COMPARATIVE CLINICAL EVALUATION OF TETRACYCLINE FIBERS WITH CURCUMIN INCORPORATED COLLAGEN FIBERS - A RANDOMISED CLINICAL STUDY

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In the partial fulfillment of the requirement for the degree

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MASTER OF DENTAL SURGERY

In

PERIODONTOLOGY

By

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Under the guidance of

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LIST OF ABBREVIATIONS

PI	Plaque index
GI	Gingival index
PPD	Probing pocket depth
GCF	Gingival crevicular fluid
BOP	Bleeding on probing
p. gingivalis	Porphyromonas gingivalis
p. intermedia	Pervotella intermedius
CU	Curcumin
CHX	Chlorhexidine
TC	Tetracycline
LDD	Local drug delivery
SRP	Scaling and root planing
MMP	Matrix Metallo Proteinases
PCR	Polymerase Chain Reaction

Periodontitis is an inflammatory disease that cause destruction of tooth supporting structure like periodontal ligament and alveolar bone. Anti- microbial therapy is essential along with conventional therapy in the management of periodontal disease. Due to limitation of these therapy local application of herbal drugs has been initiated. Turmeric is not just remedy, it is the cure. To assess the clinical efficacy 30 sites with 5-6 mm pockets were divided into 2 groups i.e tetracycline group (control) and curcumin incorporated collagen fiber.(Experimental group). Clinical parameter including Plaque score, Gingival score, Pocket probing depth were recorded at baseline ,7^{th} day,14^{th} day and 21^{st} day. Result showed that the Gingival score decrease significant (P value< 0.001) in curcumin group at 14^{th} day as compared to both 0 and day 7.Plaque score showed significant decrease (P<0.01) or (P<0.001) in tetracycline group at both day 14^{th} and 21^{st} as compared to baseline and day 7.PPD reduced significant decrease in tetracycline group (P<0.001) at both day 14 and 21as compared to both day 0 and day7. It further reduce significant at day 7 as compared to base line.Incurcumin group PPD also reduced significant (P<0.05 or P<0.001) at day 21^{st} as compared to day 0,7,14. Mean %variation observed in gingival score for curcumin and tetracycline group was 12% and 4.8% respectively. Mean %variation observed in plaque score for curcumin and tetracycline group was 2.7% and 8.7% respectively. Mean %variation observed in pocket probing for curcumin and tetracycline group was 46.3% and 22.5% respectively. Hence curcumin can be effectively use in the treatment of gingivitis.

INTRODUCTION

Periodontal disease is an infectious, inflammatory disease and it is initiation and progression is done by specific invasion of anaerobic bacteria that contribute in destruction of tooth supporting structure. Highly organized and colonized bacterial population form the apically advancing front of periodontal pockets in close proximity to connective tissue and distruct alveolar bone . Elimination or adequate suppression of putative periodontopathic microoganisms in the subgingival area is essential for periodontal healing[1].

Non surgical treatment of periodontal diseases primarily involves scaling and root planing. Scaling and root planing fails to completely remove all pathogens due to their ability to penetrate deeper tissue or because of inappropriate instrumentation often leading behind significant number of bacteria to recolonize within 42days after single debridement session[2].

Systemic periodontal antibiotic therapy aims to reinforce mechanical debridement and to support the host defense system in overcoming the infection by killing sub gingival pathogens that remain after conventional mechanical periodontal therapy[3].Drugs administered systemically are well absorbed into the blood stream and distributed throughout the body through the circulation. However, systemic drug therapy is limited by its adverse reactions such as toxicity, acquired bacterial resistance, and drug interactions. Patient compliance is also a recognized problem. In contrast, local administration of the drug allows the therapeutic agent to be delivered at the diseased periodontal site with increased therapeutic effect and minimal side effects[4]. A local route of drug delivery (LDD) can attain various time higher concentration of antimicrobial agent in sub gingival sites when compared with a systemic therapy[5]. Commonly used methods for local drug delivery are sub-gingival irrigation and sustain release of drug.

The antimicrobial agents used as local drug delivery agents include tetracycline, ofloxacin, clindamycin chlorhexidine, etc[6]. Tetracycline as well its derivatives doxycycline and minocycline are the most commonly used antimicrobial agents in the treatment of periodontal infections[6]. Tetracycline is a broad-spectrum antimicrobial and it may be used as a adjunct to periodontal therapy. Tetracyclines are the most commonly and frequently prescribed antimicrobials in periodontal therapy. The groups of tetracyclines are generally more effective against Gram-positive bacteria

than Gram-negative bacteria. As it has bacteriocidal activity it kills most spirochetes as well as many anaerobic and facultative bacteria. High drug concentrations have been reported in gingival crevicular fluid making them particularly suitable for periodontal applications[4].The disadvantage of tetracycline is the ability to kill benign organisms associated with healthy as well pathogenic bacteria[7].

Several herbal drugs have been an area of interest in the treatment of periodontal diseasessuch as Turmeric[8,] Neem[9], Aloe vera[10], Lemon grass, Tea tree oil, Green tea[11] etc. The medicinal properties of turmeric, the source of curcumin, have been known for thousands of years; however the ability to determine the exact mechanism of action and bioactive components of CU also have been recently investigated. Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione), also called diferuloylmethan is the main natural polyphenol found in the rhizome of *Curcuma longa* (turmeric) and in others *Curcuma* spp[12]. Curcumin (diferuloylmethane), a constituent of *Curcuma longa* plant, possess antioxidant[13], anti-inflammatory[14], anti-carcinogenic[15], and anti-microbial[16] properties. Studies have shown that curcumin is not toxic to humans[17]. Its therapeutic implementation has been observed ina variety of conditions, with few studies analyzing the efficacy of Curcumin as a localdrug delivery agent in the treatment of periodontitis[18].

With the recent advent of newer herbal drugs and local drug delivery systems, the aim of the present study is formulated to compare the efficacy of an indigenously developed local drug delivery module, i.e., Curcumin with that of tetracycline fibre (Periodontal Plus AB).

AIM AND OBJECTIVES

1. AIM

The aim of the present study was to evaluate the clinical efficacy of curcumin incorporated collagen fibers and compared with the tetracycline incorporated fibers.

2. OBJECTIVES

1. To assess the clinical efficacy (Gingival index, Plaque index, Pocket probing depth) of *Curcuma longa* (Turmeic) incorporated collagen fiber in chronic periodontitis.
2. To assess the clinical efficacy (Gingival index, Plaque index, Pocket probing depth) of tetracycline incorporated fiber in chronic periodontitis.
3. To compare the clinical efficacy of curcumin incorporated fiber with tetracycline incorporated fibers.

REVIEW OF LITERATURE

Mousques T et al (1980)[2] Investigated the effect of a single session of scaling and root planing on the subgingival periodontal flora of 14- adult human subjects under darkfield microscopy. The results indicated that a single session of scaling and root planing is capable of disturbing the proportions of certain bacterial forms in the subgingival periodontal flora, and that it may require approximately 42 days for the proportions to return to baseline levels.

Deodhar SD et al (1980)[19]Conducted a preliminary double-blind, randomized controlled trial (RCT), in which curcumin was compared to phenylbutazone in patients with rheumatoid arthritis. Curcumin was given 1200 mg daily and it was observed that curcumin effective in improving joint swelling, morning stiffness, and walking time.

Srivastava et al(1985)[20] Investigated that curcumin may increase the risk of bleeding due to its antiplatelet properties, as it was shown to inhibit the cyclooxygenase pathway by blocking the GPIIb/IIIa receptor. Additionally, it causes an increase in prostacyclin activity, an inhibitor of aggregation. Therefore it is not recommended for patients on anticoagulant drugs or those with pre-existing bleeding disorders.

Satoskar RR et al(1986)[21] Examined the effects of curcumin compared to phenylbutazone or placebo for spermatic cord edema after surgery for inguinal hernia or hydrocele. Forty-five patients received 400 mg curcumin (Group A), 250 mg lactose powder placebo (Group B), or 100 mg phenylbutazone (Group C) three times daily for six days postoperatively. Parameters measured were spermatic cord edema, spermatic cord tenderness, operative site pain, and operative site tenderness and reflected by intensity score (TIS). TIS on day 6 decreased in Group A (curcumin) by 84.2 percent, by 61.8 percent in Group B (placebo), and by 86 percent in Group C (phenylbutazone). Although TIS scores for curcumin andphenylbutazone were similar on day 6, curcumin proved to be superior by reducing all four parameters of inflammation. Phenylbutazone did not reduce tenderness at the operative site.

Slots J and Rams TE (1990)[22] in their article discussed about the disadvantages of tetracycline. These were discoloration and hyperplasia of teeth and depressed skeletal growth and also Photosensitivity, Antibiotic resistance, superinfection and systemic complictions due to decreased absorption of tetracycline due to chelation with

antacids, alumunium. and bismuth. This proved the importance of local drug delivery in periodontal disease as compared to system2ic antibiotics.

Ciando SG et al. (1992)[23] evaluated the concentration and location of tetracycline hydrochloride in tissue adjacent to periodontal pockets treated with a tetracycline impregnated fiber. A secondary objective was to determine if the pre surgical placement of fibers had any adverse effects on healing following periodontal surgery. The study population consisted of 10 patients with minimum 2 pockets of ≥ 5 mm in depth and exhibiting bleeding on probing in both maxillary quadrants. After an initial scaling and root planing, 2 non -adjacent pockets were selected, placebo or tetracycline fibers were randomly used. Fibers were removed at the time of surgery; i.e., day 8, and periodontal surgery was performed utilizing a flap incision that allowed biopsy of inter dental papilla from each of the 2 test sites in each quadrant. One biopsy was analyzed for tetracycline concentrations by high performance liquid chromatography (HPLC). Light and ultraviolet fluorescence microscopy were used to determine the location of residual tetracycline and the intensity of inflammatory cell in second biopsy and concluded presurgical use of site-specific, controlled delivery of tetracycline does not interfere with post-surgical healing.

Seymour RA and Heasman PA (1995)[24]in their systemic review on use of tetracycline fibers in chronic periodontitis patient stated about the effects of tetracycline apart from their anti-bacterial effect. These include collagenase inhibition, anti-inflammatory actions, inhibition of bone resorption, and their ability to attach fibroblasts to root surfaces.Consequently tetracycline has also been used for root conditioning purpose.

