trial was begun after obtaining ethical clearance and registering at Clinical Trail registry of India. Study was randomized controlled trial conducted at Karnataka Cancer Therapy Research Institute Hubballi, Karnataka. Study sample of 70 in each arm was (Control- CCRT and study arm- CCRT+MB) was considered after calculating the sample size. Randomization was done with envelop method after considering the Inclusion and exclusion criteria with participant blinding.

A total of 257 subjects were screened, out of which 218 were eligible based on Inclusion criteria. Among them 140 consented for the study and each arm had 38 Head and Neck, 22 Cervical and 10 Esophagus Cancer subjects. Both Control group (CCRT, n=70) and Trail group [CCRT+MB, n=70] received Concurrent

Chemoradiation therapy with weekly Cisplatin (40mg/m^2) and Radiation fractions based on type of cancer (25-35#). Trail group additionally received *Jeevanthyadi ghrita Matra basti* for three consecutive days just before every chemotherapy cycle for six weeks.

All the subjects were assessed for Primary outcome i,e Quality of Life using EORTC-QLQ-30 core questionnaire as a tool along with supplement scales of respective cancers (H&N-43, CX-24 and OES-18) every week. Secondary outcomes were assessed at three time points (Before, Mid and Post Trial) namely Adverse effects (assessed through CTCAE version 5), Safety parameter through CBC, Liver function test, serum urea and creatinine. Performance status was assessed by ECOG-PS scale.

Overall, Quality of life was significantly different ($p<0.05$) between CCRT and CCRT+MB group subjects. CCRT+MB had better mean scores in domains of **Physical, social, emotional, cognitive** functions and in symptoms like **nausea, vomiting, pain, dyspnoea, insomnia, constipation, diarrhoea and financial difficulty**.

In Head and Neck cancer subjects, Quality-of-Life scores of CCRT and CCRT+MB group was significantly different [$p<0.05$] in **Physical, Role, Social, Cognitive functions** and Symptoms namely**, Fatigue, Nausea & Vomiting, Pain, Dyspnoea, Insomnia, Appetite, Constipation, Diarrhoea and financial difficulty** group. Independent 't' test showed significant difference [$p<0.001$] in scores between CCRT and CCRT+MB groups in majority of symptoms. However, there was no statistical difference observed in swallowing, Dry mouth, sticky saliva, Pain opening mouth and cough but the mean scores were better in

CCRT+MB. indicating the role of *Jeevanthaydi ghrita* in sustaining quality of life and amelioration of CCRT induced side effects in Head and Neck cancer subjects

In Cervical cancer subjects, Quality-of-Life scores of CCRT and CCRT+MB group over a period was significantly different [$p<0.05$] **in all domains and symptoms** except for Fatigue, Appetite and Diarrhoea. However, the mean score values of these parameters were better in CCRT+MB group. Independent 't' test showed significant difference [$p<0.05$] in scores between CCRT and CCRT+MB groups in all scale namely symptom score, body image, Peripheral neuropathy and menopausal symptoms.

In oesophagus cancer subjects, Quality-of-Life scores of CCRT and CCRT+MB group over a period showed significant difference [$p>0.05$] in all domain and symptoms except Global Health, Physical function and pain score. In symptoms scale Independent 't' test showed no significant difference [$p>0.05$] in scores between CCRT and CCRT+MB groups in symptoms scales.

There were totally 40 symptoms noted in entire study. Independent 't' test showed significant difference [ranging from $p<0.001$ – $p<0.05$] in symptoms grading in 13 major symptoms induced by CCRT at 5^{th} week in CCRT and CCRT+MB. Independent 't' test showed significant difference [$p<0.001$] in both CCRT and CCRT+MB groups in 11 symptoms like Tastelessness, burning sensation in oral cavity/mouth, burning micturition, fatigue, Cough, Mucositis, Sticky saliva, Dry mouth, Oral Ulcers, Skin Discoloration and skin peeling. Here the difference noted was that in CCRT group there was considerable percentage of subjects suffering from grade 3 toxicities while the same was not evident in

CCRT+MB group indicating that *Jeevanthadi ghrita* has a role in anchoring the symptoms from getting worsen or go to next grades.

There were two cases in CCRT group who suffered serious adverse effects one subject had radiation induced blurred vision and another subject had herpes infection. While one subject sustained a fracture [due to fall on the day of chemotherapy]. It was also noteworthy that Loss of appetite was ranking first in CCRT group [Annexure, weekly ranking of complaints] throughout the study for six weeks.

There was no significant difference in safety parameters like Complete blood count, Liver function test, serum urea and creatinine in both CCRT and CCRT+MB groups. This deliberates that *Jeevanthyadi ghrita* has no negative effect on the blood, renal and liver profiles when administered along with concurrent chemoradiation therapy.

Performance status showed significant difference [$p<0.001$] in between CCRT and CCRT+MB groups at mid trail and post-trial. At 5^{th} week of trial, the percentage of subjects with performance status 2 was on higher in CCRT group [72.3] in comparison to CCRT+MB [21.7].

In case of compliance and cancellation of Chemotherapy cycles there was significant difference between CCRT and CCRT+MB group. Similarly in case Adverse events like Number of Hospitalizations, Blood transfusions and Morphine prescriptions for pain was significantly different between CCRT and CCRT+MB group. Additionally, if one sees the percentage of blood transfusions there was difference in CCRT and CCRT+MB group as mentioned earlier. This hints that there

is an undeniable role of *JG matra basti* in preventing hematological toxicity or thrombocytopenia.

Another major finding was loss of weight, which was significant in CCRT group when compared to CCRT+MB group. This was predominantly seen in Head and Neck cancer subjects and not so significant in cervical and esophagus cancer subjects.

Jeevanthyadi ghrita has demonstrated the presence of various bioactive compounds, such as terpenoids and alkaloids, which are known to inhibit lipid peroxidation and downregulate pro-inflammatory cytokines like TNF-α, IL-6, and IL-2, indicating their anti-inflammatory, immunomodulatory, analgesic, anti-pyretic, and anti-cancerous properties.

In present study the complaints of appetite, insomnia, pain was ameliorated by *JG matra basti* and anxiety and depression showed no difference form baseline to last week, which indicate that *JG matra basti* might have its role in anchoring them. Pearson correlation coefficient showed positive relation between taking *basti* and compliance of chemotherapy (r =0.349**) and a negative co-relation between cancelation and Basti taken (r = - 0.423**) Pearson correlation coefficient showed positive relation between taking *JG matra Basti* and compliance of chemotherapy (r =0.349**) and a negative co-relation between cancelation and *JG matra Basti* taken (r = - 0.423**). Basti treatment may work as a stimulant for both the entire body and the gastrointestinal tract. Serotonin, enteroglucagon, and vasoactive intestinal polypeptide (VIP), which stimulate the dopaminergic neural system, are examples of regulatory peptides produced in the colon. There are encouragements and evidences tracing up saying that *Ayurveda* may not be substitute to conventional therapies but has potential

to be supportive and palliative care in coherence to conventional therapies. This study can be an evidence-based document to strengthen the dialogue of safety concern and efficacy note of Traditional medicines especially Indian system of medicine Ayurveda.

9. CONCLUSION

Jeevanthyadi Ghrita matra basti shows trend of improvement in Quality of life in Physical, Role, Emotional and Social functioning.

Jeevanthyadi Ghrita matra basti showed Amelioration of GI tract symptoms like Loss of Appetite, Constipation and Nausea Vomiting. It also showed effect over pain, insomnia and urinary urgency.

Jeevanthyadi Ghrita matra basti showed no statistically significant difference in drymouth, sticky saliva, mucositis and fatigue. However, the mean scores were better in comparison to CCRT group.

Jeevanthyadi Ghrita matra basti was also significant in managing neurological symptoms like Anxiety and depression.

Jeevanthyadi Ghrita matra basti was also significant in Sustenance of Physical strength assessed by ECOG.

Jeevanthyadi Ghrita matra basti was also significant in reducing the Adverse events like Hospitalizations, Blood Transfusions and Morphine prescriptions for Pain.

Jeevanthyadi Ghrita matra basti showed that it is safe to be administered along with concurrent chemoradiation therapy as seen through complete blood count, liver function test, serum urea and creatinine.

Additionally, *Jeevanthyadi Ghrita matra basti* showed that it can prevent weight loss especially in Head and neck cancer subjects.

Above all *Jeevanthyadi Ghrita matra basti* showed tangible outcome of better compliance to concurrent chemoradiation therapy.

10. LIMITATION OF STUDY

1. Heterogenous populations.
2. Oesophagus cancer subjects were only 10.
3. Acceptance of *Matra Basti* as a mode of therapy in conventional setting was initially a sceptical approach however later it was accepted.

11. RECOMMENDATIONS FOR FURTHER STUDY

1. Inflammatory markers can complete the circle of evidence-based medicine.

2. Plain Ghee can be used as another group or as standalone.

3. Esophagus cancer subjects can be taken in larger sample.

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ANNEXURES

ANNEXURE 1 : ETHICAL CLEARANCE AND CTRI REGISTRATION

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Formerly known as KLE University)
(Deemed-to-be-University established u/s 3 of the UGC Act, 1956)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC Campus, Nehru Nagar, Belagavi-590 010, Karnataka State, India
☎: 0831-2444444 FAX: 0831-2493777 Web: http://www.kledeemeduniversity.edu.in E-mail: info@kledeemeduniversity.edu.in

Ref.No.KAHER/EC/19-20/ 290619005 28th June 2019

To,
Dr. Santosh F. Patil
Part-Time Ph.D. Research Scholar,
2018-19 Batch, Faculty of Ayurveda,
KAHER, Belagavi.

Dear Research Scholar,

The KAHER Ethics Committee on Human Subjects for Ph.D. Research Project met on th **14th May 2019** to consider your application for approval of the research project **"Evaluation of Jeevanthyadi Ghrita Matra Basti on Chemo-radiation induced adverse events in Cancer patients."**

As there are no ethical issues involved in your proposed research project, the committee has provided approval for this research project.

You are requested to report to Ethical Committee of the following:

1. Any deviation from or change of the protocol.
2. Any changes in study documents.

(Dr. Anita Dalal)
Member-Secretary
Ethical Committee (Human) for Ph. D. Research
KAHER, Belagavi.

(Dr. B.C. Kotinatot)
Chairman
Ethical Committee (Human) for Ph. D. Research
KAHER, Belagavi.

CC to: - The Director Research Foundation, KAHER, Belagavi.
- The Director Academic Affairs, KAHER, Belagavi.
- The Registrar, KAHER, Belagavi.
- Special Officer to Hon. Vice Chancellor, KAHER, Belagavi.

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Formerly known as KLE University)
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☎: 0831-2444444 FAX: 0831-2493777 Web: http://www.kledeemeduniversity.edu.in E-mail: info@kledeemeduniversity.edu.in

Ref.No.KAHER/EC/22-23/ 2504 22001 12th April 2022

To,
Dr. Santosh F. Patil
Part-Time Ph.D. Research Scholar,
2018-19 Batch, Faculty of Ayurveda,
KAHER, Belagavi.

Dear Research Scholar,

Your application for change in the Study was forwarded to the KAHER Ethics Committee on Human Subjects for Ph.D. Research Project to consider for the research project **"Evaluation of Jeevanthyadi Ghrita Matra Basti on Chemo-radiation induced adverse events in Cancer patients".** The same has been approved by the committee.

As there are no ethical issues involved in your proposed research project, the committee has provided approval for this research project.

You are requested to report to Ethical Committee of the following:

1. Any deviation from or change of the protocol.
2. Any changes in study documents.

(Dr. Sheetal U. Harakuni)
Member-Secretary
Ethical Committee (Human) for Ph. D. Research
KAHER, Belagavi.

(Dr. B.C. Kotinatot)
Chairman
Ethical Committee (Human) for Ph. D. Research
KAHER, Belagavi.

CC to: - The Director Research Foundation, KAHER, Belagavi.
- The Director Academic Affairs, KAHER, Belagavi.
- The Registrar, KAHER, Belagavi.
- Special Officer to Hon. Vice Chancellor, KAHER, Belagavi.

CLINICAL TRIALS REGISTRY - INDIA
ICMR - National Institute of Medical Statistics

PDF of Trial
CTRI Website URL - http://ctri.nic.in

Clinical Trial Details (PDF Generation Date :- Mon, 29 Jan 2024 04:31:54 GMT)

CTRI Number	CTRI/2021/03/032043 [Registered on: 16/03/2021] - **Trial Registered Prospectively**
Last Modified On	09/07/2022
Post Graduate Thesis	Yes
Type of Trial	Interventional
Type of Study	Ayurveda Radiation Therapy Process of Care Changes
Study Design	Randomized, Parallel Group Trial
Public Title of Study	Ayurveda management in cancer side effects
Scientific Title of Study	Evaluation of Jeevanthyadi Ghrita matra basti on Chemo-radiation induced adverse events in cancer patients

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	Dr Santosh F Patil
Designation	Assistant Professor
Affiliation	KAHER Shri B M Kankanawadi Ayurveda Mahavidyalaya
Address	KAHER Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi, Karnataka. Belgaum KARNATAKA 590003 India
Phone	9886633099
Fax	
Email	dr.santosh19@gmail.com

Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Dr Santosh F Patil
Designation	Assistant Professor
Affiliation	KLE University
Address	KLE Shri B M Kankanawadi Ayurveda Mahavidyalaya Nath Pai circle, Shahpur Belagavi Karnataka Belgaum KARNATAKA 590003 India
Phone	09886633099
Fax	
Email	dr.santosh19@gmail.com

Details Contact Person (Public Query)

Details Contact Person (Public Query)	
Name	Dr Santosh F Patil
Designation	Assistant Professor
Affiliation	KAHER Shri B M Kankanawadi Ayurveda Mahavidyalaya
Address	KAHER Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi, Karnataka. Belgaum KARNATAKA 590003 India

ANNEXURE 2: RAW DRUG AUTHENTICATION AND ANALYSIS

Dabur
India Ltd.

12-01-2021

TO WHOMSOEVER IT MAY CONCERN

Authentication Certificate

This is to certify that following authentic Raw herbs were provided to ***Dr Santosh F Patil***, Ph.D Scholar and Assistant Professor Department of ***Agadatantra*** for his Ph.D study entitled **"Evaluation of Jeevanthyadi Ghrita matra basti on Chemo-radiation induced adverse events in cancer patients"**

Sl no	Drug	Latin name	Part
1.	Jeevanti	*Leptadenia reticulata* Wight and Am.	Whole Plant
2.	Yasthimadhu	*Glycyrrhiza glabra* linn	Root
3.	Draksha	*Vitis vinifera* Linn.	Fruit
4.	Kutaja	*Holerrhena antidysentrica* Wall.	Stem bark
5.	Pushkaramula	*Inula racemosa* Hook.F.	Root
6.	Sati	*Hedychium spicatum* Ham.Ex Smith.	Rhizome
7.	Pippali	*Piper longum* Linn.	Fruit
8.	Gokshura	*Tribulus terrestris* Linn.	Fruit
9.	Bala	*Sida cordifolia* Linn.	Root
10.	Nilothpala	*Nymphaea nouchali* Burm.F.	Flower
11.	Bhumyamalaki	*Phyllanthus amarus* Schum & Thonb.	Whole plant

Dr. Vedula. Sasibhushan
Health care Research

Dabur Research & Development Centre
Plot No. 22, Site IV, Sahibabad-201010, Ghaziabad (U.P.), India, Tel: (0120) 3378400 (30 Lines) Fax: (0120) 4552645
Regd. Office: 8/3, Asaf Ali Road, New Delhi - 110 002 (India)
CIN: L24230DL1975PLC007908, Email: corpcomm@dabur.com, Website: www.dabur.com

राष्ट्रीय पारम्परिक चिकित्साविज्ञान संस्थान
ICMR-NATIONAL INSTITUTE OF TRADITIONAL MEDICINE
(भूतपूर्व क्षेत्रीय आयुर्विज्ञान अनुसंधान केन्द्र **Formerly Regional Medical Research Centre**)
Nehru Nagar, Belagavi-590 090

भारतीय आयुर्विज्ञान अनुसंधान परिषद
INDIAN COUNCIL OF MEDICAL RESEARCH
स्वास्थ्य अनुसंधान विभाग, स्वास्थ्य और परिवार कल्याण मंत्रालय, भारत सरकार
Department of Health Research,
Ministry of Health & Family Welfare, Govt. of India

Dr. Harsha Hegde
Scientist-E
harshah@icmr.gov.in

Date: 22-02-2022

AUTHENTICATION

This is to authenticate that the plant material brought by Dr. Santosh Patil, KLE Shri BMK Ayurveda Mahavidyalaya, Belagavi, is identified as ***Gentiana kurroo* Royle.** belonging to family Gentianaceae. The herbarium specimen of the same has been deposited in our herbaria with accession number RMRC-1677.

Harsha Hegde
Scientist-E

SHRI B.M.K. AYURVEDA MAHAVIDYALAYA

A constituent unit KLE Academy of Higher Education & Research
Deemed–to-be-University
Central Research Facility
DRUG AUTHENTICATION REPORT

Submitted By: Dr. Santosh F. Patil

Submitted Date: 07/01/2020

Date of Issue: 11/01/2020

S N	Sample Name	Scientific Name	Family	Part submitted	CRF Code	Authenticated as			
						Ayurvedic Name	Scientific Name	Family	Part Authenticated
1.	Jivanti	*Leptadenia reticulata* W. & A	Asclepiadaceae	Whole plant	CRF/Auth / 2020/06	Jivanti	*Leptadenia reticulata* W. & A	Asclepiadaceae	Whole plant
2.	Yastimadhu	*Glycyrrhiza glabra* Linn.	Fabaceae	Root	CRF/Auth / 2020/07	Yastimadhu	*Glyceyrrhiza glabra* L	Fabaceae	Root
3.	Draksha	*Vitis vinifera* L	Vitaceae	Fruit	CRF/Auth / 2020/08	Draksha	*Vitis vinifera* L	Vitaceae	Fruit
4.	Kutaja	*Holarrhena antidysenterica* Wall	Apocynaceae	Stem bark	CRF/Auth / 2020/09	Kutaja	*Holarrhena antidysenterica* Wall	Apocynaceae	Stem bark
5.	Pushkarmula	*Inula racemosa* Hook.F.	Asteraceae	Root	CRF/Auth / 2020/10	Pushkarmula	*Inula racemosa* Hook.F.	Asteraceae	Root

Signature:
Authentication Expert Name: Mr. Ajit Lingayat
Date: 11/01/2020

CRF SHAHAPUR, BELGAUM

Signature of Coordinator
ASU Drug Testing Laboratory

SHRI B.M.K. AYURVEDA MAHAVIDYALAYA

A constituent unit KLE Academy of Higher Education & Research
Deemed–to-be-University
Central Research Facility
DRUG AUTHENTICATION REPORT

6.	Sati	*Hedychium spicatum* Ham Ex. Smith	Zingiberaceae	Rhizome	CRF/Auth / 2020/11	Sati	*Hedychium spicatum* Ham Ex. Smith	Zingiberaceae	Rhizome
7.	Pippali	*Piper longum* L	Piperaceae	Fruit	CRF/Auth / 2020/12	Pippali	*Piper longum* L	Piperaceae	Fruit
8.	Kantakari	*Solanum surattnse* Burm.f	Solanaceae	Root	CRF/Auth / 2020/13	Kantakari	*Solanum surattnse* Burm.f	Solanaceae	Root
9.	Gokshura	*Tribulus terrestris* L	Zygophyllaceae	Fruit	CRF/Auth / 2020/14	Gokshura	*Tribulus terrestris* L	Zygophyllaceae	Fruit
10.	Bala	*Sida cordifolia* L.	Malvaceae	Root	CRF/Auth / 2020/15	Bala	*Sida cordifolia* L.	Malvaceae	Root
11.	Nilotphala	*Nymphaea Nauchali* Burm.F.	Nymphaeaceae	Flower	CRF/Auth / 2020/16	Nilotphala	*Nymphaea Nauchali* Burm.F.	Nymphaeaceae	Flower
12.	Bhumyamalaki	*Phyllanthus amarus* S & Th.	Euphorbiaceae	Whole plant	CRF/Auth / 2020/17	Bhumyamalaki	*Phyllanthus amarus* S & Th.	Euphorbiaceae	Whole plant
13.	Trayaman	*Gentiana kurroo* Royle	Gentianaceae	Rhizome	CRF/Auth / 2020/18	Trayaman	*Gentiana kurroo* Royle	Gentianaceae	Rhizome
14.	Duralabha	*Fagonia cretica* L.	Zygophyllaceae	Whole plant	CRF/Auth / 2020/19	Duralabha	*Fagonia cretica* L.	Zygophyllaceae	Whole plant

Signature:
Authentication Expert Name: Mr. Ajit Lingayat
Date: 11/01/2020

K.L.E. University's Shri B. M. Kankanwadi Ayurveda Mahavidyalaya CRF SHAHAPUR, BELGAUM

Signature of Coordinator
ASU Drug Testing Laboratory

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/159/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Jeevanti — Batch No. : NA — Part/Form : Whole plant
Product : PLANT — Sample Qty: 50 gm — Report Date : 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	RESULTS
PART	: Whole plant
COLOUR	: Dull yellowish
TASTE	: Bitter
ODOUR	: Odourless

Physico Chemical Standards :

TESTS	RESULTS
Foreign Matter	:Nil
Ash Value	:6.280 %
Acid insoluble Ash	:1.483 %
Water soluble extractive	:5.834 %
Alcohol soluble extractive	:1.916 %

Note : **API** Standards are not Available.Given results are of the submitted sample.

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/RM/159/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample :Jeevanti — Batch No.: NA — Part/Form :Whole plant
Product : PLANT — Sample Qty:50gm — Report Date :27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Negative
Test for Monosaccharides	Positive	Negative
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Positive	Positive
Test for Flavonoids	Positive	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Negative	Negative
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/160/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Yashtimadhu — Batch No. : NA — Part/Form : Root
Product : PLANT — Sample Qty : 50 gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Root	: Root
COLOUR	Yellowish brown or dark brown	: Yellowish brown or dark brown
TASTE	Sweetish	: Sweetish
ODOUR	Faint and Characteristic	: Faint and Characteristic

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Nil	:Nil
Ash Value	Not more than 10%	:7.157 %
Acid insoluble Ash	Not more than 2.5%	:1.590 %
Water soluble extractive	Not less than 20%	:22.231 %
Alcohol soluble extractive	Not less than 10%	:11.460 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/RM/160/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Yastimadhu — Batch No. : NA — Part/Form : Root
Product : PLANT — Sample Qty: 50gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Positive
Test for Monosaccharides	Positive	Positive
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Positive	Negative
Test for Amino Acids	Positive	Negative
Test for Steroids	Negative	Positive
Test for Flavonoids	Positive	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Positive
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/176/2021-22

Reference No:CRF/RM/161/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Draksha — Batch No. : NA — Part/Form : Fruit
Product : PLANT — Sample Qty: 50 gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT

Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Fruit	: Fruit
COLOUR	Dark brown to black	: Dark brown to black
TASTE	Sweet	: Sweet
ODOUR	Sweetish and Pleasant	: Sweetish and Pleasant

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 2%	:Nil
Ash Value	Not more than 3%	:1.870 %
Acid insoluble Ash	Not more than 0.2%	:0.146 %
Water soluble extractive	Not less than 70%	:82.982 %
Alcohol soluble extractive	Not less than 25%	:33.492 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/RM/161/2021-22 — Registration Dt:-31/05/2021
Submitted by: Dr.Santosh Patil — Requisition No:-------
Sample : Draksha — Batch No. : NA — Part/Form : Fruit
Product : PLANT — Sample Qty:50gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT

Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Positive
Test for Monosaccharides	Negative	Negative
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Positive
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Negative	Positive
Test for Flavonoids	Negative	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Negative
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/214/2021-22

Reference No:CRF/RM/162/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Kutaja — Batch No. : NA — Part/Form : Stem bark
Product : PLANT — Sample Qty: 50 gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT

Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Stem Bark	: Stem bark
COLOUR	Buff to Brownish	: Buff to Brownish
TASTE	Acrid and bitter	: Acrid and bitter

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 2%	:Nil
Ash Value	Not more than 7%	:6.552 %
Acid insoluble Ash	Not more than 1%	:0.880 %
Water soluble extractive	Not less than 10%	:15.933 %
Alcohol soluble extractive	Not less than 18%	:22.187 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/RM/162/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Kutaja — Batch No. :NA — Part/Form: Stem Bark
Product : PLANT — Sample Qty:50gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT

Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Negative
Test for Monosaccharides	Positive	Positive
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Positive
Test for Proteins	Negative	Positive
Test for Amino Acids	Negative	Positive
Test for Steroids	Negative	Negative
Test for Flavonoids	Negative	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Positive
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST — AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/[illegible]/2021-22

Reference No:CRF/RM/163/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Pushkarmula — Batch No. : NA — Part/Form : Root
Product : PLANT — Sample Qty: 50 gm — Report Date:27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Root	: Root
COLOUR	Brownish grey	: Brownish grey
TASTE	Bitter and camphoraceous	: Bitter and camphoraceous
ODOUR	Camphoraceous and aromatic	: Camphoraceous and aromatic

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 2%	:Nil
Ash Value	Not more than 5%	:4.886 %
Acid insoluble Ash	Not more than 0.6%	:0.345 %
Water soluble extractive	Not less than 20%	:25.824 %
Alcohol soluble extractive	Not less than 10%	:14.342 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

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Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/RM/163/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Pushkarmula — Batch No. : NA — Part/Form:Root
Product : PLANT — Sample Qty:50gm — Report Date:27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Positive
Test for Monosaccharides	Positive	Positive
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Negative	Negative
Test for Flavonoids	Positive	Positive
Test for Alkaloids	Negative	Positive
Test for Tannins	Positive	Positive
Test for Glycosides:		
A.Cardiac Glycosides	Positive	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Negative	Negative

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Outward No:-BMK/CRF/[illegible]/2021-22

Reference No:CRF/RM/164/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Sati — Batch No. : NA — Part/Form : Rhizome
Product : PLANT — Sample Qty: 50 gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Rhizome	: Rhizome
COLOUR	Yellowish-brown to dark brown	: Yellowish-brown to dark brown
TASTE	Bitter	: Bitter
ODOUR	Camphoraceous	: Camphoraceous

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 1%	: Nil
Ash Value	Not more than 8%	:7.870 %
Acid insoluble Ash	Not more than 2%	:1.377 %
Water soluble extractive	Not less than 8%	:9.101 %
Alcohol soluble extractive	Not less than 4%	:7.824 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

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Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/RM/164/2021-22 — Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil — Requisition No:-----
Sample : Sati — Batch No. : NA — Part/Form: Rhizome
Product : PLANT — Sample Qty:50gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Negative
Test for Monosaccharides	Positive	Negative
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Positive
Test for Amino Acids	Negative	Positive
Test for Steroids	Negative	Positive
Test for Flavonoids	Negative	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Negative
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

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Outward No:-BMK/CRF/376/2021-22

Reference No:CRF/RM/165/2021-22
Submitted by: Dr.Santosh Patil
Sample : Pippali
Product : PLANT
(* N/A - Not Available)
Batch No. : NA
Sample Qty: 50 gm
Registration Dt:-31/05/2021
Requisition No:-------
Part/Form: Fruit
Report Date:27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Fruit	: Fruit
COLOUR	Greenish-black to black	: Greenish-black to black
TASTE	Pungent	: Pungent
ODOUR	Aromatic	: Aromatic

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 2%	:Nil
Ash Value	Not more than 7%	:6.611 %
Acid insoluble Ash	Not more than 0.5%	:0.386 %
Water soluble extractive	Not less than 7%	:43.027 %
Alcohol soluble extractive	Not less than 5%	:9.258 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

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Outward No:-BMK/CRF/376/2021-22

Reference No:CRF/RM/165/2021-22
Submitted by: Dr.Santosh Patil
Sample : Pippali
Product : PLANT
(* N/A - Not Available)
Batch No : NA
Sample Qty: 50gm
Registration Dt:-31/05/2021
Requisition No:-------
Part/Form : Fruit
Report Date: 27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Positive
Test for Monosaccharides	Negative	Positive
Test for Pentose Sugar	Positive	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Positive
Test for Steroids	Negative	Negative
Test for Flavonoids	Positive	Positive
Test for Alkaloids	Negative	Positive
Test for Tannins	Positive	Positive
Test for Glycosides:		
A.Cardiac Glycosides	Positive	Positive
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Negative	Negative

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Outward No:-BMK/CRF/377/2021-22

Reference No:CRF/RM/166/2021-22
Submitted by:Dr.Santosh Patil
Sample : Kantakari
Product : PLANT
(* N/A - Not Available)
Batch No. : NA
Sample Qty : 50 gm
Registration Dt:-31/05/2021
Requisition No:-------
Part/Form : Root
Report Date : 27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	RESULTS
PART	: Root
COLOUR	: Light Brownish
TASTE	: Bitter
ODOUR	: No Characteristics odour

Physico Chemical Standards :

TESTS	RESULTS
Foreign Matter	: Nil
Ash Value	:6.875 %
Acid insoluble Ash	:0.913 %
Water soluble extractive	:6.088 %
Alcohol soluble extractive	:2.921 %

Note : **API** Standards are not Available.Given results are of the submitted sample.

