"COMPARATIVE EFFICACY OF MUCOADHESIVE FILM CONTAINING SILVER NANO PARTICLES AND MUCOADHESIVE FILM CONTAINING CURCUMIN ON WOUND HEALING AFTER PERIODONTAL SURGERY – A RANDOMIZED CONTROLLED TRIAL"

BY

REG NO. IK0222003

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This is to certify that the dissertation **"Comparative efficacy of mucoadhesive film containing silver nano particles and mucoadhesive film containing curcumin on wound healing after periodontal surgery – A Randomized Controlled Trial"** *is a bonafide research work done by* ***REG NO. IK0222003.***

Dr. MENAKA K. B *M.D.S*
Professor and Head,
Department of Periodontics,
KAHER's KLE V. K. Institute of
Dental Sciences, Belagavi

Date: 18/4/25
Place: Belagavi

Professor and Head
Department of Periodontics
KLE V. K. Institute of Dental Sciences
Belagavi

Dr. ALKA KALE *M.D.S, PhD*
Principal,
KAHER's KLE V. K. Institute of
Dental Sciences, Belagavi'

PRINCIPAL
KLE V.K. Institute of Dental Sciences
Nehru Nagar, BELAGAVI-590010.

Date: 17/4/25
Place: Belagavi

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I, ***REG NO. IK0222003,*** a postgraduate student in Department of Periodontics, have completed my research work on the topic *"***Comparative efficacy of mucoadhesive film containing silver nano particles and mucoadhesive film containing curcumin on wound healing after periodontal surgery – A Randomized Controlled Trial***"* in the year 2022-2025.

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Date:19-04-2025

Place: Belagavi

REG NO. IK0222003

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LIST OF ABBREVIATIONS

AgNPs / AgNP	**Silver nano particles**
ATCC	**American Type Culture Collection**
BHI agar	**Brain Heart Infusion Agar**
DMSO	**Dimethyl sulfoxide**
E. Coli	***Escherichia coli***
FDA	**Food and Drug Administration**
M	**Molar**
MBC	**Minimum Bactericidal Concentration**
mg	**Milligram**
MIC	**Minimal Inhibitory Concentration**
ml	**Milliliter**
mm	**Millimeter**
MTT Assay	**3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide**
nm	**Nanometer**
NSAIDS	**Non-steroidal Anti-inflammatory Drugs**
PBS	**Phosphate buffer solution**
RPM	**Revolutions per minute**
S. aureus	***Staphylococcus aureus***
SRP	**Scaling and Root Planing**
ZOI	**Zone of inhibition**
µl	**Microliter**

ABSTRACT

INTRODUCTION

The periodontium supports and preserves teeth, but periodontitis, which affects up to half of the global population, undermines these structures. Periodontal dressings (pack) are protective materials applied over the wound created by periodontal surgical procedures. The main objectives of periodontal dressings are to obtain an optimized healing and ensure minimum discomfort to the patient along with wound protection. While periodontal dressings aid in healing, they may also encourage bacterial growth. To address this, drug-loaded dressings including substances such as silver nanoparticles and curcumin have been investigated for antibacterial and anti-inflammatory activities. Given the potential of mucoadhesive films for targeted administration, this study assesses and compares the wound-healing efficacy of curcumin- and silver nanoparticle-based films after periodontal surgery.

AIM

To assess and juxtapose the impact of mucoadhesive films containing silver nano particles and mucoadhesive films containing curcumin on wound healing after periodontal surgery.

MATERIALS AND METHODS

A total of 45 patient with chronic periodontitis following flap surgery were allocated into 3 groups; where group 1 received only periodontal pack, group 2 received silver nanoparticle film with periodontal pack and group 3 received curcumin film with periodontal pack. All of them were assessed for wound healing at the end of 7^{th} and 14^{th} day using the Wound Healing Index and the antibacterial effect was assessed by colony forming units at baseline and 7^{th} day after surgery. The statistical test to be done for the following parameters were: Descriptive statistics,

Normality of data assessed by Shapiro – Wilk test, Wilcoxon Matched Pairs test for baseline and post intervention comparison of groups, Intergroup comparison with Unpaired t-test/ Mann-Whitney U test. Statistical significance to be accepted at a confidence level greater than 95% ($p < 0.05$).

RESULTS

The mean age group of the study participants was 47.33 ± 6.21. Intergroup comparison by Mann-Whitney U test showed improved healing scores in group 2 and group 3 with a very statistically significant difference with 'p' value of 0.0020, 0.0079 at day 7 and 'p' value of 0.0004, 0.0011 at day 14 respectively. Intragroup comparison of day 7 and day 14 wound healing scores were statistically significant 'p' values of 0.0007 in all the groups. Intergroup comparison of colony forming units at day 7 was reduced in group 2 with a statistically significant 'p' value of 0.0001 and percentage reduction of 56%. Intragroup comparison of baseline and post operative colony forming units by paired t test showed a reduction in the colonies postoperatively in all 3 groups with a statistically significant 'p' value of 0.0001.

CONCLUSION

In light of the observations from the study, drug-loaded dressings used alongside conventional periodontal dressings significantly enhance healing following periodontal surgery. Among the materials studied, silver nanoparticles demonstrated the most effective antibacterial and wound-healing properties. Curcumin also exhibited similar effects, albeit to a lesser degree, suggesting its potential as an alternative for promoting wound healing.

KEYWORDS

Chronic Periodontitis, periodontal dressing, wound healing, silver, curcumin, mucoadhesive film

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INTRODUCTION

"***All truths are easy to understand once they are discovered; the point is to discover them***"

- Galileo Galilei

Periodontium comprises specialized tissues that not only anchor and support the teeth but also protect the underlying neurovascular structures and form a defensive barrier against the oral microbiota. Periodontitis is one of the most prevalent dental conditions, characterized by the breakdown of the tooth's supporting structures. It is primarily caused by bacterial colonization of the oral tissues and affects approximately 20–50% of the global population. [1]

The healing of periodontal wounds varies from cutaneous wound healing in that it leaves minimal scarring, similar to embryonic healing. Periodontal dressings are protective materials used over surgical wounds following treatments including gingivectomy, flap surgery, crown lengthening, mucogingival, and periodontal regeneration.[2]

By protecting the wound from food, saliva, trauma, these dressings promote the best possible healing environment and increase post-operative comfort. Although studies have shown plaque accumulation beneath periodontal dressings, which may cause discomfort and transient bacteraemia, these dressings also provide indirect protection against infection at the wound site.[3]

Due to these concerns, researchers designed drug-loaded periodontal dressings that act as antimicrobial barriers, promoting optimal wound healing while preventing subsequent infections. Numerous antibacterial medications, such as tetracycline, zinc bacitracin, and chlorhexidine digluconate salts, have been studied. Silver has gained

popularity among these because of its broad-spectrum antibacterial activity and low systemic toxicity.[3]

The use of silver nanoparticles (AgNPs) in surgical instruments, bone prostheses, wound dressings, and contraceptives is growing. In animal models, silver nanoparticles have been shown to improve wound healing by reducing pro-inflammatory markers. They are a viable option for clinical usage because of their capacity to lower inflammation in the preliminary phases of healing. By suppressing both Gram-positive and Gram-negative microbial strains, silver nanoparticles can help prevent oral diseases such as periodontal and peri-implant infections, as reported by Song and Gealso in a systematic review.[3]

Plant-derived compounds like curcumin have shown considerable therapeutic promise as complementary agents alongside conventional wound-healing treatments. Curcumin is well known for its inflammation reducing, antimicrobial, free radical neutralizing, and tissue-repairing effects.[4]

Certified by the U.S. regulatory agency, the FDA as a safe substance, curcumin is not only affordable and readily available but also exhibits a multi-modal mechanism that targets the cellular signaling pathways, unlike NSAIDs. However, despite its biological potential, clinical application of curcumin is limited due to its reduced biological availability, resulting from limited uptake, rapid breakdown, and fast removal from the body.[4]

Since curcumin produces greater concentrations in the oral cavity than systemic administration, it has been included into localized drug delivery systems such gels, mouth washes, subgingival irrigation solutions, and curcumin- infused collagen fibers to get around these limitations.[4]

Mucoadhesive films, a type of local drug delivery technology, increase absorption and therapeutic effectiveness by ensuring targeted drug release through the transmucosal pathway. Nevertheless, nothing is known about curcumin's ability to cure wounds with mucoadhesive films following periodontal surgery.

In light of these factors, the goal of the current project was to analyse and contrast the ability of mucoadhesive films comprising curcumin and silver nanoparticles to improve wound healing after periodontal surgery.

AIMS AND OBJECTIVES

AIM:

To assess and juxtapose the impact of mucoadhesive films containing silver nano particles and mucoadhesive films containing curcumin on wound healing after periodontal surgery.

OBJECTIVES:

1. Formulation of mucoadhesive films containing silver nano particles and mucoadhesive films containing curcumin.

2. To assess and compare the effect of mucoadhesive film containing silver nano particles and mucoadhesive film containing curcumin on wound healing after periodontal surgery using Wound Healing index (Landry, Turnbull and Howley 1988)

3. To compare the antibacterial efficacy of mucoadhesive film containing silver nano particles and mucoadhesive film containing curcumin.

REVIEW OF LITERATURE

Surgical wound dressings have been used for millennia to protect sites of surgery, minimize postoperative infections, and expedite recovery. Periodontal dressings, often referred to as periodontal packs, provide similar benefits when applied following surgical procedures. Dressings are generically classified as either eugenol-based or non-eugenol dressings. Through the years, many alterations have been introduced to the formulations of such dressings to enhance their physical and curative benefits.[5] Periodontal dressings have been used for nine decades, but their effectiveness and benefits are being called into question. Periodontal dressings vary in their formulation, hardening characteristics, texture, and dissolution rate. Numerous researchers have investigated the features and performance of these dressings.

Most research has predominantly emphasized the compatibility with biological tissues and the healing potential of these materials. Biologically derived dressings are gaining traction owing to their favorable interaction with tissues and their capacity to support regeneration. The existing literature presents a range of perspectives on the utilization of periodontal dressings across different clinical scenarios. Given the lack of a definitive agreement on their clinical use, practitioners are required to exercise their own judgment based on individual case conditions [6]

Joy Fong et al (2006)[7] in this paper discussed the properties and clinical applications of nanocrystalline silver dressings, specifically Acticoat™, and reviews supporting evidence for their use in wound care. Acticoat uses nanotechnology to distribute nanocrystalline silver, which makes silver more accessible while releasing much less silver cations than silver sulfadiazine or silver nitrate. Acticoat has demonstrated cytotoxicity to keratinocytes and fibroblasts in laboratory settings, despite evidence

from in vitro and animal studies showing it is efficient against common wound infections, provides broad-spectrum antibacterial action, and can operate as a protective barrier over skin grafts. wound healing, according to research on animals. Although there are few high-quality human clinical trials, the data that is currently available indicates that Acticoat is affordable, improves healing in chronic wounds, and lowers infections, dressing change frequency, discomfort, wound exudate, bioburden, and matrix metalloproteinase activity. When using these dressings on wounds that are epithelializing or proliferating, care should be taken even though there is no in vivo proof that they are harmful to human skin cells. To better understand the function of nanocrystalline silver in wound care, more randomized controlled trials are required.

Jun Tian et al. (2007)[8] discussed the benefits of silver nanoparticles for wound healing in their review. He demonstrated its benefits using an animal model, in which researchers investigated the ability of silver nanoparticles to heal wounds and discovered that they do so in a dose-dependent manner, promoting both faster healing and improved cosmetic appearance. Furthermore, using quantitative PCR and proteomic analyses, they demonstrated that silver nanoparticles are beneficial due to their antibacterial capabilities, modulation of fibrogenic cytokines, and reduction in wound inflammation. These findings have defined the mechanism of action of silver and introduced a unique curative technique for management of wounds in clinical trials.

Joseph J Castellano et al., (2007)[9] To assess the antibacterial efficiency of eight commercially available silver-containing dressings, researchers compared them to three topical antimicrobial creams, a silver-containing topical gel, and a control group. The results revealed that all silver dressings and topical antimicrobials had

antibacterial action against three pathogens. Some treatments were able to almost completely eliminate bacterial development within 24 hours. Although silver-containing dressings may not have the same bactericidal and bacteriostatic qualities as commonly used topical antimicrobial medicines, they are likely to provide an effective barrier against infection and aid in its treatment.

Rakesh Das (2011)[10] performed a comparative experiment to investigate the healing efficacy of rhEGF (recombinant human epidermal growth factor) powder and plant extracts as mucoadhesive buccal patches on five human volunteers. Using polyvinylpyrrolidone, mucoadhesive buccal patches of 1.5 x 1.5 cm were created. The active ingredient extracts from Curcuma longa and Centella asiatica, respectively, included curcumin, Asiaticoside, and madecassoside, which was used as therapeutic agents. Plant extracts and rhEGF have average healing times of 36.6 ± 0.46 hours and 52.16 ± 2.82 hours, respectively, with SEM values of 0.232 and 1.262. He concluded that plant extract, curcumin, and Centella Asiatica as a mucoadhesive buccal patch had good healing potential as the difference in the healing lesion time interval was not too long when compared to rhEGF.

Chiara Rigo et al., (2013)[11] evaluated the efficacy of silver nanoparticle-based dressing was on a fibroblast cell line in vitro and on a burn patient. According to this investigation, Ag NPs drastically reduced mitochondrial activity, despite the fact that cellular staining methods revealed that nuclear integrity was maintained and there were no signs of cell death. Skin biopsies collected from a single patient throughout therapy were evaluated for the first time using spectrometry and electron microscopy. Findings revealed that Ag NPs are present in the cytoplasm of fibroblasts and are released as aggregates. The nanoparticles were dispersed differentially in the cells of the dermis, and no cell death was observed. In depth profiles of Ag levels were

obtained. While the silver penetrated deeper in the unhealed sample, the mended sample retained the majority of its silver in the superficial layers. The experimental findings and clinical observations gathered here favour the safety of Ag NP-based dressings in wound care and are consistent with earlier publications.

LetIcia Mazzarino et al., (2014)[12] in an vitro study assessed a novel strategy of buccal curcumin administration. chitosan-coated with curcumin and polycaprolactone nanoparticles were mixed into chitosan formulations to produce films via casting. To optimize the film characteristics, various glycerol concentrations and chitosan molar weights were tested. Microscopic evaluation revealed that films containing medium and high molar mass chitosan were homogeneous, flexible, and had a uniform distribution of nanoparticles. In vitro, the films demonstrated continuous, regulated curcumin release and good hydration in simulated saliva, with a maximum swelling of roughly 80%. These observations specify that films incorporating nanoparticles represent a hopeful strategy for curcumin delivery, especially for treating periodontal diseases that require prolonged drug release.

Lin YH et al (2016)[13] In his research study assessed the effects of 3 silver-comprising dressings on wound healing and bacterial survival were examined. In vitro research was done on these dressings' capacity to keep internal microorganisms and prevent germs from entering from the outside. The study also examined the amount of collagen synthesis in vivo and compared the healing effectiveness of the three dressings using a rat model. According to in vitro data, the silver-containing dressings stopped bacteria from growing in wounds by keeping the germs inside the dressing and preventing external bacteria from entering. According to an in vivo investigation, wound healing was expedited by a decrease in the bacterial burden. Gauze-treated wounds did not heal as well as those treated with silver-comprising dressings.

Additionally, KoCarbonAg® promoted the synthesis and organization of collagen, which further facilitated wound healing.

Woei Yenn Tong et al., (2017)[14] In this work assessed the effectiveness of cellulose nanocrystal film's effectiveness both in vitro and in vivo as a means of delivering antimicrobial drugs to a diabetic wound dressing. It was possible to separate cellulose nanocrystals from medical-grade cotton fibers. The curcumin-developed film has a thickness of 0.4 mm and a consistent yellow tint. The mechanical characterization examination of the film revealed that it was soft and flexible. The curcumin release test hit a plateau after 36 hours, with a total release of 98.9% from the nanocrystal film. Five bacteria, and one yeast were all significantly inhibited by the film. The skin sample's histology analysis also revealed that the film containing curcumin greatly enhanced the skin's sebaceous gland and hair follicle regeneration. Our findings suggest that cellulose nanocrystal films loaded with curcumin may be applied to diabetic wound healing.

Rathi VC et al., (2019)[15] estimated the efficiency of neem and turmeric on wound healing in orthodontic extraction sockets, a clinical trial was carried out. Forty-five patients in all were enrolled. They were split up into three groups; one test group received neem gel, the other test group received turmeric gel, and the control received a betadine pack after extraction. After a day, three days, and seven days, they were evaluated. In comparison to the herbal groups, the betadine group experienced the highest levels of discomfort, inflammation, and infection, according to the results. Patients receiving neem and turmeric treatment showed no signs of wound dehiscence. They came to the conclusion that herbal extract appeared to have a greater therapeutic effect.

Yanping Huang et al., (2019)[16] in their work created a new clay-reinforced polycaprolactone composite film with curcumin. Attenuated complete reflection was one of the characteristics of the created Cur-loading composite films. Differential scanning calorimetry, microscopic evaluation, infrared spectroscopy, SEM, thermogravimetric analysis, and X-ray diffraction all revealed good clay dispersion in the composite films. It was discovered that adding nanoclay greatly increased the tensile strength. Additionally, compared to membranes without clay, the clay-enriched drug-comprised films showed superior controlled-release of Curcumin. Skin disinfection test showed, film infused with curcumin shielded the lesion against bacterial infection. The composite films' strong biocompatibility was demonstrated by cytotoxicity analysis. For wound care, the clay-enriched Curcumin-comprising films may be a good option.

Federica Paladini et al., (2019)[17] in this review have discussed the antimicrobial effect of silver nanoparticles on healing of wounds. Since infections are a major cause of amputations among the increasing number of senior diabetics, diabetic foot ulcers in particular are a serious problem. One of the major obstacles to healing is the formation of biofilms - organized bacterial communities encased in a self-produced matrix that renders resistance to conventional antimicrobial treatments. New anti-biofilm tactics and creative antimicrobial drugs are now desperately needed as a result. In this regard, the medicinal potential of silver nanotechnology has drawn a lot of attention. Because of their inherent antibacterial qualities and wide-ranging effectiveness, silver nanoparticles have created exciting new opportunities for infection prevention and better wound healing results.