Radvar et al. (1996)[25] evaluated the efficacy of three local drug delivery agents as adjuncts to scaling and root planning(SRP) in treatment of sites with persistent periodontal lesions. 54 patients with 4 pockets ≥ 5 mm and bleeding on probing were randomized in 4 treatment groups including: SRP with application of 25% tetracycline fiber (S + Tet) in 13 patients, SRP with application of 2% minocycline gel (S + Min) in14 patients, SRP with 25% metronidazole gel (S + Met) in14 patients and SRP alone in 13 patients. Clinical measurements were taken at baseline and after 6 weeks. All treatments were applied using the protocols and resulted in significant improvement in probing depth, attachment level, modified gingival index (MGI)

scores and bleeding on probing. The improvements in clinical parameters were imporved in all three adjunctive treatment groups than SRP alone and concluded that a treatment regimen of scaling and root planing plus tetracycline fiber substitute gave the greatest advantage in the treatment of persistent periodontal lesions atleast during the 6-week period following treatment.

Shoba et al (1998)[26]examined thatcurcumin is poorly absorbed from the gastrointestinal tract after oral intake and is mostly excreted unchanged with the feces. The small portion that is absorbed is completely eliminated by biliary and renal excretion, and is not stored in any organ. Moreover, the levels of parent curcumin in blood plasma, bile, and urine are extremely low even after high doses. Thus, any effects on peripheral tissues must be considered to be mediated by the degradation products or the metabolites of curcumin. In order to enhance the bioavailability of curcumin, it is combined with other spices such as piperine, a component of black pepper. This compound has been shown to increase the bioavailability of curcumin by as much as 154% through suppression of its glucuronidation that occurs primarily in the liver and in the intestine.

Sidhu G Set al (1998)[27]Studied on curcumin and investigated that Curcumin has an advantage over aspirin,as it selectively inhibit synthesis of prostaglandin E2 and thromboxane while not affecting prostacyclin. Curcumin reduces inflammatory mediators and causes shrinkage of wound by reducing inflammatory edema and vascular engorgement of connective tissues. It also promotes migration of fibroblasts in the wound bed and result in reduction of vascularization. It enhances wound healing by increase in fibronectinand transforming growth factor beta transcription.

Asai, Nakagawa et al (1999)[28]Conducted a study on mice, showed that turmeric extract inhibited membrane phospholipid peroxidation and increased liver lipid metabolism, which indicates turmeric extract has the ability to prevent the deposition of triacylglycerols in the liver. Dietary supplementation for one week (1% w/w of diet) with a turmeric extract showed lower phospholipids hydroperoxide level in mice red blood cells (RBC). The liver lipid peroxidizability induced with Fe^{2+}/ascorbic acid was effectively suppressed by dietary supplementation with turmeric.

Cobb C M(2002)[29] presented his perspective based on the evidence on the clinicalsignificance of non-surgical periodontal therapy. Sub-gingival debridement and SRP are the traditional methods of controlling sub-gingival microflora. The primary objective of SRP is the removal of both calculus and contaminated cementum. Evidence from clinical trials reveals a consistency of clinical response in the treatment of chronic periodontitis by SRP using manual, sonic, or ultrasonic instrumentation.The effectiveness of either procedure decreases with increasing probing depth,especially when probing depths exceed 5mm. Each method of instrumentation appears to yield the same degree of subgingival calculus removal and controlof sub gingival plaque,and both provoke a similar healing response.The conflicting studies suggest that the supra gingival plaque control is effective in early and moderate disease but not in advanced periodontal disease.

Chattopadhay I et al (2004)[12]On their study on Curcumin, found that the main bioactive component of turmeric has posed to be a good anti-inflammatory agent because it cause downregulation of cyclo-oxygenase pathway via arachidonic acid inhibition. It was found that the anti-inflammatory properties of curcumin are also mediated through their effects on cytokines, lipid mediators, eicosanoids and proteolytic enzymes. It also acts as an anti-oxidant agent by scavenging the superoxide radicals, hydrogen peroxide and nitric oxide from activated macrophages and inhibits lipid peroxidation.

Divya P.V et al.(2006)[30] reported that topical administration of mouthwash, dentifrice or gels can be used effectively in controlling supra gingival plaque. Irrigation systems can deliver agents into deep pockets but clinically not effective in stopping the progression of periodontal attachment loss and concluded local drug delivery appears to be as effective as SRP with regards to reducing signs of inflammatory disease - redness, bleeding on probing, probing depth and loss of clinical attachment.

Lao CD et al (2006)[31]. Reviewed that the conventional oral formulation of curcumin resulted in a very low availability of curcumin in the blood circulation to achieve therapeutic effects. So there is a Various types of nanoparticle (NPs), such as polymer NPs, polymeric micelles, liposome/phospholipid, nano-/microemulsions, nanogels,

solid lipid NPs, polymer conjugates, self-assemblies, are suitable for the delivery of an active form of curcumin.

Lopez N J S et al. (2006)[32]determined the effect of systemic administration of metronidazole plus amoxicillin (M+A) as the sole therapy, on the subgingivalmicrobiota of chronic periodontitis with twenty-two patients with untreated chronic periodontitispatient were randomly assigned to a group that received M+A for 7 days, or to a group receiving scaling and root planing (SRP) and two placebos with clinical measurements and concluded that changes in clinical and microbiological parameters were parallel after receiving systemically administered M+A as the sole therapy or after receiving SRP only.

Suhag (2007)[33] conducted a study in which periodontal sites were treated by scaling and root planing and later selected sites were irrigated with either chlorhexidine (0.2%), curcumin (1%), saline (0.9%), or control sites (nonirrigated).As a subgingivalirrigant, the inflammatory signs were better resolved by 1% curcumin solution when compared to saline and chlorhexidine irrigation.

Cheng W H R et al. (2008)[34]followed the periodontal healing response changes over a 12-month period after non-surgical conventional periodontal therapy with the adjunctive use of chlorhexidine and periodic recalls in adults with down syndrome who presented initially with chronic periodontitis. They studied 21 subjects with down syndrome (14 males and seven females; 25.3 – 5.5 years of age) chronic periodontitis patient were treated by non-surgical conventional periodontal therapy(followed by monthly recalls)and the adjunctive use of chlorhexidine gel for brushing, chlorhexidine mouthwash twice daily. Clinical data were recorded and concluded that satisfactory healing responses were achieved after non-surgical conventional periodontal therapy with the adjunctive use of chlorhexidine and monthly recalls in adults with down syndrome with chronic periodontitis and mild-to-moderate learning disabilities.

Jurenka JS (2009)[35] Reviewed that Curcumin modulates the inflammatory response by down-regulating the activity of cyclooxygenase-2 (COX-2), lipoxygenase, and inducible nitric oxide synthase (iNOS) enzymes; inhibits the production of the inflammatory cytokines tumor necrosis factoralpha (TNF-a), interleukin (IL) -1, -2, -

6, -8, and -12, monocyte chemoattractant protein (MCP), and migration inhibitory protein; and down-regulates mitogen-activated and Janus kinases.

Panwar M C L et al. (2009)[36] reported SRP is the basic treatment for periodontal disease. Conventional treatment is limited by biochemical considerations and physical impediments. Antimicrobial agents can be used as an adjunct to overcome limitations of conventional therapy. In Group A scaling and root planing was alone carried out whereas in Group B tetracycline fibers were used along with scaling and root planing. Result: using TF as an adjunct to scaling and root planing was found to be more effective in reducing inflammation. The number of sites with bleeding on probing were 12 in Group A and 4 in Group B after 30 days. The mean decrease in probing depth was more in Group B than Group A after 30 and 90 days. The decrease in probing depth was statistically significant with both conventional therapy as well as with tetracycline fibers. Concluded that local drug delivery with tetracycline fiber is an effective non surgical method to improve periodontal status.

Srivastava R et al. (2009)[37]undertook a study to evaluate clinically, the newly released sustained drugs, PerioCol (Chlorhexidine - CHX- chip) with Periodontal Plus ABTM (Tetracycline fibers) Patients were allocated in 3 experimental treatment groups, Group A- SRP + CHX Chip, Group B- SRP + TF, and Group C- SRP alone (control group). Forty-five sites in 14 patients (9 females and 5 males) with chronic periodontitis were evaluated clinically for probing depth (PD) (5-8mm probing depth) and relative attachment level (RAL) and concluded that the Combination of SRP + CHX chip (Group A) resulted in added benefits compared to the other two treatment groups.

Soares F B P et al. (2009)[38]evaluated the influence of scaling and root planing (SRP), with and without the use of tetracycline-loaded bovine absorbent membrane, in the reduction of periodontal pockets, probing pocket depth (PPD), bleeding on probing (BOP) and plaque index (PI) reduction. 24 patients were selected totalizing 144 random teeth divided in 2 groups, n=72 teeth, control (SRP) and experimental (SRP with tetracycline-loaded absorbent membrane). PPD, BOP and PI were evaluated preoperatively and 28 days after the treatment. At the end of the treatment the PPD values always lower than the baseline values. There was a reduction of the PI in both methods, but it was more evident on the experimental group. Concluded that the use

of tetracycline-loaded absorbent membrane resulted in a better prognosis compared to scaling and root planing after only 28 days of evaluation.

Gill JS et al. (2011)[39] compared the clinical efficacy of tetracycline fibers and a xanthan based chlorhexidine gel in the treatment of chronic periodontitis with 30 patients in age group of 30-50 years.In each subject two experimental sites were chosen that had probing depth of 5 mm and were located in symmetric quadrants and sites. It was arandomized and split mouth study with one site receiving tetracycline fibers and other chlorxidine gel. It was concluded that the long term studies with more samples are needed to further evaluate and compare the efficacy of both materials.

Behal R et al (2011)[40]Studied on turmeric and examined that Applying the paste made from 1 tsp turmeric and ½ tsp salt and ½ tsp mustard oil provide relief from gingivitis and periodontitis. Rub the teeth and gums with this paste twice daily.

Sachdev S et al. (2011)[41] compared the clinical efficacy of tetracycline impregnated fibrillar collagen in conjunction with SRP, SRP alone in the treatment of chronic periodontitis. The study was conducted in a split mouth manner. 35 patients having atleast two non adjacent sites in different quadrants with periodontal pockets 5mm and with bleeding on probing at initial visit were treated with both scaling and root planing plus tetracycline fibers or with either scaling and root planing alone. Baseline and follow up measurements included plaque index, gingival index, probing pocket depth and clinical attachment level. Both treatment modalities were effective in improving clinical parameters over 3 months recall. The combined antimicrobial and mechanical debridement therapy has shown better results as compared to SRP alone. Application of tetracycline in modified collagen matrix following SRP shows better treatment of chronic adult periodontitis and improving periodontal parameters for 3 months duration.