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Outward No:-BMK/CRF/377/2021-22

Reference No:CRF/RM/166/2021-22
Submitted by: Dr.Santosh Patil
Sample : Kantakari
Product : PLANT
(* N/A - Not Available)
Batch No : NA
Sample Qty: 50gm
Registration Dt:-31/05/2021
Requisition No:-------
Part/Form : Root
Report Date: 27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Positive
Test for Monosaccharides	Positive	Negative
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Negative	Positive
Test for Flavonoids	Positive	Positive
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Negative
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

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Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/167/2021-22 — Registration Dt:-31/05/2021
Submitted by: Dr.Santosh Patil — Requisition No:-------
Sample : Gokshura — Batch No. : NA — Part/Form : Fruit
Product : PLANT — Sample Qty : 50 gm — Report Date : 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Fruit	: Fruit
COLOUR	Light or Greenish yellow	: Light or Greenish yellow
TASTE	Slightly astringent	: Slightly astringent
ODOUR	NA	: Characteristic

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 1%	:Nil
Ash Value	Not more than 15%	:13.667 %
Acid insoluble Ash	Not more than 2%	:1.702 %
Water soluble extractive	Not less than 10%	:16.772 %
Alcohol soluble extractive	Not less than 6%	:7.509 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

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Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/167/2021-22 — Registration Dt:-31/05/2021
Submitted by: Dr.Santosh Patil — Requisition No:-------
Sample : Gokshura — Batch No : NA — Part/Form : Fruit
Product : PLANT — Sample Qty: 50gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Negative
Test for Monosaccharides	Positive	Negative
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Positive	Negative
Test for Amino Acids	Positive	Negative
Test for Steroids	Positive	Positive
Test for Flavonoids	Positive	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Negative
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

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Outward No:-BMK/CRF/275/2021-22

Reference No:CRF/RM/168/2021-22 — Registration Dt:-31/05/2021
Submitted by: Dr.Santosh Patil — Requisition No:-------
Sample : Bala — Batch No. : NA — Part/Form : Root
Product : PLANT — Sample Qty : 50 gm — Report Date : 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	RESULTS
PART	: Root
COLOUR	: Brownish
TASTE	: Not Specific
ODOUR	: Not Specific

Physico Chemical Standards :

TESTS	RESULTS
Foreign Matter	:Nil
Ash Value	:1.588 %
Acid insoluble Ash	:0.962 %
Water soluble extractive	:12.340 %
Alcohol soluble extractive	:3.594 %

Note : **API** Standards are not Available.Given results are of the submitted sample.

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Outward No:-BMK/CRF/275/2021-22

Reference No:CRF/RM/168/2021-22 — Registration Dt:-31/05/2021
Submitted by: Dr.Santosh Patil — Requisition No:-------
Sample : Bala — Batch No : NA — Part/Form : Root
Product : PLANT — Sample Qty: 50gm — Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Negative	Negative
Test for Monosaccharides	Positive	Positive
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Positive	Positive
Test for Flavonoids	Positive	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Positive
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

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Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/169/2021-22 | Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil | Requisition No:-------
Sample : Nilothpala | Batch No. : NA | Part/Form : Flower
Product : PLANT | Sample Qty : 50 gm | Report Date: 22/09/2020
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	RESULTS
PART	: Flower
COLOUR	: Creamish to dark brown
TASTE	: Sour and Astringent
ODOUR	: No Characteristic odour

Physico Chemical Standards :

TESTS	RESULTS
Foreign Matter	:Nil
Ash Value	:12.964 %
Acid insoluble Ash	:3.326 %
Water soluble extractive	:29.002 %
Alcohol soluble extractive	:7.077 %

Note : **API** Standards are not Available.Given results are of the submitted sample.

ANALYST — AUTHORISED SIGNATORY

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Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/169/2021-22 | Registration Dt:-31/05/2021
Submitted by:Dr.Santosh Patil | Requisition No:-------
Sample : Nilothpala | Batch No : NA | Part/Form : Flower
Product : PLANT | Sample Qty: 50gm | Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Negative
Test for Monosaccharides	Positive	Positive
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Positive	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Negative	Positive
Test for Flavonoids	Positive	Positive
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Positive
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST — AUTHORISED SIGNATORY

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Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/170/2021-22 | Registration Dt:-31/05/2021
Submitted by: Dr.Santosh Patil | Requisition No:-------
Sample : Bhumyamalaki | Batch No. : NA | Part/Form : Whole Plant
Product : PLANT | Sample Qty : 50 gm | Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Whole plant	: Whole Plant
COLOUR	Greenish brown	: Greenish brown
TASTE	Slightly bitter	: Slightly bitter
ODOUR	Indistinct	: Indistinct

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 2.0%	: Nil
Ash Value	Not more than 16%	:6.372 %
Acid insoluble Ash	Not more than 7.0%	:0.910 %
Water soluble extractive	Not less than 13%	:15.077 %
Alcohol soluble extractive	Not less than 3%	:4.760 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

ANALYST — AUTHORISED SIGNATORY

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Outward No:-BMK/CRF/274/2021-22

Reference No:CRF/RM/170/2021-22 | Registration Dt:-31/05/2021
Submitted by: Dr.Santosh Patil | Requisition No:-------
Sample : Bhumyamalaki | Batch No : NA | Part/Form : Whole Plant
Product : PLANT | Sample Qty: 50gm | Report Date: 27/07/2021
(* N/A - Not Available)

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Negative
Test for Monosaccharides	Positive	Positive
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Positive
Test for Proteins	Negative	Positive
Test for Amino Acids	Negative	Positive
Test for Steroids	Negative	Negative
Test for Flavonoids	Positive	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Positive
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST — AUTHORISED SIGNATORY

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Outward No:-BMK/CRF/214/2021-22

Reference No:CRF/RM/171/2021-22
Submitted by: Dr.Santosh Patil
Sample : Trayamana
Product : PLANT
(* N/A - Not Available)
Batch No. : NA
Sample Qty : 50 gm
Registration Dt:-31/05/2021
Requisition No:------
Part/Form: Rhizome
Report Date : 27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Rhizome	: Rhizome
COLOUR	Dark brown with yellowish patches	:Dark brown with yellowish patches
TASTE	Bitter	: Bitter
ODOUR	Characteristically Aromatic	: Characteristically Aromatic

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 2%	:Nil
Ash Value	Not more than 7%	:6.450 %
Acid insoluble Ash	Not more than 2%	:1.772 %
Water soluble extractive	Not less than 13%	:31.558 %
Alcohol soluble extractive	Not less than 28%	:29.531 %

(Standards reffered above are as per **API**)
In my opinion the Sample is standard quality

NALYST

CRF BHANAPUR, BELGAUM

AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/214/2021-22

Reference No:CRF/RM/171/2021-22
Submitted by: Dr.Santosh Patil
Sample : Trayamana
Product : PLANT
(* N/A - Not Available)
Batch No : NA
Sample Qty: 50gm
Registration Dt:-31/05/2021
Requisition No:-------
Part/Form : Rhizome
Report Date: 27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Negative	Negative
Test for Monosaccharides	Positive	Negative
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Negative	Negative
Test for Flavonoids	Positive	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Negative
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST

CRF SHAHAPUR, BELGAUM

AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/215/2021-22

Reference No:CRF/RM/172/2021-22
Submitted by: Dr.Santosh Patil
Sample : Duralabha
Product : PLANT
(* N/A - Not Available)
Batch No. :
Sample Qty : 50 gm
Registration Dt:-31/05/2021
Requisition No:-------
Part/Form : Whole Plant
Report Date : 27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Description Macroscopic :

TESTS	LIMITS	RESULTS
PART	Whole plant	: Whole Plant
COLOUR	Yellowish white	: Yellowish white
TASTE	Bitter	: Bitter
ODOUR	NA	: Characteristics

Physico Chemical Standards :

TESTS	LIMITS	RESULTS
Foreign Matter	Not more than 2%	: Nil
Ash Value	Not more than 10%	:9.081 %
Acid insoluble Ash	Not more than 0.4%	:0.397 %
Water soluble extractive	Not less than 10%	:24.072 %
Alcohol soluble extractive	Not less than 5%	:6.712 %

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

ANALYST

CRF SHAHAPUR, BELGAUM

AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/215/2021-22

Reference No:CRF/RM/172/2021-22
Submitted by: Dr.Santosh Patil
Sample : Duralabha
Product : PLANT
(* N/A - Not Available)
Batch No : NA
Sample Qty: 50gm
Registration Dt:-31/05/2021
Requisition No:-------
Part/Form : Whole Plant
Report Date: 27/07/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Preliminary Phytochemical Screening:

TESTS	WATER	ALCOHOL
Test for Carbohydrates	Positive	Positive
Test for Reducing sugar	Positive	Negative
Test for Monosaccharides	Positive	Negative
Test for Pentose Sugar	Negative	Negative
Test for Non reducing sugar	Negative	Negative
Test for Hexose Sugar	Negative	Negative
Test for Proteins	Negative	Negative
Test for Amino Acids	Negative	Negative
Test for Steroids	Positive	Positive
Test for Flavonoids	Positive	Negative
Test for Alkaloids	Negative	Negative
Test for Tannins	Positive	Negative
Test for Glycosides:		
A.Cardiac Glycosides	Negative	Negative
B.Anthraquinone glycosides	Negative	Negative
C.Saponin glycosides	Positive	Negative

ANALYST

CRF SHAHAPUR, BELGAUM

AUTHORISED SIGNATORY

ANNEXURE 3: JEEVANTHYADI GHRITA ANALYSIS

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/911/2021-22

Reference No:CRF/RM/225/2021-22 | Registration Dt:-17/09/2021
Submitted by:Dr.Santosh Patil | Requisition No:------
Sample: Ghrita | Batch No:NA | Product:Animal
(* N/A - Not Available) | Sample Qty: 50 gm | Report Date :01/10/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Organoleptic Characters :

TESTS	LIMITS	RESULTS
Form	Semisolid With granular Texture	: Semisolid With granular Texture
Colour	White to light yellow	: White to light yellow
Odour	Rich & Characteristic	: Rich & Characteristic
Taste	Pleasant	: Pleasant

Physico Chemical Standards :

Moisture Content	Not more than 0.5 %	: 0.291%
Acid Value	NA	: 4.115
Saponification Value	Not more than 225	: 201.24
Iodine Value	Not more than 35	: 33.60

(Standards reffered above are as per **API**)
* In my opinion the Sample is standard quality

ANALYST | AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/FG/271/2021-22 | Registration Dt:-23/09/2021
Submitted by:Dr.Santosh Patil | Requisition No:------
Sample: Jeevanthyadi Ghrita | Batch No.: NA | Part/Form: Ghrita
Ref: Rajyaksham Chikitsa,AH 5/16-17 | Sample Qty: 100ml | Report Date:07/10/2021
(* N/A - Not Available) | Mfg Date:NA | Exp. Date: NA

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Test for specified Micro -Organisms (Qualitative)

	LIMITS (As per IP)	RESULTS
E coli	Absent/100ml	Absent
S aureus	Absent/100ml	Absent
P aeruginosa	Absent/100ml	Absent
S abony	Absent/100ml	Absent

Microbial limit test (Quantitative)

	LIMITS (As per IP)	RESULTS
Total Bacterial Count	30 - 300 cfu/ml	:07cfu/ml
Total Fungal Count	10 - 100 cfu/ml	:01cfu/ml

(Standards reffered above are as per **IP**/In house Specification)
*** In my opinion the Sample is standard quality**

ANALYST | AUTHORISED SIGNATORY

SHRI B M KANKANAWADI AYURVED MAHAVIDYALAYA
A Constituent Unit of KLE ACADEMY OF HIGHER EDUCATION & RESEARCH (DEEMED-TO-BE-UNIVERSITY)
(Re-Accredited 'A' Grade by NAAC (2nd Cycle) || Placed under Category 'A' by MHRD GoI)
CENTRAL RESEARCH FACILITY
(AYUSH Approved ASU Drug Testing Laboratory Lic. No.TL-8/2011)

Outward No:-BMK/CRF/ /2021-22

Reference No:CRF/FG/271/2021-22 | Registration Dt:-23/09/2021
Submitted by:Dr.Santosh Patil | Requisition No:------
Sample: Jivantyadi Ghrita | Batch No: NA | Part/Form:Ghrita
Ref: Rajyaksham Chikitsa,AH 5/16-17 | D/Mfg: NA | D/Exp: NA
(* N/A - Not Available) | Sample Qty: 100ml | Report Date :07/10/2021

TEST REPORT
Form-50 [See Rule 160-D (f)]
(The Drugs & Cosmetic Act 1940 and the rules there under)

Organoleptic Characters :

TESTS	LIMITS	RESULTS
Form	Ghrita	: Ghrita
Colour	Greenish yelllow	: Greenish yelllow
Odour	Pleasant	: Pleasant
Taste	Sweet & Bitter	: Sweet & Bitter

Physico-Chemical Standards :

TESTS	LIMITS	RESULTS
Loss on Drying at 110 C	Not More than 1%	: 0.184%
Saponification Value	220 to 232	: 221.59
Iodine Value	30 to 40	: 32.09
Refractive index at 40 C	1.4524 to 1.4545	: 1.4540
Acid Value	Not more than 3	: 2.893

(Standards reffered above are as **PSAF**)
* In my opinion the Sample is standard quality

ANALYST | AUTHORISED SIGNATORY

CARe KERALAM
Confederation for Ayurvedic Renaissance Keralam Ltd
A joint venture of Ayurvedic Entrepreneurs & KINFRA (Govt. of Kerala), supported by Dept. of AYUSH, Govt. of India

TEST REPORT

Test Report No : CKL/22/ T376 | Date : 26-05-2022

- Name of Customer : Dr Santosh F Patil
- Customer Address : Ph.D Scholar & Asst professor Department of Agada tantra , B.M. Kankanwadi Ayurvedic Mahavidyalaya, Shahpur, Belagavi, Karnataka 590065,
- Manufacturing License no. : Not mentioned
- Test Requisition No. & Date : LWF128 & 09-05-2022
- Date of Sample Received : 09-05-2022
- Sample Analysis Date : 09-05-2022 To 26-05-2022
- Sample Name : Jeevanthyadi Ghrita
- Sample ID : T376
- Batch No : Not mentioned
- Batch Size : Not mentioned
- Date of Manufacturing : Not mentioned
- Date of Expiry : Not mentioned
- Quantity of Sample Received : 100 ml
- Sample Drawn by : The Customer
- Sample Condition : Received in good condition

Parameters	Unit	Result	Test Method
Phytochemical Screening			
Alkaloids	-	Present	Dragendroff's reagent test
Flavonoids	-	Absent	Shinoda test
Glycosides	-	Absent	Picric acid test
Phenol	-	Absent	Folin ciocalteu reagent test
Saponins	-	Absent	Foam test
Tannins	-	Absent	Lead Acetate test
Terpenoids	-	Present	Salkowski reaction test
Steroids	-	Absent	Salkowski reaction test

Page 1 of 2

Authorized Signatory
BASIL ELDHO
TECHNICAL MANAGER

Address: KINFRA Small Industries Park, Nalukettu road, Koratty-680309, Ph: 0480 2735837, Fax: 0480 2735737, E-mail: lab@carekeralam.com

CARe KERALAM

Confederation for Ayurvedic Renaissance Keralam Ltd

A joint venture of Ayurvedic Entrepreneurs & KINFRA (Govt. of Kerala), supported by Dept. of AYUSH, Govt. of India

TEST REPORT

Test Report No : CKL/22/ T376 Date : 26-05-2022

Parameters	Unit	Result	Test Method
Quantification of Phytochemicals			
Alkaloids	%	0.32	Experimental Phytopharmacognosy
Saponins	-	Absent	Standardisation of Botanicals
Flavonoids	-	Absent	CKL/ANL/UV-003
Phenol	-	Absent	CKL/ANL/UV-002
Tannin	-	Absent	CCRAS 40.3
HPTLC Analysis	-	Profile attached	Reference API
GCMS Analysis	-	Profile attached	CKL/ANL/GC-001

Total Number of Determination: 15 only

Page 2 of 2

Authorized Signatory
BASIL ELDHO
TECHNICAL MANAGER

Note: The test results relate only to the sample tested. The report shall not be reproduced except in full, without the written approval of the laboratory

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FAZAL MANZIL, 36, SUVIDHA COLONY, KESHWAPUR, HUBLI - 580023 (KARNATAKA)

E-mail : [illegible] Customer care No : (0836) 2368666, 2268786, 3501089

TEST REPORT

Sheet No 1 of 1

Client	Dr.Santosh Patil,	Report No.	G/ESSAR/SP/003
	KLE BMK, Ayurvedic College	Date of Sampling	18/12/2021
	Belagavi.	Date of Analysis	22/12/2021

Sample Description / Name of the commodity	Sample as submited by the party : Plain (Hallikar Breed) Ghee.
Batch No.	--
Test Device Details	Volumetric, Gravimetric & Instrumental
Test Reference	IS 3508

SL.NO.	PARAMETER	UNIT	OBSERVED VALUE	GRADE SPECIFICATIONS
1.	Baudouin test	--	Negative	Negative
2.	Butro-refractometer reading @ 40 C	--	41.6	40.0 – 43.0
3.	Reichert Meissel Value	--	25.8	Min. 24
4.	Polenske value	--	1.40	1.0 – 2.0
5.	Moisture content	%	0.32	0.3-0.5
6.	Free fatty acid. (as oleic)	%	1.14	2.8 Max
7.	Colour	--	7.50	10
8.	Saturated Fat	%	65.5	--
9.	MUFA	%	17.6	--
10.	PUFA	%	2.80	--
11.	DHA	%	0.04	--
12.	Milk Fat	%	99.2	99-99.5
13.	Cholesterol	%	0.18	0.5 Max

STATEMENT :

- *This report is CONFIDENTIAL and should not be reproduced except in full without written approval of that laboratory.*
- *The test results relate only to the items/samples tested. Endorsement of the product is not implied.*
- *This report is strictly confidential and if any claim in legal disputes is not permitted.*
- *Total liability of our Laboratory is limited to tested invoice amount*
- *Any dispute arising out of this report is subject to Hubli Jurisdiction.*
- *Samples not drawn by us unless otherwise stated.*

Tested By:	Approved By:
Designation: Chemist	Designation: Managing Partner

HUBLI

ESSAR LABORATORIES & RESEARCH CENTRE

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ISO 9001 : 2015 Certified

FAZAL MANZIL, 36, SUVIDHA COLONY, KESHWAPUR, HUBLI - 580023 (KARNATAKA)

E-mail : [illegible] Customer care No : (0836) 2 360666, 2268786, 3501089

TEST REPORT

Sheet No 1 of 1

Client	Dr.Santosh Patil,	Report No.	G/ESSAR/SP/004
	KLE BMK, Ayurvedic College	Date of Sampling	18/12/2021
	Belagavi.	Date of Analysis	22/12/2021

Sample Description / Name of the commodity	Sample as submited by the party : Jeevantyadi Ghee.
Batch No.	--
Test Device Details	Volumetric, Gravimetric & Instrumental
Test Reference	IS 3508

SL.NO.	PARAMETER	UNIT	OBSERVED VALUE	GRADE SPECIFICATIONS
1.	Baudouin test	--	Negative	Negative
2.	Butro-refractometer reading @ 40 C	--	42.2	40.0 – 43.0
3.	Reichert Meissel Value	--	26.5	Min. 24
4.	Polenske value	--	1.36	1.0 – 2.0
5.	Moisture content	%	0.30	0.3-0.5
6.	Free fatty acid. (as oleic)	%	1.24	2.8 Max
7.	Colour	--	7.90	10
8.	Saturated Fat	%	67.5	--
9.	MUFA	%	18.2	--
10.	PUFA	%	2.50	--
11.	DHA	%	0.03	--
12.	Milk Fat	%	99.26	99-99.5
13.	Cholesterol	%	0.20	0.5 Max

STATEMENT :

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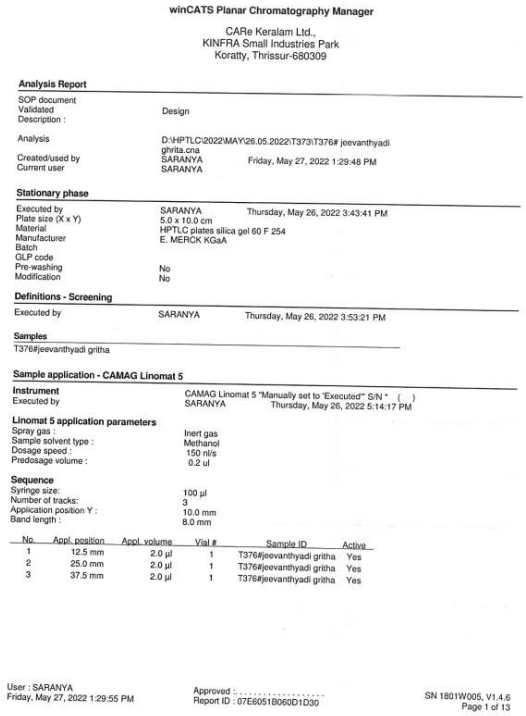
- *Any dispute arising out of this report is subject to Hubli Jurisdiction.*
- *Samples not drawn by us unless otherwise stated.*

Tested By:	Approved By:
Designation: Chemist	Designation: Managing Partner

HUBLI

HPTLC REPORTS



winCATS Planar Chromatography Manager

CARe Keralam Ltd.,
KINFRA Small Industries Park
Koratty, Thrissur-680309

Analysis Report

SOP document
Validated
Description : Design

Analysis D:\HPTLC\2022\MAY\26.05.2022\T373\T376# jeevanthyadi ghrita.cna
Created/used by SARANYA Friday, May 27, 2022 1:29:48 PM
Current user SARANYA

Stationary phase

Executed by SARANYA Thursday, May 26, 2022 3:43:41 PM
Plate size (X x Y) 5.0 x 10.0 cm
Material HPTLC plates silica gel 60 F 254
Manufacturer E. MERCK KGaA
Batch
GLP code
Pre-washing No
Modification No

Definitions - Screening

Executed by SARANYA Thursday, May 26, 2022 3:53:21 PM

Samples

T376#jeevanthyadi gritha

Sample application - CAMAG Linomat 5

Instrument
Executed by CAMAG Linomat 5 "Manually set to "Executed"" S/N * ( )
SARANYA Thursday, May 26, 2022 5:14:17 PM

Linomat 5 application parameters

Spray gas : Inert gas
Sample solvent type : Methanol
Dosage speed : 150 nl/s
Predosage volume : 0.2 ul

Sequence

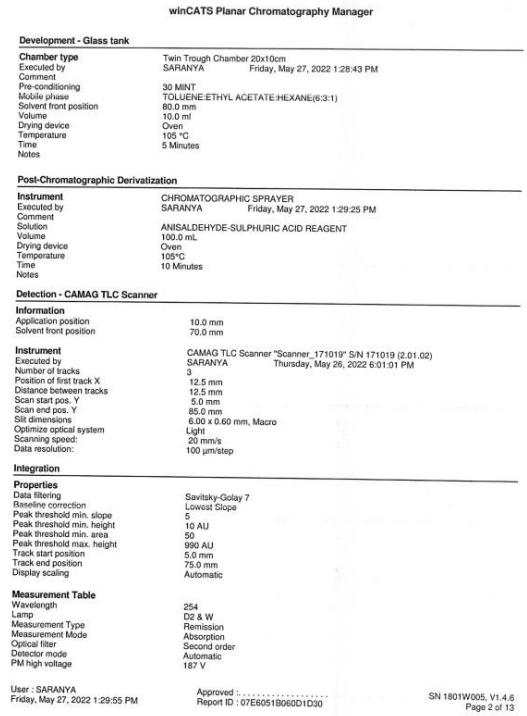
Syringe size: 100 µl
Number of tracks: 3
Application position Y : 10.0 mm
Band length : 8.0 mm

No.	Appl. position	Appl. volume	Vial #	Sample ID	Active
1	12.5 mm	2.0 µl	1	T376#jeevanthyadi gritha	Yes
2	25.0 mm	2.0 µl	1	T376#jeevanthyadi gritha	Yes
3	37.5 mm	2.0 µl	1	T376#jeevanthyadi gritha	Yes

User : SARANYA
Friday, May 27, 2022 1:29:55 PM

Approved : . . . . . .
Report ID : 07E6051B060D1D30

SN 1801W005, V1.4.6
Page 1 of 13



winCATS Planar Chromatography Manager

Development - Glass tank

Chamber type Twin Trough Chamber 20x10cm
Executed by SARANYA Friday, May 27, 2022 1:28:43 PM
Comment
Pre-conditioning 30 MINT
Mobile phase TOLUENE:ETHYL ACETATE:HEXANE(6:3:1)
Solvent front position 80.0 mm
Volume 10.0 ml
Drying device Oven
Temperature 105 °C
Time 5 Minutes
Notes

Post-Chromatographic Derivatization

Instrument CHROMATOGRAPHIC SPRAYER
Executed by SARANYA Friday, May 27, 2022 1:29:25 PM
Comment
Solution ANISALDEHYDE-SULPHURIC ACID REAGENT
Volume 100.0 mL
Drying device Oven
Temperature 105°C
Time 10 Minutes
Notes

Detection - CAMAG TLC Scanner

Information
Application position 10.0 mm
Solvent front position 70.0 mm

Instrument CAMAG TLC Scanner "Scanner_171019" S/N 171019 (2.01.02)
Executed by SARANYA Thursday, May 26, 2022 6:01:01 PM
Number of tracks 3
Position of first track X 12.5 mm
Distance between tracks 12.5 mm
Scan start pos. Y 5.0 mm
Scan end pos. Y 85.0 mm
Slit dimensions 6.00 x 0.60 mm, Macro
Optimize optical system Light
Scanning speed: 20 mm/s
Data resolution: 100 µm/step

Integration

Properties
Data filtering Savitsky-Golay 7
Baseline correction Lowest Slope
Peak threshold min. slope 5
Peak threshold min. height 10 AU
Peak threshold min. area 50
Peak threshold max. height 990 AU
Track start position 5.0 mm
Track end position 75.0 mm
Display scaling Automatic

Measurement Table
Wavelength 254
Lamp D2 & W
Measurement Type Remission
Measurement Mode Absorption
Optical filter Second order
Detector mode Automatic
PM high voltage 187 V

User : SARANYA
Friday, May 27, 2022 1:29:55 PM

Approved : . . . . . .
Report ID : 07E6051B060D1D30

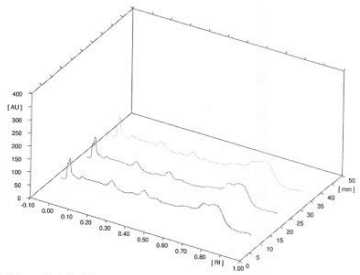
SN 1801W005, V1.4.6
Page 2 of 13

winCATS Planar Chromatography Manager

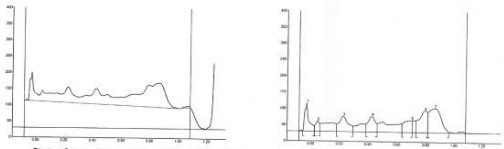
Detector properties

Y-position for 0 adjust	5.0 mm
Track # for 0 adjust	0
Analog Offset	10%
Sensitivity	Automatic (224)