Nadda Chiaoprakobkij et al (2020)[18] in an vitro study successfully created biopolymer composites film that were multifunctional using economical casting procedure. SEM images confirmed uniform structural distribution. The composites showed water contact angles of 50–70° and water vapor permeability values (300–800 g/m²/24h) comparable to commercial dressings. The flexible films exhibited adequate stiffness, adhered well to the skin, and maintained hydration. Mucoadhesion on pig mucosa in artificial saliva lasted 0.5 to 6 hours. Curcumin-infused films displayed strong antimicrobial activity against 2 bacterial strains *E.coli* and *S. aureus,* and also presented potent anticancer effects on oral cancer cells, and remained non-cytotoxic to human keratinocytes and gingival fibroblasts. As a result, these curcumin-loaded films showed promise as a topical treatment modality and sould be used in treatment of oral cancer, periodontitis, and wounds.

Meghana MVS et al., (2020)[19] carried out a cross over split mouth clinical trial to measure and contrast the efficacy of a gel comprising curcumin and non-eugenol dressing in wound healing after flap surgery. 20 patients were recruited, and one site gel with curcumin was administered and the other with non-eugenol dressing. As the main study endpoints, tissue response and wound healing were evaluated at postoperative sites. Assessments of pain and the quantity of analgesics taken by the participants were the secondary outcomes. There were no significant differences in tissue reactivity, early wound healing, or pain perception between the two groups. The group that took curcumin used less analgesics than the group that received periodontal dressing. They came to the conclusion that curcumin and periodontal dressings work well to ease pain perception, improve wound healing, normalize TC, and lower TE.

Iris Xiaoxue Yin et al., (2020)[20] in his review highlighted the antibacterial properties, dental applications, and safety considerations of AgNPs in clinical practice. Because of its few side effects, silver has been frequently employed as a disinfectant and antibacterial agent. They have broad-spectrum antimicrobial action. Their nanoscale size and high surface area-to-volume ratio allow them to penetrate microbial cell walls, impair membrane integrity, create reactive oxygen species, and hinder DNA replication and finally result in cell death. In dentistry, AgNPs are incorporated into titanium implant coatings, endodontic irrigants and obturation materials, orthodontic adhesives, guided tissue regeneration membranes, acrylic resins for dentures, and composite resins for restorations. Although their safety is still under investigation and not yet universally accepted, no systemic toxicity from ingestion has been reported. However, environmental concerns persist due to the potential for nanoparticles to interact with harmful substances, potentially altering their toxicity.

Atanu Naskar et al., (2020)[21] put forward a review on the benefits of nanomaterial-based therapeutics in wound healing. Nanomaterial-based wound-healing approaches have shown superior performance compared to traditional methods that primarily rely on dressings. These materials offer antibacterial, anti-inflammatory, and anti-proliferative properties and can influence multiple stages of the wound-healing process. However, several critical challenges must be addressed before their effective clinical application. Most existing studies focus on single-target bacteria or are limited to in vitro experiments. Therefore, more comprehensive in vivo research involving major bacterial strains, as well as skin microbiota, is essential for advancing their use in wound-healing therapies.

Chaushu L et al., (2021)[22] performed an animal study to observe the outcomes of a paste with 2 % curcumin on wound healing in a palatal rat model using 56 male Wistar rats. Following mucoperiosteal flap elevation on the maxillary alveolar ridge, rats were divided into four groups: 2% curcumin, orabase, incision-only, and intact control. Curcumin and orabase were applied 12 hourly for three days. Rats were sacrificed at one and two weeks for histological analysis. After one week, both Cur and O groups showed complete epithelial closure, while the C group had residual gaps. Curcumin treatment led to a significant upregulation of connective tissue stem cell markers ($P < .05$) and increased, though not statistically significant, expression of epithelial markers compared to orabase. The study concluded that 2% curcumin may enhance primary wound healing by promoting connective tissue stem cell activation, aiding epithelial regeneration.

Aggarwal K et al. (2021)[3] formulated a clinical trial to inspect the potential of a nano-silver membrane on healing of wound after flap surgery in 42 systemically healthy participants with chronic periodontitis. Post-surgery, the test group received a nanocrystalline silver dressing, whereas the control received a non-eugenol dressing. Clinical parameters - PI and WHI were assessed on days 7 and 14. Microbiological analysis and VEGF levels were evaluated at baseline and day 7. The test group showed significantly better healing, lower bacterial counts, and increased VEGF levels. From the results it can be concluded that nano-silver dressings enhance post-surgical wound healing by reducing microbial colonization and promoting angiogenesis

Bhavya et al. (2021)[23] conducted a split-mouth study to compare gingival tissue response and patient compliance following flap surgery in 11 patients with chronic periodontitis. Group I received only Coe-Pak™ (non-eugenol dressing), while Group

II received an AgNP membrane (ACTICOAT®) combined with Coe-Pak™. Clinical parameters namely plaque index and bleeding scores were assessed on day 7 post-surgery. Group II showed improved healing and tissue response compared to Group I. Although pain and discomfort scores were statistically significant, patients reported no unpleasant taste or odor and preferred the AgNP membrane. The study concluded that the AgNP membrane with Coe-Pak™ enhances healing, tissue response, and patient acceptability.

Stefania Vitale et al. (2022)[24] in a review, discussed the biological activity of various medicinal plants in healing of wounds. Because healing is a complicated biological mechanism, effective wound treatment is still quite difficult. Natural remedies are becoming more and more essential in the treatment of infections and skin diseases because of the negative effects of conventional pharmaceuticals and the lower cost of herbal products. Compiling the most recent research papers on significant herbal preparations, their phytochemical components, and innovative wound care formulations is the aim of the current study. According to research, phenolic compounds, alkaloids, flavonoids, and saponins all play important roles in many herbal treatments' ability to heal wounds. Phytochemical compounds function at different phases of the process via a number of mechanisms, including anti-inflammatory, angiogenic, antibacterial, antioxidant, collagen synthesis-stimulating. The application of natural chemicals via nanotechnology devices has the potential to significantly improve wound care effectiveness.

Varun Arora et al. (2022)[25] studies the wound healing effectiveness of nanocrystalline silver membranes post periodontal flap surgery in 60 periodontitis patients. Participants were grouped into, Group I – who were administered with a nanocrystalline silver dressing, while Group II was administered with a non-eugenol

dressing. Clinical parameters including wound healing index, VEGF levels, and microbiological analysis were assessed on days 7 and 14 postoperatively. In Group I, the mean healing index was 3.75 on day 7 and 4.12 on day 14. Bacterial colony-forming units (CFU/ml $\times 10^6$) decreased from 3.4 at baseline to 1.6 by day 7, and VEGF levels increased from 0.021 to 0.032. These statistically significant improvements suggest that nanocrystalline silver dressings offer strong antibacterial properties and promote effective wound healing.

Sorina Mihaela Solomon et al., (2022)[26] In this review discussed the benefits of the Curcuma longa extract in the periodontal disease therapy. While SRP remain the benchmark for managing periodontal disease, they are often unable to fully eliminate periodontopathogenic bacteria residing in the cementum, dentinal tubules, and periodontal soft tissues. Recently, there has been growing interest in phytotherapeutic approaches for periodontal therapy. Curcumin, in particular, has shown promising anti-inflammatory, antioxidant, anticancer, and chemo preventive properties in numerous laboratory and clinical experiments. It has been found to curtail oxidative stress and enhance antioxidant defense by regulating superoxide dismutase levels It has also been noted that the enzymes xanthine hydrogenase/oxidase and lipo-oxygenase/cyclooxygenase are inhibited.

Yaseen Hussain et al., (2022)[27] in this review discussed the anti-microbial potential of curcumin. The bioactive substance curcumin, which comes from Curcuma longa, is well known for having broad-spectrum antibacterial qualities. Curcuminoids, its main ingredients, have potent antioxidant properties. Curcumin has demonstrated encouraging effects against pathogens that cause surgical and implant-related disorders, including S. aureus and E. coli. It is also effective against a variety of bacteria, including ones that are resistant to antibiotics. Curcumin also exhibits

antiviral potential against potentially fatal viral infections and antifungal actions against dermatophytes and Candida species. Curcumin exhibits synergistic antibacterial effects when combined with other phytochemicals, which makes it a viable option for co-loaded, pro-regenerative coatings on orthopaedic implants. However, its rapid disintegration, low bioavailability, and low solubility in water limit its therapeutic usefulness. A solution is provided by delivery systems based on nanotechnology, which improve the stability and efficacy of curcumin, especially in orthopaedic and surgical applications. In situations of periprosthetic joint infections, curcumin-loaded nanoparticles have demonstrated significant antibacterial efficacy against S. aureus.

Marieta Constantin et al. (2022)[28] intended to formulate a new biocomposite film with antibacterial, anti-inflammatory properties for the treatment of periodontal pockets. To achieve an environmentally benign synthesis, silver nanoparticles (AgNPs) were incorporated into polyvinyl alcohol cross-linked with oxidized chitosan. The inclusion of up to 1.44 wt% AgNPs improved the films' physicochemical qualities. Films had robust mucoadhesion (0.6 N), a large swelling ratio (162%), and sufficient tensile strength (1.46 MPa). The optimized formulation contained ibuprofen, which allowed for prolonged medication release for 72 hours. These biocomposite films also had strong antibacterial properties against oral infections.

Prithyani Saurabh et al. (2023)[29] designed a study that measured wound healing with a nano-crystalline silver membrane and a Coe-Pak dressing. The individuals were randomized to either the test or control groups after flap surgery. The postsurgical wound in the test group was covered with both Coe-Pak and nano-crystalline silver membrane, while the control group only received Coe-Pak. At days

7 and 14, the test group's healing was noticeably superior to that of the control group, according to the results. The plaque index (PI) scores did not differ between the two groups.

Abdullah Saleem (2025)[30] In his systematic study, examined the effectiveness of AgNPs as a supplement to antimicrobial therapy for periodontitis. AgNPs have strong antibacterial action against periodontal infections, according to the review's findings. They are just as effective as common medications like tetracycline and can stop the growth of bacteria at the right concentrations. AgNPs improved periodontal health by supplementing conventional therapies, as demonstrated by in vivo investigations. Because silver nanoparticles have an antibacterial action, they may be used as adjuncts for periodontitis treatment. However, numerous studies have not yet conclusively demonstrated their long-term safety and efficacy.

MATERIALS AND METHODS

SOURCE OF DATA

The trial was a randomized controlled, single-blind clinical trial. The study was conducted in the Department of Periodontics, KAHER's KLE Vishwanath Katti Institute of Dental Sciences, KLE's Dr. Prabhakar Kore Basic Science Research Centre (BSRC), and KLE College of Pharmacy KLE Academy of Higher Education and Research, Belagavi, Karnataka. An ethical clearance (Annexure 1) was obtained before conducting the study from Ethical Committee, KAHER's KLE Vishwanath Katti Institute of Dental sciences, Belagavi.

STUDY PARTICIPANTS

A total of 45 patients diagnosed as having moderate chronic periodontitis (1999 International Workshop for Classification of Periodontal Disease and Condition), reporting to the out-patient Department of Periodontics, KAHER's KLE Vishwanath Katti Institute of Dental sciences, Belagavi, were selected for the study.

Participants meeting the specified inclusion and exclusion criteria were enrolled in the study

INCLUSION CRITERIA:

- Systemically healthy patients requiring periodontal therapy - periodontal flap surgery.
- Patients between the age of 35 – 60 years.
- Patients interested in taking part in the study.

EXCLUSION CRITERIA:

- Pregnant individuals and nursing mothers.
- Patients with underlying medical conditions or those on treatments that may affect tissue healing.
- Individuals who have received periodontal treatment within the past six months.
- Patients who have taken antibiotics or NSAIDs in the previous six months.
- Smokers or individuals with any history of harmful habits.
- Patients with known or suspected allergies to curcumin or silver.

STUDY DESIGN:

IN VITRO STUDY

The film formulation was conducted at KLE's Dr. Prabhakar Kore Basic Science Research Centre (BSRC), and KLE College of Pharmacy KLE Academy of Higher Education and Research, Belagavi, Karnataka

FILM FORMULATION:

i. Curcumin was purchased from Kancor limited. (Figure 1)
ii. Silver nitrate solution was procured from Sigma Aldrich company.

SYNTHESIS OF SILVER NANOPARTICLES:

Armamentarium required:

- Beakers
- Volumetric flasks
- Amber storage bottles

- Sodium citrate
- Silver nitrate
- Sodium borohydride
- Sodium hydroxide (1.25 M)
- Milli-Q water (Type 1 ultra-pure water)
- Magnetic stirrer with stir bar
- Pipettes (micropipettes & graduated pipettes)
- Burette (for pH adjustment)
- Cold bath setup (maintaining 6–10°C)
- Thermometer or temperature probe

Procedure:

To synthesize silver nanoparticles, 185 mL of Milli-Q Type 1 water was mixed with 5 mL of 0.05 M sodium citrate and 5 mL of 0.05 M silver nitrate. The mixture was placed in a cold bath maintained at 6–10°C and stirred at 3000 RPM for three minutes. Subsequently, 5 mL of 0.05 M sodium borohydride was gradually added dropwise. The pH of the mixture was adjusted to 10 using 1.25 M sodium hydroxide. The formed silver nanoparticles (AgNPs) (Figure 2) were stored in amber-colored bottles at 4°C. A UV- visible spectrophotometric method was used to verify the presence of AgNPs in the final solution.

MIC AND MBC ESTIMATION:

Armamentarium required:

- *Staphylococcus aureus*
- *Pseudomonas aeruginosa*
- *Porphyromonas gingivalis*
- Weighing Scale
- Dimethyl Sulfoxide (DMSO)
- Eppendorf Tubes
- Pipette with micro pipette tips
- Brain heart Infusion culture broth
- Anaerobic Jar
- Incubator
- Brain heart Infusion agar
- Platinum bacterial inoculation loop
- Electric loop sterilizer

Procedure:

Inoculum preparation: BHI broth and ATCC strains of *Staphylococcus aureus, Pseudomonas aeruginosa,* and *Porphyromonas gingivalis* were used to prepare the inoculum. Using a sterile loop, colonies were selected and transferred into BHI broth. The stock culture was then conditioned for 8 to 14 hours at 37°C, until the turbidity matched the 0.5 McFarland standard. The cloudiness of the actively proliferating bacterial suspension was calibrated with fresh broth to align with the 0.5 McFarland standard.

Broth dilution method [Resazurin] for determining Minimum Inhibitory Concentration: 5.5 grams of BHI powder were dispersed in 150 mL of water and thoroughly mixed. The broth was then autoclaved at 120°C and 15 psi. Dilutions of the broth were prepared in a sterile 96-well plate, with each step performed in triplicate. In the first well, 100 µL of the curcumin working solution was added and serially diluted to the required concentrations up to the ninth well. The same procedure was repeated for the other two rows of the well plate. The 96-well plates were then incubated in a McIntosh and Fildes' anaerobic jar for 48 hours (Figure 8). After incubation, 30 µL of Resazurin reagent was added, and the wells were observed for color changes after 4 hours. A shift from blue/violet to pink/slightly pink/magenta indicated the MIC of the emulsion. The results were documented by capturing high-quality photographs (Figures 3-5).

Minimum Bactericidal Concentration MBC: The MBC values of curcumin were determined with the help of agar plates. 7.8 grams of BHI powder were dispersed in 150 mL of water and thoroughly mixed. The solution was then autoclaved at 120°C and 15 psi. After cooling for 10-15 minutes, the agar was poured into plates and allowed to solidify. Using an inoculating loop, bacterial streaks were applied to the agar plates, which were then sealed with paraffin film and incubated in a bacteriological incubator for 12 hours. The minimum concentration at which no bacterial growth was observed was recorded as the MBC value (Figures 6-8). The film formulation was developed based on the MIC and MBC results obtained from these procedures

CYTOTOXICITY ASSESSMENT:

MTT Assay was performed to evaluate the cytocompatibility.

Armamentarium required:

- L929 Mouse fibroblast cell line
- MTT reagent
- DMSO (Dimethyl sulfoxide)
- Culture medium - DMEM
- PBS (Phosphate Buffered Saline)
- 96 - well plates
- Sterile pipettes and tips
- CO_2 incubator
- Micropipettes
- Microplate reader
- Microscope

All materials were procured from Himedia.

Methodology:

Cell Line Maintenance:

L929 cells were sourced from the National Center for Cell Sciences (NCCS), Pune. These cells were authenticated using a data sheet containing sixteen short tandem repeat (STR) loci, confirming a 100% identity match with the ATCC STR database. Upon acquisition, the cells were cultured and expanded in a complete growth medium composed of 89 mL of DMEM, 10 mL FBS, and 1 mL of antibiotic

solution, totalling 100 mL. Cells were maintained in a humidified 5% CO_2 incubator and monitored using an inverted phase-contrast microscope. Subculturing and trypsinization were performed when cells reached approximately 85% confluence, following standard aseptic techniques.

MTT Assay:

MTT assay was conducted on logarithmic-phase cells using a 96-well plate, with untreated wells as negative controls. Silver nanoparticles and curcumin were tested at concentrations from 500 to 15.6 µg/mL in triplicate. Cells (5×10^3/well) were seeded in 150 µL of medium and incubated at 37°C with 5% CO_2 for 24 hours. After adherence, test compounds were added and incubated for another 24 hours. Then, 20 µL of MTT reagent was added, and plates were incubated in the dark for 4 hours. Formazan crystals were dissolved with 100 µL of 1% DMSO, followed by 25 µL of glycine buffer. Absorbance was measured at 570 nm, and cell viability was calculated as a percentage of control OD. (Figure 9)

FILM FORMULATION:

Armamentarium Required:

- Curcumin
- Silver nanoparticle
- Ethyl cellulose
- Eudragit
- Hydroxypropyl methylcellulose
- Polyethylene glycol
- Glycerine

- Beaker
- Petri plates
- Silicone Molds
- Magnetic stirrer

Procedure:

Films were prepared using solvent casting. Ethyl cellulose, Eudragit, and HPMC were dispersed separately in 10 mL of ethanol with a magnetic stirrer to form a polymer solution. The plasticizer, curcumin, and silver nanoparticles were then added to the solution while stirring. After thorough mixing, the solution was transferred into a sterilized petri plates placed horizontally. A cotton-plugged glass funnel was inverted over the dish to allow slow solvent evaporation. The setup was left at room temperature for 24 hours. Once the solvent evaporated, the cast films were removed, wrapped in aluminum foil, and stored in a desiccator. (Figure 10 – 12)

Formulated films were then sterilized using gamma sterilisation, packed and stored for use in the clinical trial. (Figure 13, 14)

Characterization of Films:

Thickness:

Thickness was assessed using a digital vernier caliper, with readings taken at multiple points across the film.