Bhardwaj A et al. (2012)[42]reviewed various approaches of local drug delivery systems for the administration of drugs to the periodontal pocket and effectiveness of these systems in the periodontal therapy and concluded that as a monotherapy, local drug delivery systems incorporating a assortment of drugs can improve periodontal health. Local drug delivery was effective as SRP with regards to reducing signs of

periodontal inflammation. Local delivery may be an adjunct to conventional therapy. The recent advances in periodontal local drug delivery systems are - free mucoadhesive, biodegradable nanoparticles technology.This has an immense opportunity for the designing of new, low-dose and valuable treatment method by the use of controlled device. These devices are more convenient, easy-to-use and more effective than the regular drugs and medicines which act systemically.

Dodwad et al. (2012)[43] reviewed about the local drug delivery in periodontics: a strategic intervention. They concluded that adjunctive use of local drug delivery may provide a defined but limited beneficial response. However the magnitude of change anticipated by combined therapy must be interpreted in light of the severity of the defects being treated. Therefore the clinician will need to make decisions based on the desired outcomes of the therapy.

Jain R et al. (2012)[44] evaluated the long term efficacy of a locally delivered 2% minocycline gel as an adjunct to scaling and root planing in managing chronic periodontitis by twenty two pairs of sites with similar probing depths. Subjects were randomly allocated to test and control groups. All sites were treated with SRP plus minocycline gel in the test sites.PPD, relative attachment levels, plaque index, and microbiological parameters were evaluated for both the groups over a 9-month period and concluded that investigation did not show any significant advantage of using 2% minocycline gel over SRP.

Venkatesh A et al.(2012)[45] discussed the various anti microbials used in treating periodontal disease which were delivered as local drug delivery agents and concluded that the local drug delivery system is effective for treating the single rooted teeth than multirooted teeth.

Shavetha S et al (2012)[46] did a study in which they formulated 2% curcumin gel by simple dispersion method.Carbopol-940 was soaked in purified water containing 0.2% w/v sodium benzoate overnight. Using tissue homogenizer hydroxypropyl methylcellulose (HPMC) solution was mixed in propylene glycol. 2 mg of curcumin (Rajesh Chemicals, Mumbai) was transferred into HPMC solution and homogenized. This drug solution was transferred to carbopol solution and homogenized. Triethanolamine was added quantity sufficient to neutralize the ph. Then, distilled

water was added to make quantity sufficient to 100 ml. The gel was stored at ambient temperature.

Mugliker et al (2013)[47] Studied the efficacy of curcumin mouth wash as an adjunct to scaling and root planing in the treatment of chronic gingivitison 30 patients and compare it with the chlorhexidine in terms of its anti-inflammatory and antimicrobial Properties. Significant reduction of gingival inflammation was reported in the test group compared to the control group at the end of the 21-day observation period. They concluded that curcumin is comparable to chlorhexidine as an anti-inflammatory mouth wash and it is an effective adjunct to mechanical periodontal therapy.

Kaplish V et al. (2013)[48] approaches the main delivery systems for the administration of drugs to the periodontal pocket, the advancement of these systems effectiveness in the periodontal therapy and concluded that local drug delivery system is used effectively in controlling tissue associated bacteria, it eradicates the pathogens for several weeks, local drug delivery system is effectual for treating single rooted teeth than multi rooted teeth and mode of treatment for shallow periodontal pockets and recurrent periodontal disease.

Balappanavar AY et al (2013)[49] evaluated and compared the effectiveness of 0.5% tea, 2% neem, and 0.2% chlorhexidine mouthwashes on oral health. 30 healthy subjects were selected and randomly assigned into 3 groups i.e..group A - 0.2% chlorhexidinegluconate (bench mark control), Group B - 2% neem, and group C- 0.5% tea of 10 subjects per group. Mean plaque and gingival scores were reduced over the 3 week trial period for experimental and control groups. Anti- plaque effectiveness was highest in group C. Neem and tea showed comparative effectiveness on gingiva better than chlorhexidine. The salivary pH rise was sustained and significant in Group B and C compared to Group A.

Ashtapure V et al. (2014)[50] reviewed the concepts of local drug delivery in periodontics and emphasize on various drug systems available to date and rationales of using those antibacterial drugs systems through local delivery into the periodontal pockets.

Bhatia et al. (2014)[51] Conducted a study on 25 patients with chronic periodontitis with periodontal pockets of at least 5 mm in depth. The test group received scaling and root planing along with intrapocket application of a gel containing 1% curcumin at baseline and at 1-, 3-, and 6-month intervals. The control group received scaling and root planing alone. At the end of the observation period, there were significant improvements in the clinical parameters of periodontitis, including reduction in pocket depth and bleeding, and gain in clinical attachment levels in both groups but with more pronounced improvement in the test group. In regard to the microbiological parameters, curcumin significantly reduced the levels of P. gingivalis, P. intermedia, F. nucleatum and Capnocytophaga sp. at the end of the six-month observation period.

Kotwal V et al. (2014)[52]studied about the Clinical Evaluation of Tetracycline Gel as a Local Drug Delivery System in Association With SRP in Patients with CP - An in Vivo with A double blind study was designed to test the effectiveness of the gel using clinical parameters like gingival index, Plaque index, PPD and Sulcus bleeding index. These indices were recorded at baseline,15th , 30th ,60th and 90th day in 40 sites, > 4mm pockets in 11 patients. 20 received tetracycline gel and rest 20 received placebo gel, following SRP. The study was compared and concluded that cost-effective tetracycline gel could be a capable local drug delivery system when used in adjunct to scaling and root planing.

Plessas A et al. (2014)[53]discussed the evidence behind the current clinical practice for the administration of the CP patients including oral hygiene methods, different periodontal therapeutic modalities currently available are discussed and concluded that the nonsurgical periodontal treatment remains the gold standard for managing the periodontal patients. It can result in reduction of inflammation, PPD and clinical attachment gain. There is no certain amount of initial PPD where nonsurgical periodontal therapy is no longer effective. However, it needs to be emphasized that the root instrumentati on is only indicated for sites with probing depth 4mm and above as instrumenting shallow sites will potentially develop loss of attachment.

Rajesh H et al. (2014)[54] reviewed the various local drug delivery devices used to treat periodontal disease and concluded that devices is that it reduces the number of patient's visit and ensures compliance.

Suchetha A et al. (2014)[55] compared the efficacy of tetracycline fibres, povidone iodine when locally delivered to the moderately deep periodontal pocket. 30 subjects were selected for the study and divided into two groups; Group I treated with Tetracycline fibers (Periodontal AB Plus), Group II treated with povidoneiodine . The Gingival Index (GI), Probing Pocket Depth (PPD) and Clinical Attachment Level (CAL) were measured at baseline and at 3 months and concluded that tetracycline fibers were more efficacious in improving the periodontal health status when compared to povidone Iodine.

Garg S et al. (2015)[56] reviewed the current status of controlled local delivery and their usefulness, as well as the advancement of these systems in the treatment of periodontitis and concluded that additional randomized, controlled studies are needed to help delineate the types of lesions, periodontal diseases, or specific situations where local delivery systems would be most beneficial.

Kataria S et al. (2015)[57] evaluated the efficacy of tetracycline fiber (used as local drug delivery) along with scaling and root planing for the treatment of CP, and compare the results with those ensuing after scaling and root planing alone. 50 patients were selected for the study and the treatment sites were divided into two groups using split mouth technique. In each patient, periodontal pockets were treated with SRP alone (control site), or treated by SRP with placement of tetracycline fiber (test site), with the aim of evaluating A. actinomycetemcomitans in CP and concluded that compared with SRP alone, tetracycline fiber therapy along with SRP improves clinical parameters and significantly reduces bacterial colony count in treatment of chronic periodontitis.

Mehta W P et al. (2015)[58] studied about the neem extract incorporated in LDD system used as adjunct to SRP in 15 patients having CP (7 males and 8 females) with an average age of 25-55 yrs. Clinical parameters such as Plaque index, Gingival index, probing pocket depth were determined and microbiological study was done to assess the subgingival flora of P. gingivalis, P. intermedia, Fusobacteriumnucleatum, A.actinomycetemcomitans. All clinical parameters were evaluated at baseline, first month and third months. Full mouth scaling and root planing was performed. 3 groups were made Group A- SRP, Group B- SRP plus tetracycline fibers, Group scaling and root planing along with placement of neem fibers. The three selected sites were

randomly assigned to one of the groups. The test sites in group B & C received intra pocket placement of tetracycline &neem fiber respectively and con cluded that Neem extracts exhibited good antibacterial property, and was found to be marginally better but not statistically significant than commercially available tetracycline fibres.

Nidhi G et al. (2015)[59]evaluated the clinical outcome following non surgical periodontal therapy alone compared to tetracycline fiber therapy used adjunctively with SRP in the treatment of CP patients and concluded that Locally delivered tetracycline therapy has a specific purpose, to control localized infection, whereas scaling is utilized to remove calculus and other deposits.

Sweatha C et al. (2015)[60] evaluated the efficacy of the adjunctive use of minocycline plus SRP as compared with SRP alone in the treatment of the CP and to compare the effects of local drug delivery of minocycline microspheres as an adjunct SRP, SRP alone with total number of 72 sites from 18 patients with pocket depth ≥5 mm in CP cases. The selected groups were randomly divided into control group (group I) test group (group II). Only SRP were done at the baseline visit for the control sites as well as for test sites with application of Arestin™ (1 mg) and redelivery of Arestin™ (1 mg) was done on 30th day. Clinical parameters such as plaque index, gingival index, and gingival bleeding index were recorded at baseline, 30, 90 daysand day 180 in the selected sites of both the groups. Probing pocket depth and Clinical attachment level also was recorded at baseline, day 90, and day 180 for both the groups and study confirmed that Arestin (1mg Minocycline microspheres) delivered in biodegradable system, are a safe and efficient adjunct to SRP, and produced significant clinical benefits when compared to SRP alone.