All tracks at WavelengthSc4



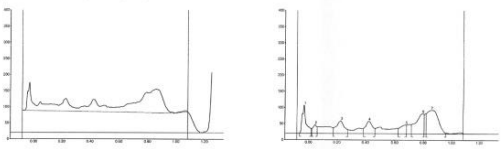
Track 1, ID: T376#jeevanthyadi gritha



Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	-0.05	2.0	-0.03	86.2	21.98	0.02	17.0	1805.6	12.17	unknown *
2	0.02	17.1	0.04	31.7	8.09	0.05	24.0	605.3	4.08	unknown *
3	0.15	23.6	0.19	47.5	12.10	0.25	17.9	2126.4	14.33	unknown *
4	0.33	25.0	0.36	47.6	12.12	0.40	26.2	1737.5	11.71	unknown *
5	0.55	27.6	0.60	37.2	9.48	0.60	35.9	1426.3	9.61	unknown *
6	0.63	37.1	0.68	67.0	17.09	0.70	63.7	2726.6	18.38	unknown *
7	0.70	63.9	0.74	75.0	19.13	0.83	2.5	4410.0	29.72	unknown *

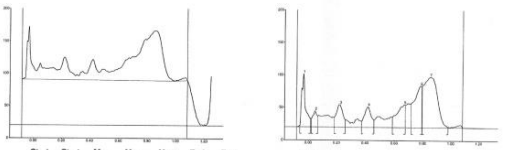
winCATS Planar Chromatography Manager

Track 2, ID: T376#jeevanthyadi gritha



Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	-0.06	0.4	-0.03	87.0	24.60	0.02	14.9	1668.5	13.54	unknown *
2	0.02	15.2	0.04	27.0	7.64	0.05	19.4	508.1	4.12	unknown *
3	0.15	16.7	0.19	39.5	11.16	0.24	12.0	1497.7	12.16	unknown *
4	0.33	15.7	0.36	38.0	10.73	0.40	16.7	1265.2	10.27	unknown *
5	0.54	16.7	0.58	27.3	7.73	0.58	26.5	802.4	6.51	unknown *
6	0.61	28.7	0.68	62.2	17.58	0.69	60.0	2523.6	20.48	unknown *
7	0.70	61.9	0.73	72.7	20.55	0.82	2.1	4055.7	32.92	unknown *

Track 3, ID: T376#jeevanthyadi gritha



Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	-0.05	1.9	-0.03	81.6	23.34	0.01	13.4	1551.7	11.67	unknown *
2	0.02	13.0	0.04	24.7	7.05	0.06	17.1	544.1	4.09	unknown *
3	0.16	14.9	0.19	34.7	9.91	0.22	11.8	1105.8	8.32	unknown *
4	0.32	9.6	0.36	31.9	9.12	0.40	11.6	1065.2	8.01	unknown *
5	0.50	16.2	0.57	35.3	10.09	0.58	34.2	1423.9	10.71	unknown *
6	0.62	36.7	0.67	64.2	18.35	0.68	63.2	2376.6	17.88	unknown *
7	0.68	63.4	0.73	77.4	22.13	0.84	0.8	5226.6	39.32	unknown *

winCATS Planar Chromatography Manager

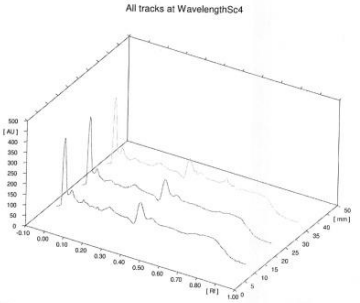
Measurement Table

Wavelength	366
Lamp	Hg
Measurement Type	Remission
Measurement Mode	Fluorescence
Optical filter	K400
Detector mode	Automatic
PM high voltage	187 V

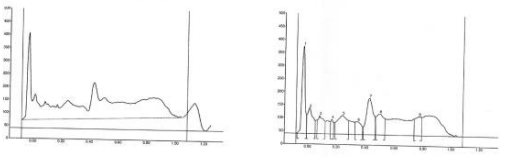
Detector properties

Y-position for 0 adjust	5.0 mm
Track # for 0 adjust	0
Analog Offset	10%
Sensitivity	Automatic (224)

All tracks at WavelengthSc4



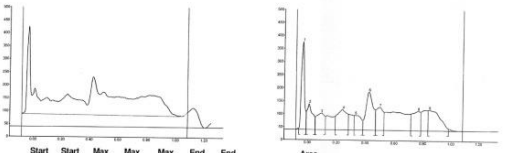
Track 1, ID: T376#jeevanthyadi gritha



winCATS Planar Chromatography Manager

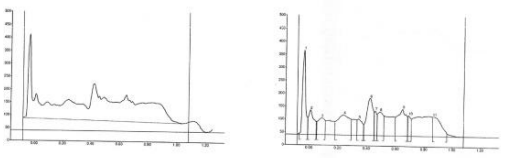
Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	-0.06	2.4	-0.03	335.6	34.55	-0.01	71.2	5121.6	20.52	unknown *
2	-0.01	71.4	0.01	97.7	10.06	0.04	49.2	2703.4	10.83	unknown *
3	0.06	51.9	0.07	69.0	7.11	0.10	47.4	1996.2	8.00	unknown *
4	0.14	46.1	0.14	56.1	5.78	0.16	43.7	739.6	2.96	unknown *
5	0.16	44.7	0.21	72.1	7.42	0.25	52.6	3448.4	13.82	unknown *
6	0.28	46.7	0.30	48.7	5.01	0.33	29.7	1387.8	5.56	unknown *
7	0.33	29.8	0.37	139.0	14.31	0.40	69.6	4497.9	18.02	unknown *
8	0.41	70.3	0.43	80.1	8.25	0.46	62.4	2838.2	11.37	unknown *
9	0.63	63.7	0.66	72.9	7.51	0.68	71.0	2223.7	8.91	unknown *

Track 2, ID: T376#jeevanthyadi gritha



Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	-0.05	5.5	-0.03	336.2	32.90	-0.01	70.2	5050.1	15.93	unknown *
2	-0.01	70.5	0.01	98.7	9.66	0.04	49.3	2725.8	8.60	unknown *
3	0.05	49.6	0.08	63.6	6.23	0.11	50.5	2452.3	7.74	unknown *
4	0.16	52.1	0.21	78.4	7.67	0.24	59.7	3710.3	11.70	unknown *
5	0.28	56.0	0.28	57.1	5.59	0.33	37.2	1893.8	5.97	unknown *
6	0.33	37.5	0.36	145.9	14.28	0.40	78.3	5135.0	16.20	unknown *
7	0.40	78.7	0.43	88.1	8.62	0.45	70.2	2934.1	9.26	unknown *
8	0.61	63.9	0.66	74.7	7.31	0.67	72.4	3091.0	9.75	unknown *
9	0.72	77.9	0.72	79.0	7.74	0.84	8.3	4710.6	14.86	unknown *

Track 3, ID: T376#jeevanthyadi gritha



winCATS Planar Chromatography Manager

Peak	Start Rf	Start Height	Max Rf	Max Height	Max %	End Rf	End Height	Area	Area %	Assigned substance
1	-0.06	4.5	-0.03	326.1	26.80	-0.01	66.8	4995.4	15.30	unknown *
2	-0.01	67.0	0.01	95.4	7.84	0.04	51.1	2533.0	7.76	unknown *
3	0.05	51.3	0.07	65.4	5.38	0.10	54.9	2128.0	6.52	unknown *
4	0.15	52.0	0.21	78.4	6.44	0.25	61.1	4617.9	14.14	unknown *
5	0.29	60.2	0.29	62.6	5.14	0.32	43.6	1547.3	4.74	unknown *
6	0.33	43.7	0.36	143.4	11.78	0.39	89.0	4472.9	13.70	unknown *
7	0.39	89.5	0.39	95.0	7.81	0.40	82.5	1069.8	3.28	unknown *
8	0.41	83.1	0.42	91.6	7.53	0.45	77.2	2491.3	7.63	unknown *
9	0.51	72.1	0.56	103.9	8.54	0.59	75.7	4468.8	13.69	unknown *
10	0.59	76.1	0.59	79.4	6.52	0.61	66.7	1173.2	3.59	unknown *
11	0.74	75.9	0.74	75.9	6.23	0.83	12.7	3156.1	9.67	unknown *

Visualizer Document - Plate state Developed

User : SARANYA
Friday, May 27, 2022 1:29:55 PM

Approved : .....
Report ID : 07E6051B060D1D30

SN 1801W005, V1.4.6
Page 7 of 13

Gas chromatography and Mass spectrometry Reports

CARe KERALAM LTD

Area Percent Report

Data Path : D:\GCMSD\2022\MAY\24.05.2022\
Data File : T_376.D
Acq On : 24 May 2022 15:06
Sample : JEEVANTHYADI GHRITA

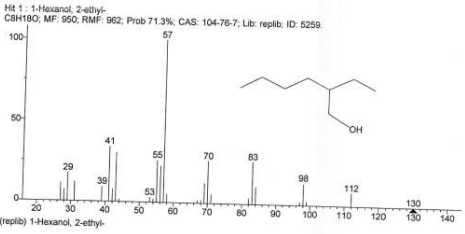
peak #	R.T. min	first scan	max scan	last scan	PK TY	peak height	corr. area	corr. % max.	% of total
1	10.461	616	625	692	BB	2512781	105595666	38.57%	7.882%
2	21.098	1849	1861	1876	PV	436808	17657042	6.45%	1.318%
3	24.405	2201	2246	2266	BV 5	678897	49791145	18.18%	3.717%
4	29.924	2869	2887	2914	BV 2	1174266	78539179	28.68%	5.862%
5	30.258	2914	2926	2965	VB	213105	24438016	8.93%	1.824%
6	33.233	3259	3272	3281	M6	368227	27596568	10.08%	2.060%
7	33.717	3310	3328	3344	BV 3	1184616	54008940	19.73%	4.031%
8	35.245	3497	3506	3531	PV 2	651348	24652949	9.00%	1.840%
9	36.587	3649	3662	3700	BV	1726110	124713796	45.55%	9.309%
10	39.107	3930	3955	3978	PV	910330	88617154	32.36%	6.615%
11	39.389	3978	3988	3999	VV	4039296	142691797	52.11%	10.651%
12	41.390	4212	4220	4235	PV 2	657347	35902737	13.11%	2.680%
13	41.568	4235	4241	4271	VV	4686528	273806472	100.00%	20.438%
14	42.061	4287	4298	4316	PV 2	1232053	60613841	22.14%	4.524%
15	42.993	4384	4407	4415	BV	1493093	49730433	18.16%	3.712%
16	43.143	4415	4424	4433	VV	3899782	125053285	45.67%	9.334%
17	43.640	4466	4482	4495	BV 2	1305774	56307914	20.56%	4.203%

Sum of corrected areas: 1339716934

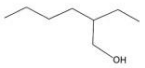
GCMS_PROFILING2022.M Tue May 24 17:00:00 2022

COMPOUND 1

Hit 1 : 1-Hexanol, 2-ethyl-
C8H18O; MF: 950; RMF: 962; Prob 71.3%; CAS: 104-76-7; Lib: replib; ID: 5259.



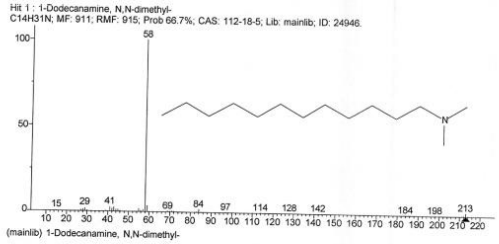
(replib) 1-Hexanol, 2-ethyl-



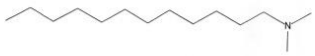
Name: 1-Hexanol, 2-ethyl-
Formula: $C_8H_{18}O$
MW: 130 CAS#: 104-76-7 NIST#: 288735 ID#: 5259 DB: replib
Other DBs: Fine, TSCA, RTECS, EPA, HODOC, NIH, EINECS, IRDB
Contributor: James Little,Eastman Chem.Co.,Kingsport,TN
10 largest peaks:
57 999 | 41 337 | 43 300 | 70 260 | 83 259 | 55 258 | 56 222 | 29 172 | 98 130 | 69 122 |
Synonyms:
1.Ethylhexanol
2.2-Ethyl-1-hexanol
3.2-Ethylhexan-1-ol
4.2-Ethylhexanol
5.2-Ethylhexyl alcohol
6.2-Ethyl-hexanol-1
7.Ethylhexyl alcohol
8.2-EH
9.Aerofroth 88
10.Octyl alcohol
11.Surfynol 104

COMPOUND 2

Hit 1 : 1-Dodecanamine, N,N-dimethyl-
C14H31N; MF: 911; RMF: 915; Prob 66.7%; CAS: 112-18-5; Lib: mainlib; ID: 24946.



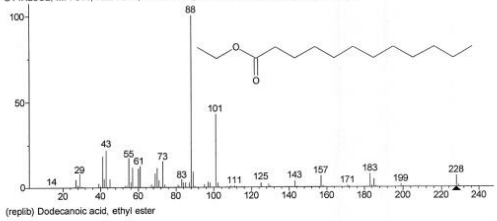
(mainlib) 1-Dodecanamine, N,N-dimethyl-



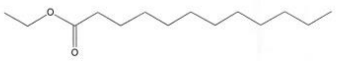
Name: 1-Dodecanamine, N,N-dimethyl-
Formula: $C_{14}H_{31}N$
MW: 213 CAS#: 112-18-5 NIST#: 231563 ID#: 24946 DB: mainlib
Other DBs: Fine, TSCA, RTECS, NIH, EINECS, IRDB
Contributor: Japan AIST/NIMC Database- Spectrum MS-NW-2730
10 largest peaks:
58 999 | 59 36 | 41 27 | 43 25 | 213 19 | 84 18 | 42 17 | 55 17 | 29 16 | 44 13 |

COMPOUND 3

Hit 1 : Dodecanoic acid, ethyl ester
C14H28O2; MF: 914; RMF: 914; Prob 73.3%; CAS: 106-33-2; Lib: replib; ID: 11106.



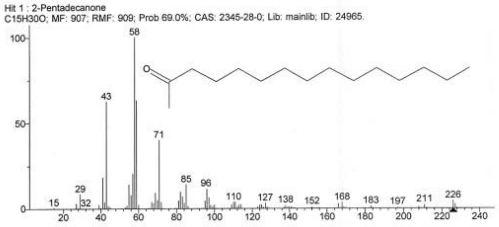
(replib) Dodecanoic acid, ethyl ester



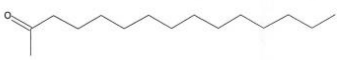
Name: Dodecanoic acid, ethyl ester
Formula: $C_{14}H_{28}O_2$
MW: 228 CAS#: 106-33-2 NIST#: 10881 ID#: 11106 DB: replib
Other DBs: Fine, TSCA, HODOC, NIH, EINECS, IRDB
10 largest peaks:
88 999 | 101 425 | 43 217 | 41 183 | 55 171 | 73 153 | 61 125 | 57 116 | 70 113 | 60 111 |
Synonyms:
1. Lauric acid, ethyl ester
2. Ethyl dodecanoate
3. Ethyl dodecylate
4. Ethyl laurate
5. Ethyl laurinate
6. Ethyl n-dodecanoate

COMPOUND 4

Hit 1 : 2-Pentadecanone
C15H30O; MF: 907; RMF: 909; Prob 69.0%; CAS: 2345-28-0; Lib: mainlib; ID: 24965.



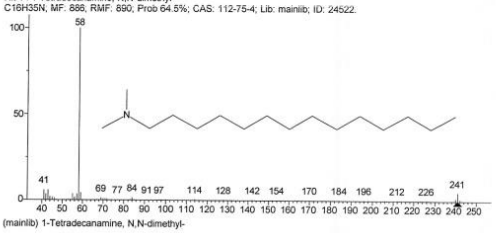
(mainlib) 2-Pentadecanone



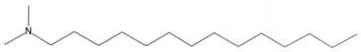
Name: 2-Pentadecanone
Formula: $C_{15}H_{30}O$
MW: 226 CAS#: 2345-28-0 NIST#: 236978 ID#: 24965 DB: mainlib
Other DBs: TSCA, HODOC, EINECS
Contributor: Japan AIST/NIMC Database- Spectrum MS-IW- 215
10 largest peaks:
58 999 | 59 630 | 43 623 | 71 398 | 57 205 | 41 182 | 85 141 | 55 140 | 96 114 | 82 97 |
Synonyms:
1. Methyl tridecyl ketone
2. Pentadecan-2-one

COMPOUND 5

Hit 1 : 1-Tetradecanamine, N,N-dimethyl-
C16H35N; MF: 886, RMF: 890, Prob 64.5%; CAS: 112-75-4; Lib: mainlib; ID: 24522.

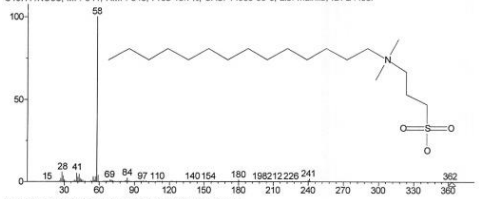


(mainlib) 1-Tetradecanamine, N,N-dimethyl-

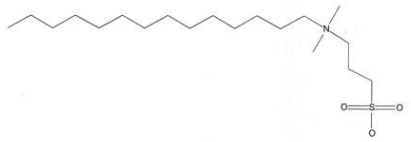


Name: 1-Tetradecanamine, N,N-dimethyl-
Formula: $C_{16}H_{35}N$
MW: 241 CAS#: 112-75-4 NIST#: 129243 ID#: 24522 DB: mainlib
Other DBs: Fine, TSCA, NIH, EINECS
Contributor: LAC, NIDDK, NIH, Bethesda, MD 20892
10 largest peaks:
58 999 | 41 59 | 43 58 | 241 49 | 59 42 | 55 37 | 42 35 | 57 35 | 44 20 | 45 17 |
Synonyms:
1. Tetradecylamine, N,N-dimethyl-
2. Armeen DM 14D
3. Armine DM14D
4. Dimethyl myristamine
5. Dimethyltetradecylamine
6. Myristyl dimethyl amine
7. N,N-Dimethyl-n-tetradecylamine
8. N,N-Dimethylmyristylamine
9. N,N-Dimethyltetradecanamine
10. N,N-Dimethyltetradecylamine
11. Tetradecyldimethylamine
12. Dimethyl-n-tetradecylamine
13. Robaxine
14. Adma 14
15. Empigen AH
16. N,N-Dimethyl-1-tetradecanamine #

Hit 2 : 3(N,N-Dimethylmyristylammonio)propanesulfonate
C19H41NO3S; MF: 841; RMF: 846; Prob 13.7%; CAS: 14933-09-6; Lib: mainlib; ID: 24453.



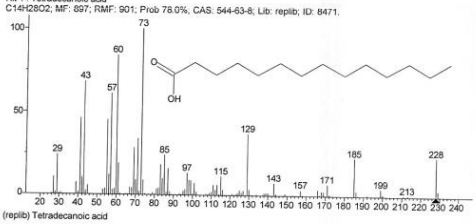
(mainlib) 3(N,N-Dimethylmyristylammonio)propanesulfonate



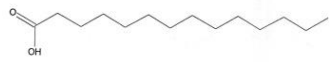
Name: 3(N,N-Dimethylmyristylammonio)propanesulfonate
Formula: $C_{19}H_{41}NO_3S$
MW: 363 CAS#: 14933-09-6 NIST#: 236253 ID#: 24453 DB: mainlib
Other DBs: Fine, EINECS
Contributor: Japan AIST/NIMC Database- Spectrum MS-NW-6953
10 largest peaks:
58 999 | 28 58 | 41 52 | 43 44 | 59 39 | 29 35 | 55 30 | 42 29 | 57 29 | 84 23 |
Synonyms:
1.1-Tetradecanaminium, N,N-dimethyl-N-(3-sulfopropyl)-, hydroxide, inner salt

COMPOUND 6

Hit 1 : Tetradecanoic acid
C14H28O2; MF: 897; RMF: 901; Prob 78.0%; CAS: 544-63-8; Lib: replib; ID: 8471.



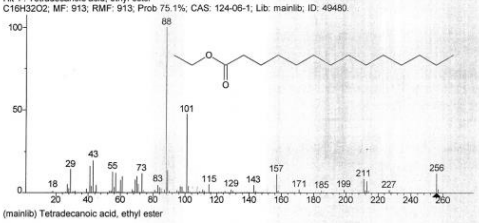
(replib) Tetradecanoic acid



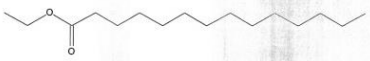
Name: Tetradecanoic acid
Formula: $C_{14}H_{28}O_2$
MW: 228 CAS#: 544-63-8 NIST#: 189107 ID#: 8471 DB: replib
Other DBs: Fine, TSCA, RTECS, EPA, HODOC, NIH, EINECS, IRDB
Contributor: Chemical Concepts
10 largest peaks:
73 999 | 60 841 | 43 681 | 57 609 | 41 461 | 55 451 | 129 371 | 71 338 | 69 282 | 85 241 |
Synonyms:
1.Myristic acid
2.n-Tetradecanoic acid
3.n-Tetradecoic acid
4.Neo-Fat 14
5.Univol U 316S
6.1-Tridecanecarboxylic acid
7.Coconut oil fatty acids
8.Crodacid
9.Emery 655
10.Hydrofol acid 1495
11.Hystrene 9014
12.n-Tetradecan-1-oic acid
13.Emery 654
14.Hystrene 9514
15.Philacid 1400
16.Prifac 2940

COMPOUND 7

Hit 1 : Tetradecanoic acid, ethyl ester
C16H32O2; MF: 913; RMF: 913; Prob 75.1%; CAS: 124-06-1; Lib: mainlib; ID: 49480.



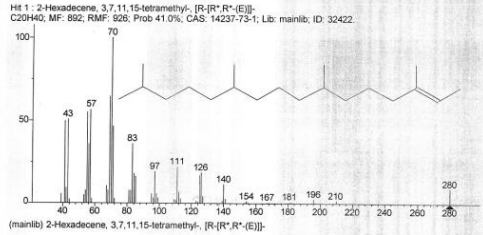
(mainlib) Tetradecanoic acid, ethyl ester



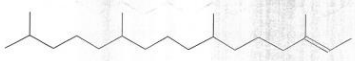
Name: Tetradecanoic acid, ethyl ester
Formula: $C_{16}H_{32}O_2$
MW: 256 CAS#: 124-06-1 NIST#: 229118 ID#: 49480 DB: mainlib
Other DBs: Fine, TSCA, EPA, HODOC, NIH, EINECS, IRDB
Contributor: Japan AIST/NIMC Database- Spectrum MS-NW-3755
10 largest peaks:
88 999 | 101 473 | 43 195 | 41 161 | 29 143 | 89 136 | 55 127 | 57 119 | 256 118 | 73 117 |
Synonyms:
1.Myristic acid, ethyl ester
2.Ethyl myristate
3.Ethyl tetradecanoate
4.Ethyl ester of tetradecanoic acid
5.Ethyl N-tetradecanoate

COMPOUND 8

Hit 1 : 2-Hexadecene, 3,7,11,15-tetramethyl-, [R-[R*,R*-(E)]]-
C20H40; MF: 892; RMF: 926; Prob 41.0%; CAS: 14237-73-1; Lib: mainlib; ID: 32422.



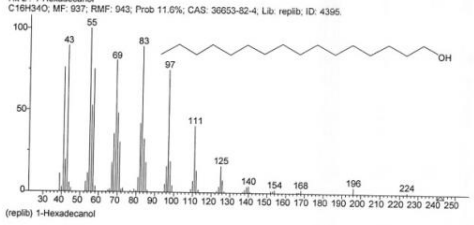
(mainlib) 2-Hexadecene, 3,7,11,15-tetramethyl-, [R-[R*,R*-(E)]]-



Name: 2-Hexadecene, 3,7,11,15-tetramethyl-, [R-[R*,R*-(E)]]-
Formula: $C_{20}H_{40}$
MW: 280 CAS#: 14237-73-1 NIST#: 67754 ID#: 32422 DB: mainlib
Other DBs: None
Contributor: V.P.FLANAGAN US DEPT. AGRICULTURE, WASHINGTON, D.C., USA
10 largest peaks:
70 999 | 69 645 | 57 564 | 55 550 | 43 506 | 41 497 | 71 464 | 83 360 | 56 359 | 111 220 |
Synonyms:
1.(2E)-3,7,11,15-Tetramethyl-2-hexadecene #

COMPOUND 9

Hit 2 : 1-Hexadecanol
C16H34O; MF: 937; RMF: 943; Prob 11.6%; CAS: 36653-82-4; Lib: replib; ID: 4395.

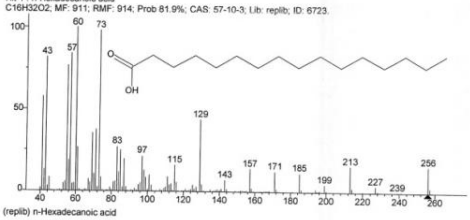


(replib) 1-Hexadecanol

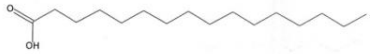
Name: 1-Hexadecanol
Formula: $C_{16}H_{34}O$
MW: 242 CAS#: 36653-82-4 NIST#: 313200 ID#: 4395 DB: replib
Other DBs: Fine, TSCA, RTECS, EPA, HODOC, NIH, EINECS, IRDB
Contributor: Dr. P.K. Shah, NYC Police Laboratory, NY
10 largest peaks:
55 999 | 43 894 | 83 889 | 69 805 | 41 759 | 57 751 | 97 745 | 56 526 | 70 479 | 82 415 |
Synonyms:
1.n-Cetyl alcohol
2.n-Hexadecan-1-ol
3.n-Hexadecanol
4.n-1-Hexadecanol
5.Adol 52
6.Adol 52 NF
7.Adol 54
8.Aldol 54
9.Alfol 16
10. Atalco C
11. Cachalot C-51
12. Cachalot C-52
13. Cetaffine
14. Cetal
15. Cetalol CA
16. Cetanol

COMPOUND 10

Hit 1 : n-Hexadecanoic acid
C16H32O2; MF: 911; RMF: 914; Prob 81.9%; CAS: 57-10-3; Lib: replib; ID: 6723.



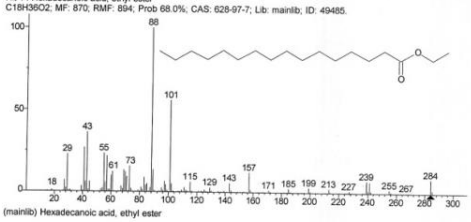
(replib) n-Hexadecanoic acid



Name: n-Hexadecanoic acid
Formula: $C_{16}H_{32}O_2$
MW: 256 CAS#: 57-10-3 NIST#: 335494 ID#: 6723 DB: replib
Other DBs: Fine, TSCA, RTECS, EPA, HODOC, NIH, EINECS, IRDB
Contributor: Drug Lab
10 largest peaks:
60 999 | 73 980 | 57 840 | 43 817 | 55 767 | 41 574 | 129 435 | 71 373 | 69 351 | 83 267 |
Synonyms:
1.Hexadecanoic acid
2.n-Hexadecoic acid
3.Palmitic acid
4.Pentadecanecarboxylic acid
5.1-Pentadecanecarboxylic acid
6.Cetylic acid
7.Emersol 140
8.Emersol 143
9.Hexadecylic acid
10.Hydrofol
11.Hystrene 8016
12.Hystrene 9016
13.Industrene 4516
14.Prifrac 2960
15.Glycon P-45
16.Prifac 2960
17.Univol U332

COMPOUND 11

Hit 1 : Hexadecanoic acid, ethyl ester
C18H36O2; MF: 870; RMF: 894; Prob 68.0%; CAS: 628-97-7; Lib: mainlib; ID: 49485.

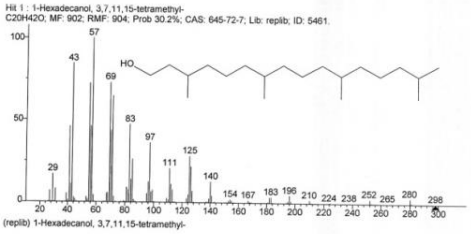


(mainlib) Hexadecanoic acid, ethyl ester

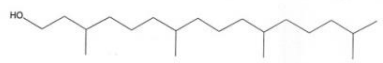
Name: Hexadecanoic acid, ethyl ester
Formula: $C_{18}H_{36}O_2$
MW: 284 CAS#: 628-97-7 NIST#: 233204 ID#: 49485 DB: mainlib
Other DBs: Fine, TSCA, EPA, HODOC, NIH, EINECS, IRDB
Contributor: Japan AIST/NIMC Database- Spectrum MS-NW-5396
10 largest peaks:
88 999 | 101 559 | 43 362 | 41 268 | 55 233 | 29 227 | 57 217 | 73 156 | 89 136 | 69 132 |
Synonyms:
1.Palmitic acid, ethyl ester
2.Ethyl hexadecanoate
3.Ethyl palmitate

COMPOUND 12

Hit 1 : 1-Hexadecanol, 3,7,11,15-tetramethyl-
C20H42O; MF: 902; RMF: 904; Prob 30.2%; CAS: 645-72-7; Lib: replib; ID: 5461.