Film Weight:

Films (1 cm × 1 cm) were individually cut and weighed using an electronic balance.

Surface pH Measurement

The film was gently moistened with water, and the pH was measured by placing an electrode in contact with the surface of the film.

Percentage Moisture Loss

Moisture loss was estimated by placing the films in a desiccator. The percentage moisture loss was quantified with the following formula:

$$\text{Percentage Moisture Loss} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weigth}} \times 100$$

Percentage Moisture Absorption

Moisture absorption was assessed by placing pre-weighed films of known size in a desiccator with 100 mL of saturated aluminum chloride solution, maintaining a relative humidity (RH) of 79.5%. After 3 days, the films were reweighed. The percentage of moisture absorption was then quantified with the following formula.:

$$\text{Percentage Moisture Absorption} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weigth}} \times 100$$

Folding Endurance

This was tested by repeatedly folding a single film at the same spot until it either broke or reached 200 folds, the threshold for good mechanical properties. The number of folds endured without breaking was recorded.

Swelling Index (SI)

The swelling index of the films was measured in simulated salivary fluid (pH 6.6). A 1 cm^2 film sample was weighed and placed in a pre-weighed stainless-steel sieve, which was then immersed in 15 mL of simulated salivary fluid in a porcelain dish. At

specified time intervals, the sieve was removed, excess fluid was blotted with tissue, and the film was reweighed. The swelling index was obtained with the formula.:

$$\text{Swelling Index} = \frac{Wt - W0}{Wt} \times 100$$

Where:

- W_t = weight of the swollen film at time t
- W_0 = initial weight of the dry film

In Vitro Antibacterial Activity (Disk Diffusion test):

Film samples (1 cm^2) were evaluated for antibacterial activity. Nutrient agar medium (60 mL) was prepared, sterilized at 15 lb pressure for 20 minutes, and poured into Petri dishes under aseptic conditions, allowing it to solidify. A 0.1 mL microbial suspension of known concentration was evenly spread over the agar surface. The cut films were placed on the agar and incubated at 37°C for 24 hours. Antibacterial activity was determined by measuring the zone of inhibition (in mm) against the three microorganisms. (Figure 15 – 17)

CLINICAL STUDY:

Clinical part of the study was performed at KAHER's KLE Vishwanath Katti Institute of Dental Sciences, Belagavi.

The trial was registered with the Clinical Trial Registry of India - CTRI/2024/09/073827.

Participants who provided consent with full knowledge were incorporated in the study.

The trial was a randomized controlled, single-blinded clinical trial, where participants were assigned to their group using a simple random sampling method (computer-based software).

CLINICAL ARMAMENTARIUM REQUIRED: (Figure 18, 19)

1. Surgical drape
2. Mouth mask
3. Disposable gloves
4. Mouth mirror, Explorer, Tweezers, Straight probe
5. Kidney tray
6. Cotton swabs and gauze
7. Glass slab
8. Sterilized set of Gracey curette
9. Saline
10. Sterilized microcentrifuge tubes – Eppendorff tubes
11. Petri plates
12. Pipettes
13. Nutrient agar medium
14. Peptone water
15. Mucoadhesive film containing silver nano particles
16. Mucoadhesive film containing curcumin
17. Periodontal dressing (Coe Pak)
18. Cement Spatula

PROCEDURE FOR PERIODONTAL THERAPY

All patients received a full mouth SRP. Following re-evaluation at 1 week, patients requiring periodontal flap surgery underwent random allocation into

Group 1 (Control), After periodontal flap surgery they received periodontal pack (Perio – pack) as a periodontal dressing. (Figure 20)

Group 2, After periodontal flap surgery they received a mucoadhesive film containing silver nano particles and periodontal pack as a periodontal dressing. (Figure 21)

Group 3, After periodontal flap surgery they received a mucoadhesive film containing curcumin and periodontal pack as a periodontal dressing. (Figure 22)

Plaque samples were collected at baseline following which periodontal surgery was conducted. All the patients were recalled on the 7^{th} day for suture removal, wound healing was assessed and plaque samples were obtained to assess the CFU. Later, they were recalled on the 14^{th} day for wound healing assessment.

A customized proforma (Annexure 6) was developed for the study to ensure systematic and structured documentation of all observations and information. Relevant details, including the patient's personal information, chief complaint, and dental history, were documented using this form. Subsequently, microbiological samples were obtained, and a clinical examination was performed on a dental chair under standard lighting using a mouth mirror, explorer, William’s graduated periodontal probe, and tweezer.

MICROBIOLOGICAL ASSESSMENT

A sterile Gracey's curette was used to collect plaque samples from both the test and control groups at baseline and at day 7. The samples were collected in a sterilized microcentrifuge tube containing thioglycolate broth (Transport media) and transported to KAHER's Dr. Prabhakar Kore Basic Research Center, Belagavi for microbial evaluation within 20 minutes from collection. (Figure 23, 24)

1. Sample Preparation and Serial Dilution

The sterile nutritional agar medium was autoclaved, transferred onto sterile petri plates, and allowed to solidify. The subgingival sample collected in the thioglycolate broth (Transport media) was mixed well by vortexing. The dilution of the sample was prepared using sterile saline solution in test tubes whereby 1 mL of the original sample was transferred into 9 mL of diluent (10^{-1} dilution) using a new sterile pipette.

2. Plating Method

Spread Plate Method: 0.1 mL of the dilution was transferred onto the surface of a pre-solidified nutrient agar plate and evenly distributed using a sterile swab. The plate was allowed to absorb the sample before incubating.

3. Incubation

Incubation was carried out for 24 hours with the plates positioned in an inverted manner at 37°C

4. Colony Counting and Calculation

Post-incubation, colony counts were performed using a colony counter.

Microbiological parameter was assessed at baseline and 7 days. (Figure 25 - 26)

WOUND HEALING INDEX:

Wound healing index was assessed at 7th day and 14th day after periodontal surgery. (27 -29)

Wound healing was assessed using Landry, Turnbull and Howley Healing Index (1988)

Healing Index	Tissue Color	Bleeding on Palpation	Granulation Tissue	Incision Margin	Suppuration
1 – Very Poor (2 or more signs present)	≥ 50 % of red gingiva	Yes	Yes	Not epithelized, with loss of epithelium beyond incision margin	Yes
2 – Poor	≥ 50 % of red gingiva	Yes	Yes	Not epithelized, with exposed connective tissue	No
3 – Good	25 – 50 % of red gingiva	No	No	No exposed connective tissue	No
4 – Very Good	< 25% of red gingiva	No	No	No exposed connective tissue	No
5 - Excellent	All pink tissues	No	No	No exposed connective tissue	No

STATISTICAL ANALYSIS

Study data obtained was entered to Microsoft Excel Software, which was then exported to Statistical Package for Social Sciences (SPSS) Version 25, IBM Statistics, USA.

Descriptive statistics were computed, and the Shapiro-Wilk test was employed to evaluate data normality. For intergroup comparisons, the Kruskal-Wallis ANOVA test and the Mann-Whitney U test were used. For intragroup comparisons, the Wilcoxon matched-pairs test and the paired t-test were applied, depending on the data's normality. Statistical significance was accepted at a confidence level greater than 95% ($p < 0.05$).

Figure 1: Curcumin

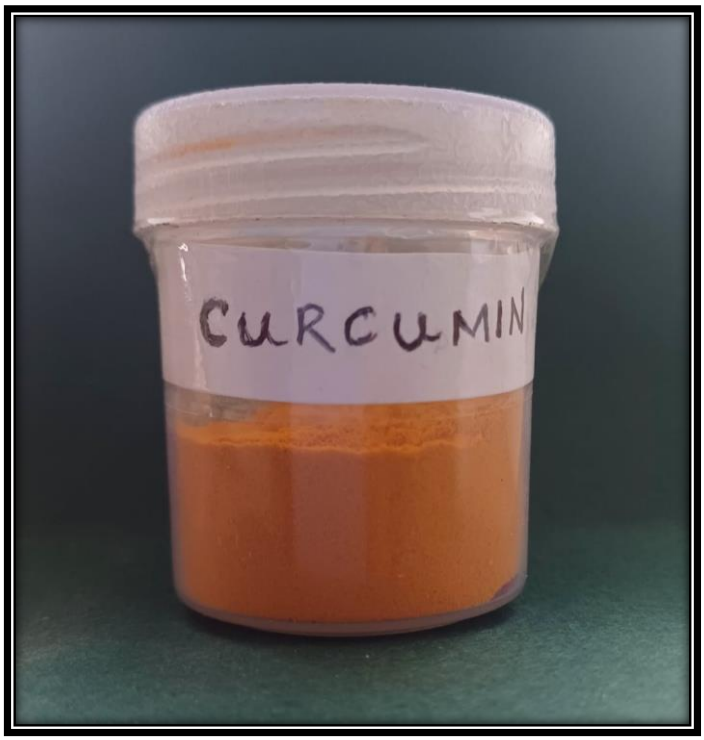


Figure 2: Synthesized Silver nano particle solution:

Figure 3: Broth dilution method [Resazurin] for Minimum Inhibitory Concentration of *Staphylococcus aureus*

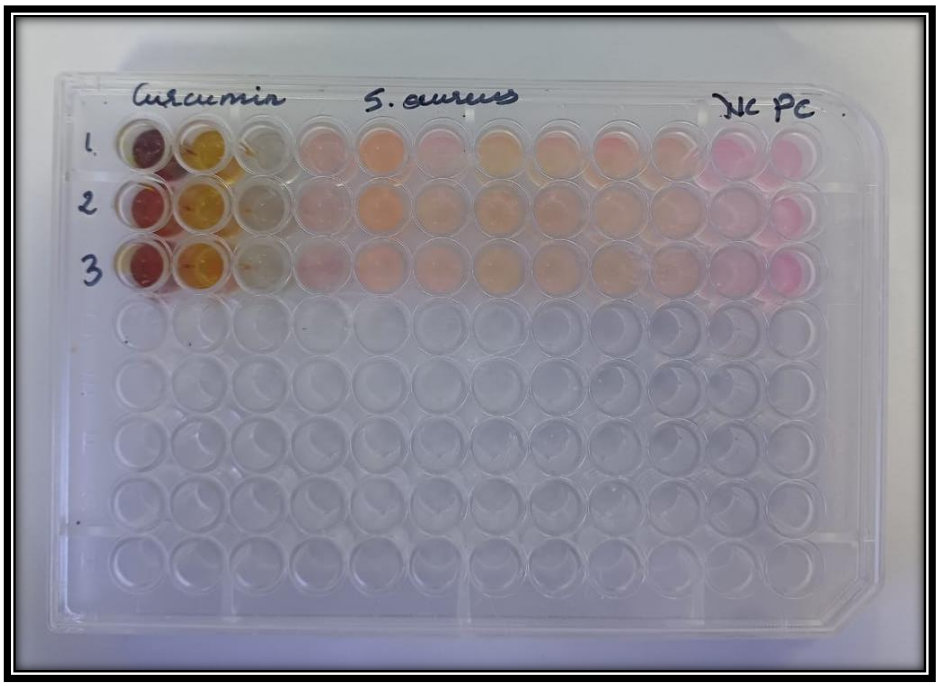


Figure 4: Broth dilution method [Resazurin] for Minimum Inhibitory Concentration of *Pseudomonas aueroginosa* and *Porphyromonas gingivalis*

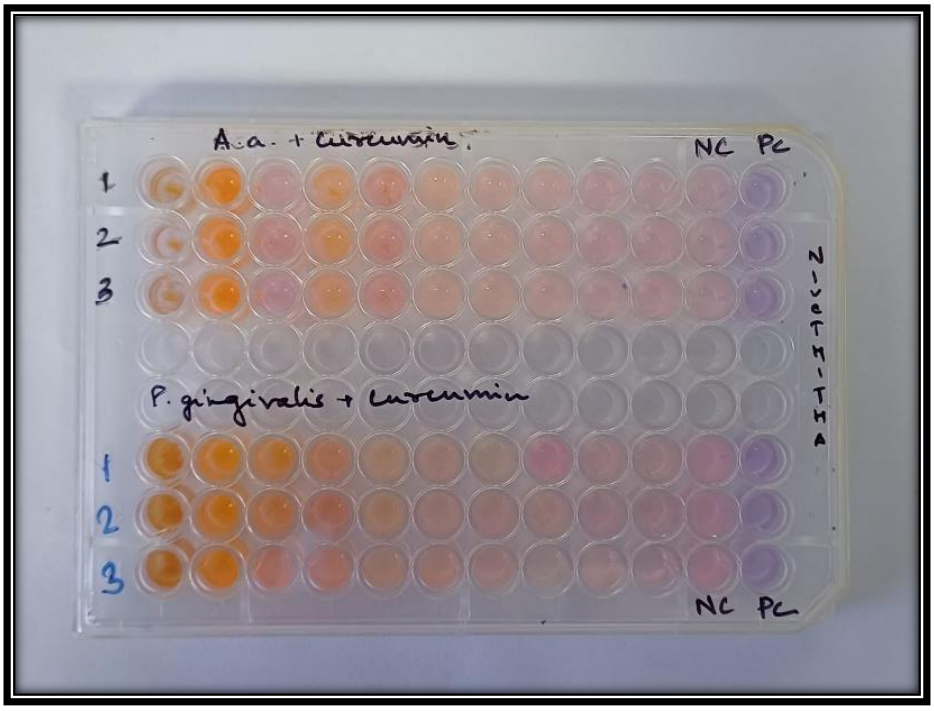


Figure 5: Minimum Bactericidal Concentration of Curcumin against *Staphylococcus aureus*

Figure 6: Minimum Bactericidal Concentration of Curcumin against *Porphyromonas ginigvalis*

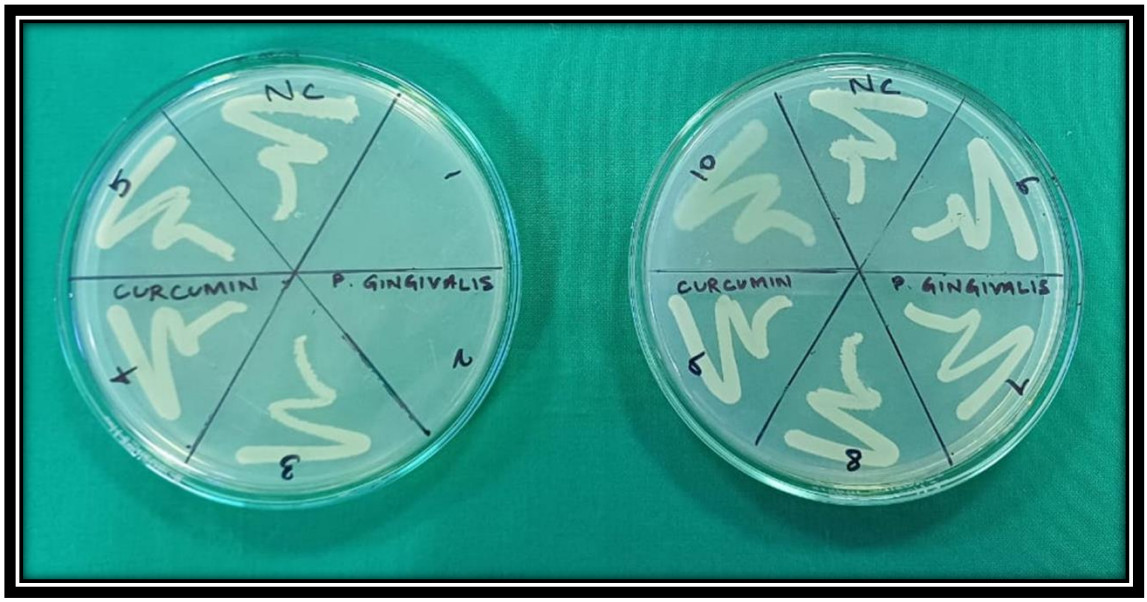


Figure 7: Minimum Bactericidal Concentration of Curcumin against *Pseudomonas aueroginosa*

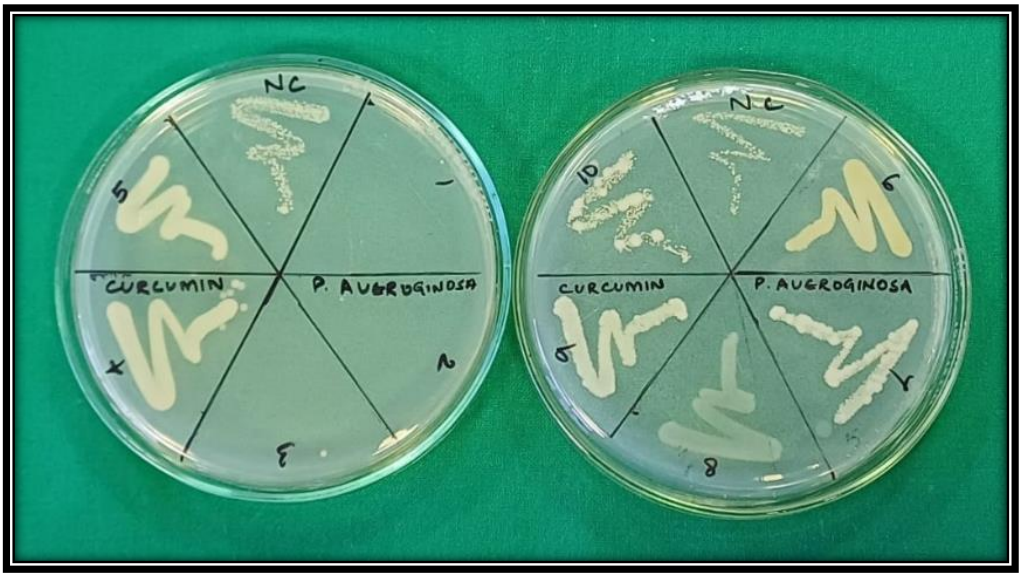


Figure 8: Bacteriological Incubator

Figure 9: Cytotoxicity test showing viable cells:

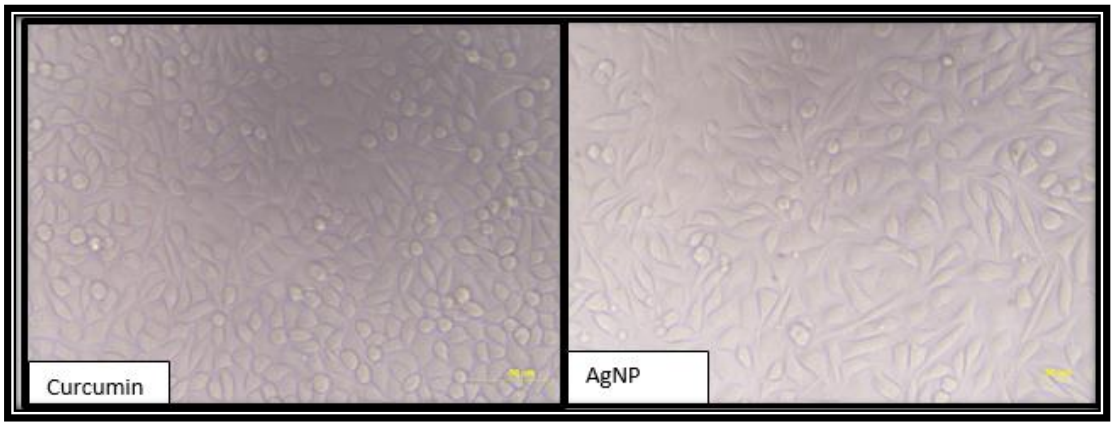


Figure 10: Chemical Reagents for Film formulation

Figure 11: Magnetic Stirrer

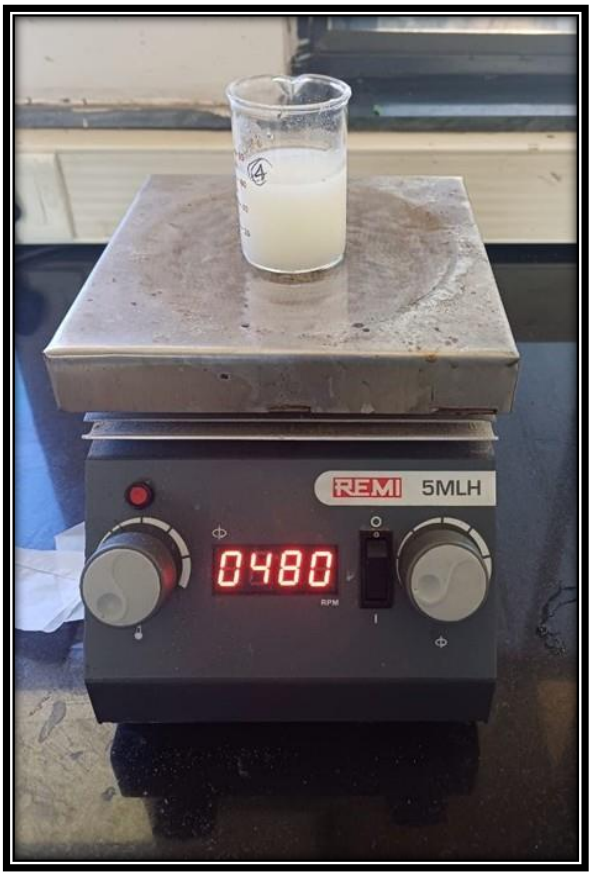


Figure 12: Polymer solution being poured for film formulation onto silicone molds and petri plates

Figure 13: Formulated, sterilized and packed AgNP films

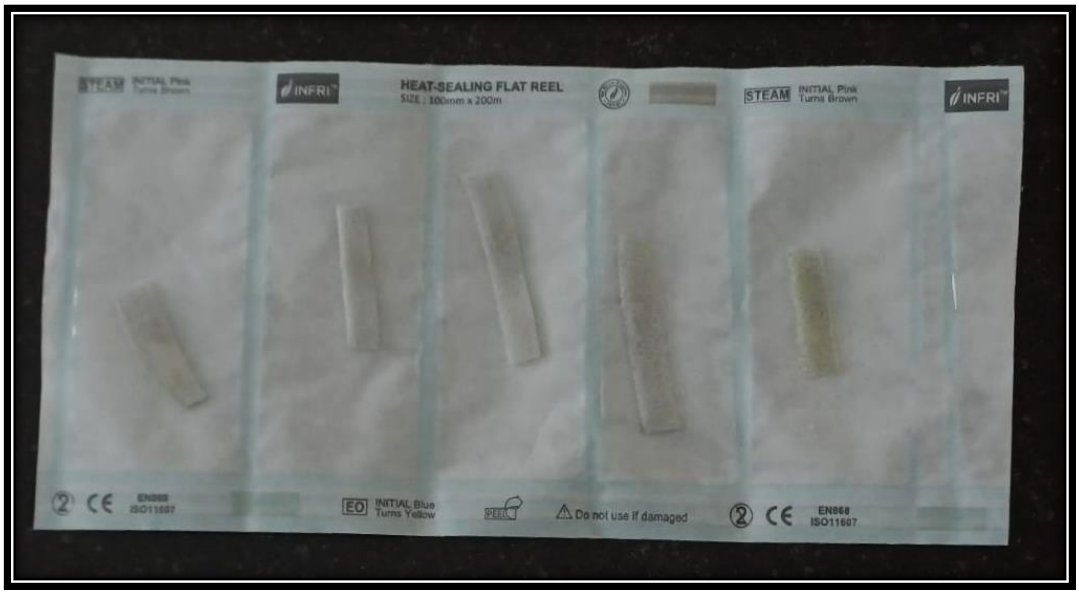


Figure 14: Formulated, sterilized and packed Curcumin films

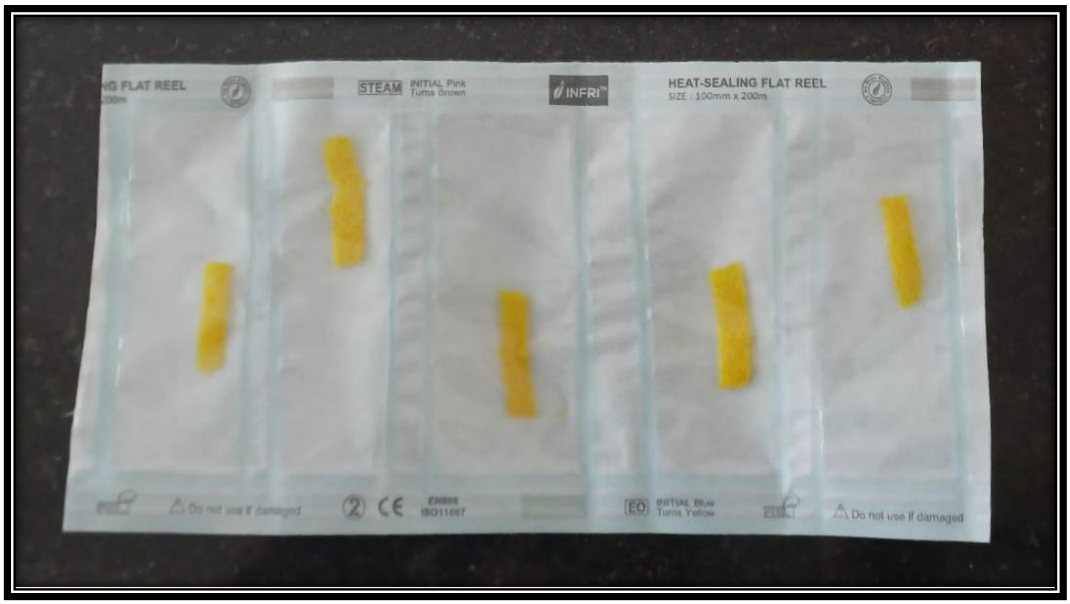


Figure 15: Zone of Inhibition of the films against *Staphylococcus aureus*

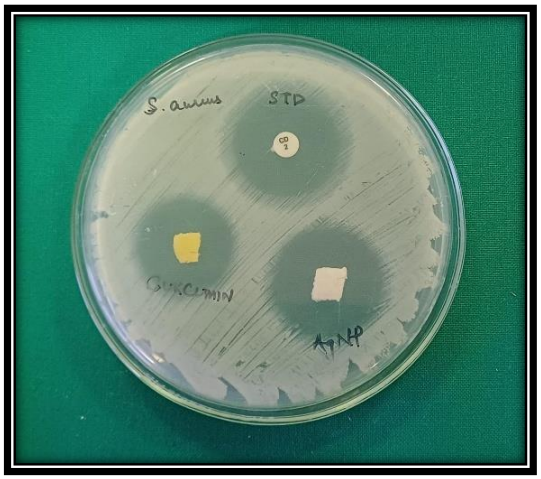


Figure 16: Zone of Inhibition of the films against *Porphyromonas gingivalis*

Figure 17: Zone of Inhibition of the films against *Pseudomonas auroginosa*

Figure 18: Clinical Armamentarium

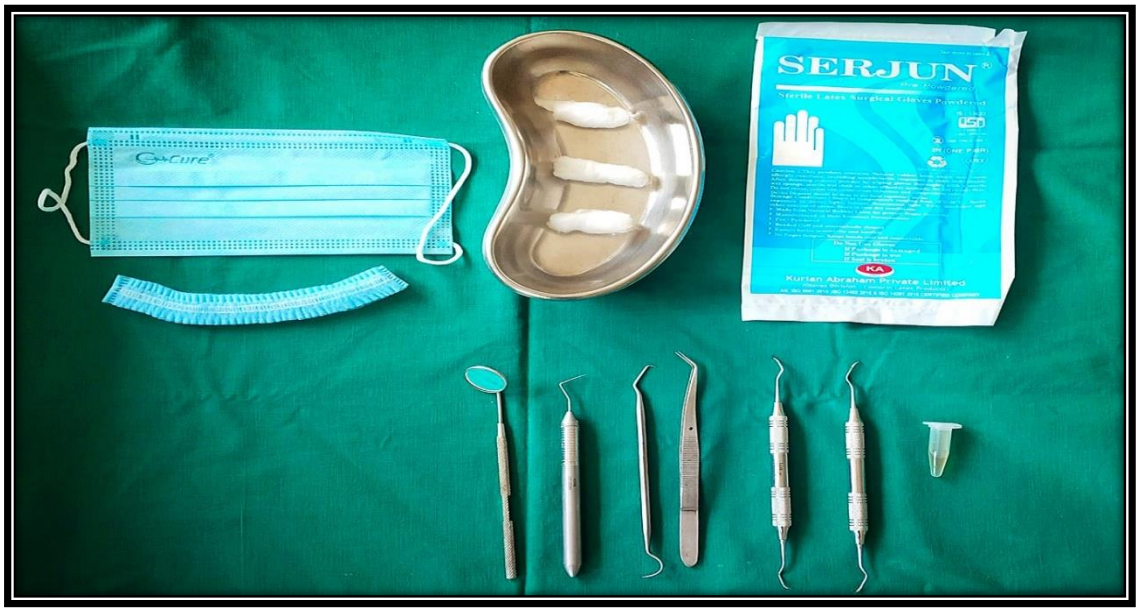


Figure 19: Periodontal Pack – Coe Pak

Figure 20: Periodontal pack placement

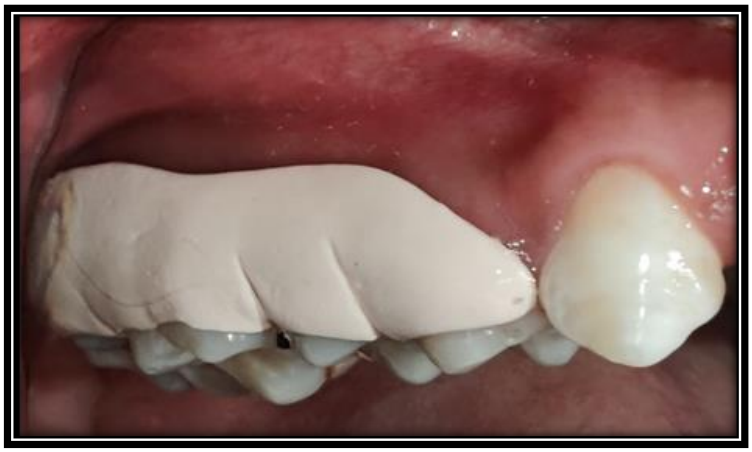


Figure 21: Placement of AgNP Film

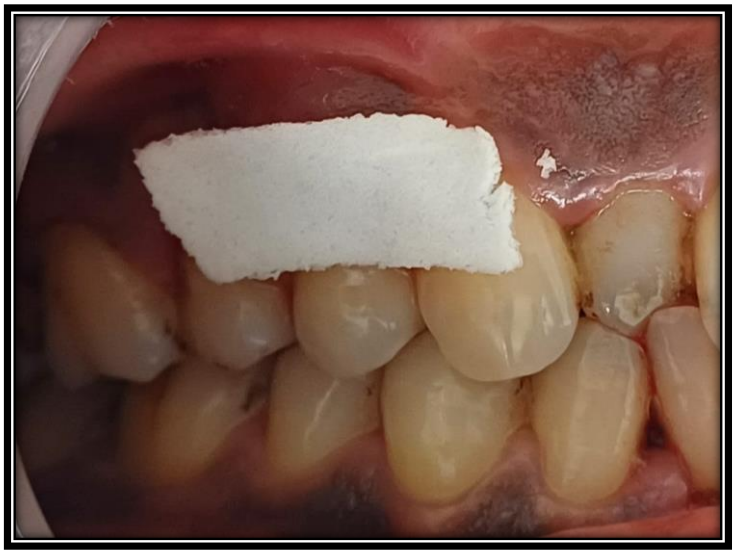


Figure 22: Placement of curcumin film

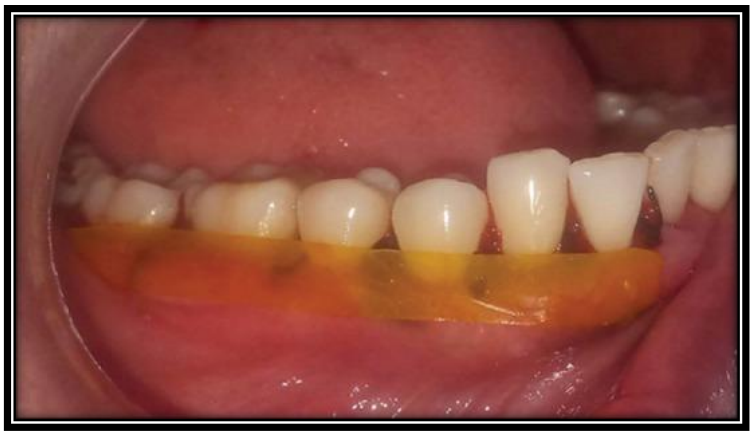


Figure 23: Laboratory Armamentarium

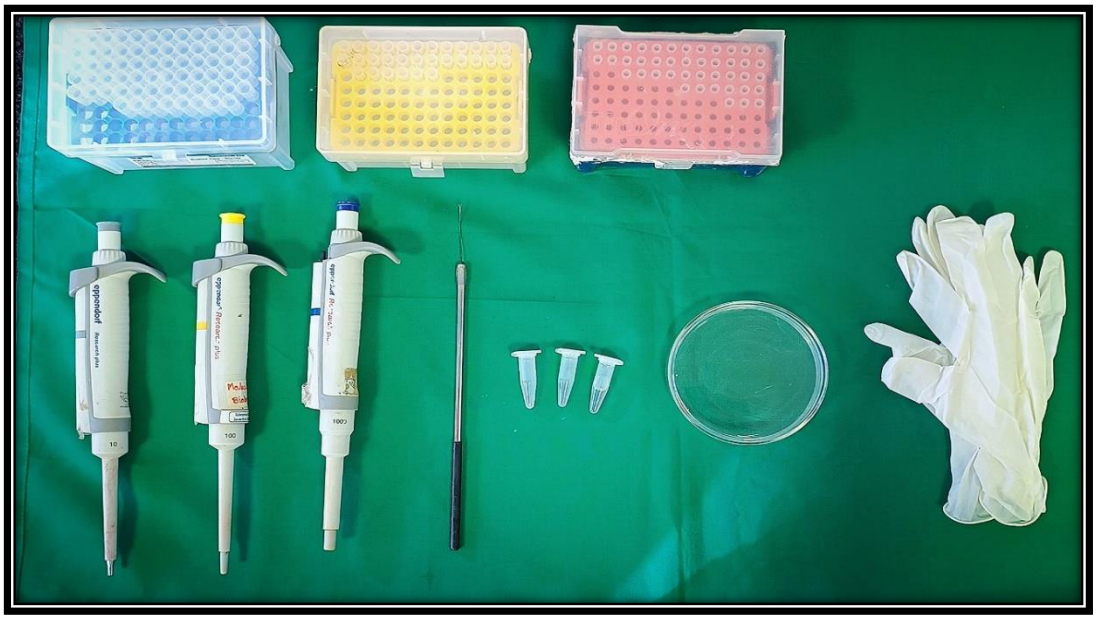


Figure 24: Laminar air flow chamber

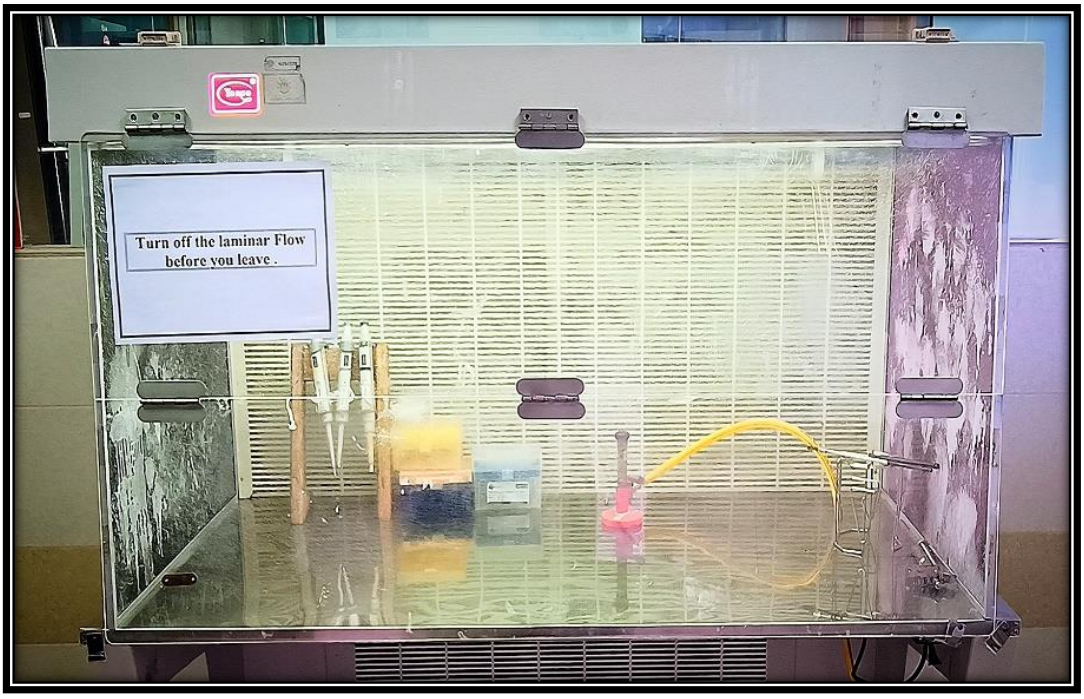


Figure 25: Agar Plate Inoculated with Subgingival Plaque Sample and Colonies observed at baseline