Christopher J. (2015)[61] Conducted a meta-analysis on 72 articles on the effectiveness of SRP with or without the systemic antimicrobials, a systemic host inoculator (subantimicrobial-dose doxycycline). locally delivered antimicrobials chlorhexidine chips, doxycycline hyclate gel. and minocycline microspheres), and a variety of nonsurgical lasers (photodynamic therapy with a diode laser, a diode laser. neodymium yttrium-aluminum-garnet lasers, and erbium lasers). The panel judged 4 adjunctive therapies as beneficial with a moderate level of certainty: systemic subantimicrobial-dose doxycycline systemic antimicrobials, chlorhexidine chips, and photodynamic therapy with a diode laser.

Anuradha BR etal(2015)[62] Preparation of gel using simple dispersion method Accurately weighed polymer was taken in beaker and dispersed in 50 ml of water and kept aside for 30 min, it was stirred at 1200 rpm for 30 min under mechanical stirrer. To it required quantity of CUR+β-CD, which is dissolved in water, is added. DMSO, menthol, and parabens which were dissolved in methanol were added to the above preparation and final volume was adjusted with the water and pH was adjusted with triethylamine.

Roopa DA et al (2016)[63] evaluated the clinical efficacy of oral curcuma gel in the management of gingivitis, to assess the adverse effects & tolerance of gel. Fifteen control sites were treated by subgingival scaling and root planing alone, and 15 test sites were treated with subgingival scaling and root planing followed by gingival massage with 1% curcumin gel. It was concluded that the gel containing curcuma longa extract was efficient in treating gingivitis as an anti-inflammatory agent as a local application adjunct to scaling.

MATERIAL AND METHODS

A Comparative clinical evaluation of tetracycline fibers with curcumin incorporated collagen fibers- A Randomised clinical study was conducted in the department of periodontology, Babu Banarasi Das College of Dental Sciences, Lucknow, Uttar Pradesh in Collaboration with School of pharmacy, Babu Banarasi Das University.The approval for the experimental protocol was taken from ethics committee, Babu Banarasi Das College of Dental Sciences, Lucknow. (ANNEXURE 1.ANNEXURE 2)

MATERIALS –

Materials required for extraction of curcumin.

Grinder

Sieve

Flask

Micro pipette

Soxhlet apparatus.

Plant:

Kingdom: Plantae

Subkingdom: Tracheobionta

Superdivision: Spermatophyta

Division: Magnoliophyta

Subclass: Zingiberidae

Order: Zingiberales

Family: Zingiberaceae

Genus: Curcuma

Species: longa

Scientific name: Curcuma longa

Common names: Turmeric, Haldi, indian saffron

Part used: Rizome

PLATE 1: UNIFORM SIZED POWDER OF CURCUMIN RHIZOMES

Chemical composition of Curcumin:

Curcumin is a main active phytochemicals. Active Constituents Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxy-curcumin, and bisdemethoxycurcumin.

Collection and Validation of plant material.

Curcumin was collected from local market and formed a fine powder in school of pharamacy. BBDU LUCKNOW. It was collaborated and validated by CSIR-NATIONAL INSTITUTE OF SCIENCE COMMUNICATION AND INFORMATION RESOURCES. Rref no-NISCAIR/RHMD/Consult/2020/3721-22.(ANNEXURE-3)

PREPARATION OF EXTRACT:

Taxonomic identification of curcumin was performed by CSIR-NISCAIR. Delhi: where voucher specimens were deposited. Rref No- NISCAIR/RHMD/ Consult/2020/3721-22. ANN

The rizome of turmeric was dried and made in crystal powder form, then using soxhlet apparatus extraction process was carried out.

Soxhlet apparatus: PLATE-2

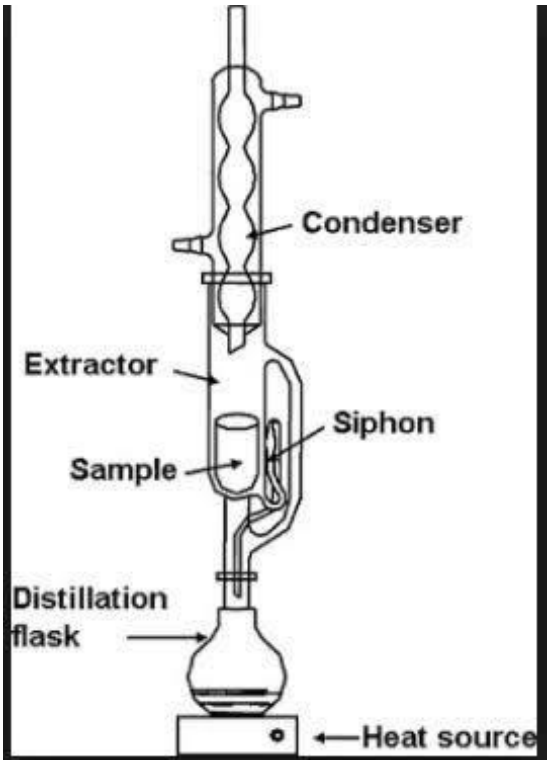


PLATE 2: SOXHLET APPARATUS

It was originally designed for the extraction of a lipid from a solid material. Typically used when the desired compound has a limited solubility in a solvent. A Soxhlet extractor has three main sections: a percolator (boiler and reflice which circulates the salvent. a thimble (usually made of thick filter paper) which retains the solid to be extracted, and a siphon mechanism, which periodically empties the thimble.

The solvent is heated to reflux. The solvent vapour travels up a distillation am and floods into the chamber housing the thimble of solid. The condenser ensure that any solvent vapour cools, and drips back down into the chamber housing the solid

material. The chamber containing the solid material slowly fills with warm solvent. Some of the desired compound dissolves in the warm solvent. When the Soxhlet chamber is almost full, the chamber is emptied by the siphon. The solvent is returned to the distillation flask. The thimble ensures that the rapid motion of the solvent does not transport any solid material to the still pot. This cycle may be allowed to repeat many times, over hours or days

During each cycle, a portion of the non-volatile compound dissolves in the solvent After many cycles the desired compound is concentrated in the distillation flask. The advantage of this system is that instead of many portions of warm solvent being passed through the sample, just one batch of solvent is recycled.

After extraction the solvent is removed, typically by means of a rotary evaporator, yielding the extracted compound. The non-soluble portion of the extracted solid remains in the thimble, and is usually discarded. The curcumin were extracted with absolute ethanol solvent.

The yield curcumin extract was then filter through filter paper, and was kept in an air tight amber coloured glass container.

PLATE 3: EXTRACTION PROCESS BY OF CURCUMIN RIZOME BYSOXHLET APPARATUS

INCORPORATION OF CURCUMIN IN TO STERILE COLLAGEN FIBERS

A single vial of type 1 sterile collagen fibers weighed 25 mg, were soaked into 5 ml of Pure curcumin extract.

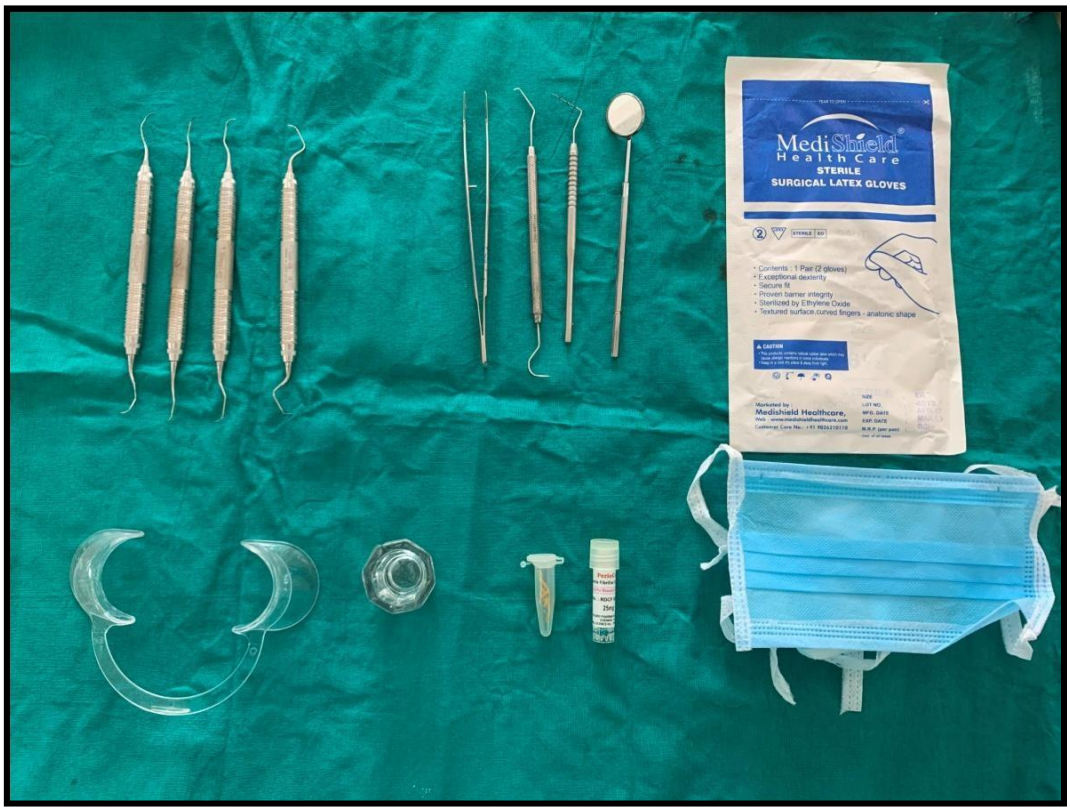


PLATE 4: ARMAMENTARIUM

IN VIVO STUDY

Total of 30 sites were selected including both males and females in the age group 30-60 years.

Inclusion criteria

1) A total of 30 patients including both males and females in the age group of 30 -60 years.

2) Patients diagnosed to have chronic periodontitis with probing pocket depth >5mm

3) Free from any systemic disease and who had not undergone any form of periodontal therapy in the last 6 months.

Exclusion Criteria

1) Pregnant ladies or lactating mothers

2) Patients having systemic diseases

3) Smokers

4) Patients who had received any topical or systemic antibiotic treatment for any purpose in the past 3 months including the use of mouth wash or currently on systemic antibiotic

5) Drug allergies

6) Teeth with traumatic occlusion

CLINICAL STUDY DESIGN

On the basis of inclusion and exclusion criteria, 30 sites in 15 patients were randomly selected and treatment protocol for the selected site weres decided randomly by lottery method. These sites were divided into 2 groups - SRP+ TTC and SRP+ Curcumin according the treatment to be given.

Experimental group: these sites received scaling and root planing along with Curcumin incorporated collagen fibers.