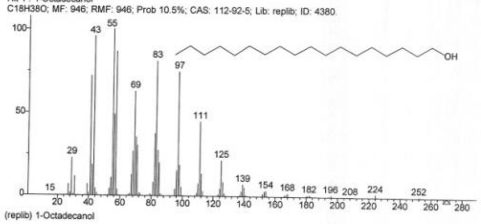
(replib) 1-Hexadecanol, 3,7,11,15-tetramethyl-



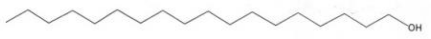
Name: 1-Hexadecanol, 3,7,11,15-tetramethyl-
Formula: $C_{20}H_{42}O$
MW: 298 CAS#: 645-72-7 NIST#: 194527 ID#: 5461 DB: replib
Other DBs: HODOC, EINECS
Contributor: Chemical Concepts
10 largest peaks:
57 999 | 43 845 | 69 726 | 55 722 | 71 644 | 83 471 | 56 460 | 41 457 | 70 433 | 97 359 |
Synonyms:
1.Dihydrophytol
2.3,7,11,15-Tetramethylhexadecanol
3.3,7,11,15-Tetramethyl-1-hexadecanol #

COMPOUND 13

Hit 1 : 1-Octadecanol
C18H38O; MF: 946; RMF: 946; Prob 10.5%; CAS: 112-92-5; Lib: replib; ID: 4380.



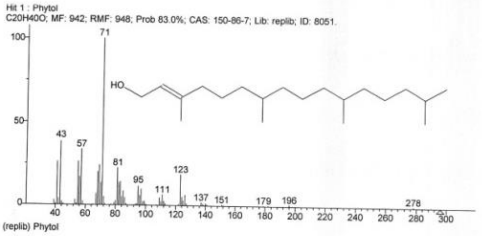
(replib) 1-Octadecanol



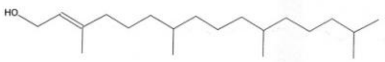
Name: 1-Octadecanol
Formula: $C_{18}H_{38}O$
MW: 270 CAS#: 112-92-5 NIST#: 333926 ID#: 4380 DB: replib
Other DBs: Fine, TSCA, RTECS, EPA, HODOC, NIH, EINECS, IRDB
Contributor: NIST Mass Spectrometry Data Center
10 largest peaks:
55 999 | 43 958 | 57 866 | 83 808 | 97 747 | 41 721 | 69 628 | 56 489 | 111 447 | 82 374 |
Synonyms:
1.n-Octadecanol
2.n-Octadecyl alcohol
3.n-1-Octadecanol
4.Aldol 62
5.Alfol 18
6.Atalco S
7.Cachalot S-43

COMPOUND 14

Hit 1 : Phytol
C20H40O; MF: 942; RMF: 948; Prob 83.0%; CAS: 150-86-7; Lib: replib; ID: 8051.



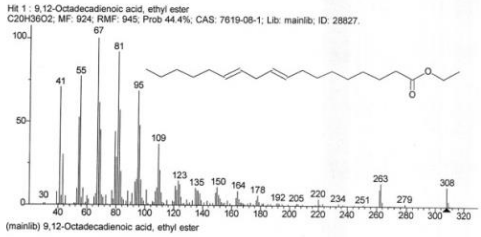
(replib) Phytol



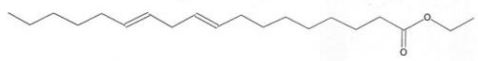
Name: Phytol
Formula: $C_{20}H_{40}O$
MW: 296 CAS#: 150-86-7 NIST#: 108727 ID#: 8051 DB: replib
Other DBs: Fine, TSCA, RTECS, HODOC, EINECS
Contributor: Philip Morris R&D
10 largest peaks:
71 999 | 43 381 | 57 334 | 41 260 | 55 259 | 69 239 | 81 223 | 68 199 | 123 184 | 56 169 |
Synonyms:
1.2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, [R-[R*,R*-(E)]]-
2.trans-Phytol
3.3,7,11,15-Tetramethyl-2-hexadecen-1-ol
4.(2E)-3,7,11,15-Tetramethyl-2-hexadecen-1-ol #

COMPOUND 15

Hit 1 : 9,12-Octadecadienoic acid, ethyl ester
C20H36O2; MF: 924; RMF: 945; Prob 44.4%; CAS: 7619-08-1; Lib: mainlib; ID: 28827.



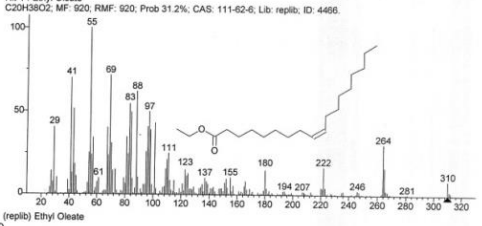
(mainlib) 9,12-Octadecadienoic acid, ethyl ester



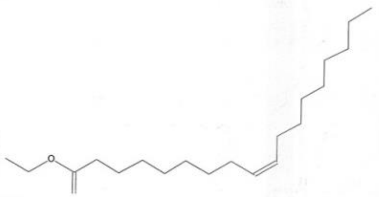
Name: 9,12-Octadecadienoic acid, ethyl ester
Formula: $C_{20}H_{36}O_2$
MW: 308 CAS#: 7619-08-1 NIST#: 249157 ID#: 28827 DB: mainlib
Other DBs: HODOC
Contributor: TNO Volatile Compounds in Food - Chemical Concepts
10 largest peaks:
67 999 | 81 919 | 55 772 | 41 707 | 95 683 | 68 613 | 82 569 | 54 525 | 96 478 | 69 448 |
Synonyms:
1.Ethyl (9E,12E)-9,12-octadecadienoate #

COMPOUND 16

Hit 1 : Ethyl Oleate
C20H38O2; MF: 920; RMF: 920; Prob 31.2%; CAS: 111-62-6; Lib: replib; ID: 4466.

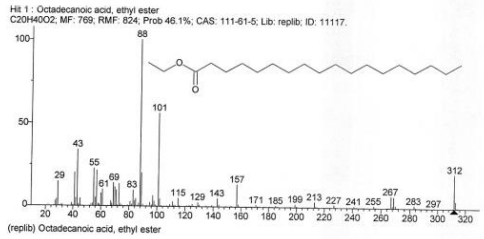


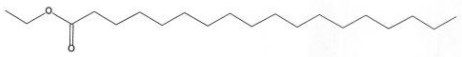
(replib) Ethyl Oleate



Name: Ethyl Oleate
Formula: $C_{20}H_{38}O_2$
MW: 310 CAS#: 111-62-6 NIST#: 150151 ID#: 4466 DB: replib
Other DBs: Fine, TSCA, RTECS, USP, HODOC, NIH, EINECS, IRDB
Contributor: Chemical Concepts
10 largest peaks:
55 999 | 69 714 | 41 699 | 88 618 | 83 543 | 43 515 | 97 496 | 84 495 | 101 429 | 96 407 |
Synonyms:
1.9-Octadecenoic acid (Z)-, ethyl ester
2.Oleic acid, ethyl ester
3.(Z)-9-Octadecenoic acid ethyl ester
4.Ethyl cis-9-octadecenoate
5.Ethyl Z-9-octadecenoate
6.Ethyl (9Z)-9-octadecenoate #

COMPOUND 17





Name: Octadecanoic acid, ethyl ester
Formula: $C_{20}H_{40}O_2$
MW: 312 CAS#: 111-61-5 NIST#: 36393 ID#: 11117 DB: replib
Other DBs: Fine, TSCA, RTECS, HODOC, NIH, EINECS, IRDB
Contributor: R.T.HOLMAN,UNIVERSITY OF MINNESOTA
10 largest peaks:
88 999 | 101 559 | 43 339 | 55 226 | 57 213 | 312 203 | 41 200 | 89 200 | 29 146 | 69 139 |
Synonyms:
1.Stearic acid, ethyl ester
2.Ethyl n-octadecanoate
3.Ethyl octadecanoate
4.Ethyl stearate
5.Radia 7185

Liquid chromatography and Mass spectrometry Reports

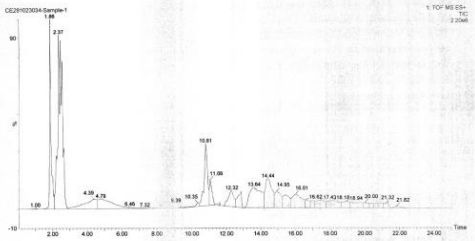
LCMS Analysis of Sample-1:

Mobile Phase-A: 0.1% Formic acid in water
Mobile Phase-B: Acetonitrile
Diluent: Methanol and Tetrahydrofuran
Sample Preparation: About 10mg of sample is dissolved in 1ml of THF and diluted to 10mL with methanol. Filtered and injected.
Injection Volume: 10uL
Gradient Programme:

Time	Flow	%A	%B
Initial	0.500	95.0	5.0
1.00	0.500	95.0	5.0
6.00	0.500	50.0	50.0
12.00	0.500	5.0	95.0
17.00	0.500	5.0	95.0
18.00	0.500	95.0	5.0
20.00	0.500	95.0	5.0

LC Make: Waters, USA **Model:** 1525µ Binary Pump
MS Make: Waters, USA **Model:** Xevo G2-XS QTof
Column: Accucore C18, 50 x 4.6, 5µ Particle size from ThermoScientific.
Capillary Voltage: 3.0KV
Collision Energy: 20V
Ramp Collision Energy: 30-90V
Source Temp: 150°C
Desolvation Temp: 450°C
Cone gas: 50L/Hr
Desolvation Gas Flow: 800L/Hr
Processing Software: MassLynx V4.1

Positive mode TIC Chromatogram of Sample-1



Time	Height	Area	Area%
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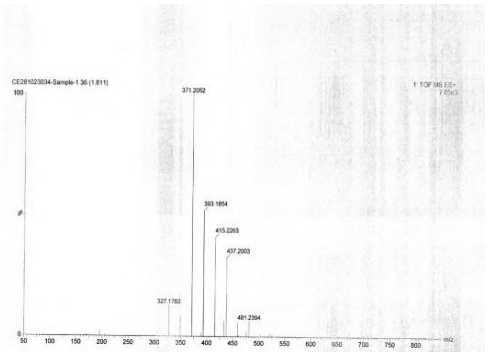
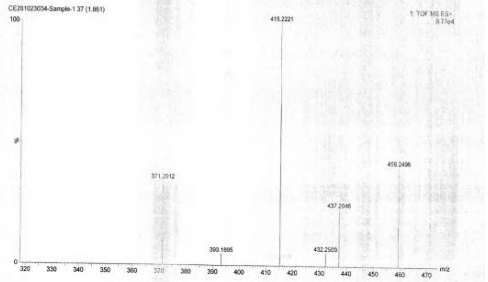
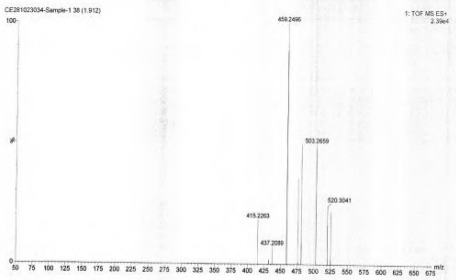
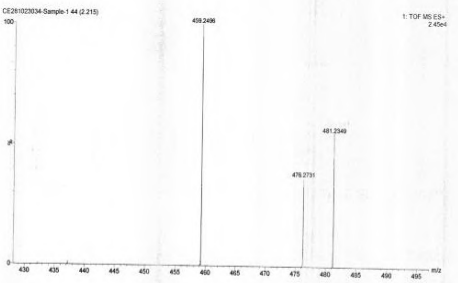
1.861	2203296	213302.703	9.377
2.367	2019474	592274.938	26.038
4.388	112847	97023.883	4.265
4.792	113366	113250.484	4.979
6.459	19076	5335.006	0.235
7.318	6465	445.511	0.020
9.390	16786	2112.389	0.093
9.643	9201	1077.609	0.047
9.896	5153	494.962	0.022
10.350	41156	8556.579	0.376
10.805	715399	156520.469	6.881
11.058	291889	49806.313	2.190
11.614	35683	1803.445	0.079
12.321	182668	66701.867	2.932
12.877	183466	51364.020	2.258
13.636	232787	184243.797	8.100
14.444	332627	151705.188	6.669
14.950	191205	75134.945	3.303
15.455	149389	66857.102	2.939
16.011	155138	99804.609	4.388
16.617	92618	25789.912	1.134
16.921	82417	20044.010	0.881
17.426	88549	52613.094	2.313
18.184	84894	64458.609	2.834

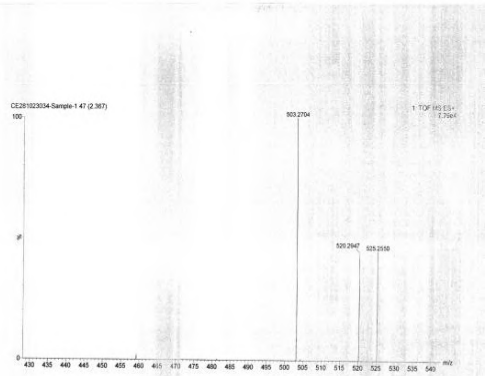
18.942	78415	35626.605	1.566
19.195	68797	46493.609	2.044
20.003	61232	20301.051	0.892
20.357	53317	12739.650	0.560
20.660	52885	12955.064	0.570
20.964	56896	16298.657	0.717
21.317	87153	18542.449	0.815
21.823	22060	9714.357	0.427

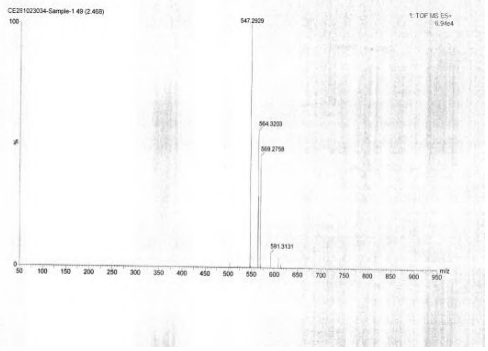


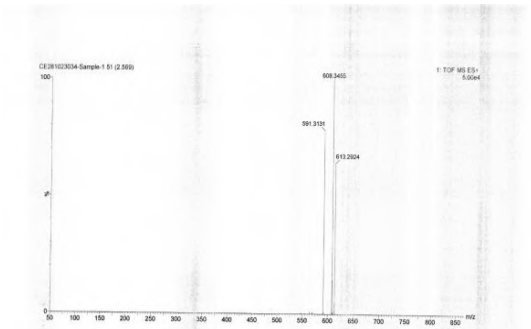








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1: TOF MS ES+
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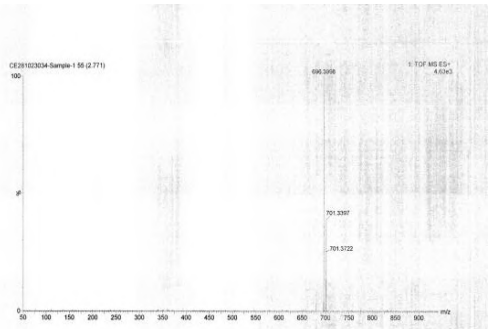
608.3455
591.3131
613.2924
m/z


CE281023034-Sample-1 55 (2.771)
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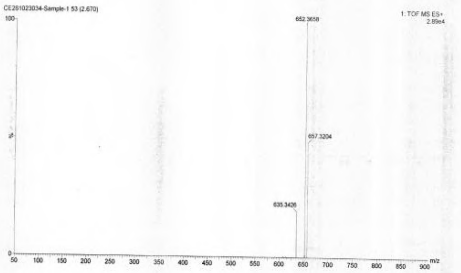
701.3397
701.3722
m/z


CE281023034-Sample-1 53 (2.670)
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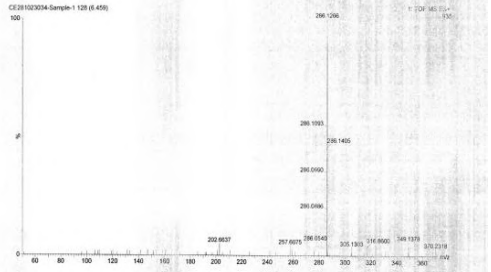
657.3204
635.3436
m/z


CE281023034-Sample-1 128 (6.459)
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286.1405
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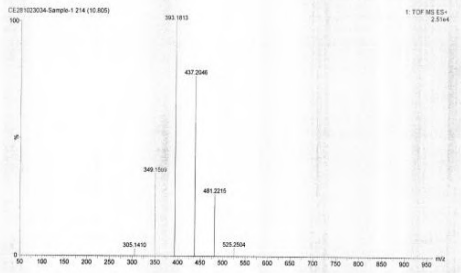
m/z


CE281023034-Sample-1 214 (10.605)
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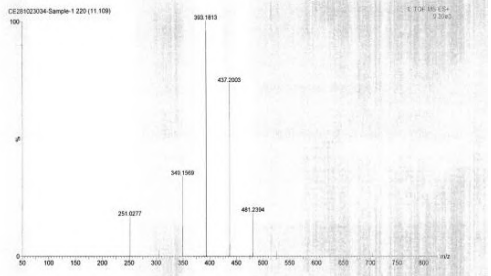
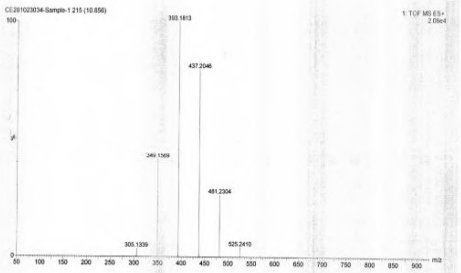
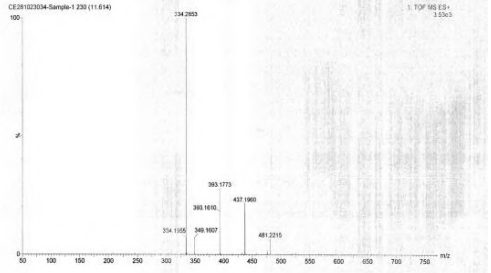
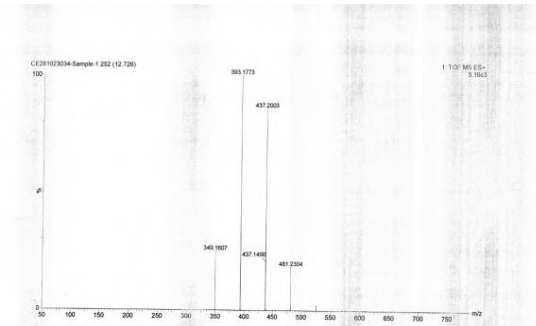
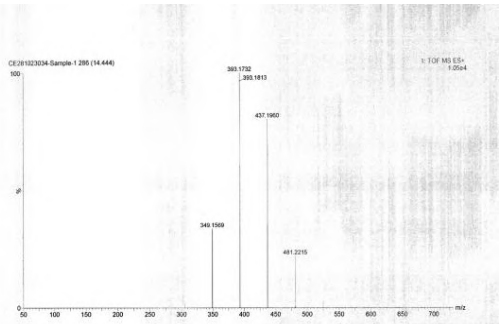
349.1569
481.2215
305.1410
525.2504
m/z

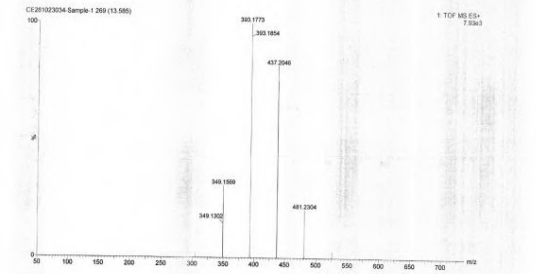

CE281023034-Sample-1 220 (11.109)
1: TOF MS ES+
2.03e3
393.1813
437.2003
349.1569
481.2394
251.0277
m/z

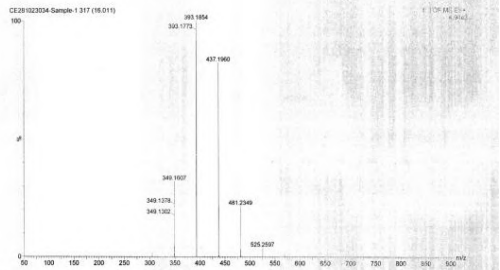

CE281023034-Sample-1 215 (10.656)
1: TOF MS ES+
2.06e4
393.1813
437.2046
349.1569
481.2304
305.1339
525.2410
m/z

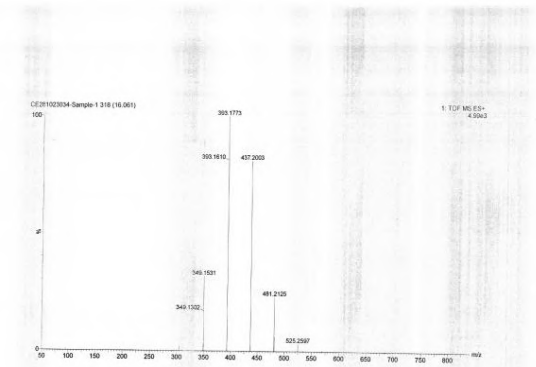

CE281023034-Sample-1 230 (11.614)
1: TOF MS ES+
3.53e3
334.2853
393.1773
437.1960
393.1610
334.1955
349.1607
481.2215
m/z

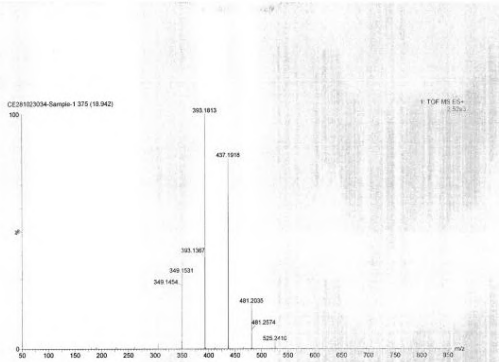

CE281023034-Sample-1 252 (12.726)
1: TOF MS ES+
5.16e3
393.1773
437.2003
349.1607
437.1498
481.2304
m/z

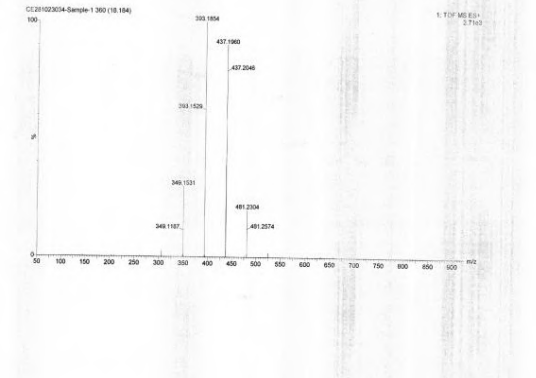

CE281023034-Sample-1 286 (14.444)
1: TOF MS ES+
1.05e4
393.1732
393.1813
437.1960
349.1569
481.2215
m/z

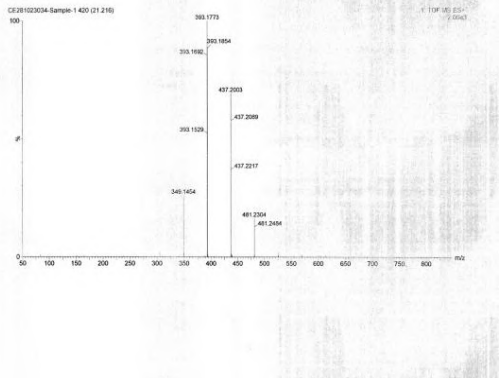

CE281023034-Sample-1 269 (13.585)
1: TOF MS ES+
7.93e3
393.1773
393.1854
437.2046
349.1569
349.1302
481.2304
m/z


CE281023034-Sample-1 317 (16.011)
393.1854
393.1773
437.1960
349.1607
349.1378
349.1302
481.2349
525.2597
m/z

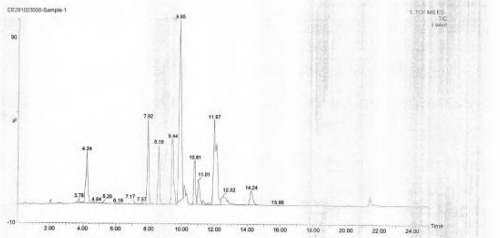

CE281023034-Sample-1 318 (16.061)
1: TOF MS ES+
4.50e3
393.1773
393.1610
437.2003
349.1531
349.1302
481.2125
525.2597
m/z


CE281023034-Sample-1 375 (18.942)
1: TOF MS ES+
393.1813
437.1918
393.1367
349.1531
349.1454
481.2035
481.2574
525.2410
m/z

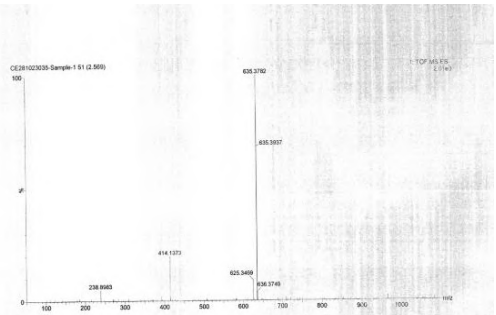

CE281023034-Sample-1 360 (18.184)
1: TOF MS ES+
2.71e3
393.1854
437.1960
437.2046
393.1529
349.1531
481.2304
349.1187
481.2574
m/z

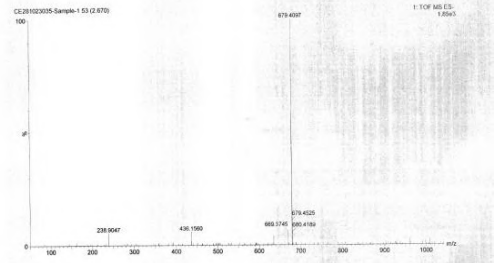

CE281023034-Sample-1 420 (21.216)
393.1773
393.1854
393.1692
437.2003
437.2089
393.1529
437.2217
349.1454
481.2304
481.2454
m/z

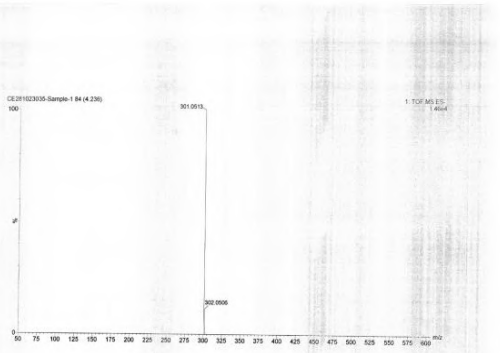
Negative Mode TIC Chromatogram of Sample-1

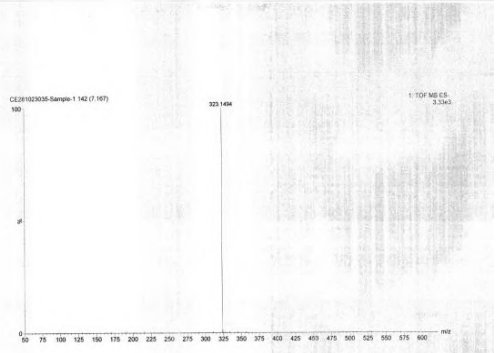


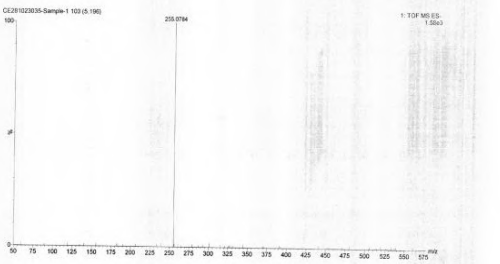
Time	Height	Area	Area%
3.782	45445	2648.325	0.263
4.236	538093	75140.148	7.460
4.843	11571	2468.905	0.245
5.196	10136	977.746	0.097
5.449	2923	332.952	0.033
6.156	4188	671.284	0.067
6.813	3666	259.603	0.026
7.167	16282	1157.424	0.115
7.369	10606	700.156	0.070
7.571	20364	1413.255	0.140
7.925	888217	95424.695	9.474
8.582	621345	62710.387	6.226
9.037	3518	480.912	0.048
9.441	683638	101173.414	10.045
9.846	1898383	297187.469	29.506
10.806	460140	54658.766	5.427
11.008	248765	35533.633	3.528
11.311	42028	4741.546	0.471
11.614	19622	2082.284	0.207
11.968	884703	197704.594	19.629
12.524	91131	37279.699	3.701
13.383	4617	857.335	0.085
13.686	2714	520.121	0.052
14.242	151322	30998.092	3.078
15.860	1578	100.831	0.010