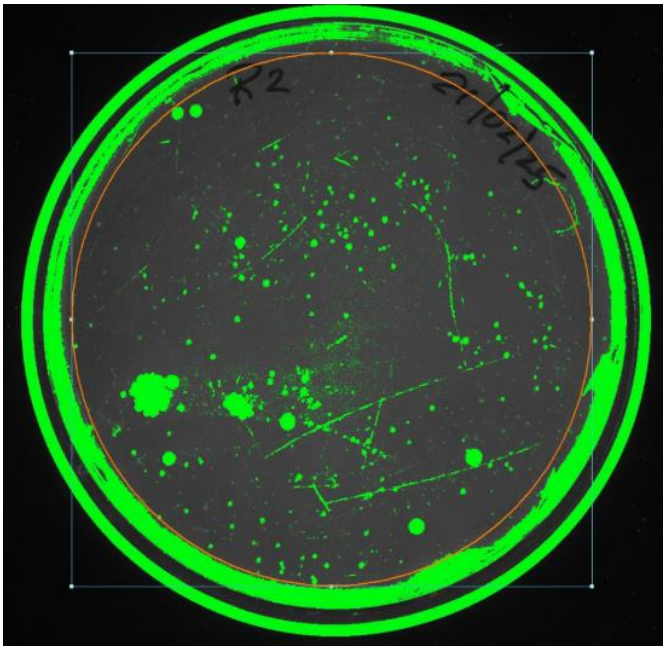


Figure 26: Agar Plate Inoculated with Subgingival Plaque Sample and Colonies observed at day 7

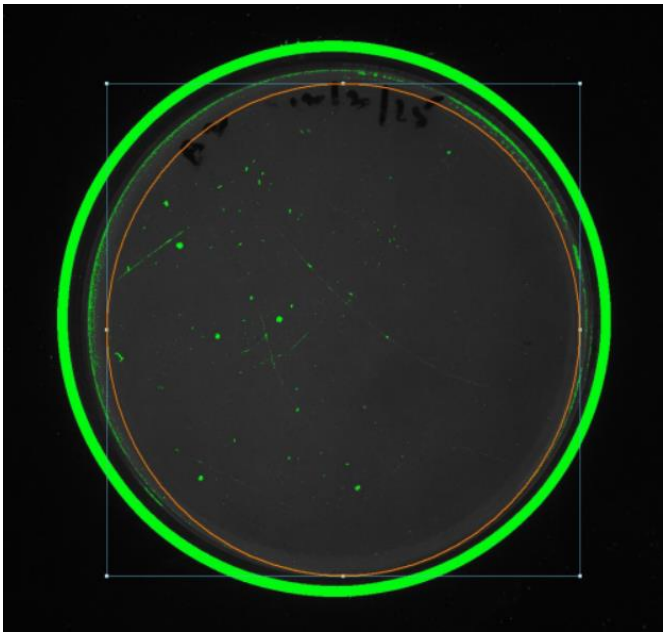


Figure 27: Intraoperative pictures after periodontal surgery - Baseline

Figure 27 a: Group 1

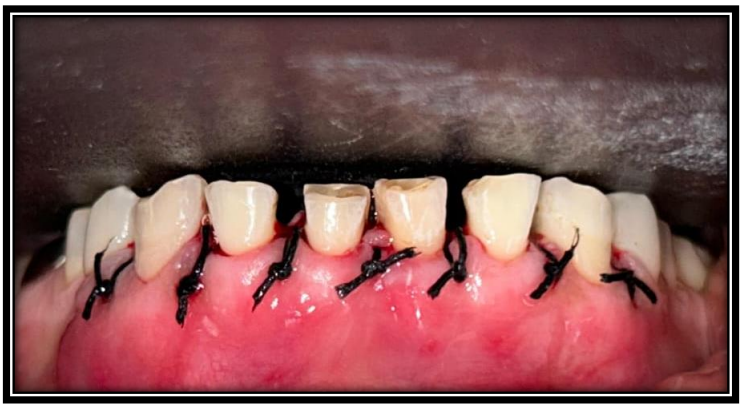


Figure 27 b: Group 2

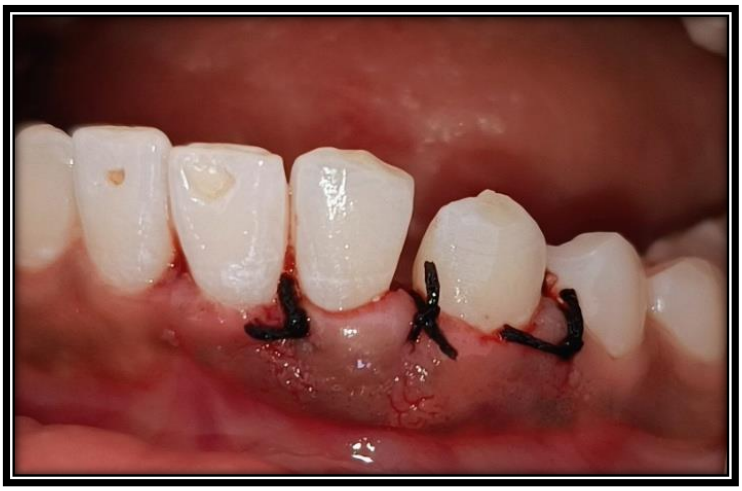


Figure 27 c: Group 3

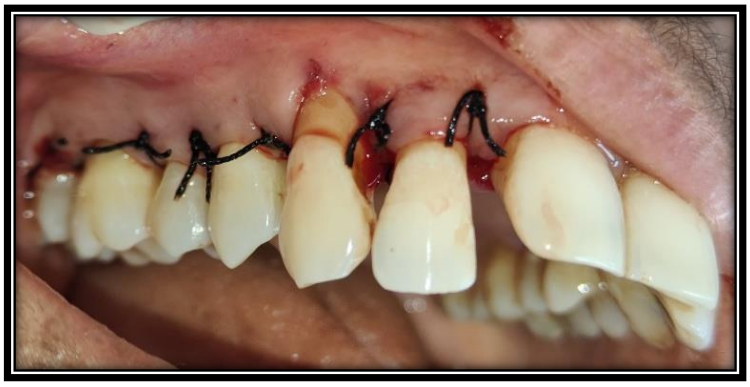


Figure 28: WHI assessment on Day 7

Figure 27 a: Group 1

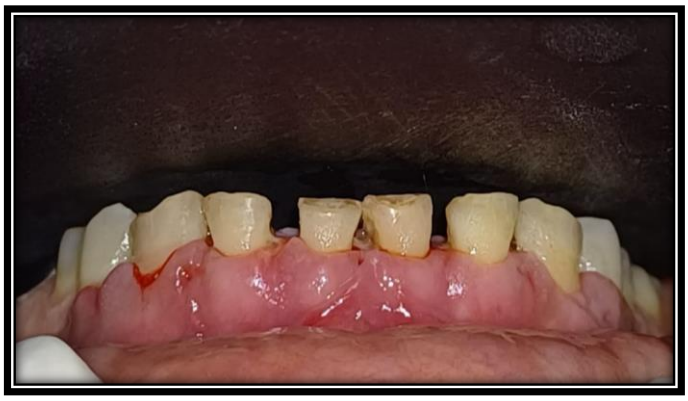


Figure 27 b: Group 2

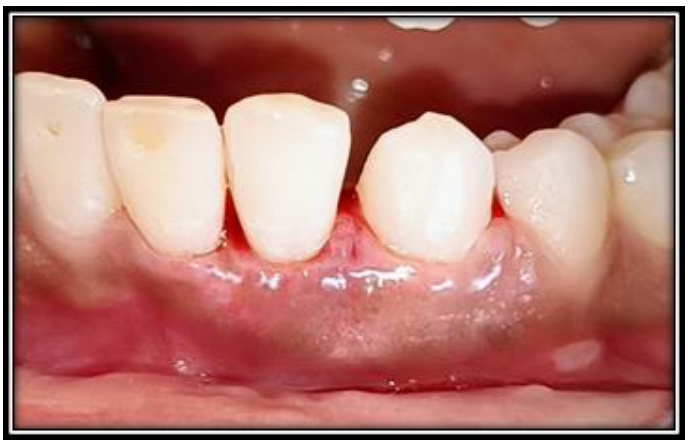


Figure 27 c: Group 3

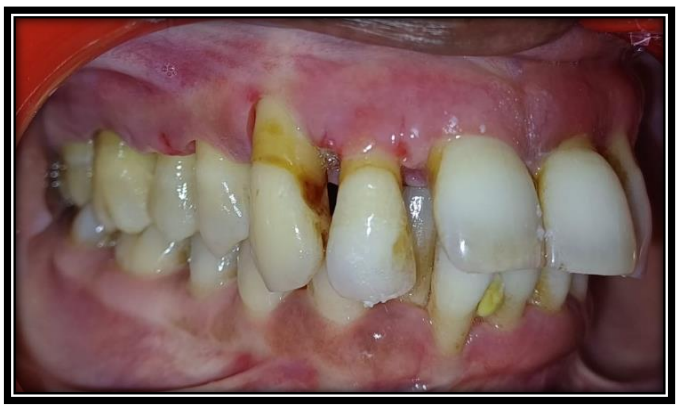


Figure 28: WHI assessment on Day 14

Figure 28 a: Group 1

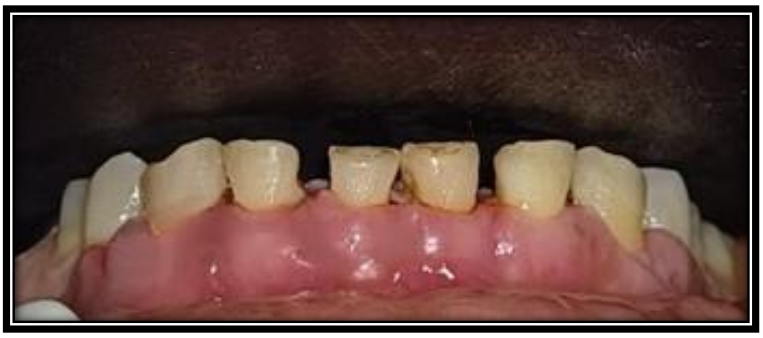


Figure 28 a: Group 2

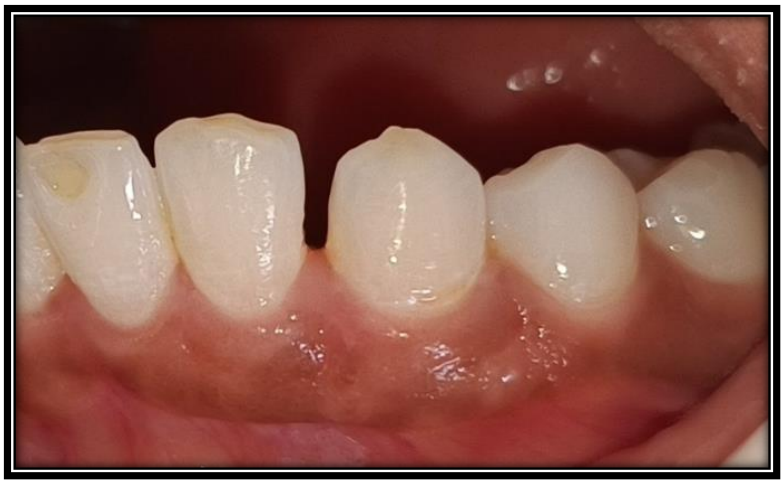
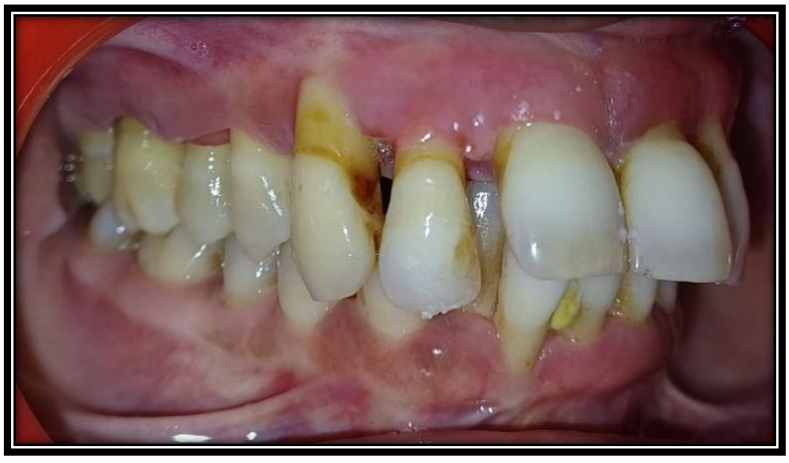


Figure 28 a: Group 3



RESULTS

The goal of the current project was to analyse and contrast the ability of mucoadhesive films containing silver nanoparticles and mucoadhesive films containing curcumin on wound healing after periodontal surgery. A total of 45 participants identified with chronic periodontitis and in need of periodontal surgery were assigned randomly into:

- Group 1: Administration of periodontal dressing only
- Group 2: Administration of mucoadhesive film containing silver nanoparticles
- Group 3: Administration of mucoadhesive film containing curcumin

Wound healing was assessed using the Wound Healing Index on Day 7 and Day 14, and microbial evaluation was conducted by measuring Colony Forming Units (CFUs) at baseline and Day 7.

The data were entered into Microsoft Excel and analyzed using SPSS version 2.5.

- Descriptive statistics were computed, and the Shapiro-Wilk test was employed to evaluate data normality.
- For intergroup comparisons, the Kruskal-Wallis ANOVA test and the Mann-Whitney U test were used.
- For intragroup comparisons, the Wilcoxon matched-pairs test and the paired t-test were applied, depending on the data's normality.

Table 1: Gender wise distribution of participants

Sex	Number	Percent (%)	Mean Age (years)	SD Age (years)
Male	24	53.33	47.75	6.58
Female	21	46.67	47.14	5.69
Total	45	100.00	47.33	6.21

Observation:

Table 1 shows that among 45 patients, male were 24 in number and female were 21 in number and a mean age of 47.33 $\pm$ 6.21 years

Table 2: Normality of scores of wound healing and log CFU at different treatment time points in three groups by Shapiro-Wilk test

Parameters	Time points	Group	Shapiro-Wilk	df	p-value
Wound healing	Day 7	Group 1	0.6300	15	0.0001*
		Group 2	0.7580	15	0.0010*
		Group 3	0.7900	15	0.0030*
	Day 14	Group 1	0.6300	15	0.0001*
		Group 2	0.6300	15	0.0001*
		Group 3	0.5610	15	0.0001*
	Day 7 to Day 14	Group 1			
		Group 2	0.4130	15	0.0001*
		Group 3	0.4130	15	0.0001*
Log CFU	Day 7	Group 1	0.9750	15	0.9190
		Group 2	0.9360	15	0.3360
		Group 3	0.9340	15	0.3090
	Day 14	Group 1	0.9500	15	0.5260
		Group 2	0.9260	15	0.2370
		Group 3	0.9110	15	0.1390
	Day 7 to Day 14	Group 1	0.9250	15	0.2270
		Group 2	0.9280	15	0.2560
		Group 3	0.8580	15	0.0630

*$p<0.05$

Observation:

Table 1 shows the normality of the all the parameters i.e., Wound healing Index and Colony forming units in the three study groups at different points using Shapiro-Wilk test which shows statistically notable difference in the wound healing score in all groups at different points with a p value of less than 0.05.

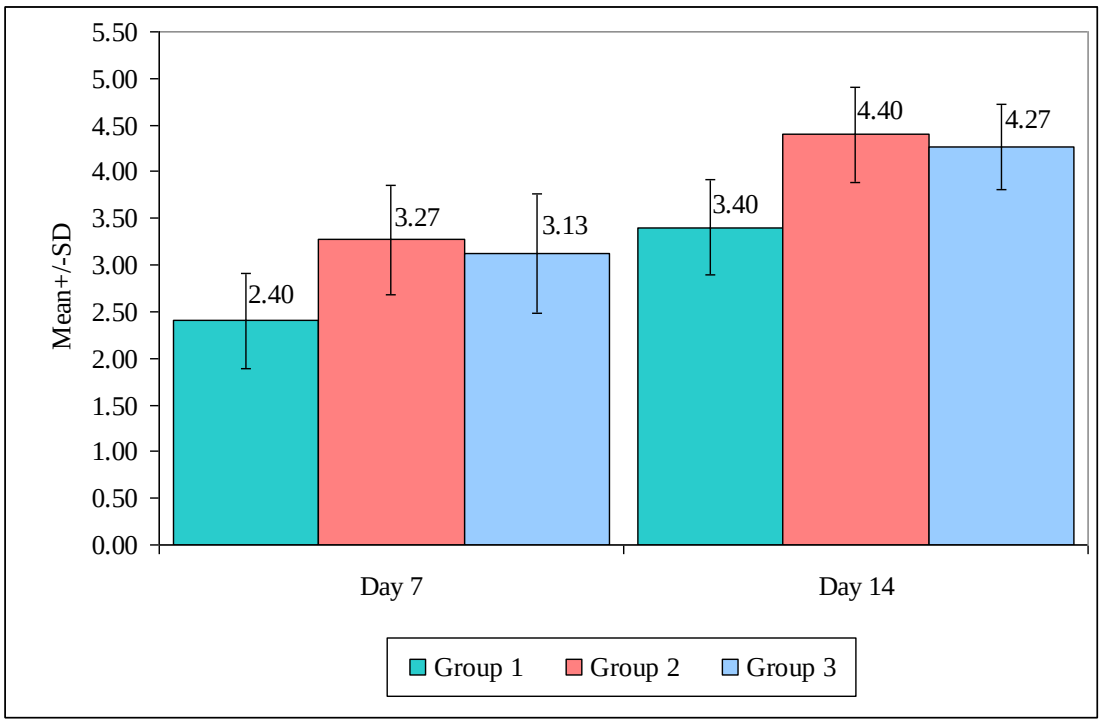
Note that, the scores of wound healing at different treatment time points in three groups did not follow a normal distribution. Therefore, the non-parametric tests were applied. But the log CFU counts follow normal distribution. Hence, parametric tests were utilized.