To wet the Sterile collagen fibers , 2 drops of Curcumin extract was added by 1 ml syringe 2 hours before placement in periodontal pocket.

Similarly few drops of sterile saline solution was added on the tetracycline fibers(Periodontal AB Plus) and 2 drops before placement in periodontal pockets.

Required portion of the wet fibers were taken and placed into the pocket site with periodontal probe gently. The gingiva was subsequently adapted to close the entrance of the site and hand pressure was applied for just a few minutes to encourage haemostasis.

After the placement of fibers in control and experimental groups, the treated sites were given Coe-pack. The clinical parameters of the selected target areas were undertaken after placement of the fibers at baseline,7 days, 14 days, 21 days .

The following clinical parameters were used to assess the periodontal status:

- Plaque index (silness and Loe 1964)[64]

- Gingival index(Loe and silness 1963)[65]

- Pocket probing depth (PPD)[66]

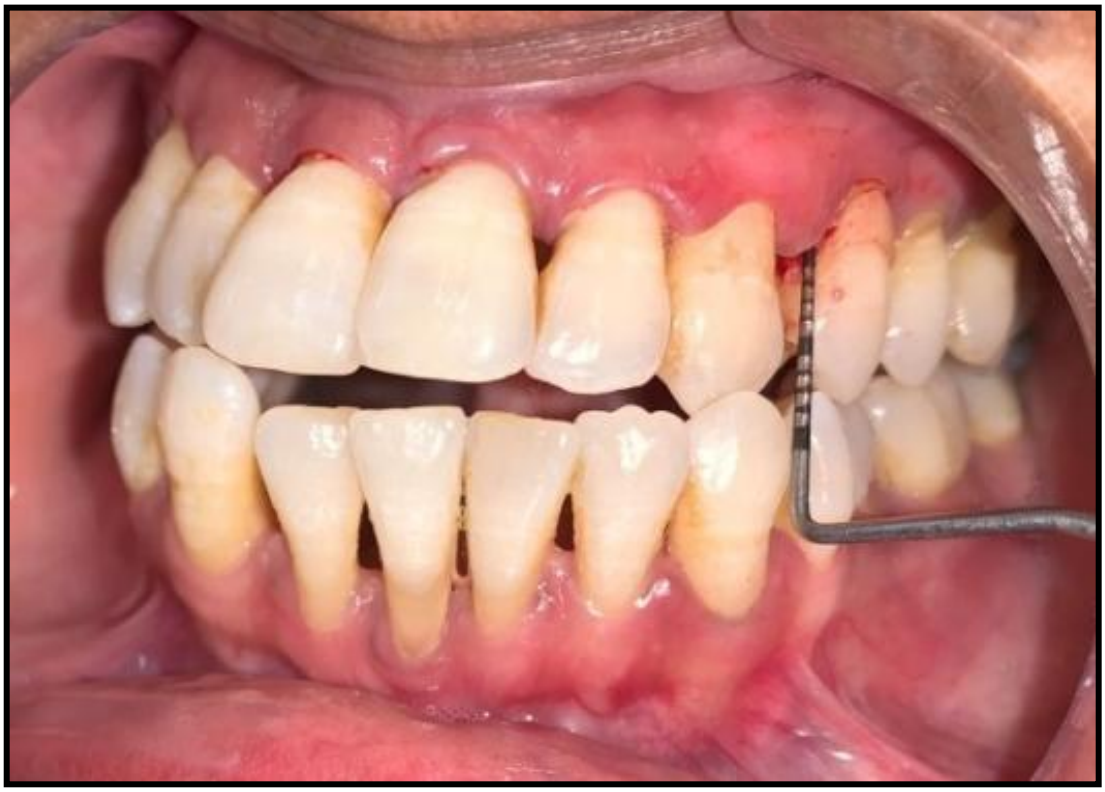


PLATE 5: BASELINE EVALUATION OF CURCUMIN FIBERS

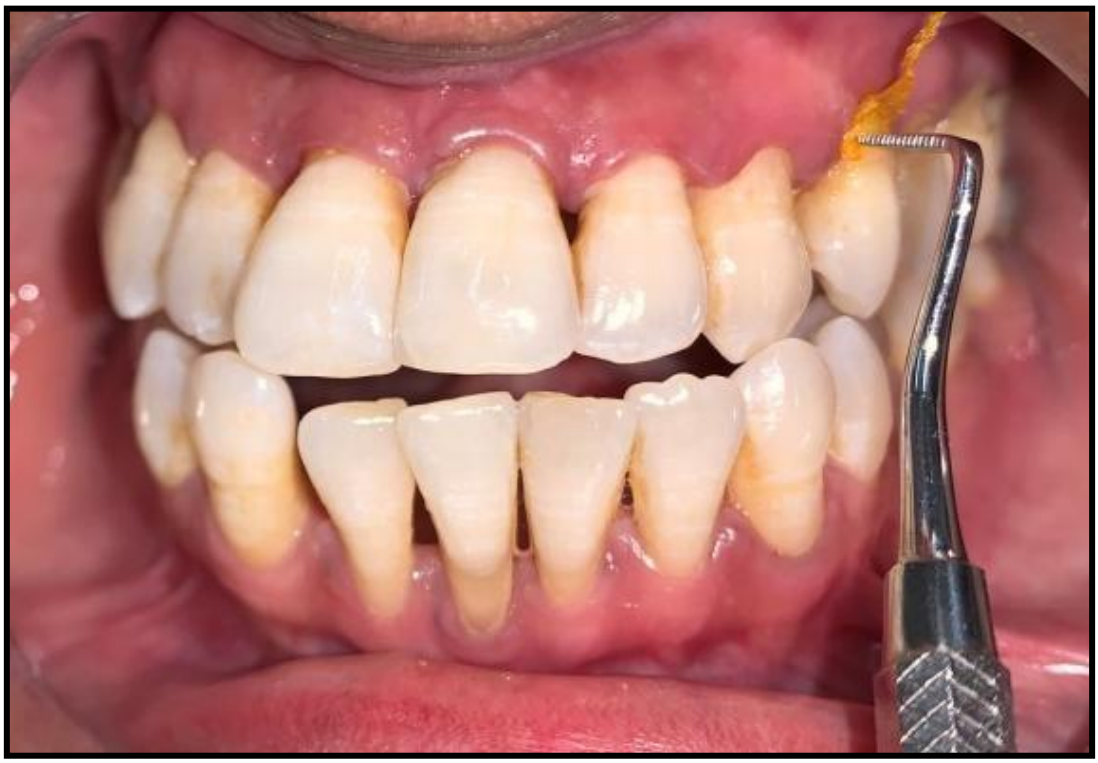


PLATE 6: PLACEMENT OF CURCUMIN FIBERS

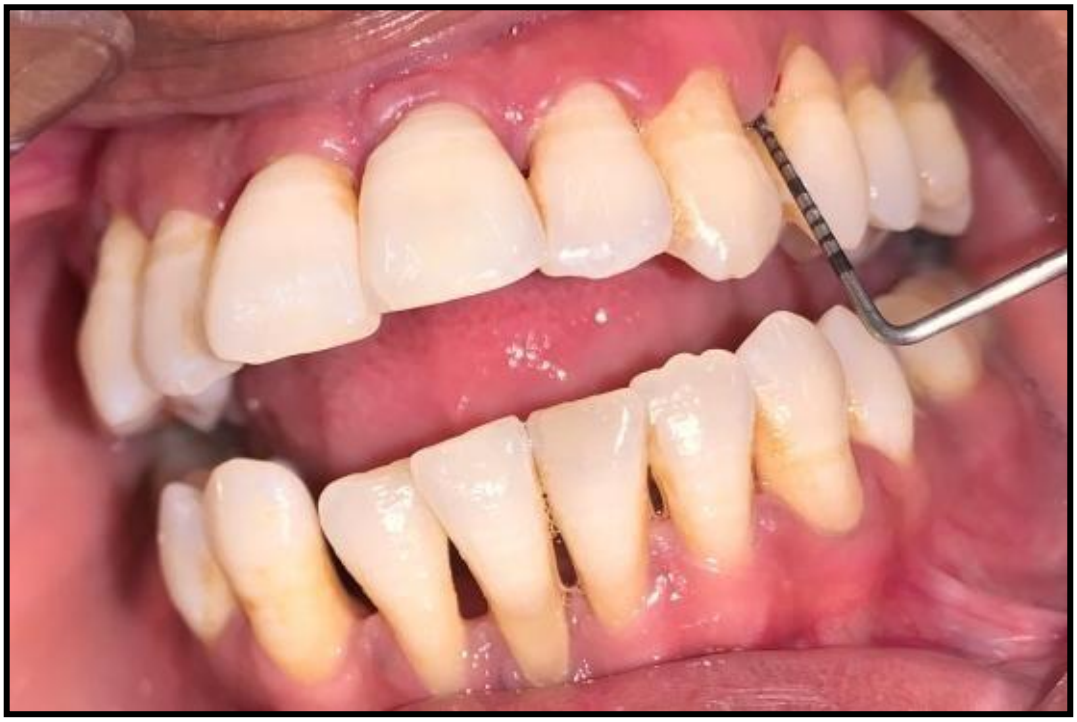


PLATE7: EVALUATION ON DAY 21 FOR CURCUMIN FIBERS

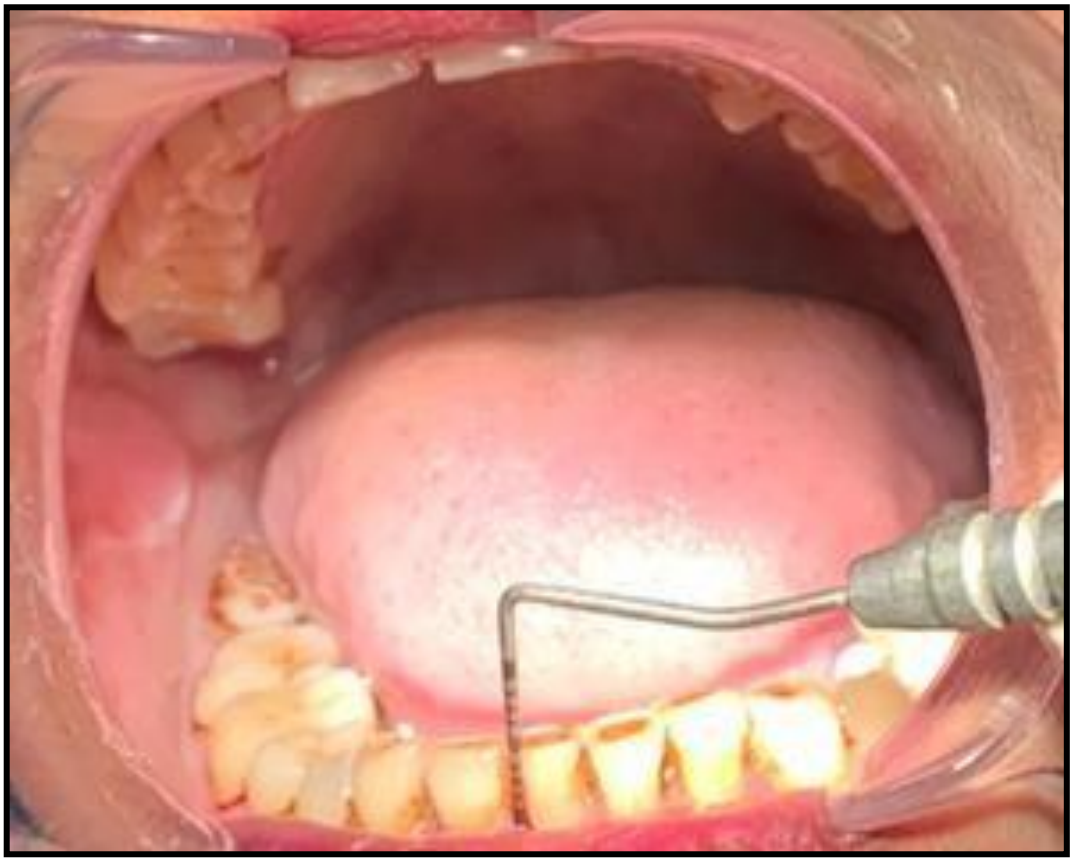


PLATE 8: BASELINE EVALUATION OF TETRACYCLINE FIBERS

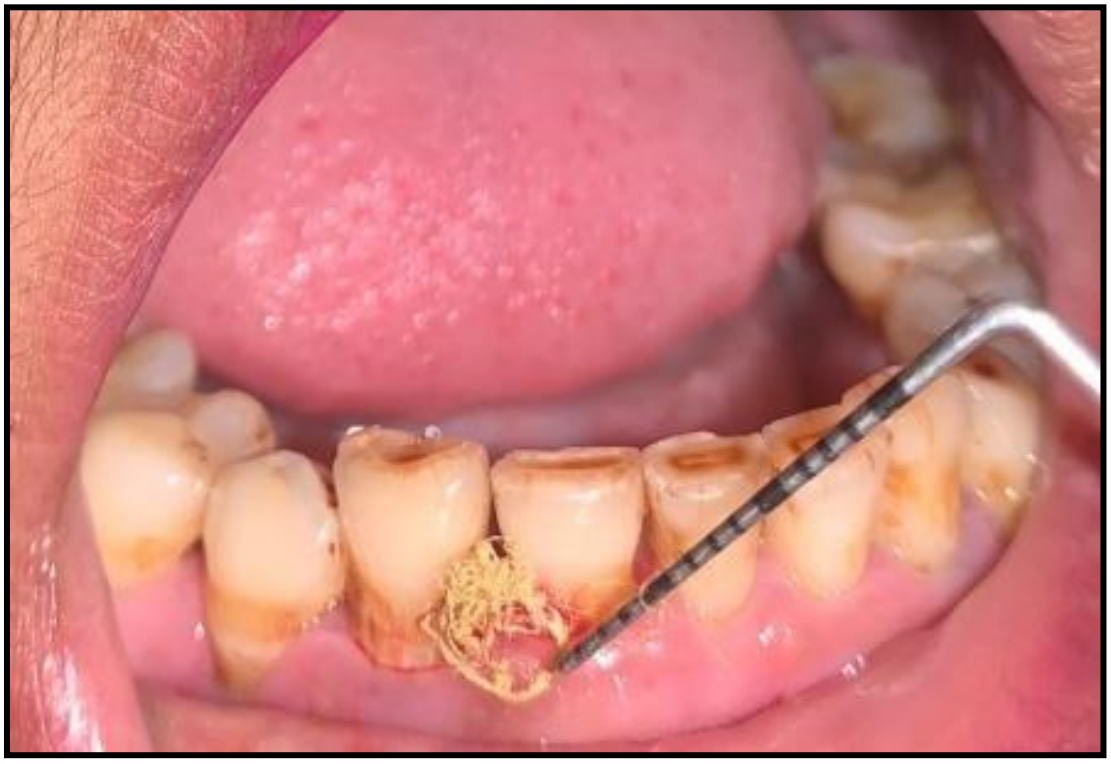


PLATE 9: PLACEMENT TETRACYCLINE FIBERS

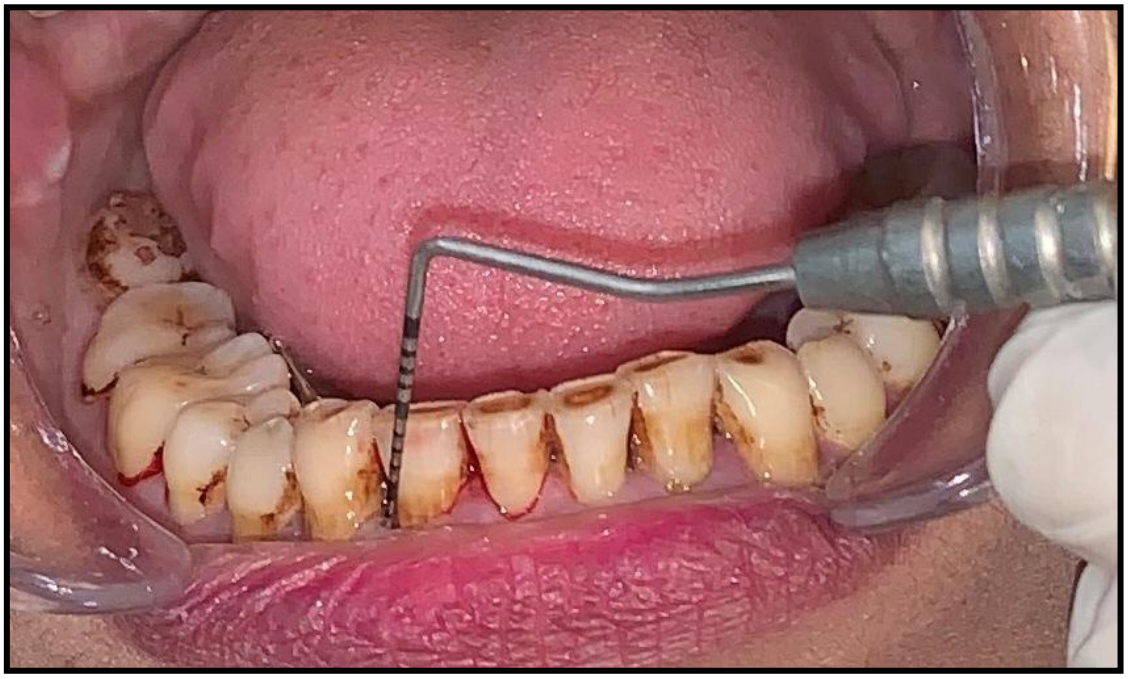


PLATE 10: EVALUATION ON DAY 21 FOR TETRACYCLINE FIBERS

RESULTS AND OBSERVATIONS

I. Gingival index (GI)