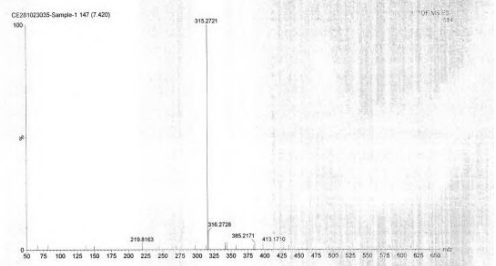


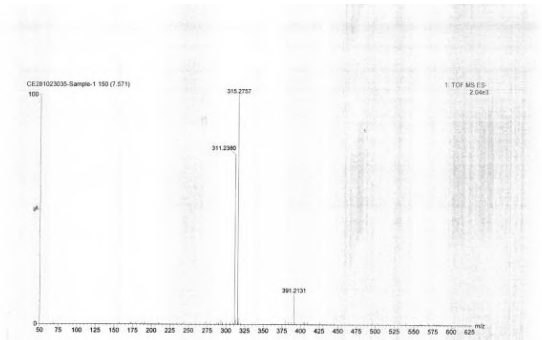


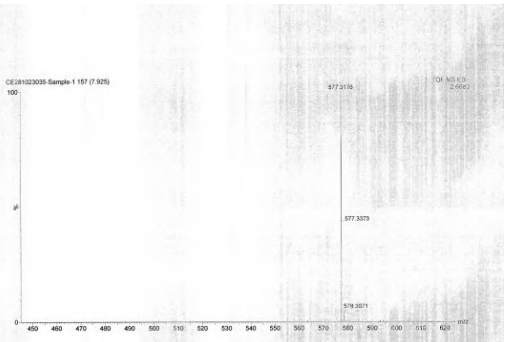


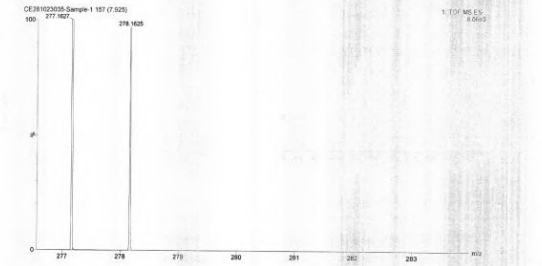


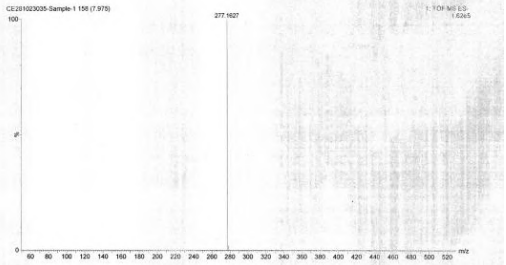


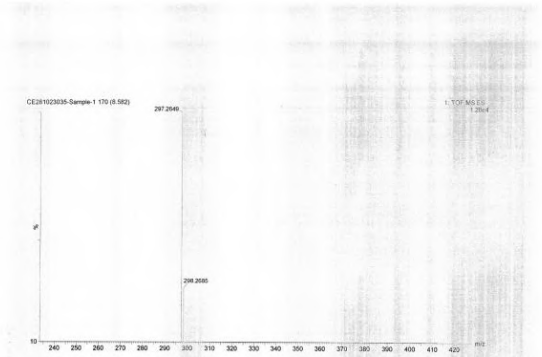


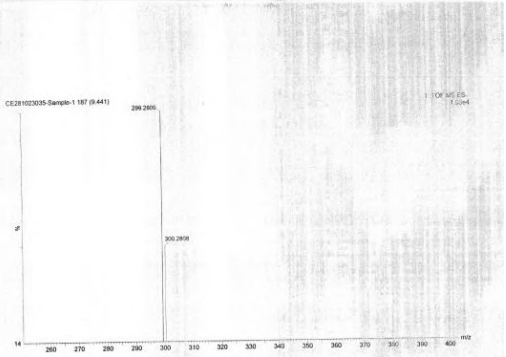

CE281023035-Sample-1 150 (7.571)
315.2757
311.2380
391.2131
m/z

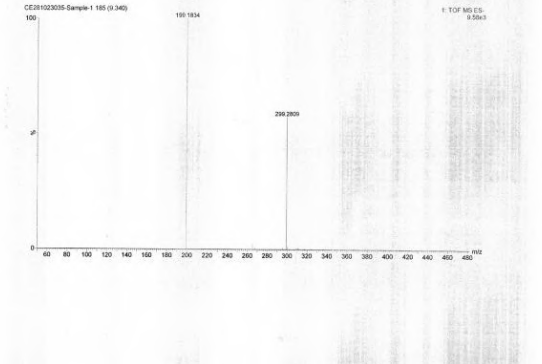

CE281023035-Sample-1 157 (7.925)
577.3178
577.3373
578.3071
m/z

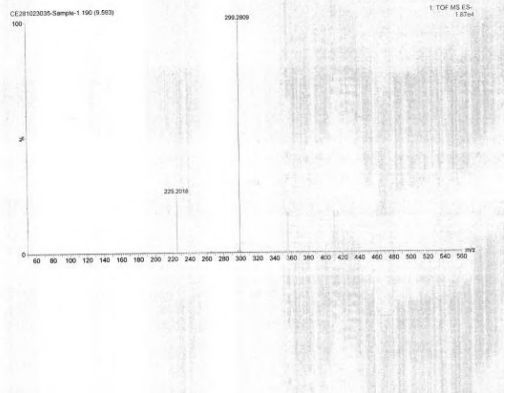

CE281023035-Sample-1 157 (7.925)
277.1627
278.1625
m/z

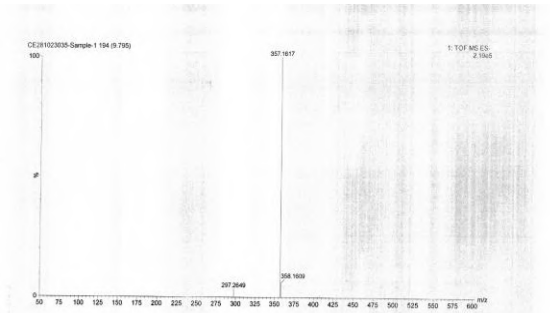

CE281023035-Sample-1 158 (7.975)
277.1627
m/z

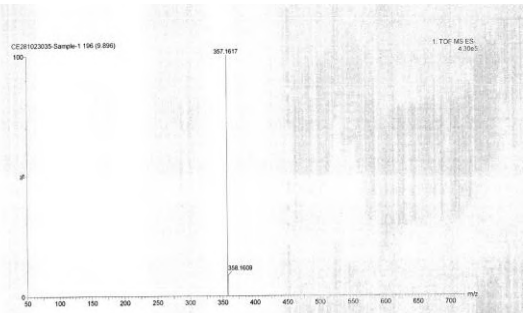

CE281023035-Sample-1 170 (8.582)
297.2649
298.2686
m/z

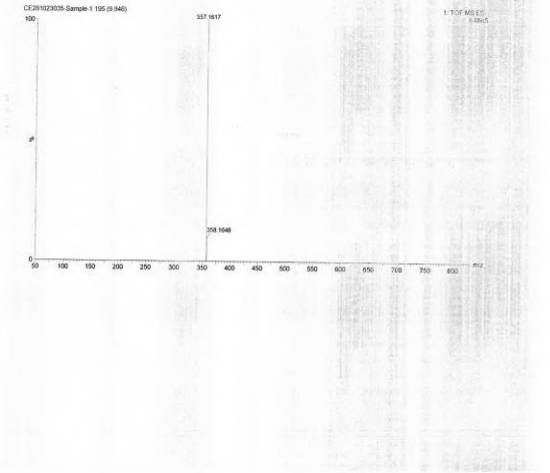

CE281023035-Sample-1 187 (9.441)
299.2805
300.2808
m/z

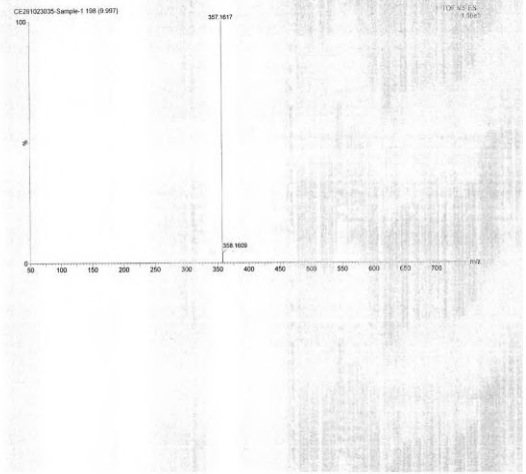

CE281023035-Sample-1 185 (9.340)
100.1834
299.2809
m/z

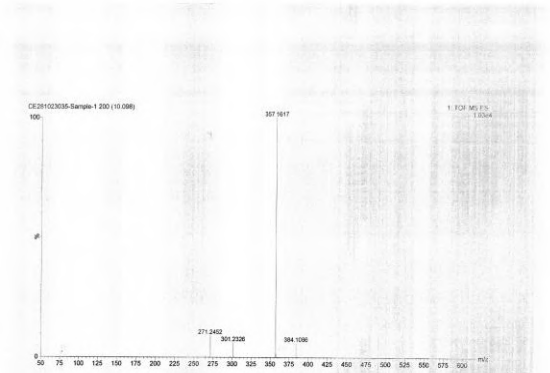

CE281023035-Sample-1 190 (9.593)
299.2809
225.2018
m/z

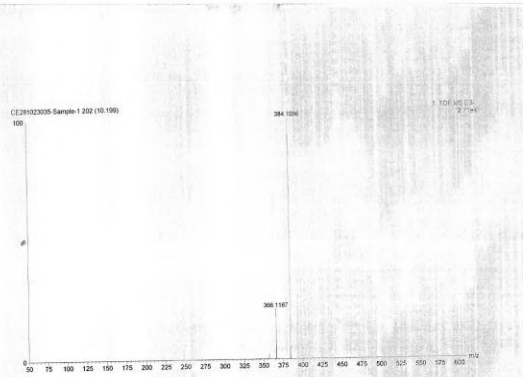

CE281023035-Sample-1 194 (9.795)
1: TOF MS ES+
2.19e5
100
%
357.1617
358.1639
297.2649
0
50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550 575 600
m/z

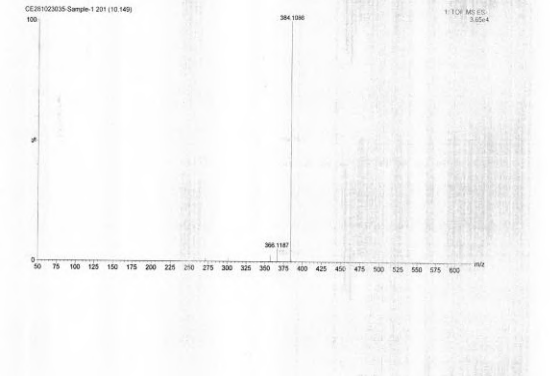

CE281023035-Sample-1 196 (9.896)
1: TOF MS ES+
4.39e5
100
%
357.1617
358.1609
0
50 100 150 200 250 300 350 400 450 500 550 600 650 700
m/z

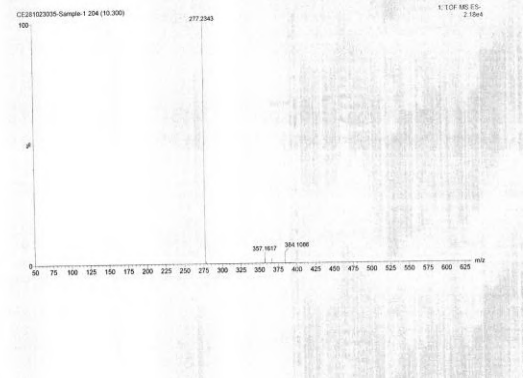

CE281023035-Sample-1 195 (9.846)
1: TOF MS ES+
6.68e5
100
%
357.1617
358.1648
0
50 100 150 200 250 300 350 400 450 500 550 600 650 700 750 800
m/z

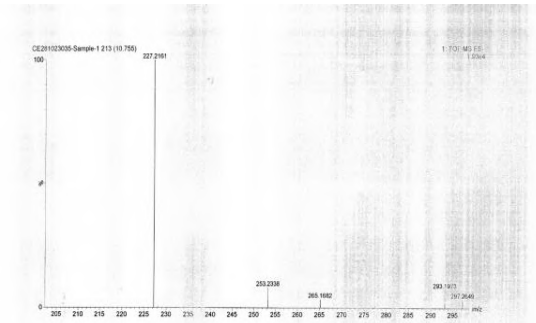

CE281023035-Sample-1 198 (9.997)
1: TOF MS ES+
100
%
357.1617
358.1609
0
50 100 150 200 250 300 350 400 450 500 550 600 650 700
m/z

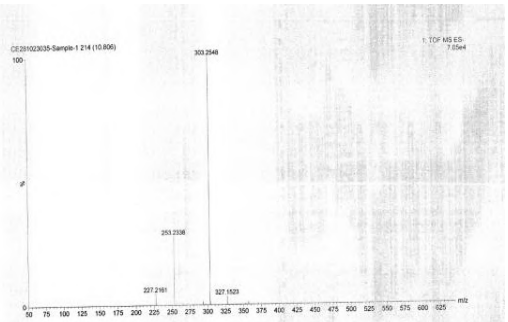

CE281023035-Sample-1 200 (10.098)
1: TOF MS ES+
1.92e4
100
%
357.1617
271.2452
301.2326
384.1086
0
50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550 575 600
m/z

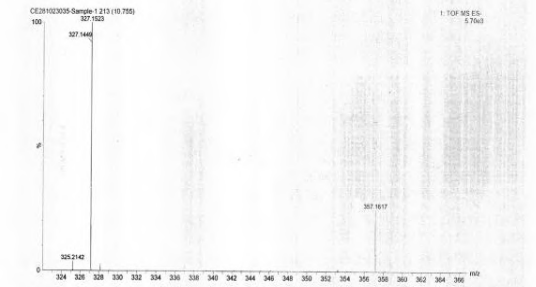

CE281023035-Sample-1 202 (10.199)
1: TOF MS ES+
2.71e4
100
%
384.1086
366.1187
0
50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550 575 600
m/z

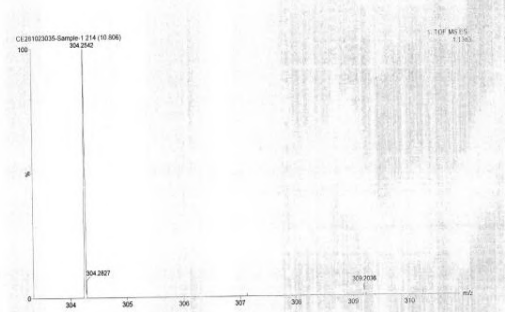

CE281023035-Sample-1 201 (10.149)
1: TOF MS ES+
3.65e4
100
%
384.1086
366.1187
0
50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550 575 600
m/z

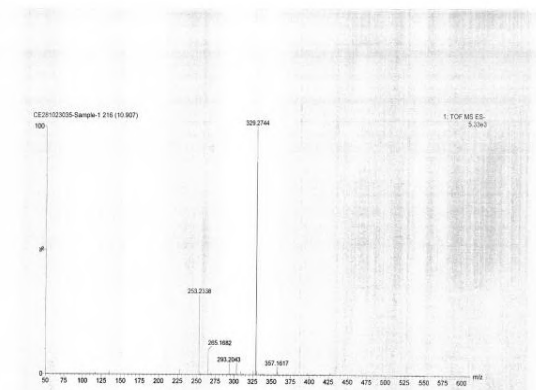

CE281023035-Sample-1 204 (10.300)
1: TOF MS ES+
2.18e4
100
%
277.2343
357.1617
384.1086
0
50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550 575 600 625
m/z

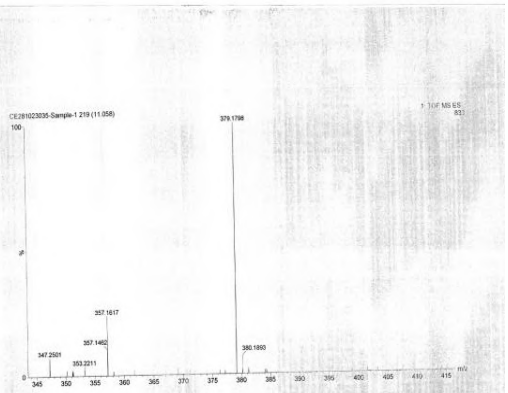

CE281023035-Sample-1 213 (10.755)
1: TOF MS ES-
227.2161
253.2338
265.1682
293.1973
297.2646
m/z

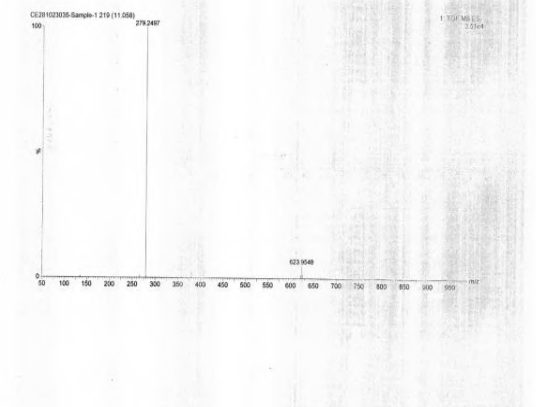

CE281023035-Sample-1 214 (10.806)
1: TOF MS ES-
303.2548
253.2338
227.2161
327.1523
m/z

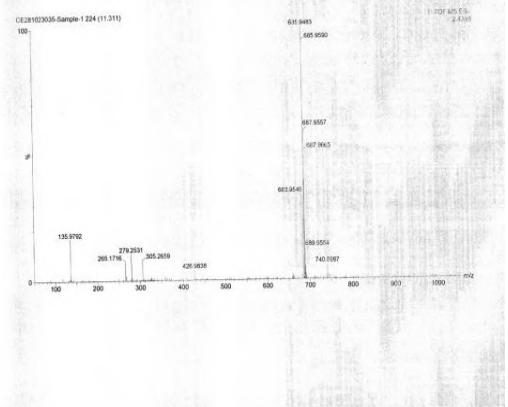

CE281023035-Sample-1 213 (10.755)
1: TOF MS ES-
327.1523
327.1440
357.1617
325.2142
m/z


CE281023035-Sample-1 214 (10.806)
304.2542
304.2827
309.2036
m/z


CE281023035-Sample-1 216 (10.907)
1: TOF MS ES-
329.2744
253.2338
265.1682
293.2043
357.1617
m/z


CE281023035-Sample-1 219 (11.058)
1: TOF MS ES-
379.1798
357.1617
357.1462
347.2501
353.2211
380.1893
m/z


CE281023035-Sample-1 219 (11.058)
1: TOF MS ES-
279.2497
623.9548
m/z


CE281023035-Sample-1 224 (11.311)
1: TOF MS ES-
631.9483
685.9590
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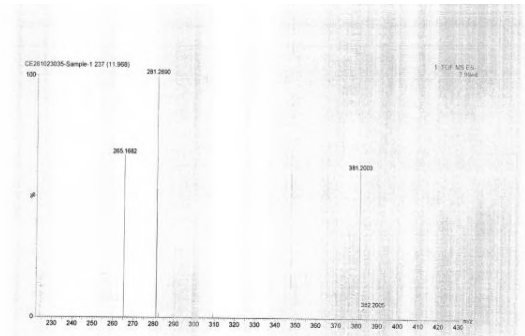
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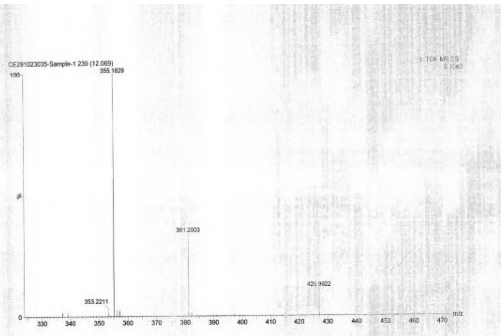
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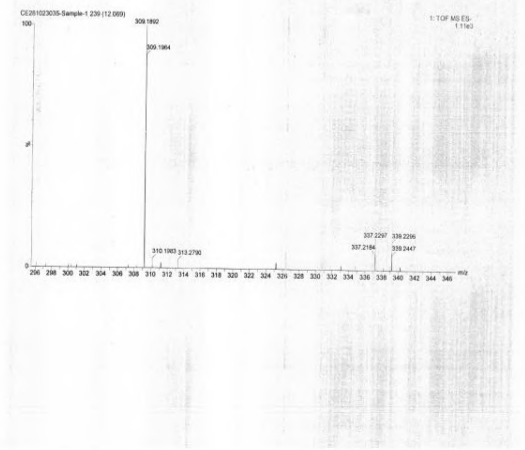
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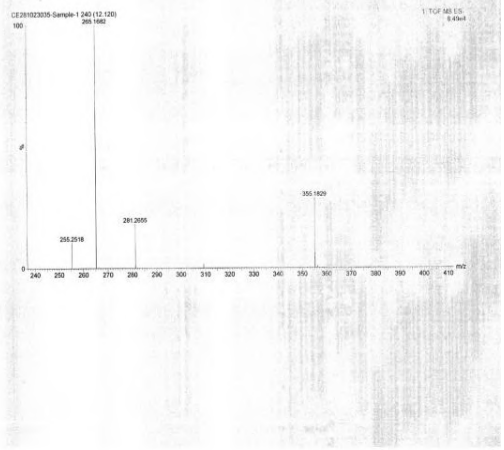
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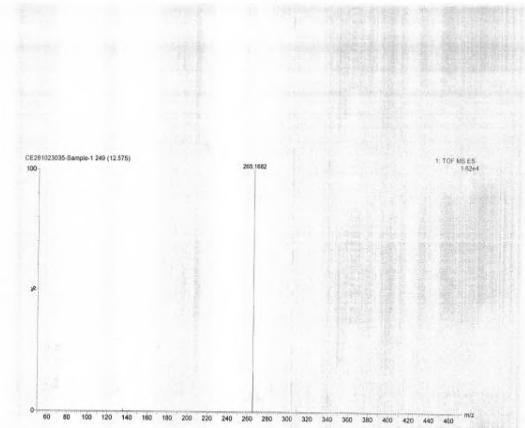
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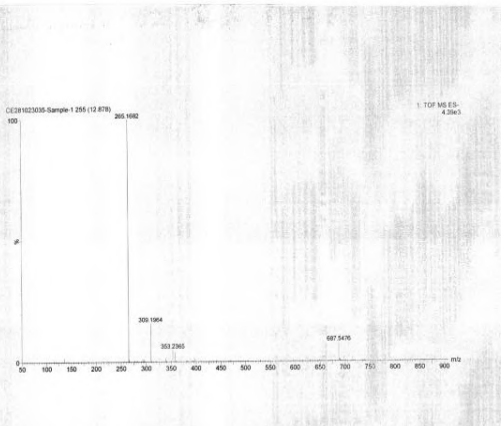
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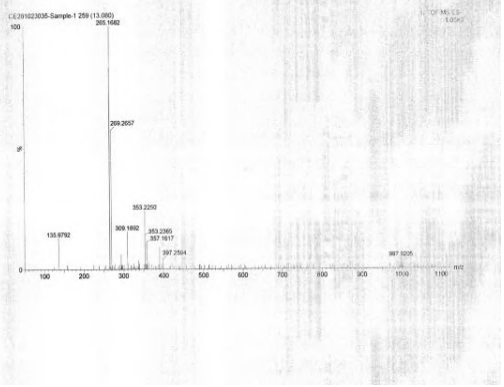
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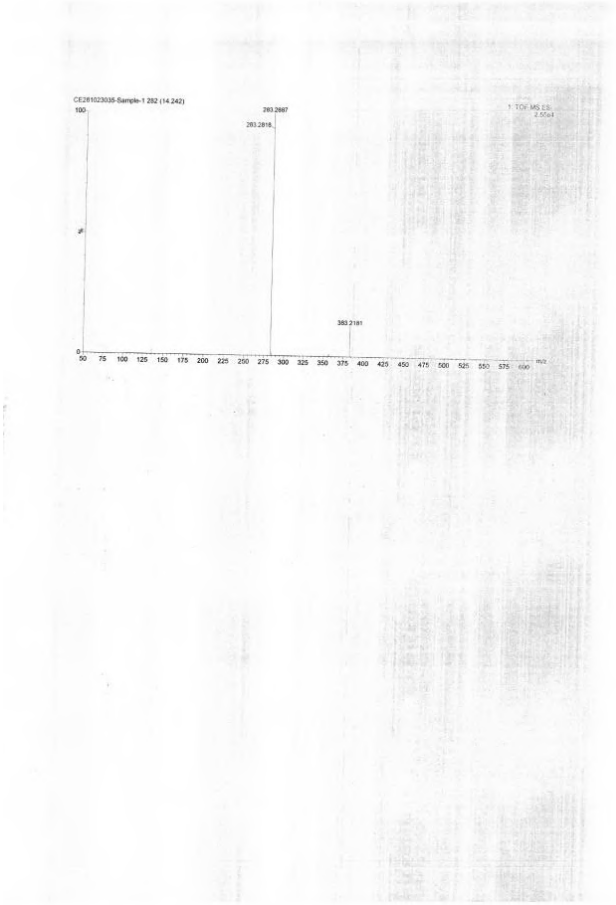
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ANNEXURE 4: CLINICAL STUDY

Patient Information Sheet

Instructions to Participant

1. You are being invited to participate in this research.
2. Before you take part in this research, the research must be explained to you and you must be given the chance to ask questions.
3. Please read carefully the information provided here and in the attached consent form. These two documents seek to provide you with information about the research.
4. Please ask questions about anything you don't understand before deciding whether or not to take part. If you agree to participate, please sign the consent form.
5. You will be given a copy of this document to take home with you.

DETAILS OF RESEARCH STUDY

PROTOCOL TITLE:

Evaluation of Jeevanthyadi Ghrita matra basti on Chemo-radiation induced adverse events in cancer patients

Principal Investigator: Dr. Santosh F Patil. M.D (Ayurveda)

Study Site: Karnataka Cancer Therapy and Research Centre, Hubbali, Karnataka.

INTRODUCTION

You are invited to participate in a clinical study on Jeevanthyadi Ghrita matra basti prepared with herbs based on Ayurveda classics in cancer patients receiving Concurrent chemo-radiation therapy. This document gives you a description of the study in which you are being asked to participate. Your participation in this study is voluntary, and you can enquire about all details before giving your written consent to participate in the study.

PURPOSE OF THE RESEARCH

You have been asked to participate in this research study since you have cancer and is advised concurrent chemo-radiation therapy. Also you fulfil the other selection criteria for the study. Concurrent chemo-radiation therapy advised in different cancers can cause range of known side-effects which themselves can become a barrier for continuing the indicated therapy. If these side-effects are addressed and taken care then the course of treatment can be completed which later helps to prevent loco-regional occurrence and improves quality of life.

Currently alternative system of medicine like AYUSH has been recommended to control side effects and enhance quality of life. In recent past many Ayurveda drugs have been used for this problem and given encouraging results.

In this research study you will be given Jeevanthyadi Ghruta matra basti (retention enema of medicated ghee) along with concurrent chemo-radiation therapy to see its effects in bring down side effects and improving quality of life. Jeevanthyadi Ghruta is one such Ayurveda formulation indicated in disorder called Yaksham (Debilitating condition) which include symptoms like aruchi (loss of appetite), chardi (vomiting), ruja (body pain), parswasula (lowback ache), jwara (fever), swasa (breathing problem) etc. The present study aims to create scientific evidence and your participation will help in exploring the role of Ayurveda in cancer management.