Table 3: Comparison of Group 1, Group 2 and Group 3 with Wound Healing Index scores at Day 7 and Day 14 treatment time points by Kruskal Wallis ANOVA

Time points	Group 1			Group 2			Group 3			H-value	P-value
	Mean	SD	Mean rank	Mean	SD	Mean rank	Mean	SD	Mean rank		
Day 7	2.40	0.51	10.50	3.27	0.59	20.50	3.13	0.64	19.80	14.0080	0.0010*
Day 14	3.40	0.51	9.80	4.40	0.51	21.20	4.27	0.46	20.80	20.3330	0.0001*
Day 7-Day 14	1.00	0.00	14.50	1.13	0.35	16.50	1.13	0.35	16.50	2.1460	0.3420

*p<0.05

Graph 1: Comparison of Group 1, Group 2 and Group 3 with Wound Healing Index scores at Day 7 and Day 14 treatment time points



Observation:

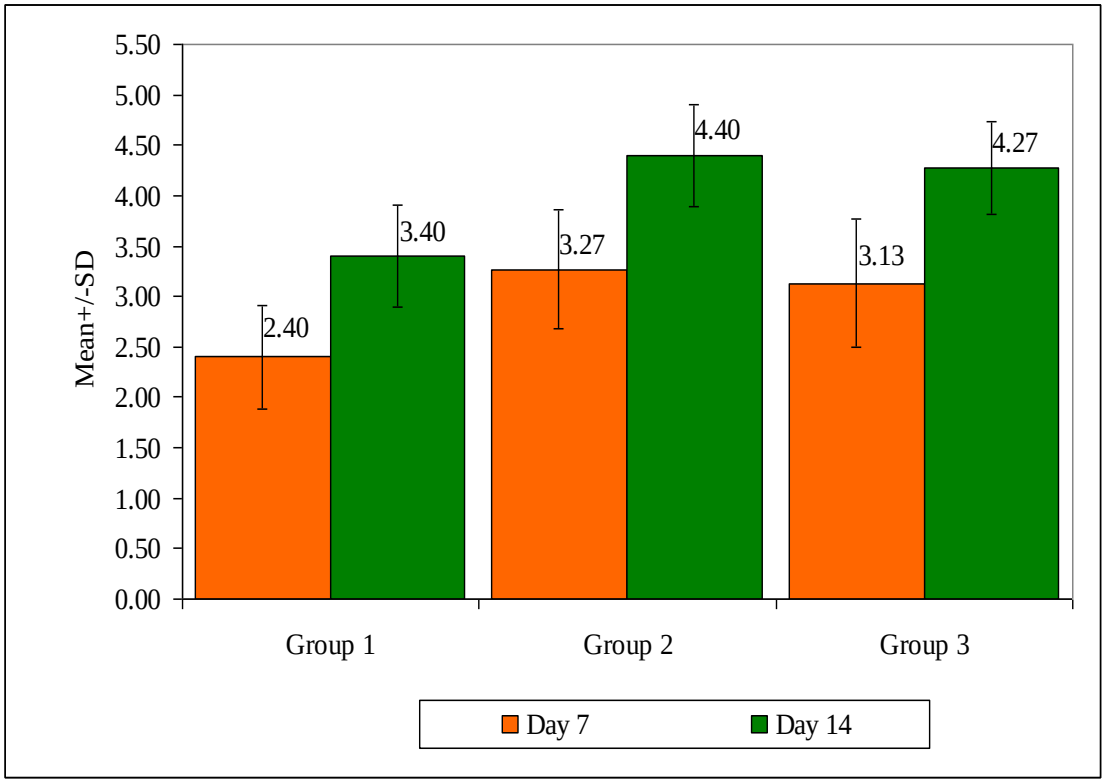
Table 3 and Graph 1 show that the mean ± standard deviation values at Day 7 were 2.30 ± 0.51, 3.27 ± 0.59, and 3.13 ± 0.64, and at Day 14 were 3.40 ± 0.51, 4.27 ± 0.51, and 4.27 ± 0.46 for each group. Based on these scores, a statistically marked difference in healing was found across the groups at both time points, with Group 2 having the highest mean healing score.

Table 4: Pair wise comparison of Group 1, Group 2 and Group 3 with Wound Healing Index scores at Day 7 and Day 14 treatment time points by Mann-Whitney U test

Time points	Groups	Mean	SD	Mean rank	U-value	Z-value	p-value
Day 7	Group 1	2.40	0.51	10.5			
	Group 2	3.27	0.59	20.5	37.50	-3.0901	0.0020*
	Group 1	2.40	0.51	11.2			
	Group 3	3.13	0.64	19.8	48.00	-2.6546	0.0079*
	Group 2	3.27	0.59	16.3			
	Group 3	3.13	0.64	14.7	100.50	0.4770	0.6334
Day 14	Group 1	3.40	0.51	9.8			
	Group 2	4.40	0.51	21.2	27.00	-3.5256	0.0004*
	Group 1	3.40	0.51	10.2			
	Group 3	4.27	0.46	20.8	33.00	-3.2768	0.0011*
	Group 2	4.40	0.51	16.5			
	Group 3	4.27	0.46	14.5	97.50	0.6014	0.5476
Day 7 to Day 14	Group 1	1.00	0.00	14.5			
	Group 2	1.13	0.35	16.5	97.50	-0.6014	0.5476
	Group 1	1.00	0.00	14.5			
	Group 3	1.13	0.35	16.5	97.50	-0.6014	0.5476
	Group 2	1.13	0.35	15.5			
	Group 3	1.13	0.35	15.5	112.50	-0.0207	0.9835

*$p<0.05$

Graph 2: Comparison of Day 7 and Day 14 treatment time points with Wound Healing Index scores in Group 1, Group 2 and Group 3



Observation:

Table 4 and Graph 2 indicates that there was a notable variation between Group 2 and Group 1 at Day 7 and Day 14, with p-values of 0.0020 and 0.0004, respectively ($p < 0.05$), showing improved healing efficacy in Group 2. Similarly, Group 3 showed considerably greater healing than Group 1, with p-values of 0.0079 and 0.0011 at Day 7 and Day 14, respectively ($p < 0.05$). However, no difference was discovered between Group 2 and Group 3, indicating that the two groups had equivalent healing efficacy.

Table 5: Comparison of Day 7 and Day 14 treatment time points with Wound Healing Index scores in Group 1, Group 2 and Group 3 by Wilcoxon matched pairs test

Groups	Time points	Mean	SD	Mean Diff.	SD Diff.	% of change	Z-value	P-value
Group 1	Day 7	2.40	0.51					
	Day 14	3.40	0.51	-1.00	0.00	-41.67	3.4078	0.0007*
Group 2	Day 7	3.27	0.59					
	Day 14	4.40	0.51	-1.13	0.35	-34.69	3.4075	0.0007*
Group 3	Day 7	3.13	0.64					
	Day 14	4.27	0.46	-1.13	0.35	-36.17	3.4076	0.0007*

*$p<0.05$

Observation:

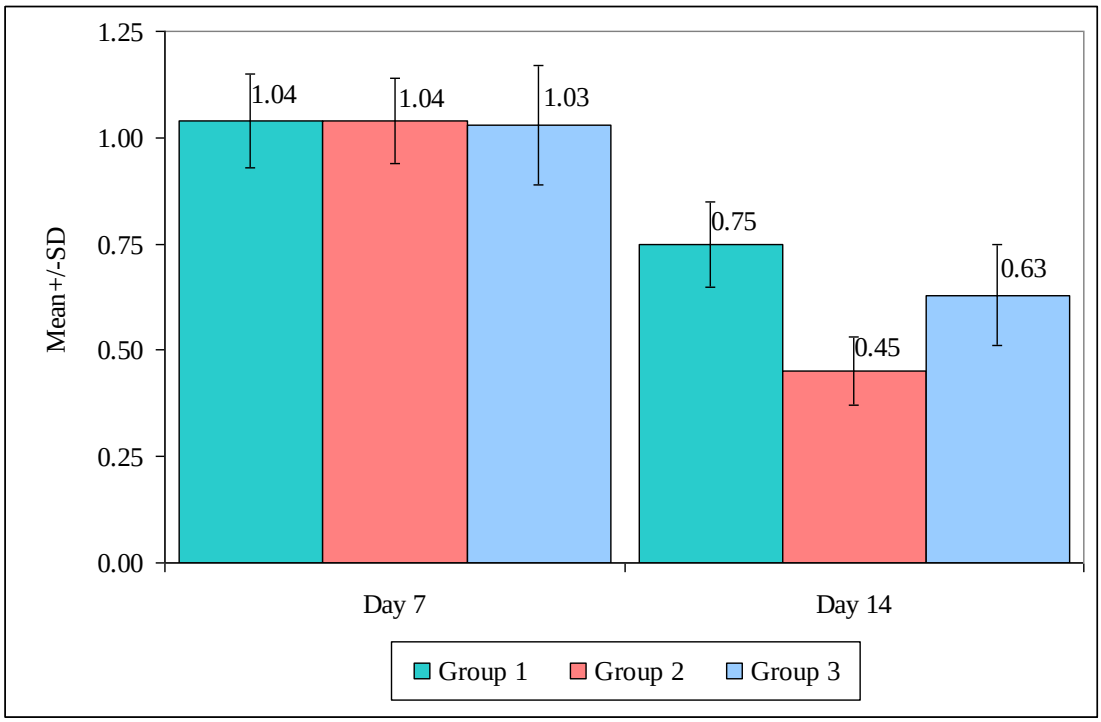
Table 5 shows that all three groups show a statistically noteworthy increase in wound healing scores from Day 7 to Day 14.

Table 6: Comparison of Group 1, Group 2 and Group 3 with log CFU counts at Baseline and Day 7 treatment time points by one way ANOVA

Time points	Group 1		Group 2		Group 3		F-value	P-value
	Mean	SD	Mean	SD	Mean	SD		
Baseline	1.04	0.11	1.04	0.10	1.03	0.14	0.0788	0.9243
Day 7	0.75	0.10	0.45	0.08	0.63	0.12	30.1150	0.0001*
Baseline -Day 7	0.30	0.03	0.59	0.05	0.40	0.05	174.0898	0.0001*

*p<0.05

Graph 3: Comparison of Group 1, Group 2 and Group 3 with log CFU counts at Baseline and Day 7 treatment time points



Observation:

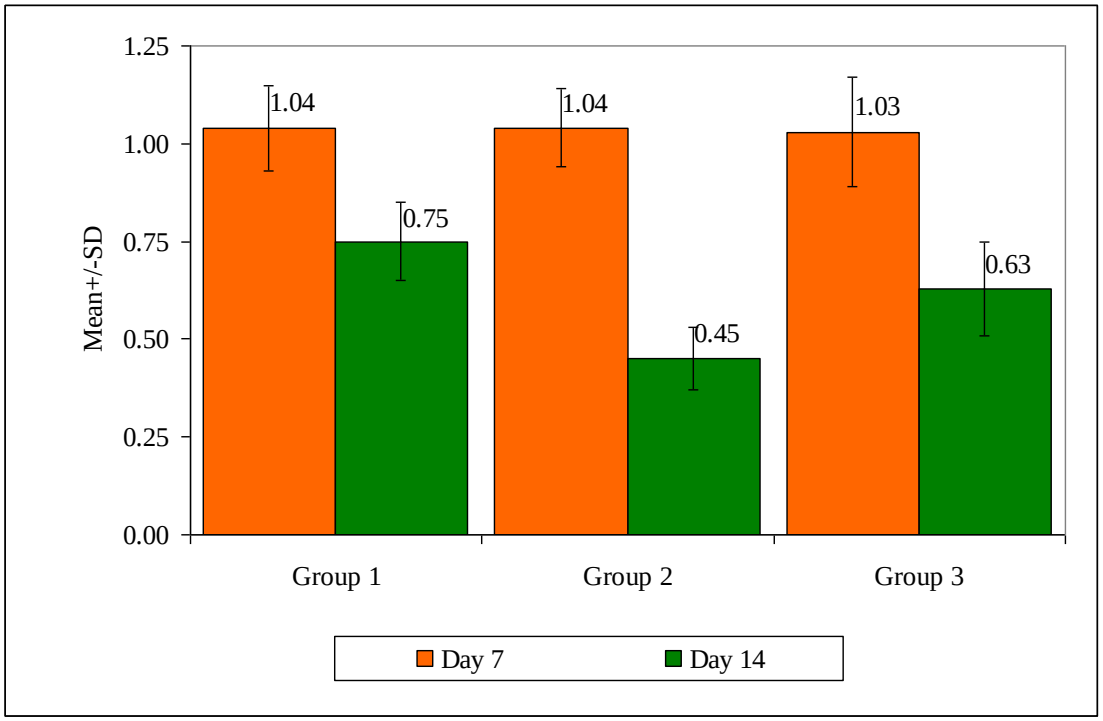
Table 6 and Graph 3 show mean ± SD values at baseline as 1.03 ± 0.11, 1.04 ± 0.10, and 1.03 ± 0.14, and at Day 7 as 0.75 ± 0.10, 0.45 ± 0.08, and 0.63 ± 0.12 for Groups 1, 2, and 3, respectively. At Day 7, all groups showed a substantial reduction (p-value = 0.0001, $p < 0.05$), with Group 2 having the greatest mean reduction.

Table 7: Comparison of Baseline and Day 7 treatment time points with log CFU counts scores in Group 1, Group 2 and Group 3 by paired t test

Groups	Time points	Mean	SD	Mean Diff.	SD Diff.	% of change	t-value	P-value
Group 1	Baseline	1.04	0.11					
	Day 7	0.75	0.10	0.30	0.03	28.52	34.6163	0.0001*
Group 2	Baseline	1.04	0.10					
	Day 7	0.45	0.08	0.59	0.05	56.67	48.5373	0.0001*
Group 3	Baseline	1.03	0.14					
	Day 7	0.63	0.12	0.40	0.05	38.76	31.1608	0.0001*

*p<0.05

Graph 4: Comparison of Baseline and Day 7 treatment time points with log CFU counts scores in Group 1, Group 2 and Group 3



Observation:

Table 6 and Figure 4 show that a statistically significant reduction was observed in all three groups at Day 7, with a p-value of 0.0001 ($p < 0.05$). The greatest decline was observed in Group 2, with a percentage reduction of 56.67% at Day 7.

INVITRO STUDY RESULTS:

MIC AND MBC ESTIMATION:

Curcumin:

Organism	MIC (mg/ml)	MBC (mg/ml)
Staphylococcus aureus	0.05	0.1
Porphyromonas gingivalis	0.05	0.1
Pseudomonas aeruginosa	0.025	0.05

AgNP:

Results given by Quintero-Quiroz et al in 2015 and Zhang et al in 2018 were taken into consideration.[31, 32]

Organism	MIC (µg/ml)	MBC (µg/ml)
Staphylococcus aureus	2.5	2.5
Porphyromonas gingivalis	4.6	2.5
Pseudomonas aeruginosa	2.5	2.5

CYTOTOXICITY ASSESSMENT:

A stock solution containing 1mg/ml of curcumin and 1 µl/ml of AgNP solution were formulated. Concentrations from 500µg/ mL – 15.6µg/ mL was considered for cytotoxicity assessment MTT Assay – L 929 cell line was carried out on and the following results were obtained.

Compound	Concentration µg/mL	Cell viability %
AgNP	500	22.26
	250	43.60
	125	74.03
	62.5	76.24
	31.2	80.10
	15.6	84.69
Curcumin	500	47.14
	250	52.44
	125	71.12
	62.5	83.46
	31.2	89.79
	15.6	95.10

At lower concentration both curcumin and AgNPs showed cytocompatibility with good viability

POST FORMULATION TEST RESULTS OF THE FILM:

Based on the cytotoxicity assessment results, the films were formulated.

The concentration of curcumin used for the formulation of the curcumin film was 0.1 mg/ml

The concentration of AgNP used for the formulation of the AgNP film was 0.1 µl/ml Film characterization was carried out, and the following results were obtained. All tests were performed in triplicate, with average values recorded.

1. Thickness:

   It was measured using calibrated digital vernier calipers, with readings taken at multiple points across each film. The average thickness was 0.56 mm for the curcumin film and 0.58 mm for the AgNP film.

2. Uniformity of Weight:

   Films of size (1 cm × 1 cm) were individually cut and weighed using an electronic balance. The average weight was 10.5 mg for the curcumin film and 11.2 mg for the AgNP film.

3. Surface pH:

   The film surface was gently moistened using water, and the pH was measured by placing a pH electrode on the surface of the film. pH of the curcumin and AgNP films was determined to be 6.7 and 6.6, respectively.

4. Percentage Moisture loss

   The curcumin film exhibited a moisture loss of 10.30%, while the AgNP film showed a moisture loss of 11.5%.

5. Percentage Moisture Absorption

   The curcumin film exhibited a moisture absorption of 12.35%, while the AgNP film showed a moisture absorption of 13.51%.

6. Folding Endurance

   Upon repeated folding, the folding endurance was recorded as 78 for the curcumin film and 84 for the AgNP film.

7. Swelling Index (SI)

   The swelling index was determined to be 15.5 for the curcumin film and 14.7 for the AgNP film.

8. Antibacterial activity:

   The assessment was done using Disk diffusion test and the ZOI of the films against the 3 organisms were observed to be

Organism	ZOI of Curcumin film (mm)	ZOI of AgNP film (mm)
Staphylococcus aureus	19	20
Porphyromonas gingivalis	14	17
Pseudomonas aeruginosa	18	18

DISCUSSION

"Nothing in life is to be feared, it is only to be understood. Now is the time to understand more so that we may fear less."