The pre Operative (day 0) and post Operative (day 7, 14 and 21) GI score of two groups (control and experimental) is summarised in Table 1 and also depicted in Fig. 1. In both groups, the mean GI score decreased linearly after the treatment and decrease was evident higher in experimental group as compared to control group.

For each group, comparing the difference in mean GI score between the periods (i.e. intra group) (Table 2 and Fig. 2), Tukey test showed insignificant ($P > 0.05$) change/decrease in GI score between periods in control group However, in experimental group, it showed significant ($P < 0.001$) decrease at day 21 as compared to both day 0 and day 7. Further, in experimental group, it also showed significant ($P < 0.01$) decrease at day 14 as compared to day 0.

Similarly, for each period, comparing the difference in mean GI score between the groups (i.e. inter group) (Table 3 and Fig. 3), Tukey test showed similar ($P > 0.05$) GI score between the two groups at all periods i.e. did not differed significantly or found to be statistically the same.

However, at final evaluation, the net mean decrease (i.e. mean change from day 0 to day 21) in GI score of experimental group (12.0%) was found 7.2% higher as compared to control group (4.8%).

Table 1: Pre and post GI score of two groups over the periods

Time period	**Control** **(n=15)**	**Experimental** **(n=15)**
day 0	1.27 ± 0.19	1.29 ± 0.14
day 7	1.25 ± 0.23	1.26 ± 0.18
day 14	1.22 ± 0.28	1.20 ± 0.21
day 21	1.21 ± 0.28	1.14 ± 0.27

The pre and post GI score of two groups were summarised in Mean ± SD.