RESEARCH PROCEDURES AND SCHEDULE

In this study you will be given Jeevanthyadi Ghruta through rectal route, in the retention enema form along with concurrent chemo-radiation therapy. This enema will be given three days continuously before every chemotherapy dose, without interfering the conventional therapy schedule.

Schedule of study

Study plan	Outcome measures and Intervention	EORTC -QLC 30	ECOG	CBC	LFT	RFT
Pre-treatment		√	√	√	√	√
Day 1-3	JGMB					
Day 4-8	1st CT + RT					
Day 9-11	JGMB	√				
Day 12- 16	2nd CT + RT					
Day 17-19	JGMB					
Day 19th		√	√	√	√	√
Day 20-24	3rd CT + RT					
Day 25-27	JGMB	√				
Day 28-32	4th CT + RT					
Day 33-35	JGMB	√				
Day 36-40	5th CT + RT					
Day 41-43	JGMB	√				
Day 44-48	6th CT + RT					
Day 49		√	√	√	√	√

Note : JGMB- Jeevanthyadi Ghrita Matra basti, CT- chemotherapy , RT - Radiation therapy.

Enema is procedure where medicine will be given through anal route. It is given after taking some food and it takes about approximately 5 minutes to administer the enema. After the enema procedure is administered the patient should be in sleeping position for atleast 30 minutes. The enema given may be retained minimum upto 3 hours and even completely absorbed. Once before starting the treatment you will be assessed for eligibility of Matra basti [Medicated ghee enema]. Investigator will examine you every week and ask you questions about your health-related quality of life up till maximum of 6 weeks. You will be asked to observe your daily symptoms during treatment in hospital. You can discuss with your study doctor regarding all your concerns or any other treatment that you may wish to take.

BENEFITS AND RISK

Jeevanthyadi Ghrita Matra Basti may help to manage your side effects and symptoms related to advised conventional therapy and disease. Your participation is helpful to provide a better service to the patients in future. During administration of Matra Basti (enema) you may feel little bit of discomfort. Post administration of Jeevanthyadi Ghrita Matra Basti you may experience few known complications like abdominal discomfort or heavy, loss of appetite and nausea. It may also cause a different set of unknown side effects. There are no other possible risks involved other than above mentioned.

SUBJECT'S RIGHTS

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you or your legal representative will be informed in a timely manner by the Principal Investigator or his/her representative.

If you agree to participate in this study, you should take the Jeevanthyadi Ghrita Matra Basti as instructed and follow the advice given to you by the study team. Inform the Principal Investigator as soon as possible about any side effects that you may have encountered.

WITHDRAWAL FROM STUDY

You are free to withdraw your consent and discontinue your participation at any time without prejudice to you or effect on your medical care. If you decide to stop taking part in this study, you should tell the Principal Investigator.

Your doctor, the Principal Investigator may stop your participation in the study at any time for one or more of the following reasons.

1. Failure to follow the instructions of the Principal Investigator and/or study staff
2. If you experience Adverse Events/Serious Adverse Events
3. If the Principal Investigator decides that continuing your participation could be harmful to you.
4. If you require any additional treatment not allowed in the study
5. If the study is cancelled
6. Other administrative reasons

CONFIDENTIALITY OF STUDY AND MEDICAL RECORDS

We will protect your records so that your name, address, and phone number will be kept confidential. Information collected for this study will be kept confidential. Your records, to the extent of the applicable laws and regulations, will not be made publicly available. Only your Investigator(s) will have access to the confidential information being collected.

However, Regulatory Agencies, Institution Ethics Committee will be granted direct access to your original medical records to check study procedures and data, without making any of your information public. By signing the Informed Consent Form attached, you or your legal representative is authorizing such access to your study and medical records.

Data collected and entered into the Case Report Forms are the property of the Institution. In the event of any publication regarding this study, your identity will remain confidential.

COSTS OF PARTICIPATION

If you take part in this study, the Jeevanthyadi ghrita matra basti will be provided free of cost.

RESEARCH RELATED INJURY AND COMPENSATION

The Hospital does not make any provisions to compensate trial subjects for research related injury. However, You will be provided medical care at this institute for any injury or illness that occurs as a direct result of your participation in this study. This medical care will be at no cost to you. By signing this consent form, you will not waive any of your legal rights.

WHOM TO CONTACT IF YOU HAVE QUESTIONS

If you have questions about this research study and your rights or in the case of any injuries during the course of this study, you may contact the Principal Investigator,

Dr.Santosh F Patil.
Assistant Professor Dept of Agadatantra
KAHER Shri B M K Ayurveda Mahavidyalaya , Shahapur Belagavi -590001
Contact No- 9886633099.

INFORMED CONSENT FORM

Details of Research Study

Protocol Title: Evaluation of Jeevanthyadi Ghrita matra basti on Chemo-radiation induced adverse events in cancer patients

Principal Investigator: Dr. Santosh F Patil.

Subject's Particulars

Name: **Subject No:**

Address:

Sex: **Date of Birth** _____ **DD/MM/YYYY**

Part I – To be filled by patient

I, _____

agree to participate in the research study as described and on the terms set out in the Patient Information Sheet. The nature of my participation in the proposed research study has been explained to me in English Language by Dr. Santosh F Patil, Principal Investigator.

I have fully discussed and understood the purpose and procedures of this study. I have been given the Patient Information Sheet and the opportunity to ask questions about this study and have received satisfactory answers and information.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons and without my medical care being affected.

I also give permission for information in my medical records to be used for research. In any event of publication, I understand that this information will not bear my name or other identifiers and that due care will be taken to preserve the confidentiality of this information.

_____ _____

[Signature/Thumbprint (Right / Left) of patient] **(Date of signing)**

Part II – To be filled by parent / legal guardian, where applicable

I, _____hereby give consent for the above patient to participate in the (parent / legal guardian) proposed research study. The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

_____ _____

[Signature/Thumbprint (Right / Left) of parent /legal guardian] **(Date of signing)**

Part III – to be filled witness, where applicable

Witnessed by: _____ _____

(Name of witness) **(Designation of witness)**

_____ _____

(Signature of witness) **(Date of signing)**

Part IV– Investigator's Statement

I, the undersigned, certify to the best of my knowledge that the patient/patient's legally acceptable representative signing this informed consent form had the study fully explained and clearly understands the nature, risks and benefits of his/her / his ward's / her ward's participation in the study.

Dr. Santosh F Patil _____ _____

Name of Investigator **Signature** **Date**

ENGLISH

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: _____

Your birthdate (Day, Month, Year): _____

Today's date (Day, Month, Year): 31 _____

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page

ENGLISH

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor Excellent

ENGLISH

EORTC QLQ – H&N43

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:	Not at All	A Little	Quite a Bit	Very Much
31. Have you had pain in your mouth?	1	2	3	4
32. Have you had pain in your jaw?	1	2	3	4
33. Have you had soreness in your mouth?	1	2	3	4
34. Have you had pain in your throat?	1	2	3	4
35. Have you had problems swallowing liquids?	1	2	3	4
36. Have you had problems swallowing pureed food?	1	2	3	4
37. Have you had problems swallowing solid food?	1	2	3	4
38. Have you choked when swallowing?	1	2	3	4
39. Have you had problems with your teeth?	1	2	3	4
40. Have you had problems because of losing some teeth?	1	2	3	4
41. Have you had problems opening your mouth wide?	1	2	3	4
42. Have you had a dry mouth?	1	2	3	4
43. Have you had sticky saliva?	1	2	3	4
44. Have you had problems with your sense of smell?	1	2	3	4
45. Have you had problems with your sense of taste?	1	2	3	4
46. Have you had problems with coughing?	1	2	3	4
47. Have you had problems with hoarseness?	1	2	3	4
48. Have you had problems with your appearance?	1	2	3	4
49. Have you felt less physically attractive as a result of your disease or treatment?	1	2	3	4

Please go on to the next page

ENGLISH

During the past week:	Not at All	A Little	Quite a Bit	Very Much
50. Have you felt dissatisfied with your body?	1	2	3	4
51. Have you had problems eating?	1	2	3	4
52. Have you had problems eating in front of your family?	1	2	3	4
53. Have you had problems eating in front of other people?	1	2	3	4
54. Have you had problems enjoying your meals?	1	2	3	4
55. Have you had problems talking to other people?	1	2	3	4
56. Have you had problems talking on the telephone?	1	2	3	4
57. Have you had problems talking in a noisy environment?	1	2	3	4
58. Have you had problems speaking clearly?	1	2	3	4
59. Have you had problems going out in public?	1	2	3	4
60. Have you felt less interest in sex?	1	2	3	4
61. Have you felt less sexual enjoyment?	1	2	3	4
62. Have you had problems raising your arm or moving it sideways?	1	2	3	4
63. Have you had pain in your shoulder?	1	2	3	4
64. Have you had swelling in your neck?	1	2	3	4
65. Have you had skin problems (e.g. itchy, dry)?	1	2	3	4
66. Have you had a rash?	1	2	3	4
67. Has your skin changed colour?	1	2	3	4
68. Have you worried that your weight is too low?	1	2	3	4
69. Have you worried about the results of examinations and tests?	1	2	3	4
70. Have you worried about your health in the future?	1	2	3	4
71. Have you had problems with wounds healing?	1	2	3	4
72. Have you had tingling or numbness in your hands or feet?	1	2	3	4
73. Have you had problems chewing?	1	2	3	4

ENGLISH

EORTC QLQ – CX24

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems. Please answer by circling the number that best applies to you.

During the past week:	Not at all	A little	Quite a bit	Very much
31. Have you had cramps in your abdomen?	1	2	3	4
32. Have you had difficulty in controlling your bowels?	1	2	3	4
33. Have you had blood in your stools (motions)?	1	2	3	4
34. Did you pass water/urine frequently?	1	2	3	4
35. Have you had pain or a burning feeling when passing water/urinating?	1	2	3	4
36. Have you had leaking of urine?	1	2	3	4
37. Have you had difficulty emptying your bladder?	1	2	3	4
38. Have you had swelling in one or both legs?	1	2	3	4
39. Have you had pain in your lower back?	1	2	3	4
40. Have you had tingling or numbness in your hands or feet?	1	2	3	4
41. Have you had irritation or soreness in your vagina or vulva?	1	2	3	4
42. Have you had discharge from your vagina?	1	2	3	4
43. Have you had abnormal bleeding from your vagina?	1	2	3	4
44. Have you had hot flushes and/or sweats?	1	2	3	4
45. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
46. Have you felt less feminine as a result of your disease or treatment?	1	2	3	4
47. Have you felt dissatisfied with your body?	1	2	3	4

Please go on to the next page

ENGLISH

During the past 4 weeks:	Not at all	A little	Quite a bit	Very much
48. Have you worried that sex would be painful?	1	2	3	4
49. Have you been sexually active?	1	2	3	4
Answer these questions only if you have been sexually active during the past 4 weeks:	**Not at all**	**A little**	**Quite a bit**	**Very much**
50. Has your vagina felt dry during sexual activity?	1	2	3	4
51. Has your vagina felt short?	1	2	3	4
52. Has your vagina felt tight?	1	2	3	4
53. Have you had pain during sexual intercourse or other sexual activity?	1	2	3	4
54. Was sexual activity enjoyable for you?	1	2	3	4

ENGLISH

EORTC QLQ – OES18

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:		Not at all	A little	Quite a bit	Very much
31.	Could you eat solid food?	1	2	3	4
32.	Could you eat liquidised or soft food?	1	2	3	4
33.	Could you drink liquids?	1	2	3	4
34.	Have you had trouble with swallowing your saliva?	1	2	3	4
35.	Have you choked when swallowing?	1	2	3	4
36.	Have you had trouble enjoying your meals?	1	2	3	4
37.	Have you felt full up too quickly?	1	2	3	4
38.	Have you had trouble with eating?	1	2	3	4
39.	Have you had trouble with eating in front of other people?	1	2	3	4
40.	Have you had a dry mouth?	1	2	3	4
41.	Did food and drink taste different from usual?	1	2	3	4
42	Have you had trouble with coughing?	1	2	3	4
43.	Have you had trouble with talking?	1	2	3	4
44.	Have you had acid indigestion or heartburn?	1	2	3	4
45.	Have you had trouble with acid or bile coming into your mouth?	1	2	3	4
46.	Have you had pain when you eat?	1	2	3	4
47.	Have you had pain in your chest?	1	2	3	4
48.	Have you had pain in your stomach?	1	2	3	4

Weekly Ranking and Percentage of Adverse effects in CCRT and CCRT+MB Groups

Symptoms Ranking of All Cancer Patients of CCRT & CCRT + MB Group After 1st week.

Sl. No	Ranking	CCRT Group [n=70]			CCRT + MB Group [n=70]		
		Symptoms	n	%	Symptoms	n	%
1.	1.	Pain	40	57.1	Pain	27	38.6
2.	2.	Loss of Appetite	30	42.9	Dysphagia	25	35.7
3.	3.	Nausea	29	41.4	loss of Appetite	21	30
4.	4.	Dysphagia	28	40	Nausea	18	25.7
5.	5.	Weakness/fatigue	27	38.6	Sleep disturbed	17	24.3
6.	6.	Constipation	19	27.1	Weakness/fatigue	14	20
7.	7.	Sleep disturbed	19	27.1	Low back ache	14	20
8.	8.	Abdominal discomfort	18	25.7	Abdominal discomfort	13	18.6
9.	9.	Sticky Saliva	16	22.9	Constipation	10	14.3
10.	10.	Tastelessness	16	22.9	Vomiting	9	12.9
11.	11.	Burning sensation	15	21.4	White Discharge	9	12.9
12.	12.	Dry mouth	14	20	Choking	8	11.4
13.	13.	Vomiting	13	18.6	Dry mouth	7	10
14.	14.	Choking	11	15.7	Burning sensation	7	10
15.	15.	White Discharge	9	12.9	Sticky Saliva	6	8.6
16.	16.	Low back ache	9	12.9	Anxiety	6	8.6
17.	17.	Mucositis	8	11.4	Tastelessness	6	8.6
18.	18.	Headache	8	11.4	Headache	5	7.1
19.	19.	Change in voice	7	10	Cough	4	5.7
20.	20.	Anxiety	6	8.6	Loose Stools	4	5.7
21.	21.	Cough	6	8.6	Bleeding P/V	3	4.3
22.	22.	Loose Stools	6	8.6	Numbness in Limbs	2	2.9
23.	23.	Numbness in Limbs	3	4.3	Change in voice	2	2.9
24.	24.	Depressive	3	4.3	Oral ulcers	2	2.9
25.	25.	Restricted Mouth Opening	2	2.9	Depressive	2	2.9
26.	26.	Giddiness	2	2.9	Bleeding	2	2.9
27.	27.	Excessive Salivation	2	2.9	Mucositis	1	1.4
28.	28.	Bleeding P/V	2	2.9	Dyspnea	1	1.4
29.	29.	Burning Micturition	2	2.9	Urinary Urgency	1	1.4
30.	30.	Urinary Urgency	2	2.9	Skin discoloration	0	0
31.	31.	Skin peeling	1	1.4	Skin peeling	0	0
32.	32.	Neuropathy	1	1.4	Restricted Mouth Opening	0	0
33.	33.	Dyspnea	1	1.4	Giddiness	0	0
34.	34.	Fever	1	1.4	Neuropathy	0	0
35.	35.	Oral ulcers	0	0	Excessive Salivation	0	0
36.	36.	Skin discoloration	0	0	Fever	0	0
37.	37.	Blurred Vision	0	0	Burning Micturition	0	0
38.	38.	Wound Discharge /Sinus/	0	0	Blurred Vision	0	0
39.	39.	Herpes	0	0	Wound Discharge /Sinus/	0	0
40.	40.	Bleeding	0	0	Herpes	0	0

Note: As this table includes all patients of CCRT group, hence here Pain could be Throat/GBS/Chest, similarly Burning sensation in mouth/Chest/Anal verge/ and Bleeding could be Per Vaginal, Rectal & Oral.

Symptoms Ranking of All Cancer Patients of CCRT & CCRT + MB Group After 2nd week.

Sl. No	Ranking	CCRT Group [n=69]			CCRT + MB Group [n= 70]		
		Symptoms	n	%	Symptoms	n	%
1.	1.	Loss of Appetite	57	82.6	Dysphagia	31	44.3
2.	2.	Weakness/fatigue	52	75.4	Pain in Throat/GB/Chest	30	42.9
3.	3.	Nausea	48	69.6	Loss of Appetite	21	30
4.	4.	Pain in Throat/GB/Chest	44	63.8	Tastelessness	19	27.1
5.	5.	Tastelessness	44	63.8	Nausea	18	25.7
6.	6.	Dry mouth	42	60.9	Weakness/fatigue	15	21.4
7.	7.	Dysphagia	39	56.5	Sleep disturbed	15	21.4
8.	8.	Sleep disturbed	39	56.5	Burning sensation	13	18.6
9.	9.	Constipation	37	53.6	Constipation	12	17.1
10.	10.	Burning sensation	36	52.2	Sticky Saliva	11	15.7
11.	11.	Sticky Saliva	32	46.4	Dry mouth	10	14.3
12.	12.	Choking	26	37.7	Abdominal discomfort	10	14.3
13.	13.	Mucositis	25	36.2	Loose Stools	8	11.4
14.	14.	Abdominal discomfort	23	33.3	Low back ache	8	11.4
15.	15.	Vomiting	20	29	Vomiting	7	10
16.	16.	Oral ulcers	17	24.6	Choking	7	10
17.	17.	Anxiety	16	23.2	Anxiety	7	10
18.	18.	Change in voice	15	21.7	Excessive Salivation	7	10
19.	19.	Loose Stools	15	21.7	Mucositis	5	7.1
20.	20.	Low back ache	11	15.9	Headache	5	7.1
21.	21.	Cough	10	14.5	Depressive	4	5.7
22.	22.	Restricted Mouth Opening	9	13	Cough	4	5.7
23.	23.	Headache	8	11.6	Change in voice	3	4.3
24.	24.	Skin discoloration	8	11.6	White Discharge	3	4.3
25.	25.	White Discharge	8	11.6	Oral ulcers	2	2.9
26.	26.	Skin peeling	7	10.1	Restricted Mouth Opening	2	2.9
27.	27.	Depressive	7	10.1	Numbness in Limbs	1	1.4
28.	28.	Burning Micturition	7	10.1	Giddiness	1	1.4
29.	29.	Urinary Urgency	6	8.7	Dyspnea	1	1.4
30.	30.	Numbness in Limbs	3	4.3	Skin discoloration	0	0
31.	31.	Neuropathy	3	4.3	Skin peeling	0	0
32.	32.	Excessive Salivation	2	2.9	Neuropathy	0	0
33.	33.	Giddiness	1	1.4	Fever	0	0
34.	34.	Dyspnea	1	1.4	Bleeding	0	0
35.	35.	Fever	1	1.4	Bleeding P/V	0	0
36.	36.	Bleeding P/V	1	1.4	Burning Micturition	0	0
37.	37.	Blurred Vision	0	0	Urinary Urgency	0	0
38.	38.	Wound Discharge /Sinus/	0	0	Blurred Vision	0	0
39.	39.	Herpes	0	0	Wound Discharge /Sinus/	0	0
40.	40.	Bleeding	0	0	Herpes	0	0

Note: As this table includes all patients of CCRT group, hence here Pain could be Throat/GBS/Chest, similarly Burning sensation in mouth/Chest/Anal verge/ and Bleeding could be Per Vaginal, Rectal & Oral.

Symptoms Ranking of All Cancer Patients of CCRT & CCRT + MB Group After 3rd week.

Sl. No	Ranking	CCRT Group [n=67]			CCRT + MB Group [n= 70]		
		Symptoms	n	%	Symptoms	n	%
1.	1.	Loss of Appetite	63	94	Pain in Throat/GB/Chest	35	50
2.	2.	Weakness/fatigue	61	91	Dysphagia	31	44.3
3.	3.	Tastelessness	59	88.1	Burning sensation	28	40
4.	4.	Nausea	58	86.6	Tastelessness	28	40
5.	5.	Sleep disturbed	54	80.6	Nausea	23	32.9
6.	6.	Dry mouth	50	74.6	Sticky Saliva	22	31.4
7.	7.	Burning sensation	50	74.6	Weakness/fatigue	22	31.4
8.	8.	Sticky Saliva	49	73.1	Loss of Appetite	20	28.6
9.	9.	Dysphagia	45	67.2	Dry mouth	18	25.7
10.	10.	Pain in Throat/GB/Chest	42	62.7	Mucositis	14	20
11.	11.	Constipation	40	59.7	Abdominal discomfort	13	18.6
12.	12.	Mucositis	39	58.2	Sleep disturbed	12	17.1
13.	13.	Choking	38	56.7	Loose Stools	12	17.1
14.	14.	Oral ulcers	33	49.3	Low back ache	10	14.3
15.	15.	Anxiety	30	44.8	Constipation	9	12.9
16.	16.	Skin discoloration	27	40.3	Vomiting	8	11.4
17.	17.	Abdominal discomfort	26	38.8	Choking	8	11.4
18.	18.	Change in voice	25	37.3	Anxiety	7	10
19.	19.	Skin peeling	25	37.3	Excessive Salivation	7	10
20.	20.	Loose Stools	22	32.8	Cough	6	8.6
21.	21.	Vomiting	21	31.3	Oral ulcers	5	7.1
22.	22.	Restricted mouth Opening	19	28.4	Restricted mouth Opening	4	5.7
23.	23.	Depressive	16	23.9	Depressive	4	5.7
24.	24.	Cough	15	22.4	Headache	3	4.3
25.	25.	Low back ache	13	19.4	Change in voice	3	4.3
26.	26.	Headache	10	14.9	Giddiness	3	4.3
27.	27.	Burning Micturition	10	14.9	Fever	3	4.3
28.	28.	Urinary Urgency	7	10.4	Burning Micturition	3	4.3
29.	29.	White Discharge	6	9	White Discharge	2	2.9
30.	30.	Numbness in Limbs	5	7.5	Numbness in Limbs	1	1.4
31.	31.	Dyspnea	3	4.5	Skin discoloration	1	1.4
32.	32.	Giddiness	2	3	Neuropathy	1	1.4
33.	33.	Neuropathy	2	3	Dyspnea	1	1.4
34.	34.	Fever	2	3	Skin peeling	0	0
35.	35.	Bleeding P/V	2	3	Bleeding	0	0
36.	36.	Excessive Salivation	1	1.5	Bleeding P/V	0	0
37.	37.	Herpes	1	1.5	Urinary Urgency	0	0
38.	38.	Bleeding	1	1.5	Blurred Vision	0	0
39.	39.	Blurred Vision	0	0	Wound Discharge /Sinus/	0	0
40.	40.	Wound Discharge /Sinus/	0	0	Herpes	0	0

Note: As this table includes all patients of CCRT group, hence here Pain could be Throat/GBS/Chest, similarly Burning sensation in mouth/Chest/Anal verge/ and Bleeding could be Per Vaginal, Rectal & Oral.

Symptoms Ranking of All Cancer Patients of CCRT & CCRT + MB Group After 4th week.

Sl. No	Ranking	CCRT Group [n=67]			CCRT + MB Group [n=69]		
		Symptoms	n	%	Symptoms	n	%
1.	1.	Loss of Appetite	66	98.5	Burning sensation	38	55.1
2.	2.	Weakness/fatigue	65	97	Tastelessness	35	50.7
3.	3.	Tastelessness	63	94	Pain in Throat/GB/Chest	33	47.8
4.	4.	Nausea	60	89.6	Dry mouth	31	44.9
5.	5.	Burning sensation	59	88.1	Dysphagia	31	44.9
6.	6.	Sleep disturbed	58	86.6	Sticky Saliva	25	36.2
7.	7.	Dry mouth	53	79.1	Loss of Appetite	25	36.2
8.	8.	Sticky Saliva	51	76.1	Weakness/fatigue	23	33.3
9.	9.	Dysphagia	46	68.7	Mucositis	22	31.9
10.	10.	Anxiety	46	68.7	Nausea	21	30.4
11.	11.	Pain in Throat/GB/Chest	44	65.7	Abdominal discomfort	15	21.7
12.	12.	Constipation	43	64.2	Loose Stools	13	18.8
13.	13.	Mucositis	41	61.2	Vomiting	12	17.4
14.	14.	Choking	41	61.2	Sleep disturbed	12	17.4
15.	15.	Oral ulcers	38	56.7	Anxiety	11	15.9
16.	16.	Skin discoloration	37	55.2	Cough	11	15.9
17.	17.	Skin peeling	36	53.7	Excessive Salivation	10	14.5
18.	18.	Restricted mouth Opening	32	47.8	Low back ache	10	14.5
19.	19.	Depressive	30	44.8	Constipation	9	13
20.	20.	Abdominal discomfort	29	43.3	Choking	9	13
21.	21.	Change in voice	28	41.8	Burning Micturition	9	13
22.	22.	Vomiting	26	38.8	Depressive	7	10.1
23.	23.	Loose Stools	19	28.4	Oral ulcers	5	7.2
24.	24.	Burning Micturition	17	25.4	Restricted mouth Opening	5	7.2
25.	25.	Headache	12	17.9	Headache	3	4.3
26.	26.	Cough	12	17.9	Change in voice	3	4.3
27.	27.	Urinary Urgency	12	17.9	Skin discoloration	3	4.3
28.	28.	Low back ache	11	16.4	Fever	3	4.3
29.	29.	Numbness in Limbs	6	9	Urinary Urgency	2	2.9
30.	30.	Neuropathy	4	6	Numbness in Limbs	1	1.4
31.	31.	White Discharge	4	6	Giddiness	1	1.4
32.	32.	Giddiness	3	4.5	Dyspnea	1	1.4
33.	33.	Fever	3	4.5	Bleeding	1	1.4
34.	34.	Dyspnea	2	3	Bleeding P/V	1	1.4
35.	35.	Excessive Salivation	1	1.5	White Discharge	1	1.4
36.	36.	Herpes	1	1.5	Skin peeling	0	0
37.	37.	Bleeding	1	1.5	Neuropathy	0	0
38.	38.	Bleeding P/V	1	1.5	Blurred Vision	0	0
39.	39.	Blurred Vision	0	0	Wound Discharge /Sinus/	0	0
40.	40.	Wound Discharge /Sinus/	0	0	Herpes	0	0

Note: As this table includes all patients of CCRT group, hence here Pain could be Throat/GBS/Chest, similarly Burning sensation in mouth/Chest/Anal verge/ and Bleeding could be Per Vaginal, Rectal & Oral.

Symptoms Ranking of All Cancer Patients of CCRT & CCRT + MB Group After 5th week.

Sl. No	Ranking	CCRT Group [n=64]			CCRT + MB Group [n= 69]		
		Symptoms	n	%	Symptoms	n	%
1.	1.	Loss of Appetite	64	100	Tastelessness	46	66.7
2.	2.	Weakness/fatigue	64	100	Burning sensation	40	58
3.	3.	Tastelessness	61	95.3	Dysphagia	37	53.6
4.	4.	Burning sensation	58	90.6	Dry mouth	35	50.7
5.	5.	Sleep disturbed	58	90.6	Pain in Throat/GBS/Chest	35	50.7
6.	6.	Nausea	55	85.9	Weakness/fatigue	30	43.5
7.	7.	Dry mouth	50	78.1	Mucositis	29	42
8.	8.	Anxiety	50	78.1	Sticky Saliva	29	42
9.	9.	Sticky Saliva	48	75.0	Loss of Appetite	23	33.3
10.	10.	Dysphagia	44	68.8	Skin discoloration	20	29
11.	11.	Pain in Throat/GBS/Chest	43	67.2	Nausea	16	23.2
12.	12.	Choking	43	67.2	Anxiety	15	21.7
13.	13.	Constipation	42	65.6	Loose Stools	13	18.8
14.	14.	Mucositis	39	60.9	Depressive	11	15.9
15.	15.	Oral ulcers	39	60.9	Cough	11	15.9
16.	16.	Skin discoloration	37	57.8	Burning Micturition	11	15.9
17.	17.	Skin peeling	37	57.8	Choking	9	13
18.	18.	Depressive	36	56.3	Excessive Salivation	9	13
19.	19.	Restricted mouth Opening	34	53.1	Vomiting	8	11.6
20.	20.	Change in voice	32	50.0	Constipation	8	11.6
21.	21.	Vomiting	25	39.1	Oral ulcers	8	11.6
22.	22.	Abdominal discomfort	24	37.5	Abdominal discomfort	7	10.1
23.	23.	Loose Stools	20	31.3	Sleep disturbed	6	8.7
24.	24.	Burning Micturition	19	29.7	Skin peeling	6	8.7
25.	25.	Cough	15	23.4	Restricted mouth Opening	6	8.7
26.	26.	Urinary Urgency	15	23.4	Low back ache	4	5.8
27.	27.	Low back ache	12	18.8	Headache	3	4.3
28.	28.	Headache	10	15.6	Fever	3	4.3
29.	29.	Numbness in Limbs	5	7.8	Urinary Urgency	3	4.3
30.	30.	Neuropathy	4	6.3	Change in voice	2	2.9
31.	31.	White Discharge	3	4.7	Giddiness	1	1.4
32.	32.	Giddiness	2	3.1	Dyspnea	1	1.4
33.	33.	Excessive Salivation	2	3.1	White Discharge	1	1.4
34.	34.	Dyspnea	1	1.6	Numbness in Limbs	0	0
35.	35.	Fever	1	1.6	Neuropathy	0	0
36.	36.	Herpes	1	1.6	Bleeding	0	0
37.	37.	Bleeding P/V	1	1.6	Bleeding P/V	0	0
38.	38.	Blurred Vision	0	0.0	Blurred Vision	0	0
39.	39.	Wound Discharge /Sinus/	0	0.0	Wound Discharge /Sinus/	0	0
40.	40.	Bleeding	0	0.0	Herpes	0	0

Note: As this table includes all patients of CCRT group, hence here Pain could be Throat/GBS/Chest, similarly Burning sensation in mouth/Chest/Anal verge/ and Bleeding could be Per Vaginal, Rectal & Oral.