- Marie Curie

Periodontal dressings have been designed to promote wound healing, alleviate patient pain and discomfort, and reduce the risk of infection and bleeding in the surgical site. Dr. Ward developed the first periodontal dressing in 1923 and advocated for its usage after periodontal surgery. [33] Because wound healing can only occur when the wound is stable, the major goals of using a periodontal dressing are blood clot stabilization and wound protection. By exerting pressure to the healing site, the dressing material minimizes dead space and promotes soft tissue adherence to the bone/root surface, reducing bacterial infiltration and boosting wound healing while maintaining tissue stability.[34] The beneficial aspects include a significant decrease in root sensitivity and the inhibition of development of plaque at the wound site.[35]

The oral cavity contains opportunistic and pathogenic bacteria that can lead to acute or chronic infections, particularly when a wound persists. Hence, taking proper precautionary measures is crucial to control microbial activity and ensure the success of the surgery.[36] These dressings act as a snug, impermeable barrier that prevents the ingress of saliva, limits bacterial proliferation, and reduces dead space beneath the periodontal flap, ultimately improving patient comfort during the postoperative period.

Periodontal dressings are regarded by many periodontists as one of the key elements influencing the therapeutic results of periodontal surgical therapy. Despite the fact antibiotics, surgical techniques, and root planing precision are all vital, they are often considered as secondary.[37] This highlights the importance of periodontal dressings in insulating and safeguarding the wound from external factors. Even though they are widely used, a clinician's preference ultimately determines whether or not to utilize them in clinical practice.[39]

Genovesi et al. (2012) reported that periodontal packs enhance the outcomes of non-surgical periodontal treatments by promoting blood clot stability, reducing bleeding, and lowering the chance of bacterial infection.[39] However, some studies have shown that these dressings may lead to increased plaque accumulation compared to cases where no periodontal dressing is used. Therefore, the composition of periodontal dressings plays a crucial role in determining key outcomes such as wound healing, plaque retention, and biocompatibility with surrounding tissues. These factors are essential for assessing the overall effectiveness of the dressing material.

Thus, in the current study, a total of 45 participants were assessed for wound healing using periodontal dressing along with a silver nano particles film and a curcumin film after periodontal surgery. The healing was assessed using WHI given by Landry *et al*., at 7^{th} and 14^{th} day and the antibacterial effect was assessed quantitatively using Colony forming units (CFU/ml) at baseline and 7 days.

The wound-healing efficacy of silver nanoparticles (AgNPs), largely due to their antimicrobial properties, has been well-documented by several researchers.[40, 41, 42] In the present study, intergroup comparison revealed that Group 2 (AgNPs) exhibited significantly higher mean healing scores than Group 1 (control) on day 7 (p

= 0.0020) and day 14 post-surgery (p = 0.0004), as shown in (Table 3 and Graph 1). This enhanced healing response is likely due to the inherent properties of AgNPs, which not only offer strong antibacterial action but also foster an inflammation-free environment that supports fibroblast proliferation and maturation.[43]

The observations of the current study align with those of Agarwal et al, Bhavya et al (2021) who reported enhanced healing when silver nanoparticles were used as a dressing succeeding flap surgery.[3, 23] Habiboallah et al. (2014), in an invitro study observed enhanced healing following the use of AgNP dressing. The histological analysis revealed a statistically notable enhancement in inflammation and tissue repair parameters (P = 0.034, 0.05) after applying the silver membrane.[44]

In the current study, intragroup comparison in Group 2 also showed a statistically significant enhancement in healing between day 7 and day 14 (p = 0.0007) (Table 4, Graph 2). This is consistent with the observations made by Metcalf et al., who studied the use of silver comprising antimicrobial dressings on 112 hard-to-heal wounds and reported improved healing in 83% of the subjects.[45] This can be attributed to the inherent antibacterial, anti-inflammatory, and hemostatic properties of AgNP that effectively contributes to effective wound healing.

Mohseni et al. conducted an in vivo study comparing antimicrobial dressings containing SSD and AgNPs for wound management. The results showed that AgNPs offered superior biocompatibility, faster healing, enhanced epithelialization, and improved skin regeneration.[46]

Curcumin, a natural polyphenol rich antioxidant isolated from the rhizome of Curcuma longa[47] (Zingiberaceae family), has inflammation curtailing[48, 49] and antioxidant traits[50, 51], rendering it a viable treatment for aiding wound healing. [52, 53]

In the present study, intergroup comparisons revealed that Group 3 (Curcumin) had significantly higher healing scores than Group 1 (Control) on day 7 ($p = 0.0079$), day 14 ($p = 0.0011$) post-surgery, as shown in (Table 4 and Graph 2). However, no changes were detected between the two test groups—Group 2 (AgNP) and Group 3 (Curcumin)—on day 7 ($p = 0.6334$) and day 14 ($p = 0.5476$), respectively.

Curcumin exhibits anti-inflammatory effects by stimulating cortisol production from the adrenal glands, lowering levels of histamine, and constraining the formation of prostaglandins and neutrophil activity. Additionally, it restrains the synthesis of pro-inflammatory cytokines and hinders their activation.[54, 55] Its wound-healing and inflammation reducing characteristics are further attributed to alleviation in edema and vascular congestion in connective tissues, along with enhanced collagen synthesis, angiogenesis, and fibroblast proliferation, all of which support tissue regeneration.[56, 57]

Muhammad and Ghani in their research, surgically induced wounds in rabbits and treated them with topically curcumin. The treated sites showed marked improvement in healing compared to the control sites.[58]

Our study is the first to examine the effects of conventional periodontal dressing, silver nanoparticle films, and curcumin films on wound healing. All three groups showed positive healing responses; however, silver nanoparticles outperformed curcumin, with statistically significant differences observed on day 7 ($p = 0.0020$) and day 14 ($p = 0.0004$) (Table 4). To sum up, both silver nanoparticles and curcumin films demonstrated superior wound healing potential compared to periodontal dressing alone.

In the present study, a substantial reduction in CFU/ml was observed across all groups by day 7 (P = 0.001) (Table 6, Graph 3), Notably, Group 2 exhibited a 56.67% decrease, whereas Group 1 showed only a 28.52% reduction (Table 7). These observations align with those of Kanika Aggarwal et al. (2021), which highlights the potent antibacterial activity of AgNPs attributed to their large surface area relative to their volume plus their ability to interact extensively with bacterial components.[3]

Additionally, Group 1 showed greater plaque accumulation beneath the dressing, with only a 28% mean reduction in plaque levels after 7 days. In contrast, Group 2 achieved a 56% mean reduction, indicating significantly less plaque buildup under the silver nanoparticle dressing (Table 7). This finding aligns with the results of Bhavya B et al. (2021), who also observed a higher percentage reduction in plaque values in the silver membrane group.[23]

Curcumin exhibits antibacterial properties through several mechanisms, including disrupting bacterial cell membranes, blocking essential bacterial enzymes and proteins, preventing biofilm formation, and displaying broad-spectrum antimicrobial activity. In our study, all groups showed a significant reduction in CFU/ml after 7 days (P = 0.001) (Table 6, Graph 3). However, Group 3 (Curcumin) demonstrated a 38.67% reduction, compared to only 28.52% in Group 1 (Control). (Table 7)

These findings are in agreement with those of Ankita Sharma et al. (2024), who found that the subgingival placement of curcumin sheets alongside (SRP) in periodontitis patients resulted in significant improvements in clinical parameters, largely attributed to curcumin's antibacterial properties.[59] Despite curcumin's effectiveness, the present study concludes that silver nanoparticles exhibited superior antibacterial and wound-healing capabilities compared to curcumin.

SUMMARY AND CONCLUSION

This study sought to examine the wound-healing potential of mucoadhesive films incorporating silver nanoparticles and curcumin following flap surgery in individuals with chronic periodontitis.

45 subjects identified with periodontitis and indicated for flap surgery were grouped into three: Group 1 was treated with only a periodontal dressing, Group 2 was treated with silver nanoparticle film along with the dressing, and Group 3 was treated with curcumin film with the dressing. Wound healing was assessed on days 7 and 14 post-surgery using the Wound Healing Index, while antibacterial activity was measured by evaluating colony-forming units (CFUs) at baseline and on day 7.

The statistical analysis was carried out using SPSS software version 2.5. Descriptive statistics were computed, and the Shapiro-Wilk test was employed to evaluate data normality. Intergroup differences were assessed using the Kruskal-Wallis ANOVA and Mann-Whitney U tests, while intragroup comparisons were conducted using either the Wilcoxon matched-pairs test or the paired t-test, depending on the distribution of the data All statistical tests were performed at a significance level of 5% ($p<0.05$).

Taking into account the outcomes of the study, it can be inferred that:

- The silver nanoparticle group showed a statistically substantial improvement in wound healing.
- Curcumin group demonstrated better healing than the control and results comparable to the silver nanoparticle group.
- Silver nanoparticle group exhibited a significant reduction in CFU/ml by day 7, indicating enhanced antibacterial activity.

To conclude, drug-loaded dressings alongside conventional periodontal dressings significantly enhances healing following periodontal surgery. Among the materials studied, silver nanoparticles demonstrated the most effective antibacterial and wound-healing properties. Curcumin also exhibited similar effects, albeit to a lesser degree, suggesting its potential as an alternative for promoting wound healing. However, further research with greater sample size is required to establish definitive guidelines for the clinical use of these materials as periodontal dressings.

Within the limitations of this study, our findings highlight the wound-healing potential of both silver nanoparticles and curcumin. A combination of these materials, or the synthesis of curcumin-based nanoparticles, may synergize their effects and yield enhanced results. Additionally, the evaluation of biomarkers such as Vascular Endothelial Growth Factor (VEGF) could provide deeper insight in regards to their wound-healing potential.

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ANNEXURES

ANNEXURE 1: ETHICAL CLEARANCE

Research and Ethics Committee
KLE VK INSTITUTE OF DENTAL SCIENCES
A Constituent Unit of KLE Academy of Higher Education & Research
Accredited 'A' Grade by NAAC | Placed in Category 'A' by MHRD (GoI)
Nehru Nagar, Belagavi - 590 010, Karnataka State
☎: 0831-2470362 | Web: http://www.kledental-bgm.edu.in
FAX: 0831-2470640 | E-mail:principal@kledental-bgm.edu.in

Sl. No. : 1641

CERTIFICATE

This is to Certify that the synopsis titled

Comparative Efficacy of Mucoadhesive film Containing Silver nano Particles and Mucoadhesive film containing curcumin on wound Healing after Periodontal Surgery - A Randomized controlled trial -

Submitted by

Dr. REG NO. IK0222003 *P. G. Student / Staff, Guided by* ____ *from Department of* Periodontics *has been critically evaluated by committee members and granted ethical clearance to conduct the above mentioned study*

Date : 8/4/22

Member Secretary
Research and Ethical Committee
KLEVK Institute of Dental Sciences
Belagavi

MEMBER SECRETARY
Research & Ethical Committee
KLEVK Institute of Dental Sciences
BELAGAVI.

Chairman
Research and Ethical Committee
KLEVK Institute of Dental Sciences
Belagavi

Chairman
Research and Ethical Committee
KLE VK Institute of Dental Sciences
Belgaum

ANNEXURE 2: COLONY FORMING UNIT – RESULT

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA
(Formerly known as KLE University) (Deemed-to-be-University u/s 3 of the UGC Act, 1956)
DR. PRABHAKAR KORE BASIC SCIENCE RESEARCH CENTER [BSRC], BELAGAVI, KARNATAKA.
III Floor, V. K. Institute of Dental Sciences Campus, Nehru Nagar, Belagavi - 590 010, Karnataka – INDIA
E-mail: research@kledeemeduniversity.edu.in; **Web**: www.klepkbsrc.org, **Phone**: 0831- 2444444, Extn. 4122

Report **Date: 29-03-2025**

Title of Research: Comparative Efficacy of Mucoadhesive Film Containing Silver Nano Particles and Mucoadhesive Film Containing Curcumin on Wound Healing After Periodontal Surgery – A Randomized Controlled Trial

Student Name: REG NO. IK0222003

Guide:

Objective Parameters

1. Formulation of mucoadhesive films containing silver nano particles and mucoadhesive films containing curcumin.
2. To assess and compare the effect of mucoadhesive film containing silver nano particles and mucoadhesive film containing curcumin on wound healing after periodontal surgery using Wound Healing index (Landry, Turnbull and Howley 1988)
3. To compare the antibacterial efficacy of mucoadhesive film containing silver nano particles and mucoadhesive film containing curcumin.

Experimental Methodology

Subgingival plaque samples were collected at baseline, 1 week and 1 month time intervals for both the test as well as control group with a sterile Gracey's curette. The samples were collected in a sterilized microcentrifuge tube containing thioglycolate broth (Transport media) and transported to KAHER's Dr. Prabhakar Kore Basic Research Center, Belagavi for microbial evaluation within 20 minutes from collection.

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DR. PRABHAKAR KORE BASIC SCIENCE RESEARCH CENTER [BSRC], BELAGAVI, KARNATAKA.
III Floor, V. K. Institute of Dental Sciences Campus, Nehru Nagar, Belagavi - 590 010, Karnataka – INDIA
E-mail: research@kledeemeduniversity.edu.in; **Web**: www.klepkbsrc.org, **Phone**: 0831- 2444444, Extn. 4122

1. Sample Preparation and Serial Dilution

A sterile nutrient agar medium was prepared and poured it into sterile petri dishes and allowed to solidify. The subgingival sample collected in the thioglycolate broth (Transport media) was mixed well by vortexing. The dilution of the sample was prepared using sterile saline solution in test tubes whereby 1 mL of the original sample was transferred into 9 mL of diluent (10^{-1} dilution) using a new sterile pipette.

2. Plating Method

Spread Plate Method: 0.1 ml of an appropriate dilution was pipetted onto the surface of a pre-prepared nutrient agar plate and spread evenly using a sterile swab. The plate was allowed to absorb the sample before incubating.

3. Incubation

The plates were inverted and incubated at 37°C for 24 hours.

4. Colony Counting and Calculation

After incubation, the visible colonies were counted on plates using a colony counter.

The study group were as follows:

Group 1: Patients will receive only Periodontal dressing

Group 2: Patients will receive a mucoadhesive film containing silver nano particles and periodontal dressing

Group 3: Patients will receive a mucoadhesive film containing curcumin and periodontal dressing

Colony forming units were assessed and counted at Baseline and 1 week.

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III Floor, V. K. Institute of Dental Sciences Campus, Nehru Nagar, Belagavi - 590 010, Karnataka – INDIA
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Result

Colony forming units were assessed and counted after test procedures at baseline and 1 week interval

At Baseline

COLONY FORMING UNIT – CFU/ml			
S.no	**Group 1**	**Group 2**	**Group 3**
1	0.98×10^2	1.06×10^2	0.76×10^2
2	1.11×10^2	1.07×10^2	0.94×10^2
3	1.09×10^2	0.97×10^2	1.09×10^2
4	0.86×10^2	0.99×10^2	1.23×10^2
5	0.89×10^2	0.85×10^2	1.1×10^2
6	0.95×10^2	1.08×10^2	0.98×10^2
7	1.17×10^2	1.19×10^2	0.77×10^2
8	1.06×10^2	1.13×10^2	1.04×10^2
9	0.92×10^2	0.94×10^2	1.13×10^2
10	0.98×10^2	1.18×10^2	1.23×10^2
11	1.01×10^2	0.87×10^2	1.09×10^2
12	1.15×10^2	1.06×10^2	0.96×10^2
13	1.19×10^2	1.09×10^2	0.93×10^2
14	1.24×10^2	1.12×10^2	1.06×10^2
15	1.04×10^2	1.07×10^2	1.12×10^2

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III Floor, V. K. Institute of Dental Sciences Campus, Nehru Nagar, Belagavi - 590 010, Karnataka – INDIA
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At 1 Week Interval

COLONY FORMING UNIT – CFU/ml			
S.no	**Group 1**	**Group 2**	**Group 3**
1	0.68×10^2	0.46×10^2	0.39×10^2
2	0.78×10^2	0.43×10^2	0.57×10^2
3	0.75×10^2	0.48×10^2	0.66×10^2
4	0.57×10^2	0.34×10^2	0.69×10^2
5	0.66×10^2	0.33×10^2	0.72×10^2
6	0.64×10^2	0.44×10^2	0.59×10^2
7	0.88×10^2	0.55×10^2	0.38×10^2
8	0.73×10^2	0.54×10^2	0.68×10^2
9	0.64×10^2	0.38×10^2	0.71×10^2
10	0.66×10^2	0.56×10^2	0.79×10^2
11	0.77×10^2	0.32×10^2	0.77×10^2
12	0.88×10^2	0.48×10^2	0.59×10^2
13	0.86×10^2	0.46×10^2	0.54×10^2
14	0.92×10^2	0.53×10^2	0.64×10^2
15	0.76×10^2	0.49×10^2	0.73×10^2

The above-mentioned data has to be subjected to further statistical analysis.

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III Floor, V. K. Institute of Dental Sciences Campus, Nehru Nagar, Belagavi - 590 010, Karnataka – INDIA
E-mail: research@kledcmcduniversity.edu.in; Web: www.klepkbsrc.org, Phone: 0831- 2444444, Extn. 4122

Lab investigations done in BSRC:

Minimum Inhibitory Concentration

Compound	SA		PG		PA	
Curcumin mg/ml	0.05	0.05	0.05	0.05	0.025	0.025
	0.05		0.05		0.025	
	0.05		0.05		0.025	

All values are expressed as mg/ml against test organisms

Minimum Bactericidal Concentration

Compound	SA		PG		PA	
Curcumin mg/ml	0.1	0.1	0.1	0.1	0.05	0.05
	0.1		0.1	0.1	0.05	
	0.1		0.1	0.1	0.05	

All values are expressed as mg/ml against test organisms

Zone of Inhibition Assessment

Groups	SA			PG			PA		
Standard (mm)	25	25	25	25	25	25	25	25	25
Curcumin film (mm)	19	19	19	14	14	14	18	18	18
Silver nanoparticles film (mm)	20	20	20	17	17	17	18	18	18

Remarks:

The results are satisfactory and relevant references have been followed.

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III Floor, V. K. Institute of Dental Sciences Campus, Nehru Nagar, Belagavi - 590 010, Karnataka – INDIA
E-mail: research@kledeemeduniversity.edu.in; **Web**: www.klepkbsrc.org, **Phone**: 0831- 2444444, Extn. 4122

11/04/25

Ms. Sayali Manjarekar,
Laboratory Assistant,
Dr Prabhakar Kore Basic Science
Research Centre, KAHER, Belagavi.

12/4/25

Dr. Rubeen D. Nadaf
Scientist Grade I,
Dr Prabhakar Kore Basic Science
Research Centre, KAHER, Belagavi.

11/4/25

Dr. Suneel Dodamani,
Scientist Grade I,
Dr Prabhakar Kore Basic Science
Research Centre, KAHER, Belagavi.