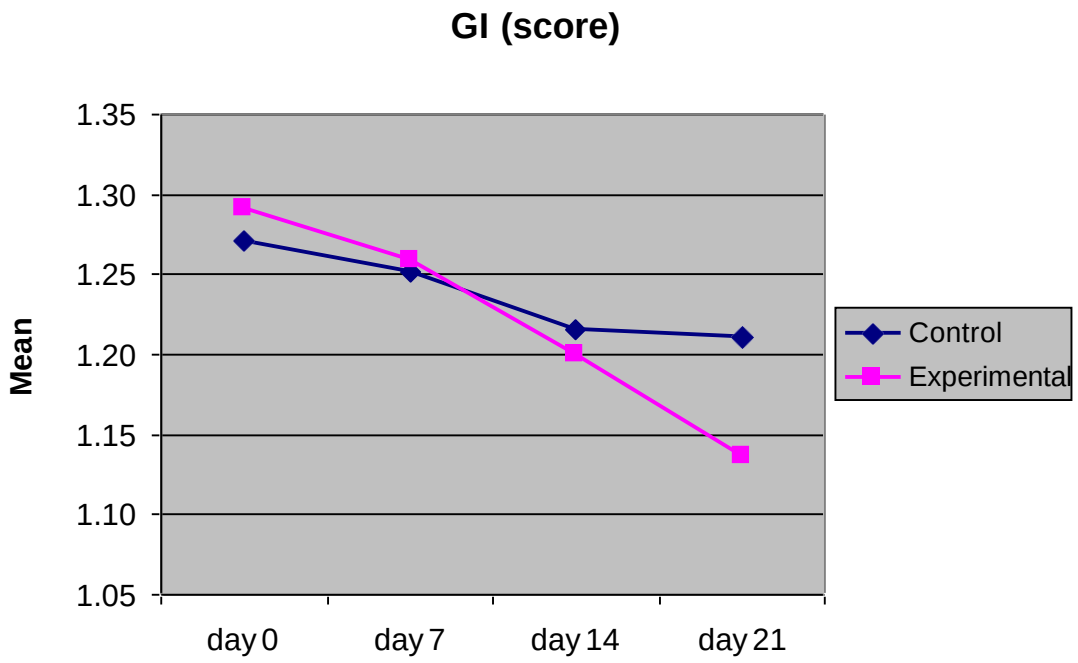
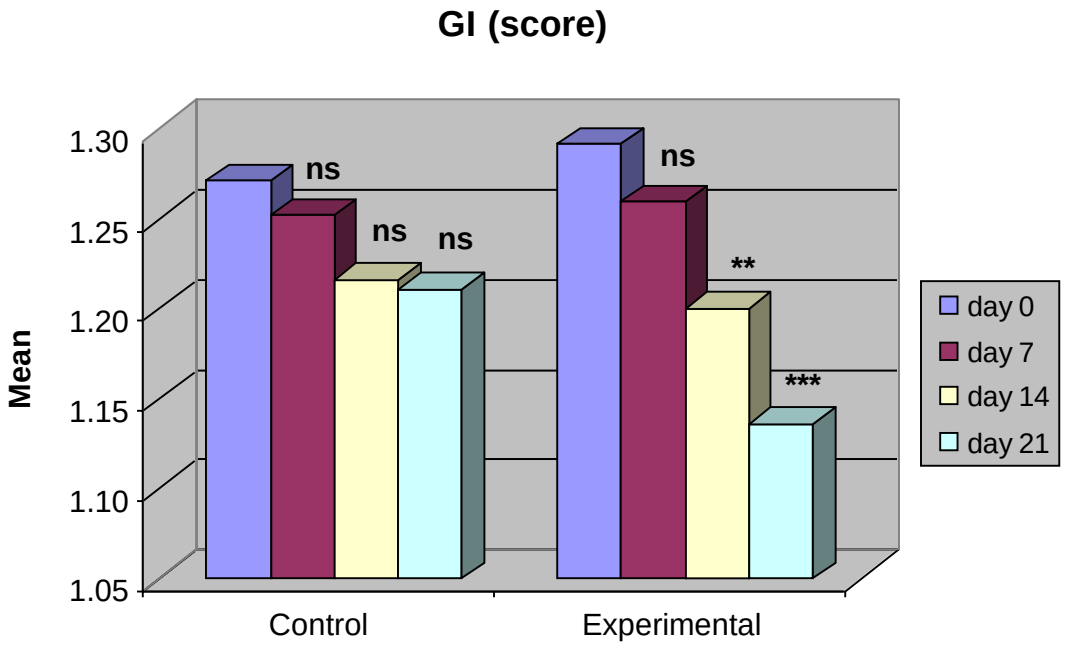


Fig. 1. Line graphs showing pre and post mean GI score of two groups over the periods.

Table 2: For each group, comparison (*P* value) of difference in mean GI score between the periods by Tukey test

Comparison	Control		Experimental	
	Mean difference	***P* Value**	**Mean difference**	***P* value**
day 0 vs. day 7	0.02	0.990	0.03	0.858
day 0 vs. day 14	0.06	0.250	0.09	0.004
day 0 vs. day 21	0.06	0.156	0.16	< 0.001
day 7 vs. day 14	0.04	0.768	0.06	0.177
day 7 vs. day 21	0.04	0.622	0.12	< 0.001
day 14 vs. day 21	0.01	1.000	0.06	0.112

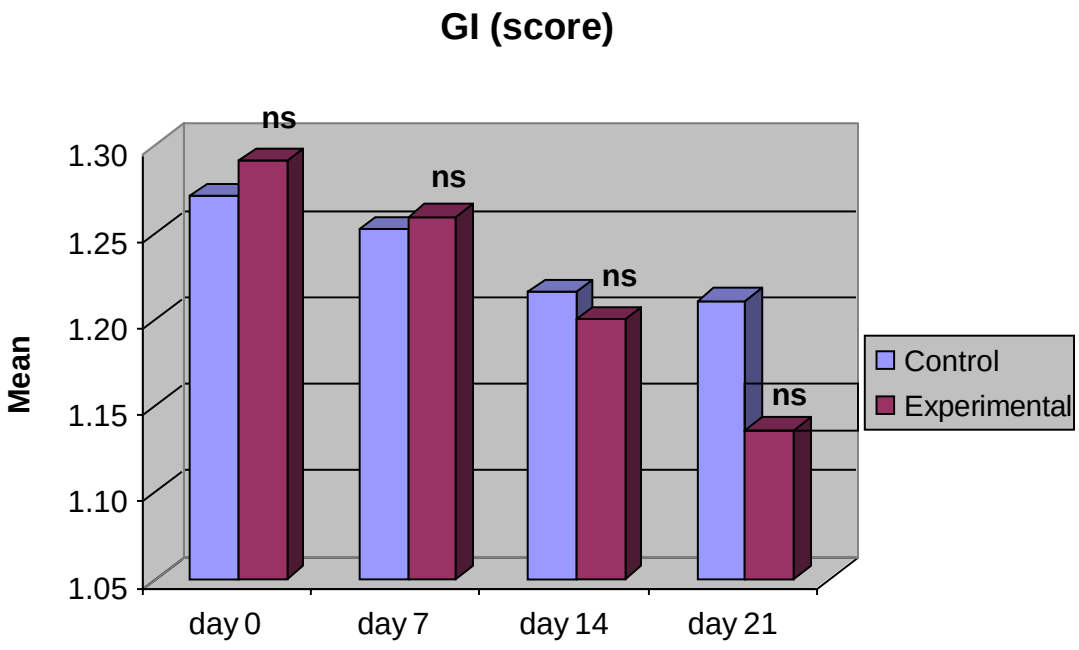


^{ns}P> 0.05 or $^{**}P$< 0.01 or $^{***}P$< 0.001- as compared to day 0

Fig. 2. For each group, bar graphs showing comparison of difference in mean GI score between the periods.

Table 3: For each period, comparison (*P* value) of difference in mean GI score between the groups by Tukey test

Time period	Control vs. Experimental	
	Mean difference	***P* value**
day 0	0.02	1.000
day 7	0.01	1.000
day 14	0.02	1.000
day 21	0.07	0.984



[ns]*P*> 0.05- as compared to control

Fig. 3. For each period, bar graphs showing comparison of difference in mean GI score between the groups.

II. Plaque index (PI)

The pre (day 0) and post (day 7, 14 and 21) PI score of two groups (control and experimental) is summarised in Table 4 and also shown in Fig. 4. In both groups, the mean PI score decreased gradually after the treatment and decrease was evident higher in control group as compared to experimental group.

For each group, comparing the difference in mean PI score between the periods (i.e. intra group) (Table 5 and Fig. 5), Tukey test showed significant ($P< 0.01$ or $P< 0.001$) change/decrease in PI score of control group at both day 14 and 21 as compared to both day 0 and 7. However, in experimental group, it showed insignificant ($P> 0.05$) change/decrease between the periods.

Similarly, for each period, comparing the difference in mean PI score between the groups (i.e. inter group) (Table 6 and Fig. 6), Tukey test showed similar ($P> 0.05$) PI score between the two groups at all periods i.e. did not differed significantly or found to be statistically the same.

However, at final evaluation, the net mean decrease (i.e. mean change from day 0 to day 21) in PI score of control group (8.7%) was found 6.0% higher as compared to experimental group (2.7%).

Table 4: Pre and post PI score of two groups over the periods

Time period	**Control (n=15)**	**Experimental (n=15)**
day 0	1.43 ± 0.12	1.45 ± 0.11
day 7	1.41 ± 0.12	1.44 ± 0.11
day 14	1.34 ± 0.12	1.44 ± 0.11
day 21	1.30 ± 0.13	1.41 ± 0.11

The pre and post PI score of two groups were summarised in Mean ± SD.