Symptoms Ranking of All Cancer Patients of CCRT & CCRT + MB Group After 6th week.

Sl. No	Ranking	CCRT Group [n=31]			CCRT + MB Group [n=41]		
		Symptoms	n	%	Symptoms	n	%
1.	1.	Dry mouth	31	100	Tastelessness	32	78
2.	2.	loss of Appetite	31	100	Dry mouth	30	73.2
3.	3.	Weakness/fatigue	31	100	Pain in Throat/GB/Chest	30	73.2
4.	4.	Tastelessness	31	100	Dysphagia	29	70.7
5.	5.	Nausea	30	96.8	Mucositis	28	68.3
6.	6.	Sticky Saliva	30	96.8	Burning sensation	28	68.3
7.	7.	Sleep disturbed	30	96.8	Sticky Saliva	26	63.4
8.	8.	Pain in Throat/GB/Chest	29	93.5	Skin discoloration	23	56.1
9.	9.	Dysphagia	29	93.5	Weakness/fatigue	22	53.7
10.	10.	Choking	29	93.5	Cough	13	31.7
11.	11.	Burning sensation	29	93.5	Oral ulcers	11	26.8
12.	12.	Anxiety	29	93.5	Loss of Appetite	9	22
13.	13.	Mucositis	28	90.3	Anxiety	9	22
14.	14.	Constipation	28	90.3	Nausea	8	19.5
15.	15.	Oral ulcers	27	87.1	Choking	8	19.5
16.	16.	Change in voice	26	83.9	Depressive	8	19.5
17.	17.	Skin discoloration	26	83.9	Skin peeling	7	17.1
18.	18.	Skin peeling	26	83.9	Restricted mouth Opening	6	14.6
19.	19.	Restricted mouth Opening	24	77.4	Constipation	4	9.8
20.	20.	Depressive	22	71	Loose Stools	4	9.8
21.	21.	Cough	13	41.9	Change in voice	3	7.3
22.	22.	Vomiting	10	32.3	Sleep disturbed	3	7.3
23.	23.	Headache	5	16.1	Excessive Salivation	3	7.3
24.	24.	Abdominal discomfort	5	16.1	Burning Micturition	3	7.3
25.	25.	Loose Stools	3	9.7	Headache	2	4.9
26.	26.	Neuropathy	2	6.5	Giddiness	2	4.9
27.	27.	Dyspnea	2	6.5	Abdominal discomfort	2	4.9
28.	28.	Giddiness	1	3.2	Vomiting	1	2.4
29.	29.	Blurred Vision	1	3.2	Fever	1	2.4
30.	30.	Wound Discharge /Sinus/	1	3.2	White Discharge	1	2.4
31.	31.	Low back ache	1	3.2	Low back ache	1	2.4
32.	32.	Burning Micturition	1	3.2	Urinary Urgency	1	2.4
33.	33.	Numbness in Limbs	0	0	Numbness in Limbs	0	0
34.	34.	Excessive Salivation	0	0	Neuropathy	0	0
35.	35.	Fever	0	0	Dyspnea	0	0
36.	36.	Herpes	0	0	Bleeding	0	0
37.	37.	Bleeding	0	0	Bleeding P/V	0	0
38.	38.	Bleeding P/V	0	0	Blurred Vision	0	0
39.	39.	White Discharge	0	0	Wound Discharge /Sinus/	0	0
40.	40.	Urinary Urgency	0	0	Herpes	0	0

Note: As this table includes all patients of CCRT group, hence here Pain could be Throat/GBS/Chest, similarly Burning sensation in mouth/Chest/Anal verge/ and Bleeding could be Per Vaginal, Rectal & Oral.

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Date : 26/07/2022

CERTIFICATE

TO WHOMSOEVER IT MAY CONCERN

This is to certify that Dr Santosh. F. Patil Assistant Professor, Department of Agadatantraevum Vidhi Vaidhya of KAHER's Shri B M Kankanawadi Ayurveda Mahavidyalaya Belgaum has attended posting at the CTRT IPD ward and OPD during his Ph.D work on concurrent basis form 01-12-2021 to 31-07-2022.

During this period, he has examined various Cancer of Head & Neck, Cervix, Esophagus and observed different techniques of radiation like conventional RT, 3DCRT, IMRT, IGRT, Radiation planning and treatment execution and follow-up of post chemo-radiation treatment cases. At same time he was able to initiate a pilot study to see the effect of JeevanthyadiGhrita over Skin toxicity in Head & Neck cancer patients under guidance of Dr Saikumari, Radiation oncologist.

We would also like to mention that he has completed the enrollment of subjects for his Ph.D thesis entitled ***Evaluation offeevanthyadiGhritamatrabasti on Chemo-radiation inducedadverse events in cancer patients***in the month of July 2022.

During this tenure he was regular and sincere.

We wish him all the best for his future endeavors.

Dr. Manjula Huggi
Chief Administrative Officer
K.C.T.R.I., Navanagar, HUBBALLI-25.

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Ph.D. PROGRAM

Evaluation of Six Monthly Reports submitted by the Candidate

Name of the Ph.D Scholar : Dr. Santosh F. Patil

Name of the Guide : Dr. Suhaskumar Shetty, Principal,
Shri. B. M. K. Ayurveda Mahavidyalaya, Belagavi

Dr. Poornachandra Tejeswi S, Hubballi- Coguide

Batch/Category/Faculty : 2018 / Part-Time / Ayurveda

Topic Evaluation of Jeevanthyadi Ghrita Matra Basti on Chemo-radiation induced adverse events in Cancer patients.

Report	Excellent	Good	Satisfactory	Poor
I			✓	
II			✓	
III			✓	
IV			✓	
V			✓	
VI			✓	
VII			✓	
VIII		✓		
IX			✓	

Note: Only when three reports are satisfactory and if the candidate has published articles as per rules then only the candidate is permitted to present second Open house seminar followed by submission of thesis

DIRECTOR ACADEMIC AFFAIRS Deemed to-be University

(Dr. Roopa M. Bellad)
Director, Academic Affairs

Cc to :
Dr. Suhaskumar Shetty, Principal, Shri. B. M. K. Ayurveda Mahavidyalaya, Belagavi -Guide
Dr. Poornachandra Tejeswi S, Hubballi - Coguide

NB: Research scholars are hereby informed in future to strictly enclose the source of documents to review half yearly reports.

ANNEXURE 5 : PUBLICATIONS

Pharmacogn. Res., 2023; 15(3):591-600.
https://www.phcogres.com

Original Article

Pharmaceutico-Analytical Assessment of *Jeevanthyadi ghrita*-A Polyherbal *Ayurveda* Formulation and its Potential Benefits

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[3]Consultant Radiation Oncologist, Padmashri Dr R B Patil The Karnataka Cancer Therapy and Reserach Institute, Hubballi, Karnataka, INDIA.

ABSTRACT

Background: Standardization and documentation of Traditional medicines have caught pace in recent past and yet remain a subject of discussion. *Jeevanthyadi ghrita* is a commonly prescribed empirically for debilitating health conditions. However, its pharmaceutical and analytical data remains untraced. Hence an attempt was made to prepare, screen the active biological constituents and review the recent activities of ingredients of the *Jeevanthyadi ghirta* to rationalize the classical indications. **Results:** Prepared *Jeevanthyadi ghrita* showed presence of Alkaloids and terpenoids. HPTLC analysis detected the presence of 7 and 11 active biological constituents at 254 nm and 366 nm respectively, which remains to be identified. No significant difference was noted between plain *ghrita* and prepared *Jeevanthyadi ghrita* in relation to AGMARK parameters. **Conclusion:** Recent activities of ingredients showed strong anti-inflammatory and immunomodulatory effect that has a relation in ceasing the pathology of debilitation.

Keywords: *Jeevanthyadi ghrita*, Debilitation, Anti-inflammatory, Alkaloids, Immunomodulatory, Pharmaceutico-Analytical.

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INTRODUCTION

Traditional Medicines are often chosen for chronic illness and there is no single best way for its documentation.[1,2] Perhaps, Ayurveda drugs are being used for varied pathological conditions and are seldom documented for all indications. Moreover, standardization of compound herbal formulation remains challenging, as it has many active biological constituents which remains unknown when tried to identify.[3] Recent advances in technology like High Power Thin Layer Chromatography (HPTLC) UV-Spectroscopy etc. are being used tools to analyze pharmaceutical products in a rational way.[4]

Jeevanthyadi ghrita [lipid-based compound formula] is one such formulation explained in Ayurveda in context of *Rajayaksham* that has been credited with qualities to cease the pathology of debilitation.[5] However, pharmaceutical analysis and clinical documentation of *Jeevanthyadi ghrita* have not been done despite its empirical usage.

Rajayaksham is a defined as a chronic debilitating disorder in Ayurveda. It is even quoted as *Roga samuha* [syndrome]. Dysregulate Oja [Immune system] is mentioned as the substrate for developing debilitation. This can happen due to four *Nidan* [etiology] namely, *ayatha balamaarambham* [physical activity surpassing one's own capacity], *vega sandharana* [suppression of the natural physiological urges], *kshaya* [depletion of tissue elements], and *vishamashanam* [irregular and unhealthy dietary habits], these etiological factors have the ability to aggravate the *vata dosha*. This unbalanced *vata dosha* is then responsible for derangement of all physiological processes and the vitality in the body i.e *Oja*. *Rajayaksham* exacerbates majorly with eleven symptoms and/or affecting various parts of the body like head, chest, back, rectum and joints based on localization of imbalanced *vata*.[6] Hence the study was aimed to analyze *Jeevanthyadi ghrita* and rationalize its potential classical indications through recent activities of its individual ingredients.

MATERIALS AND METHODS

Materials

Raw ingredients of *Jeevanthyadi ghrita* [Table 1] were procured from different reliable sources. Out of 14 herbs, 11 herbs were given for academic purpose by Dabur India Ltd., New Delhi, India. *Trayamana* [*Gentian Kurroo* Royle.] was procured from

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Table 1: Ingredients of *Jeevanthyadi ghrita*.

Sl. No.	Drug	Latin name	Part	Source
1	Jeevanti	*Leptadenia reticulata* Wight and Am.	Stem	Dabur India Ltd.
2	Yasthimadhu	*Glycyrrhiza glabra* Linn.	Root	
3	Draksha	*Vitis vinifera* Linn.	Fruit	
4	Kutaja	*Holerrhena antidysentrica* Wall.	Stem Bark	
5	Pushkaramula	*Inula racemosa* Hook. F.	Root	
6	Sati	*Hedychium spicatum* Ham. Ex Smith.	Rhizome	
7	Pippali	*Piper longum* Linn.	Fruit	
8	Gokshura	*Tribulus terrestris* Linn.	Fruit	
9	Bala	*Sida cordifolia* Linn.	Root and stem	
10	Nilothpala	*Nymphaea nouchali* Burm.F.	Flower	
11	Bhumyamalaki	*Phylanthus amarus* Schum. and Thonb.	Whole Plant	
12	Kantakari	*Solanum surattense* Burm. F.	Root	GMP Certified KLE Ayurveda Pharmacy.
13	Duralabha	*Fagonia cretica* Linn.	Whole Plant	
14	Trayamana	*Gentian Kurroo* Royle.	Rhizome	Natural Habitat.
15	Ghrita	*Hallikar Breed* Cow.		Karnataka.

its natural habitat and then authenticated at the Indian Council of Medical Research National Institute of Traditional Medicine [ICMR-NITM] Belagavi, Karnataka [Herbarium accession number RMRC-1677]. *Kantakari* [*Solanum surattense* Burm. F.], *Duralabha* [*Fagonia cretica* Linn.] were procured from GMP-certified KLE Ayurveda Pharmacy, Belagavi, Karnataka, India.

Ghrita/ghee prepared from the traditional fermentation method was procured from a farm at Kushalnagar, Madikeri District, Karnataka, India. The milk procured for preparing *ghrita* was from a native distinct breed named Hallikar cow which were reared on the same farm [Figure 1].

Methods

Preliminary Analysis of Raw Ingredients

All of the ingredients were re-authenticated and analyzed for macroscopic features [Table 2], Preliminary Physico-chemical [Table 3] and Phytochemical Analysis [Table 4] were carried out at KAHER's Shri B M Kankanawadi Ayurveda Mahavidyalaya's AYUSH approved Ayurveda Siddha Unani-Drug Testing Laboratory of Central Research Facility, Belagavi, Karnataka, India.[7]

Drug preparation: *Jeevanthyadi ghrita*

As per Ayurveda Formulary of India, the standard operating ratio of *ghrita* preparation [*Kalka:Ghrita:Jala*-1:4:16] was chosen and followed accordingly to prepare in quantum mentioned below [Table 5]. *Ghrita* was boiled until classical *Sneha siddhi* lakshana (traditional parameter for quality assessment) were achieved [Figure 2]. Processed *Jeevanthyadi ghrita* was stored in a sterile container.[8]

Drug Analysis: *Jeevanthyadi ghrita* Analysis

Plain ghee and Processed ghee (*Jeevanthyadi ghrita*) were analyzed for ghee standards as per AGMARK at ESSAR Laboratories and Research Centre [Government of India Approved AGMARK Laboratory, ISO 9000:2015 certified and NABL Accredited], Keshwapur, Hubli, Karnataka, India.

Phytochemical Screening and HPTLC Analysis of processed *Jeevanthyadi ghrita* were carried out at CARe Keralam Ltd., Koratty, Thrissur, India. [Test report number: CKL/22/ T376] for standardization.

High-Performance Thin Layer Chromatography [HPTLC] Analysis

Normal Phase: At a distance of 12.5 mm each, 2 µL sample was applied in three bands of 8mm each on pre-coated silica gel 60 G 254 aluminum plates (5mm × 10 mm) with Linomat 5 applicator attached CAMAG HPTLC system, having WINCATS software. TLC chambers were pre-saturated with Toluene: Ethyl Acetate: Hexane (6:3:1) as mobile phase for 30 min and then the plates were developed. Developed plates were read using Densitometry TLC scanner 3 at 254 and 366 nm in UV cabinet. Anisaldehyde-Sulphuric Acid Reagent was used for Post Chromatographic derivatization.

Table 2: Macroscopic Description of Ingredients of *Jeevanthyadi ghrita*.

Sl. No.	Drug	Colour	Odour	Taste
1	Jeevanti	Dull yellow	Odourless	Bitter
2	Yasthimadhu	Yellowish Brown	Faint Character	Sweetish
3	Draksha	Dark Brown	Pleasant	Sweetish
4	Kutaja	Buff to Brownish	Odourless	Acrid and Bitter
5	Pushkaramula	External brown Internal Yellowish	Bitter and Camphoraceous	Aromatic and Camphoraceous
6	Sati	Dark brown	Camphoraceous	Bitter
7	Pippali	Greenish black	Aromatic	Pungent
8	Gokshura	Light yellow	Characteristic	Slight Astringent
9	Bala	Brownish	Not specific	Not specific
10	Nilothpala	Brownish	Characteristic	Not specific
11	Bhumyamalaki	Greenish brown	Indistinct	Slightly Bitter
12	Kantakari	Yellowish green	Not distinct	Bitter
13	Duralabha	Brownish green	Characteristic	Bitter
14	Trayamana	Dark brown with yellow patches	Characteristic Aromatic	Bitter

Table 3: Physico-chemical Analysis of Ingredients of *Jeevanthyadi ghrita*.

Sl. No.	Drug	FM %	AV %	AIV %	WSE %	ASE %
1	Jeevanti	Nil	6.28	1.48	5.83	1.91
2	Yasthimadhu	Nil	7.15	1.59	22.23	11.46
3	Draksha	Nil	1.89	0.14	82.98	33.49
4	Kutaja	Nil	6.55	0.88	15.93	22.18
5	Pushkaramula	Nil	4.88	0.34	25.82	14.34
6	Sati	Nil	7.87	1.37	9.10	7.82
7	Pippali	Nil	6.61	0.38	43.02	9.25
8	Kantakari	Nil	6.87	0.91	6.08	2.29
9	Gokshura	Nil	13.67	1.70	16.77	7.50
10	Bala	Nil	1.58	0.96	12.34	3.35
11	Nilothpala	Nil	12.94	3.32	29.00	7.07
12	Bhumyamalaki	Nil	6.37	0.91	15.07	4.76
13	Trayamana	Nil	6.45	1.77	31.58	29.53
14	Duralabha	Nil	9.08	0.39	24.07	6.71

Note: All the values were under the range as specified by Ayurveda pharmacopeia. FM – Foreign Matter, AV – Ash Value, AIV – Acid Insoluble Ash, WSE – Water Soluble Extract, ASE – Alcohol Soluble Extract. All these valves are expressed in Percentage.

RESULTS

Phytochemical screening of *Jeevanthyadi ghrita* demonstrated the presence of alkaloids and Terpenoids [Tables 6 and 7]. HPTLC analysis detected the presence of 7 and 11 active biological constituents at 254 nm and 366 nm respectively, which remains to be identified [Table 8 and Figures 3, 4, 5]. No significant changes were observed in AGMARK standards of Plain ghee and *Jeevanthyadi ghrita*.

DISCUSSION

Duraipandi S, *et al.* 2015 also investigated to understand the Ayurveda Lipid-based formulation *Guggulu tiktaka ghrita*.[9] They aimed to understand the age-old ayurveda engineering

Table 4: Qualitative Phytochemical screening of Ingredients *Jeevanthyadi ghrita*.

Sl. No.	Drug Name/Test Name	Jeevanthi		Yasthimadhu		Draksha		Kutaja		Pushakarmula		Sati		Pippali	
		WE	AE	WE	AE	WE	AE	WE	AE	WE	AE	WE	AE	WE	AE
1	Carbohydrate	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2	Monosaccharaides	+	--	+	+	--	--	+	+	+	+	+	--	--	+
3	Reducing Sugar	+	--	+	+	+	+	+	--	+	+	+	--	+	+
4	Pentose sugar	--	--	--	--	--	--	--	--	--	--	--	--	+	--
5	Hexose Sugar	--	--	--	--	--	--	--	+	--	--	--	--	--	--
6	Protein	--	--	+	--	--	--	--	+	--	--	--	+	--	--
7	Amino acid	--	--	+	--	--	--	--	+	--	--	--	+	--	--
8	Steroids	+	+	--	+	--	--	--	--	--	--	--	+	--	--
9	Cardiac Glycosides	--	--	--	--	--	--	--	--	+	--	--	--	+	+
10	Saponins	+	--	+	--	+	+	+	--	--	--	+	--	--	
11	Alkaloids	--	--	--	+	--	--	--	--	--	+	--	--	--	+
12	Flavonoids	+	--	+	--	--	--	+	--	+	+	--	--	+	+
13	Tannins	--	--	+	+	+	+	+	+	+	+	+	--	+	+

Sl. No	Drug Name/Test Name	Gokshur		Bala		Nilothpala		Bhumayamlaki		Kantakari		Durlabha		Trayamana	
		WE	AE	WE	AE	WE	AE	WE	AE	WE	AE	WE	AE	WE	AE
1	Carbohydrate	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2	Monosaccharaides	+	--	+	+	+	+	+	+	+	--	+	--	+	--
3	Reducing Sugar	+	--	--	--	+	--	--	+	+	+	+	--	--	--
4	Pentose sugar	--	--	--	--	--	--	--	--	--	--	--	--	--	--
5	Hexose Sugar	--	--	--	--	+	--	+	--	--	--	--	--	--	--
6	Protein	+	--	--	--	--	--	+	--	--	--	--	--	--	--
7	Amino acid	+	--	--	--	--	--	+	--	--	--	--	--	--	--
8	Steroids	+	+	+	+	+	+	--	--	--	+	+	+	--	--
9	Cardiac Glycosides	--	--	--	--	--	--	--	--	--	--	--	--	--	--
10	Saponins	+	--	+	--	+	--	--	+	+	--	+	--	+	+
11	Alkaloids	--	+	--	+	--	--	--	--	--	--	--	--	--	+
12	Flavonoids	+	+	+	--	+	+	--	+	+	+	+	--	+	+
13	Tannins	+	+	+	+	+	+	+	+	+	--	+	--	+	--

Note: WE- Water Extract and AE- Alcoholic extract. '+' - presence and '-' - Absence.

Table 5: Ratio and quantum of ingredients used for *Jeevanthyadi ghrita* preparation.

Sl. No.	Particular	Ratio [classical method]	Taken for preparation
1	Kalka (paste of 14 drugs)	1 part	19.5 Kg
2	Ghrita	4 parts	78 L
3	Jala/Water	16 parts	312 L

involved in blending water-soluble constituents to lipid-soluble mode without using surfactants through HPTLC. It was evident through their study that active biological ingredients had eluted in *ghrita* in a monophasic oily liquid without any distinct layers. The HPTLC run with polar fractions demonstrated the presence of active biological ingredients while non-polar fractions did not. They proposed that hydrophilic contents may have been entrapped in a nano vesicular form in lipids which could control the drug delivery to targets, which seems undeniable. Pouton CW *et al.* 2000 stated that triglycerides present in foods undergo rapid

Table 6: Analysis of Plain and *Jeevanthyadi ghrita* for standard ghee parameters.

Sl. No.	Parameter	Plain *ghrita*	*Jeevanthyadi ghrita*	AGMARK Specifications
1	Baudouin test	Negative	Negative	Negative
2	Butro-Refractometer @ 40°C	41.6	42.2	40-43
3	Reichert Meissel Value	25.6	26.5	Min 24
4	Polenske Value	1.40	1.36	1.0- 2.0
5	Moisture Content	0.32%	0.30	0.3-0.5
6	Free Fatty acid (as oleic)	1.14%	1.24	2.8 Max
7	Colour	7.50	7.90	10
8	Saturated Fat	65.5%	67.5%	-
9	MUFA	17.6%	18.2%	-
10	PUFA	2.80%	2.50%	-
11	DHA	0.04%	0.03%	-
12	Milk Fat	99.2%	99.26%	99-99.5
13	Cholesterol	0.18%	0.20%	0.5 Max

Table 7: Phytochemical Screening and Quantification of *Jeevanthyadi ghrita*.

Sl. No.	Parameter	Result	Method/Test Used	Value	Method used
1	Alkaloids	Present	Dragendroff's reagent test	0.32%	Experimental Phyto pharmacognosy
2	Flavonoids	Absent	Shinoda test	---	CKL/ANL/UV-OO3
3	Glycosides	Absent	Picric acid test	---	Not Done
4	Phenols	Absent	Folin ciocalteu reagent	---	CKL/ANL/UV-OO2
5	Saponins	Absent	Foam test	---	Standardization of Botanicals
6	Tannins	Absent	Lead Acetate test	---	CCRAS 40.3
7	Terpenoids	Present	Salkowski reaction test	---	Not Done
8	Steroid	Absent	Salkowski reaction test	---	Not Done

Table 8: R_f Values of HPTLC Analysis at 254 nm and 366 nm wavelengths.

Sl. No.	254 nm R_f	% of Compound	366 nm R_f	% of Compound
1	0.01	11.76	0.01	7.76
2	0.04	4.09	0.07	6.52
3	0.19	8.32	0.21	14.14
4	0.36	8.01	0.29	4.74
5	0.57	10.71	0.36	13.70
6	0.67	17.88	0.39	3.28
7	0.73	39.32	0.42	7.63
8			0.56	13.69
9			0.59	3.59
10			0.74	9.67

digestion to form free fatty acids and 2–monoglycerides, which form colloidal dispersion of mixed micelles with bile salt-lecithin. Similarly, in this environment, lipid-based formulations containing hydrophobic drugs or poorly water-soluble drugs get solubilized.[10] This drug reservoir can lead to a partition that allows efficient, passive [transcellular] absorption of drugs

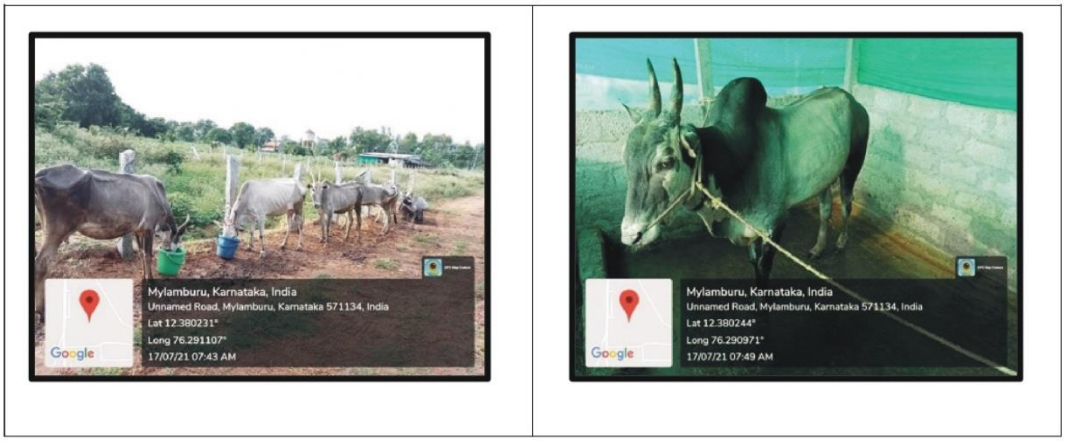

Figure 1: Hallikar Cow and Farm.

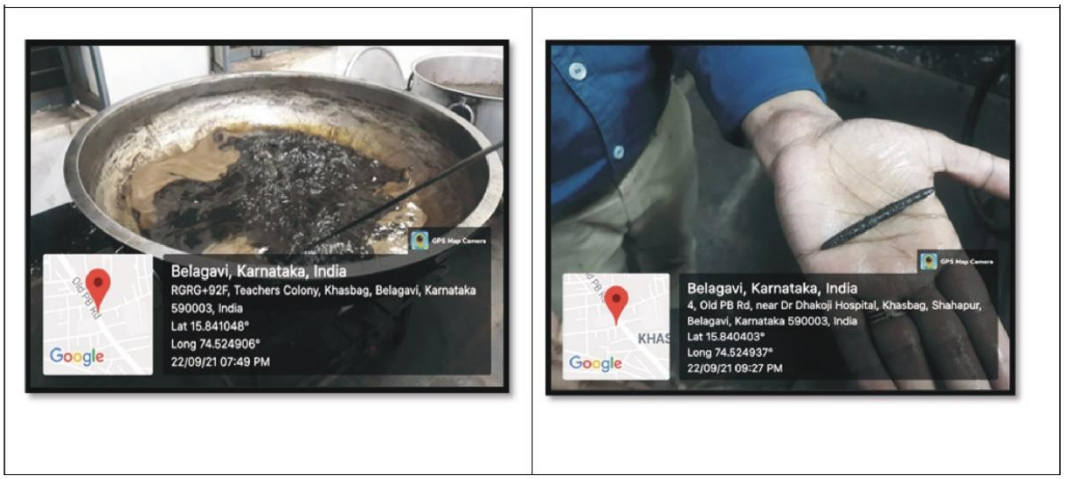

Figure 2: Ghee Processing and Siddhi Lakshana.

and prevents drug precipitation.[11] This can impact kinetics and improve bioavailability by supersaturation [intestinal absorption] and lymphatic transport.[12] These studies help to ascertain that even hydrophilic or water-soluble drugs can be targeted for purposed indications by modifying their pharmaceutical formulation. Hence nowadays the food-drug concept is evolving which was ascribed in ayurveda much before.[13] These theories explain the concept of usage of one formulation in various pharmaceutical dosage forms for target drug delivery.