15/4/2025

Dr. Ramesh S. Paranjape
Distinguished Professor, KAHER &
I/C Director,
Dr. Prabhakar Kore Basic Science
Research Centre, KAHER, Belagavi

ANNEXURE 3: CYTOTOXICITY ASSESSMENT – RESULT

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA.
(Formerly known as KLE University) (Deemed-to-be-University u/s 3 of the UGC Act, 1956)
DR. PRABHAKAR KORE BASIC SCIENCE RESEARCH CENTER [BSRC], BELAGAVI, KARNATAKA.
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E-mail: research@kledeemeduniversity.edu.in; **Web**: www.klepkbsrc.org, **Phone**: 0831- 2444444, Extn. 4122

Results Cell Culture Project-2024

Project Code:	BSRC24/12/CCP-108
Title of the Project	Comparative Evaluation of the Efficacy of Mucoadhesive Film Containing Silver Nanoparticles and Mucoadhesive Film Containing Curcumin on Wound Healing After Periodontal Surgery – A Randomized Controlled Trial
Objective	To evaluate the Cytotoxicity
Name of the Student/PhD Scholar/Faculty	
Name of the Guide	
Name of the Cell Line	L929 Mouse fibroblast cell lines
Cell Culture Assay	MTT Assay
Brief Methodology	**Maintenance of cell lines:** Cell lines of L929 were procured from National center for cell Sciences (NCCS) Pune. The data sheet with sixteen short tandem repeat (STR) loci proved to be 100% matching with ATCC STR profile. After procuring the cell lines, maintenance and sub culturing of the cells was done by preparing 100ml of complete media comprising of DMEM 89ml (Himedia, Ref: AL007S) FBS 10ml (Himedia RM 10432, LOT 573421), and antibiotics 1ml (Himedia A002, LOT 5392281) the cells were maintained in 5% CO2 incubator and observed under inverted light microscope. All the procedure of cell culture was performed in Class II cabinet by considering all the aseptic conditions. On cells reaching the 85% confluence, trypsinization was performed using trypsin (TCL007, LOT 536691) and sub culturing was done as per the standard protocol. **MTT Assay:** During the cells in log phase of growth MTT assay was performed. The assay was designed by considering negative controls without adding compound. The MTT assay was performed using treated flat bottom 96 well plate. The markings were done by considering negative control and compound of nanoparticle and curcumin concentrations from 500µg /mL- 15.6µg /mL was considered. The assay was set by in triplicate wells for all concentrations of the compound to avoid any bias. Trypan blue assay was performed and number of viable cells were counted and calculated and seeded 5 x10^3 cells per well in a 96 well plate. Later complete media was added to make the volume of 150 micro liters. After 24 hours of incubation in 5% carbon dioxide incubator once the cells got attached and reached log phase of growth test compound was added. The compounds of serial dilution were added to wells and incubated for 24 hours. The supernatant was discarded and washed with PBS and 200 micro liters of fresh media was added to the wells and incubated for 24 hours. Later media with 20 µl of MTT dye was added and the plate was wrapped in silver foil as MTT dye is photosensitive and incubated for four hours. The supernatant was slowly removed and discarded without disturbing the formazan crystals, 100 µl of 1%DMSO was added to dissolve the crystals and 25µl glycine buffer was added to optimize the pH.by using spectrophotometer at around 570nm reading was obtained and calculated the proliferative index by dividing the OD of test with

OD of control multiplied by 100.

MTT Assay –L929

Compound Code	Concentration µg /mL	Cell viability %
NP	500	22.26
	250	43.60
	125	74.03
	62.5	76.24
	31.2	80.10
	15.6	84.69
CU	500	47.14
	250	52.44
	125	71.12
	62.5	83.46
	31.2	89.79
	15.6	95.10

Results

Inference:

The submitted nanoparticles and curcumin compounds showed cytocompatibility with good viability percentage at lower concentrations

Note: Further statistical test can be applied for data analysis

7/3/25

Dr. Ramesh S. Paranjape
Distinguished Professor, KAHER & I/C
Director,
Dr. Prabhakar Kore Basic Science

7/3/2025

Dr. Deepa R. Mane
In-Charge of Cell Culture Lab, Dr Prabhakar Kore
Basic Science Research Centre
Research Centre, Belagavi

7/3/2024

Project Co-Ordinator:
Ms. Manjula Kambi
Research Associate

ANNEXURE 4: PLAGIARISM CERTIFICATE

Scientific Correspondence and Review Committee

KLE VK Institute of Dental Sciences
A Constituent Unit of KLE Academy of Higher Education and Research
(Deemed-to-be-University u/s 3 of the UGC Act, 1956)
Nehru Nagar, Belagavi - 590 010, Karnataka State
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☎: 0831-2470362 Web: http://www.kledental-bgm.edu.in
FAX: 0831-2470640 E-mail:principal@kledental-bgm.edu.in

Date : 15/4/2025 Serial No. : 410

PLAGIARISM CHECK REPORT

Name of the Applicant : **REG NO. IK0222003**
UG / PG / Ph.D / Staff : PG
Batch & Year : 2022
Department : Periodontics.

The soft copy of Research Work / Manuscript by **REG NO. IK0222003** .. entitled
"Comparative efficacy of mucoadhesive film containing Silver nano Particles & Mucoadhesive film containing Curcumin on wound healing after Periodontal surgery - A Randomized controlled Trial"
under the guidance of .. ..has been submitted for

Anti-Plagiarism check to the Scientific Correspondence & Review Committee of KLE VK Institute of Dental Sciences using "Turn-it-in" software.

The scan has been carried out and the scanned output reveals a Similarity Index of .....8.....%, which is **within** / **not within** the acceptable limits of 10% as per the UGC guidelines.

15/4/2025
Member Secretary
Scientific Correspondence and Review Committee
KLEVK Institute of Dental Sciences
KAHER-Belagavi

15/4/25
Chairman
Scientific Correspondence and Review Committee
KLEVK Institute of Dental Sciences
KAHER - Belagavi

ANNEXURE 5: BIOSTATISTICIAN CERTIFICATE

K L E
VISHWANATH KATTI
INSTITUTE OF DENTAL SCIENCES
(Constituent College of K.L.E. University, Belgaum)
J.N.M.C. Campus, Nehru Nagar, Belgaum-590 010, Karnataka, India
0831-2470362
FAX: 0831-2470640
Web: http://www.kledental-bgm.edu.in
E-mail: principal@kledental-bgm.edu.in

Biostatistics Clearance Certificate

This is to certify that Biostatistics aspect of the Dissertation/Research work of

IK0222003 **Post Graduate Student**, under the guidance of

r, Department of Periodontics, entitled **"Comparative Efficacy of Mucoadhesive Film Containing Silver Nano particles and Mucoadhesive Film Containing Curcumin on Wound Healing after Periodontal Surgery – A Randomized Controlled Trial."** has been done under my guidance and completed satisfactorily.

Place: Belagavi
Date: 15.03.2025

Name & Signature of Biostatistician

Dr. S. B. Javali. Ph.D.
Professor in Statistics
Department of Community Medicine
USM KLE International Medical Programme,
BELAGAVI-590010.

ANNEXURE 6: INFORMED CONSENT FORM

DEPARTMENT OF PERIODONTICS

KAHER'S KLE's V.K. INSTITUTE OF DENTAL SCIENCES

BELAGAVI

Comparative efficacy of the effectiveness of mucoadhesive films containing silver nano particles and mucoadhesive films containing curcumin on wound healing after periodontal surgery: A randomized controlled trial

Principal Investigator: **REG NO. IK0222003**

I _____, aged _____ years have been informed about my involvement in the study.

I agree to give my personal details like Name, Age, Gender, Residential Address, Past and Present dental history, and any other details if required for the study to the best of my knowledge.

I will co-operate with the dentist.

I will follow the instructions given by the dentist during study.

I permit the dentist to utilize the information given by me and the results obtained from this study for presentation and publication without disclosing my identity.

I will visit the dentist as and when required for the study, at the given time and date.

I have understood the nature of the study and permit the dentist to perform the required non-surgical procedure on me.

I will not claim any returns for co-operation in this study, even if it is being sponsored by any agency. I am participating with my own will and wish.

If for any reason I am unable to participate in the study, for reasons unknown, I can withdraw from the study.

In my full consciousness and presence of mind, after understanding all the procedures and related complications if any, in my vernacular language, I am willing and give my consent to participate in this study.

Date:

Name of the Patient:

Signature:

DEPARTMENT OF PERIODONTICS

KAHER'S KLE's V.K. INSTITUTE OF DENTAL SCIENCES

BELAGAVI

Comparative efficacy of the effectiveness of mucoadhesive films containing silver nano particles and mucoadhesive films containing curcumin on wound healing after periodontal surgery: A randomized controlled trial

Principal Investigator: **REG NO. IK0222003**

मी _____, वय _____ वर्षे अभ्यासातील माझ्या सहभागाबद्दल माहिती देण्यात आली आहे.

मी माझे वैयक्तिक तपशील जसे की नाव, वय, लिंग, निवासी पत्ता, भूतकाळ आणि वर्तमान दंत इतिहास आणि माझ्या माहितीनुसार अभ्यासासाठी आवश्यक असल्यास इतर कोणतेही तपशील देण्यास सहमत आहे.

मी दंतवैद्याला सहकार्य करीन.

अभ्यासादरम्यान दंतवैद्याने दिलेल्या सूचनांचे मी पालन करीन.

मी दंतचिकित्सकाला माझी ओळख उघड न करता सादरीकरण आणि प्रकाशनासाठी माझ्याद्वारे दिलेली माहिती आणि या अभ्यासातून मिळालेल्या निकालांचा वापर करण्याची परवानगी देतो.

दिलेल्या वेळी आणि तारखेला अभ्यासासाठी आवश्यक असेल तेव्हा मी दंतवैद्याला भेट देईन.

मला अभ्यासाचे स्वरूप समजले आहे आणि दंतवैद्याला माझ्यावर आवश्यक रेडियोग्राफिक, नॉन-सर्जिकल, सर्जिकल आणि लेझर ऍप्लिकेशन प्रक्रिया करण्यास परवानगी दिली आहे.

मी या अभ्यासात सहकार्यासाठी कोणत्याही परताव्याचा दावा करणार नाही, जरी ते कोणत्याही एजन्सीद्वारे प्रायोजित केले जात असले तरीही. मी माझ्या इच्छेने आणि इच्छेने सहभागी होत आहे.

कोणत्याही कारणास्तव मी अभ्यासात सहभागी होऊ शकलो नाही, अज्ञात कारणांमुळे, मी अभ्यासातून माघार घेऊ शकतो.

माझ्या पूर्ण जाणीवेने आणि मनाच्या उपस्थितीत, माझ्या स्थानिक भाषेत, सर्व प्रक्रिया आणि संबंधित गुंतागुंत समजल्यानंतर, मी या अभ्यासात सहभागी होण्यास तयार आहे आणि माझी संमती देतो.

तारीख:

रुग्णाचे नाव:

स्वाक्षरी:

DEPARTMENT OF PERIODONTICS

KAHER'S KLE's V.K. INSTITUTE OF DENTAL SCIENCES

BELAGAVI

Comparative efficacy of the effectiveness of mucoadhesive films containing silver nano particles and mucoadhesive films containing curcumin on wound healing after periodontal surgery: A randomized controlled trial

Principal Investigator: **REG NO. IK0222003**

ನಾನು _____ ವಯಸ್ಸಿನ _____ ವರ್ಷಗಳ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ತೊಡಗಿರುವ ಬಗ್ಗೆ ಮಾಹಿತಿ ಮಾಡಲಾಗಿದೆ.

ನನ್ನ ವೈಯಕ್ತಿಕ ವಿವರಗಳಾದ ಹೆಸರು, ವಯಸ್ಸು, ಲಿಂಗ, ವಾಸಸ್ಥಳದ ವಿಳಾಸ, ಹಿಂದಿನ ಮತ್ತು ಪ್ರಸ್ತುತ ದಂತ ಇತಿಹಾಸ ಮತ್ತು ನನ್ನ ಜ್ಞಾನದ ಮಟ್ಟಿಗೆ ಅಧ್ಯಯನಕ್ಕೆ ಅಗತ್ಯವಿದ್ದರೆ ಇತರ ಯಾವುದೇ ವಿವರಗಳನ್ನು ನೀಡಲು ನಾನು ಒಪ್ಪುತ್ತೇನೆ.

ನಾನು ದಂತವೈದ್ಯರೊಂದಿಗೆ ಸಹಕರಿಸುತ್ತೇನೆ.

ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ದಂತವೈದ್ಯರು ನೀಡಿದ ಸೂಚನೆಗಳನ್ನು ನಾನು ಅನುಸರಿಸುತ್ತೇನೆ.

ನನ್ನ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸದ ನಾನು ನೀಡಿದ ಮಾಹಿತಿಯನ್ನು ಮತ್ತು ಈ ಅಧ್ಯಯನದಿಂದ ಪಡೆದ ಫಲಿತಾಂಶಗಳನ್ನು ಪ್ರಸ್ತುತಿ ಮತ್ತು ಪ್ರಕಟಣೆಗಾಗಿ ಬಳಸಿಕೊಳ್ಳಲು ನಾನು ದಂತವೈದ್ಯರಿಗೆ ಅನುಮತಿ ನೀಡುತ್ತೇನೆ.

ನಾನು ದಂತವೈದ್ಯರನ್ನು ಅಧ್ಯಯನಕ್ಕೆ ಅಗತ್ಯವಿರುವಾಗ, ನಿರ್ದಿಷ್ಟ ಸಮಯ ಮತ್ತು ದಿನಾಂಕದಂದು ಭೇಟಿ ಮಾಡುತ್ತೇನೆ.

ನಾನು ಅಧ್ಯಯನದ ಸ್ವರೂಪವನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ ಮತ್ತು ನನ್ನ ಮೇಲೆ ಅಗತ್ಯವಾದ ರೇಡಿಯೋಗ್ರಾಫಿಕ್, ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯಲ್ಲದ, ಕಾರ್ಯವಿಧಾನಗಳನ್ನು ನಿರ್ವಹಿಸಲು ದಂತವೈದ್ಯರಿಗೆ ಅನುಮತಿ ನೀಡಿದ್ದೇನೆ.

ಯಾವುದೇ ಏಜೆನ್ಸಿಯಿಂದ ಪ್ರಾಯೋಜಿತವಾಗಿದ್ದರೂ ಸಹ, ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಸಹಕಾರಕ್ಕಾಗಿ ನಾನು ಯಾವುದೇ ಆದಾಯವನ್ನು ಕ್ಲೈಮ್ ಮಾಡುವುದಿಲ್ಲ. ನಾನು ನನ್ನ ಸ್ವಂತ ಇಚ್ಛೆ ಮತ್ತು ಆಶಯದೊಂದಿಗೆ ಭಾಗವಹಿಸುತ್ತಿದ್ದೇನೆ.

ಯಾವುದೇ ಕಾರಣಕ್ಕಾಗಿ ನನಗೆ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸಾಧ್ಯವಾಗದಿದ್ದರೆ, ಅಜ್ಞಾತ ಕಾರಣಗಳಿಗಾಗಿ, ನಾನು ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು.

ನನ್ನ ಪೂರ್ಣ ಪ್ರಜ್ಞೆ ಮತ್ತು ಮನಸ್ಸಿನ ಉಪಸ್ಥಿತಿಯಲ್ಲಿ, ಎಲ್ಲಾ ಕಾರ್ಯವಿಧಾನಗಳು ಮತ್ತು ಸಂಬಂಧಿತ ತೊಡಕುಗಳು ಯಾವುದಾದರೂ ಇದ್ದರೆ, ನನ್ನ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ಅರ್ಥಮಾಡಿಕೊಂಡ ನಂತರ, ನಾನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸಿದ್ಧನಿದ್ದೇನೆ ಮತ್ತು ನನ್ನ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ.

ದಿನಾಂಕ:

ರೋಗಿಯ ಹೆಸರು:

ಸಹಿ

ANNEXURE 7: PROFORMA

PROFORMA

DEPARTMENT OF PERIODONTICS

KAHER'S KLE's V.K. INSTITUTE OF DENTAL SCIENCES

BELAGAVI

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Case No: OPD No:

Name:

Age: Sex: Occupation:

Address:

Chief Complaint:

Medical History:

Dental history:

CLINICAL ASSESSMENT

Wound Healing Index (Landry, Turnbull and Howley – 1988)

WOUND HEALING SCORE

7TH DAY	
14TH DAY	

MICROBIOLOGICAL ASSESSMENT

NUMBER OF COLONY FORMING UNITS

BASELINE (CFU/ml)	
7TH DAY (CFU/ml)	

ANNEXURE 8 – MASTER CHART

Sample	Wound Healing Index					
	Group 1		Group 2		Group 3	
	Day 7	Day 14	Day 7	Day 14	Day 7	Day 14
1	2	3	3	4	3	4
2	3	4	3	4	2	4
3	3	4	4	5	3	4
4	2	3	3	5	3	4
5	2	3	4	5	2	4
6	2	3	3	4	4	5
7	3	4	3	4	3	4
8	2	3	4	5	4	5
9	3	4	3	4	3	4
10	2	3	2	4	3	4
11	3	4	4	5	3	4
12	2	3	3	4	4	5
13	3	4	4	5	3	4
14	2	3	3	4	4	5
15	2	3	3	4	3	4

Colony Forming Units CFU/ml

Sample	Group 1		Group 2		Group 3	
	Baseline	Day 7	Baseline	Day 7	Baseline	Day 7
1	0.98	0.68	1.06	0.46	0.76	0.39
2	1.11	0.78	1.07	0.43	0.94	0.57
3	1.09	0.75	0.97	0.48	1.09	0.66
4	O.86	0.57	0.99	0.34	1.23	0.69
5	0.89	0.66	0.85	0.33	1.1	0.72
6	0.95	0.64	1.08	0.44	0.98	0.59
7	1.17	0.88	1.19	0.55	0.11	0.38
8	1.06	0,73	1.13	0.54	1.04	0.68
9	0.92	0.64	0.94	0.38	1.13	0.71
10	0.98	0.66	1.18	0.56	1.23	0.79
11	1.01	0.77	0.87	0.32	1.09	0.77
12	1.15	0.88	1.06	0.48	0.96	0.59
13	1.19	0.86	1.09	0.46	0.93	0.54
14	1.24	0.92	1.12	0.53	1.06	0.64
15	1.04	0.76	1.07	0.49	1.12	0.73