Ekadasharupa of *Rajayaksham* presents symptoms like *shiroruja* [headache], *kantha dhwamsa* [dysphonia], *kasa* [cough], *svarabheda* [hoarseness of voice], *aruchi* [loss of appetite], *parshvashula* [pain in lateral side of chest], *atisara* [diarrhea], *jrumbha* [yawning], *jvara* [fever], *ura shola* [pain in the chest], *jarjarena uras* [expelling blood with phlegm] that have been correlated and studied for similarity in chronic debilitating illnesses like pulmonary tuberculosis[14] and HIV infections.[15,16] In the recent past, few opined that the acute phase of COVID-19 presents with *shadrupa* [six symptoms] and *Ekadasharupa* [eleven symptoms] of *rajayaksham*.[17] Emerging evidence of LONG TERM COVID-19 syndrome also has shown symptoms of *Rajayaksham* like chronic fatigue syndrome, headache, Allergic rhinitis, chest pain, change in taste, reduced appetite, dyspnea, memory issues, muscle/joint pain and often fever and cough especially in children.[18-21]

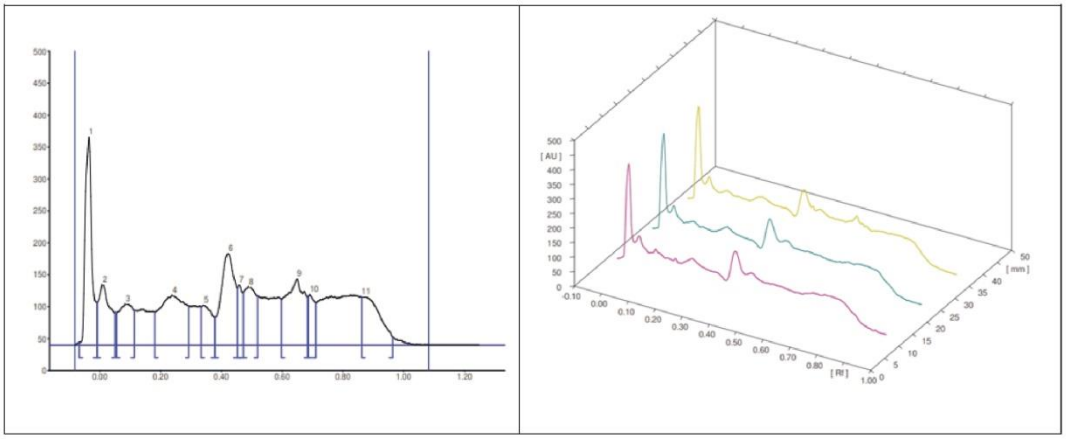

Figure 3: HPTLC of *Jeevanthyadi ghrita* at 366nm.

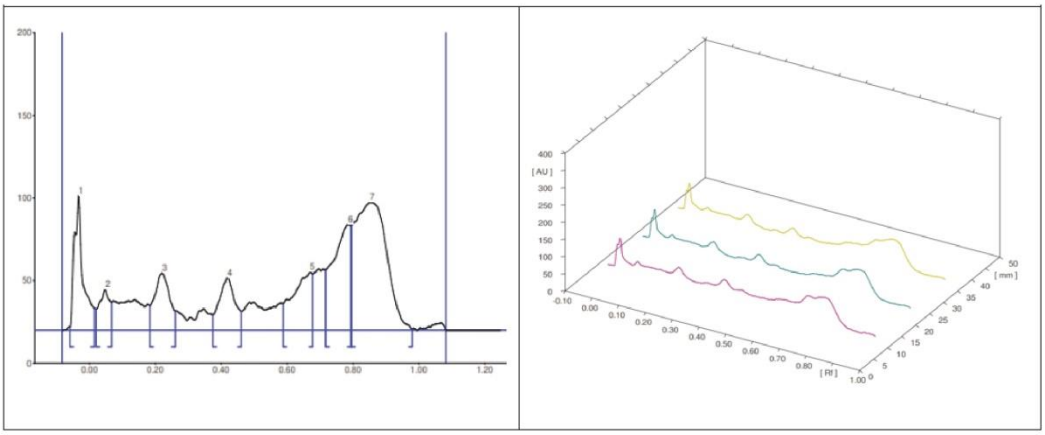

Figure 4: HPTLC of *Jeevanthyadi ghrita* at 366nm 254 nm.

On the other hand, it has also been observed that cancer therapies like radiation, chemotherapy and immunotherapy present with symptoms like gastrointestinal mucositis, fatigue, pain, body ache, sleep deprivation, and recurrent infection, etc., that have a negative impact on nutritional status leading to debilitation.[22,23]

All the above conditions that have been approximated with *Rajayaksham* have a common substrate of compromised or aberrant immune system which is orchestrated by interleukins [IL-6], tumor necrosis factor-α, nuclear factor-κB, T Helper cells like reduced CD4 and CD8 cells.[19,24-26] A compromised immune system can lead to tissue wasting.[27] This has been considered as *Ojakshaya* in Ayurveda.[28] *Ghrita* has been considered as *ojakara*[29] [immunomodulatory] and attributed with quality of *samskarasya anuvartathte* [~ selective synergistic agonist/ antagonistic] which means that *ghrita* can carry medicinal properties of herbs without forfeiting its own qualities.[30]

Jeevanthyadi ghrita is a formulation which is rich in Alkaloids and has also shown presence of terpenoids. Alkaloids are a large category of secondary plant molecules comprising of one or more nitrogen atoms. Alkaloids are considered as a chief phytoconstituents which help for performance enhancement and improving immune functions.[31]

Recent research on the ingredients of *Jeevanthyadi ghrita* has shown substantial anti-inflammatory, immunomodulatory and free radical scavenging activities. Preclinical studies on triterpenoids in aqueous extract of *Leptadenia reticulata* have downregulated pro-inflammatory cytokines like IL-2, Il-6, TNF-α and inhibited lipid peroxidation indicating its anti-inflammatory,

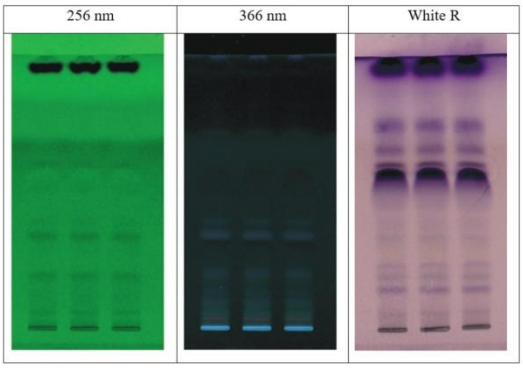

Figure 5: Image information of HPTLC of *Jeevanthyadi ghrita* at 254nm and 366 nm.

immunomodulation, analgesic, anti-pyretic and anti-cancerous activity.[32-35]

Yang R *et al.* 2016 showed that the anti-inflammatory and immunomodulatory activity can be attributed to 3 triterpenes and 13 flavonoids of *Glycyrrhiza Glabra* through a diverse route of mechanisms, especially downregulation of mediators, such as TNF-a, Matrix Metalloproteinase [MMPs], Prostaglandin E2 [PGE2], and oxidative stress on the progression of inflammation-related diseases. Glycyrrhizin exerts an anti-inflammatory action similar to hydrocortisone and other corticosteroid hormones. It inhibits phospholipase A2 activity and glycyrrhizic acid helps in inhibiting cyclooxygenase and prostaglandin formation.[36-39]

Hydro-ethanolic extract of Draksha (*Vitis Vinifera* L) inhibited pro-inflammatory markers like interleukin-6 and NF-κB transcription and downplay its successive markers through Mitogen-Activated Protein Kinase [MAPK] pathway in Lipopolysaccharide [LPS] induced inflammation. *Vitis Vinifera* can regulate leptin gene expression which is deranged in chronic inflammation via the TNF-α, IL-1β and NF-κB pathways.[40,41] different extracts of *Holarrhena Anti-dysentrica* stem bark have shown analgesic and radical scavenging activity.[42,43]

Alantolactone a sesquiterpene lactone found in *Inula racemosa* could elicit and confirm the pathway of inflammation inhibition. It was seen that extract of *Inula racemosa* was by inhibiting [LPS] induced NO production, Prostaglandin E2, TNF-alpha, Inducible nitric oxide synthase [iNOS] and COX-2.[44-46]

Methanolic extract of *Hedychium spicatum* has demonstrated for immunomodulatory effect in *in vivo* in dose-dependent manner against induced abdominal sepsis through *E. coli* and also could reverse the cyclophosphamide-induced myelosuppression.[47] Different extracts of *Hedychium spicatum* including aqueous have shown anti-inflammatory and analgesic activity in guinea pigs and mice respectively.[48]

Piperine and β-Sitosterol from pippali have shown anti-inflammatory activity by attenuating nuclear factor- κB (NF-κB) and inhibiting TNF-α induced Intercellular Adhesion Molecule-1 (ICAM-1) in endothelial cells. Piperine has also shown anti-inflammation in radiation-induced lung tissue damage in Sprague Dawley rats when irradiated for six weeks, it could anchor the Tumor Necrosis Factor alpha (TNF-α), Interleukin-1β (IL-1β) and Interleukin-6 (IL-6) and able maintain anti-oxidant enzymes like Superoxide Dismutase (SOD), Catalase (CAT) and Glutathione Peroxidase (GPx) in normal range.[49,50]

Alcoholic extract of *Solanum xanthocarpum* showed an Analgesic effect that was comparable to the standard drug Pentazocin.[51] *Tribulus terrestris* inhibited IL-6, TNF-α and is able to regulate GSH activity and bring down Malonaldehyde (MDA) which are responsible for immunomodulation and prevent cell damage.[52] Different organic extracts of *Sida cordifolia* were tested for anti-inflammatory activity using molecular markers like Prostaglandins (PGs, PGE2, PGD2, PGF2) and Thromboxane A2 (TXA2) even at the lowest dose of 10 μg/mL in the supernatant of Lipopolysaccharide (LPS)- induced RAW 264.7 cells.[53]

Nymphea nouchali showed anti-nociceptive and anti-depressant activity in a dose-dependent manner over pain which was comparable to diclofenac sodium which was persistent until 90 min.[54] *N nouchali* can mediate nuclear factor (erythroid derived2) NrF2 which is a key player in this pathway to phosphorylation of MAP kinase, extracellular signal regulated kinase 1 and 2 and p38, which confirms its antioxidant activity and DNA protection in oxidative stress.[55]

Ethanolic extract of *Phyllantus amarus* roots could regulate NF-κB gene and attenuate mRNA expression of TNF-α, IL-1β, PGE 2and COX-2 caused by phosphorylation of MAP kinase signaling induced by LPS in U937 macrophages.[56] Methanolic extract of *Gentiana kurroo* Royle showed a decrease in the release of pro-inflammatory mediators namely NO, TNF-α and IL-6 and even the expression of NF-Kappa B in mice peritoneal macrophages when stimulated by LPS which is the major transcription factor for above mediators.[57] *Fagonia indica* another variety of fagonia genus was able to down-regulate the Toll Like Receptors 4 and 9 genes which are responsible for innate immunity and pro-inflammatory markers like IL-6, Il-1B, TNF-Alpha and TGF-β.[58]

CONCLUSION

Jeevanthyadi ghrita has shown presence of alkaloids and terpenoids in phytochemical screening, HPTLC could elucidate few peaks which remains to be identified. Recent studies on ingredients of *Jeevanthyadi ghrita* rationalize the classical indications of it, based on inflammation as a substrate of pathophysiology.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

Jeevanthyadi ghrita was prepared as per classical method after collecting authenticated raw drugs. Prepared jeevanthyadi ghrita was subjected to HPTLC evaluation, preliminary phytochemical screening and standard ghee parameters [AGMARK]. *Jeevanthyadi ghrita* showed 7 and 11 peaks in HPTLC analysis, presence of Alkaloids and terpenoids in phytochemical screening and AGMARK parameters as per standard references. Review on recent activities of individual drugs of *Jeevanthyadi ghrita* showed strong anti-inflammatory and immunomodulatory effects which rationalizes its classical indications.

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Comparative quality analysis of marketed and traditionally prepared *Ghrita* and *Ayurveda* formulation *Jeevanthyadi ghrita*

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Abstract:

INTRODUCTION: Ghee is an integral part of food and medicine in the Indian system of medicine. Recent and future market indicates the increasing demand for ghee. However, it comes with shadow of adulteration and substandard quality. This can ramify to Ayurveda domain and bring down the credibility of the health system.

OBJECTIVE: Hence, we compared the quality of marketed and traditionally prepared ghee and also compared the prepared *Jeevanthyadi ghrita* (JG) with them.

MATERIALS AND METHODS: Traditionally prepared ghee was procured from Madikeri, a small town in South Karnataka, India of a single breed cow Hallikar, reared in same farm. Highly marketed ghee sample was bought. Later, the traditionally prepared ghee was processed as JG as per Ayurveda classical reference. All three samples were subjected to FSSAI–AGMARK parameters.

RESULTS AND DISCUSSION: All the samples were well within the standard range prescribed by FSSAI. However, there were nonsignificant differences in fatty acids polyunsaturated fatty acid and monounsaturated fatty acids and docosahexaenoic acid in all three samples. These variations could be due to seasonal, foliage provide to cow and method of preparation. Fortification of traditionally prepared *ghrita* with Ayurveda herbs as JG showed no deviations of standard values even after successive heating.

CONCLUSION: It was noteworthy that the market sample showed no adulteration. However, the marketed ghee is prepared from direct cream method and form pooled milk of different species, which raises concerns for processing Ayurveda *ghrita* if procured from the market.

Keywords:

Ayurveda, ghee, Ghrita kaplana, Hallikar, Jeevanthi

Ghee forms an important and integral part of food chain. In *Ayurveda*, Indigenous cow ghee (ghrita) is said as *Jeevaniya* (life sustenance and regenerative) and *Ojakara* (immune boosting)[1] and majorly used to prepare medicated ghee. This medicated ghee is prepared in a specific manner by heating the ghee with specified *kashaya's* (herbal decoctions) and *kalka* (fine paste of herbs). These medicated ghee preparations have been prescribed in many disorders for both internal (skin and neurological disorders, etc) and external usage such as topical application over wounds caused by heat or fire, painful ulcers, and many more disorders.[2] Among them, *Jeevanthyadi ghrita* (JG) is one mentioned in *Rajayaksham vyadhi* (debilitating disorder).[3] However, the quality of ghrita/ghee remains a subtle and significant factor for therapeutic efficacy. In the present scenario, mass production and demand are addressed by adopting newer methods which have its effects on the components on ghee. Recent

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studies suggest that there is slight variation in rate of recovery of ghee form milk prepared by different methods such as the indigenous method (80%–85%), the creamery butter method (88%–92%), and direct cream method (90%–95%).[4]

Major portion of milk produced to meet the demand is also converted to ghee (early 28%). The characteristic features of ghee such as color, flavor, and texture can differ based on rearing and region of the country. These characters also differ based on manufacturing technique, conditions, and materials.[5]

Increasing demand and limited supply of ghee leads to price escalations and malpractice like adulterations. It is not uncommon to adulterate *ghrita* with vegetable oil (commonly dalda or palm oil and or even partially hydrogenated oils like refined groundnut oil) and animal fat. In such scenario, their investigations are warranted to have vigilance over quality control parameters with physical and chemical tests. Quality parameters are important not only for commercial value but also for health reasons.[6]

Hence, the study was undertaken to observe the quality of marketed sample, traditionally prepared ghee and then compare fortified or processed *Jeevanthaydi ghrita* prepared out of traditionally prepare ghee for basic parameters.

Materials and Methods

Materials

One sample of Market ghee sample (MS) was procured and another sample which was prepared in traditional way (TS) was procured from Madikeri district in South Karnataka of a native and distinct Hallikar breed cow [Figure 1], cows were reared in same farm [Figure 2]. All the ingredients (authenticated) of JG [Table 1] were provided by Dabur India Limited, New Delhi, and KLE Ayurveda Pharmacy, Belagavi, Karnataka, expect the drug Trayaaman (*Gentian Kurroo* Royle.) which was collected from natural habitat and authenticated at National Institute of Traditional Medicine of Indian Council Medical Research Belagavi, Karnataka (Herbarium accession number RMRC-1677). All the ingredients were subjected to preliminary phytochemical analysis before the preparation of the study drug. Phytochemical values of ingredients were according to the Ayurveda pharmacopeia of India. After the confirmation of these values, the raw drugs and plain ghee were processed to JG in a classical way.

Traditional *ghrita* (ghee) preparation

Hallikar cow milk was collected in evening hours after the rearing. Then boiled and cooled at room temperature.

Figure 1: Hallikar breed cow

Table 1: *Jeevanthyadi ghrita* ingredients used for Kalka (fine paste)

Drug	Latin name	Part	Ratio
Jeevanti	*Leptadenia reticulata* Wight and Am.	Whole plant	1
Yasthimadhu	*Glycyrrhiza glabra* Linn.	Root	1
Draksha	*Vitis vinifera* Linn.	Fruit	1
Kutaja	*Holerrhena antidysentrica* Wall.	Stem bark	1
Pushkaramula	*Inula racemosa* Hook. F.	Root	1
Sati	*Hedychium spicatum* Ham. Ex Smith	Rhizome	1
Pippali	*Piper longum* Linn.	Fruit	1
Kantakari	*Solanum surattense* Burm. F.	Root	1
Gokshura	*Tribulus terrestris* Linn.	Fruit	1
Bala	*Sida cordifolia* Linn.	Root	1
Nilothpala	*Nymphaea nouchali* Burm. F.	Flower	1
Bhumyamalaki	*Phyllanthus amarus* Schum and Thonb	Whole plant	1
Trayamana	*Gentian kurroo* Royle	Rhizome	1
Duralabha	*Fagonia cretica* Linn.	Whole plant	1
Cow ghee			4

About 10%–15% of curd was added as initial culture, assorted, and incubated for 10–12 h at room temperature. The curd formed was manually churned until the butter was formed and floated on top of the buttermilk. Butter was later washed 1–2 times using water to remove residual buttermilk. Later the butter was processed on mild-to-moderate heat (flame) in a stainless steel container until it was clarified [Figure 3]. Clear ghee/*ghrita* was then transferred in a sterile glass container.

Jeevanthyadi ghrita preparation

It was processed in classical method as mentioned in Ayurvedic Pharmacopeia of India, "*Ghrita Paka Kalpana*" (standard operating procedure ghee-based compound formulations). As the per the reference the *Kalka* (fine paste of herbs) [Table 1], Sneha Dravya/*Ghrita* (lipids/ghee), and Drava Dravya/Jala (herbal

decoctions/water) should be taken in a ratio of 1:4:16, respectively.[7] As per the ratio the Kalka dravya (fine paste of herbs) came up to to ~20 kg, Ghrita (ghee) was 80 kg, and Drava dravya (water) was measured upto 320 L.

Initially the *Ghrita* (ghee) was taken in a stainless steel vessel and melted under moderate flame. Subsequently the *kalka* (fine paste of herbs) and *Drava Dravya* (water) were added to the same vessel. Boiling was continued on moderate flame for 8 h every day (it took 3 days) until there was complete evaporation of Drava dravya (water). Once the water evaporation was observed the flame was reduced further until the "*Sneha siddhi Lakshana*" (characteristic features of optimized ghee-based formulations) were seen [Figure 4]. The complete process was carried out on mild-to-moderate flame. The "*Sneha Siddhi Lakshana*" (characteristic features of optimized ghee-based formulations) mentioned in classical texts is disappearance of Phena (froth) in *Ghrita* (ghee) and formation of Varti (paste/wick) [Figure 5] without crackling sounds as surrogate feature of absence of water molecules [Figure 6]. After the complete observation of characteristic features was observed, the prepared JG was allowed to cool down and then transferred to glass bottles. Later the samples were sent to analysis in hygienic manner.

All the *Ghrita* samples, namely market sample (MS), traditionally prepared plain *ghirta* (TS) [Figure 7], and prepared JG samples [Figure 8] were tested at ESSAR Laboratories (Government of India Approved AGMARK Laboratory, ISO 9000:2015 certified and NABL Accredited), Hubballi, Karnataka, India and at Ayurveda Sidda Unani Drug Testing Laboratory of KLEU Shri B M Kankanawadi Ayurveda Mahavidyalaya approved by Department of AYUSH, Government of Karnataka.

Results

The results of the all the ghee samples are being tabulated in Table 2.

Figure 2: Reared in one farm

Figure 3: Traditional method of *Ghrita* preparation

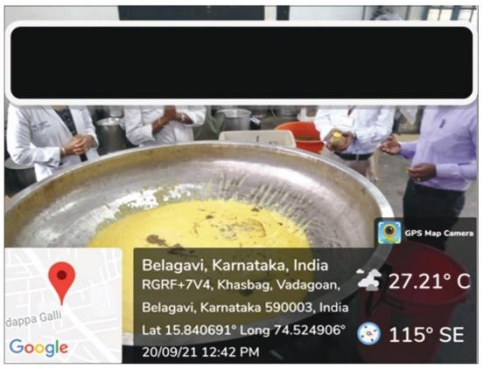

Figure 4: *Jeevanthyadi ghrita* preparation

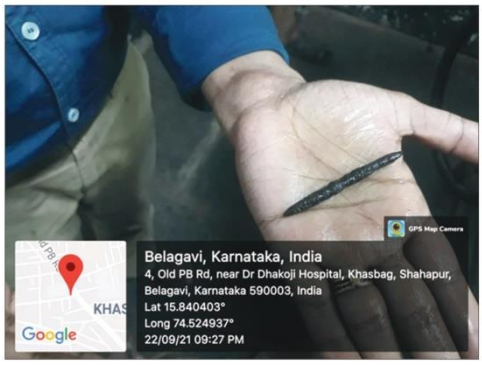

Figure 5: Varti formation (*Sneha Siddhi Lakshana*)

Figure 6: Phena Shanti (*Sneha Siddhi Lakshana*)

Figure 7: Traditionally prepared *Ghrita*

Figure 8: Prepared *Jeevanthyadi ghrita*

Discussion

The present study revealed all the *ghrita* samples confined to standard FSSAI-AGAMRK parameters and found to be of good quality. Briefly, the market sample of *ghrita* has shown to be devoid of any adulteration. Approximately 28% of milk produced in India is translated as ghee production. The texture, color, and flavor may vary from region to region and breed in India. In India, the market size of ghee reached INR 2907 billion (2022) and is projected to be 5137 billion rupees by 2028, and the compound annual growth rate was 9.9% indicating the expanding need and raising concerns.[8] This demand can influx the compromised quality of ghee that not only gives economic setback but also can become the substrate for varied health hazards.

Our study sample values namely milk fat (MS - 99.36 and TS - 99.20), Reichert Meissl value (MS - 28.6, TS - 25.8), Polenske value (MS - 1.88, TS - 1.44), and Butyro-Refractometer (at 40°C) reading (MS - 42.2, TS - 41.6) were in line with standard values prescribed by FSSAI. These tests all together indicate whether the ghee was prepared with milk fat or was adulteration done. Since even addition of 10% of the sample by any such adulteration would change the values significantly. Usually, the animal or any type vegetable oil is being added as adulterants.[9-13]

There was no significant different in other parameters except saturated fat, monounsaturated fatty acids (MUFA), and polyunsaturated fatty acids (PUFA) which were comparatively slightly on higher range in market sample in comparison to traditionally prepared method. These variations in saturated fat 13%–14%, MUFA 10%–12%, and PUFA 3%–4% could be because of seasons. It has also been stated that these differences could also be due to the grass that may modify the bacterial population in gut, which may anchor the lipid mobilization and affect the proportion of different fatty acids. This variation can also be attributed to the method of preparation.[4,14-16]

Acid value helps in understanding of shelf life and stability. The acid value indicates the presence of free fatty acids (FFA) present in ghee. FFA usually formed during process of hydrolysis of triglycerides which is again dependent on moisture in ghee. Most of the time, after processing the ghee with herbs leads to an increase in acid value due extraction of phytoconstituents from herbs. However, after the processing of *ghrita*, the increase in FFAs might be less stable and show a low shelf life as compared to raw *ghrita*. In our sample, the value was stable even after a 2-year shelf life.[17,18]

Iodine value talks about the presence of amount of PUFA in the form of a double bond that reacts with iodine. A high value indicates fats rich in PUFA which may help in reducing low-density lipoprotein cholesterol

Table 2: Physico-chemical evaluation of market *Ghrita*, Hallikar *Ghrita* and *Jeevanthyadi ghrita* formulation

Parameter	Unit	Market sample	Traditional method	*Jeevanthyadi Ghrita*	Standard value
Baudouin test	--	Negative	Negative	Negative	Negative
Butyro-refractometer (at 40°C)	--	42.2	41.6	42.2	40.0–43.0
Reichert Meissl value	--	28.6	25.8	26.5	Minimum 24
Polenske value	--	1.88	1.40	1.36	1.0–2.0
Moisture value	%	0.36	0.32	0.30	0.3–0.5
Free fatty acid (as oleic acid)	%	1.40	1.14	1.24	2.8 maximum
Color	--	8.20	7.50	7.90	10
Saturated fat	%	67.4	65.5	67.5	--
MUFA	%	21.2	17.6	18.2	--
PUFA	%	3.40	2.80	2.50	--
DHA	%	0.05	0.04	0.03	--
Milk fat	%	99.35	99.2	99.26	99.0–99.5
Cholesterol	%	0.28	0.18	0.20	0.5 maximum
pH	--	4.8	5.3	5.8	--
Iodine value	--	35	34.01	33.90	25–38
Saponification value	--	224	223	221.5	205–235
Acid value	--	1.4	1.8	2.08	--

MUFA=Mono unsaturated fatty acids, PUFA=Poly unsaturated fatty acids, DHA=Docosahexaenoic acid

levels in clinical scenario. The saponification value is also the molecular weight (or chain length) of all fatty acids present in the lipids. This value is an indicator of free acidic groups present in the fatty matter that can bring offensive odors or taste. This is caused by the reactions of hydrolysis through the supply of free oleic, linoleic, and linolenic acids that could then undergo further oxidative rancidity. It is evidenced in recent studies that during the manufacture of *Ayurveda* medicated *ghritas* there could be hydrolysis and formation or liberation of low-molecular-weight short chain fatty acids (SCFA). It is understood or hypothesized which could be due to the alkaline nature of the paste of herbal drugs and liquid media. Recently, these SCFA are believed to have a pivotal role as a fuel source for colonocytes, particularly in the distal colon. SCFA is readily absorbed and may play an important role as a protective effect for the distal colon in chronic disorders. It was observed that the saponification values of JG were in range in comparison to other Ayurveda *ghrita* and justifies its role in *rajayaksham*.[18-21]

After processing the traditionally prepared *ghrita* into JG, the values of ghee parameters didnot vary significantly expect the color of the ghee which turned slight characteristic greenish color [Figure 8]. There was reduction in moisture content though not significant which may be attributed to successive heating on moderate flame. Polenske value decreased a slight indicating that in JG it may have started to blend water-soluble compounds also into fortified or processed *ghrita*.[22] There was observed changes in saturated fat, MUFA, PUFA, and docosahexaenoic acid values, yet they were in range.

It is important for ghee standards to be in advocated manner since there are various *ghrita* preparations in Ayurveda that is practiced empirically and compromised or adulterated *ghrita* which may cloud the science. The present day pooling of milk and the preparing ghee can also pose as a major challenge to Ayurveda since qualities best owed to buffalo and cow are entirely different.

Conclusion

Market sample ghee has shown adherence to standard parameters indicting no adulteration practice. However, the difference between commercially prepared and traditionally prepared ghee showed comparative values which need to be evaluated at a larger scale. Fortification of ghee with Ayurveda drugs may have a negligible change over the parameters.

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Conflicts of interest

There are no conflicts of interest.

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