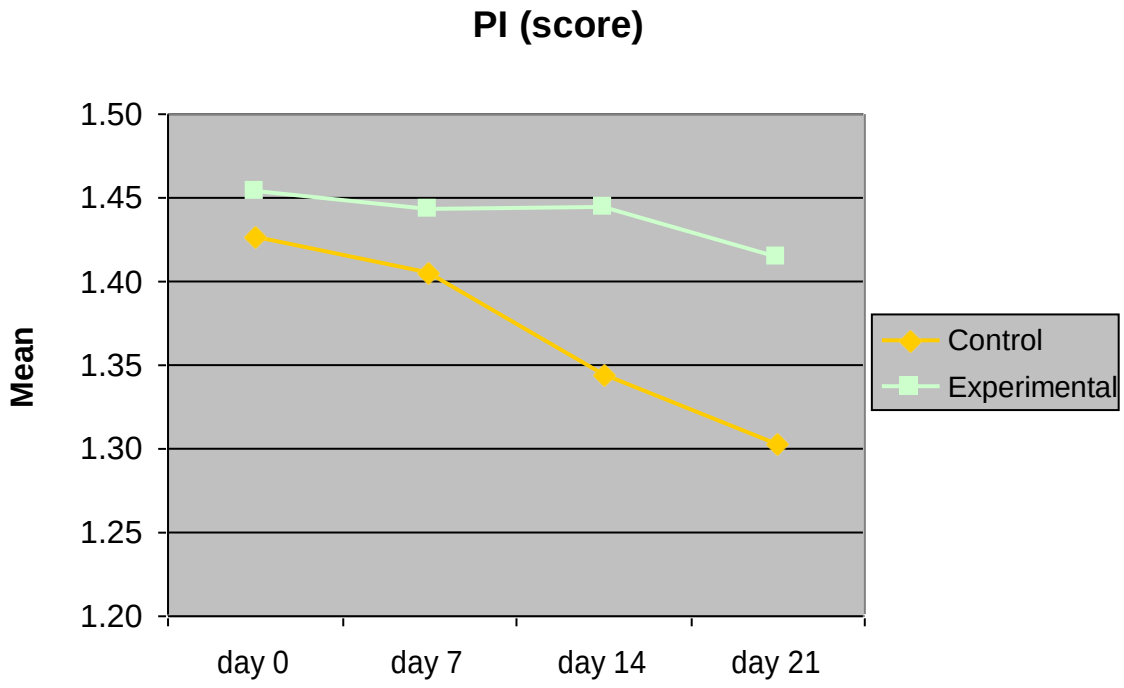
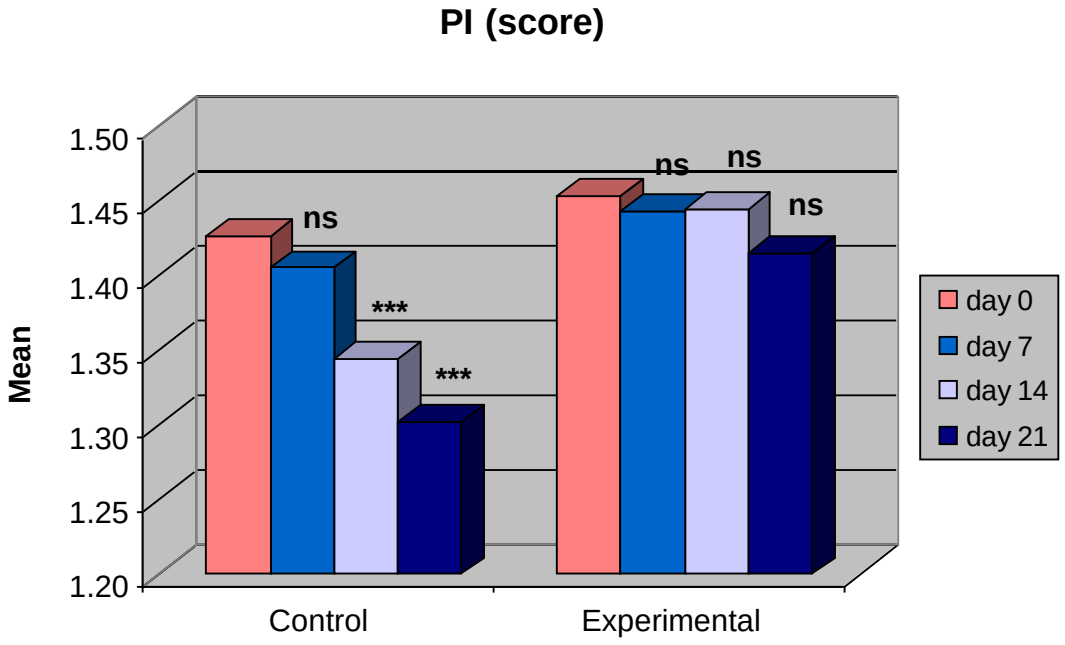


Fig. 4. Line graphs showing pre and post mean PI score of two groups over the periods.

Table 5: For each group, comparison (*P* value) of difference in mean PI score between the periods by Tukey test

Comparison	Control		Experimental	
	Mean difference	***P* Value**	**Mean difference**	***P* value**
day 0 vs. day 7	0.02	0.874	0.01	0.998
day 0 vs. day 14	0.08	< 0.001	0.01	0.999
day 0 vs. day 21	0.12	< 0.001	0.04	0.228
day 7 vs. day 14	0.06	0.005	0.00	1.000
day 7 vs. day 21	0.10	< 0.001	0.03	0.607
day 14 vs. day 21	0.04	0.147	0.03	0.579

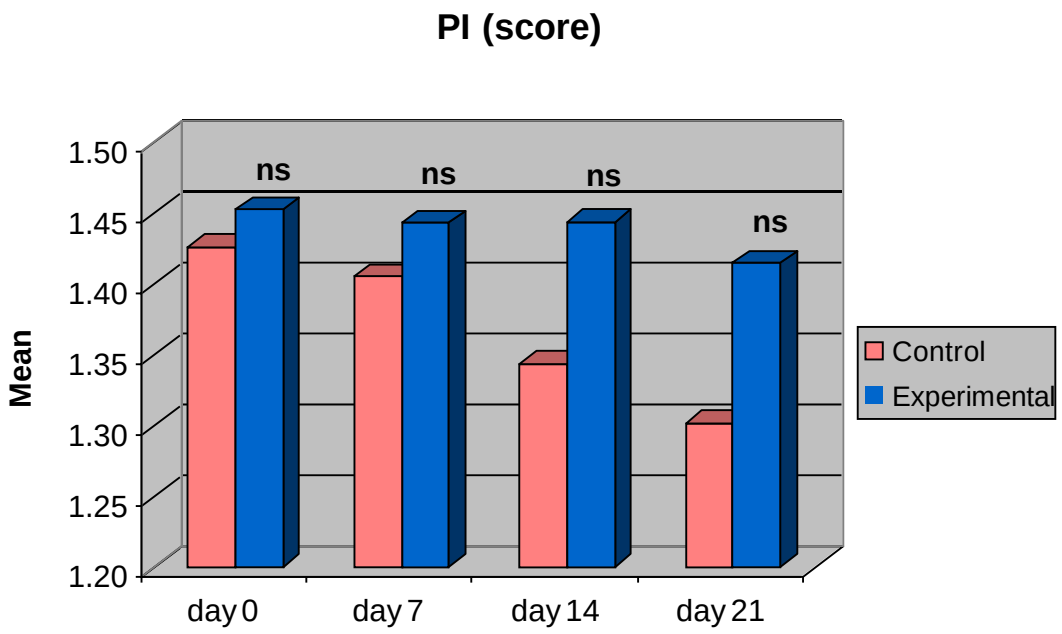


^{ns}P> 0.05 or $^{***}P$< 0.001- as compared to day 0

Fig. 5. For each group, bar graphs showing comparison of difference in mean PI score between the periods.

Table 6: For each period, comparison (*P* value) of difference in mean PI score between the groups by Tukey test

Time period	Control vs. Experimental	
	Mean difference	***P* value**
day 0	0.03	0.998
day 7	0.04	0.984
day 14	0.10	0.284
day 21	0.11	0.164



[ns]*P*> 0.05- as compared to control

Fig. 6. For each period, bar graphs showing comparison of difference in mean PI score between the groups.

III. Probing pocket depth (PPD)

The pre (day 0) and post (day 7, 14 and 21) PPD score (mm) of two groups (control and experimental) is summarised in Table 7 and also shown in Fig. 7. In both groups, the mean PPD score showed marked decrease after the treatment and decrease was evident higher in control group as compared to experimental group.

For each group, comparing the difference in mean PPD score between the periods (i.e. intra group) (Table 8 and Fig. 8), Tukey test showed significant ($P< 0.001$) change/decrease in PPD score of control group at both day 14 and 21 as compared to both day 0 and 7. Further, in control group, it also decreased significantly ($P< 0.001$) at day 7 as compared to day 0. In contrast, in experimental group, it also showed significant ($P< 0.05$ or $P< 0.001$) change/decrease at day 21 as compared to day 0, 7 and 14. Moreover, it experimental group, it also showed significant ($P< 0.01$) change/decrease at day 14 as compared to day0.

Similarly, for each period, comparing the difference in mean PPD score between the groups (i.e. inter group) (Table 9 and Fig. 9), Tukey test showed similar ($P> 0.05$) PPD score between the two groups at both day 0 and 7. However, at both day 14 and 21, it was significantly ($P< 0.01$ or $P< 0.001$) different and higher in experimental group as compared to control group.

Moreover, at final evaluation, the net mean decrease (i.e. mean change from day 0 to day 21) in PPD score of control group (46.3%) was found 23.8% higher as compared to experimental group (22.5%).

Table 7: Pre and post PPD score (mm) of two groups over the periods

Time period	**Control (n=15)**	**Experimental (n=15)**
day 0	5.47 ± 0.74	5.33 ± 0.49
day 7	4.27 ± 0.88	5.07 ± 0.59
day 14	3.33 ± 0.82	4.67 ± 0.62
day 21	2.93 ± 0.88	4.13 ± 0.52

The pre and post PPD score of two groups were summarised in Mean ± SD.

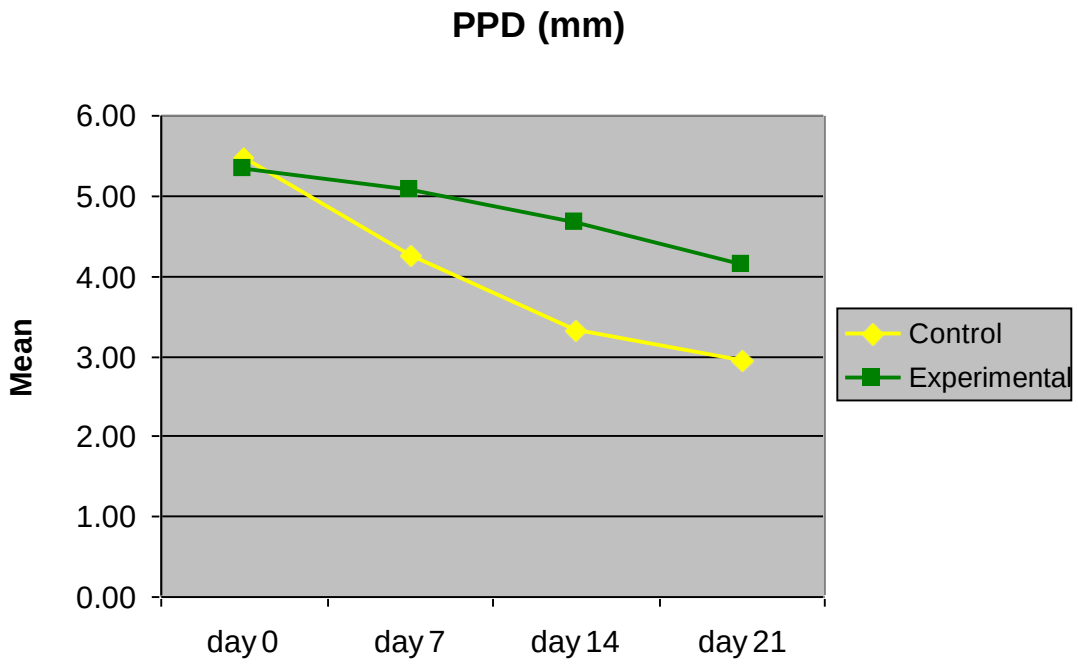
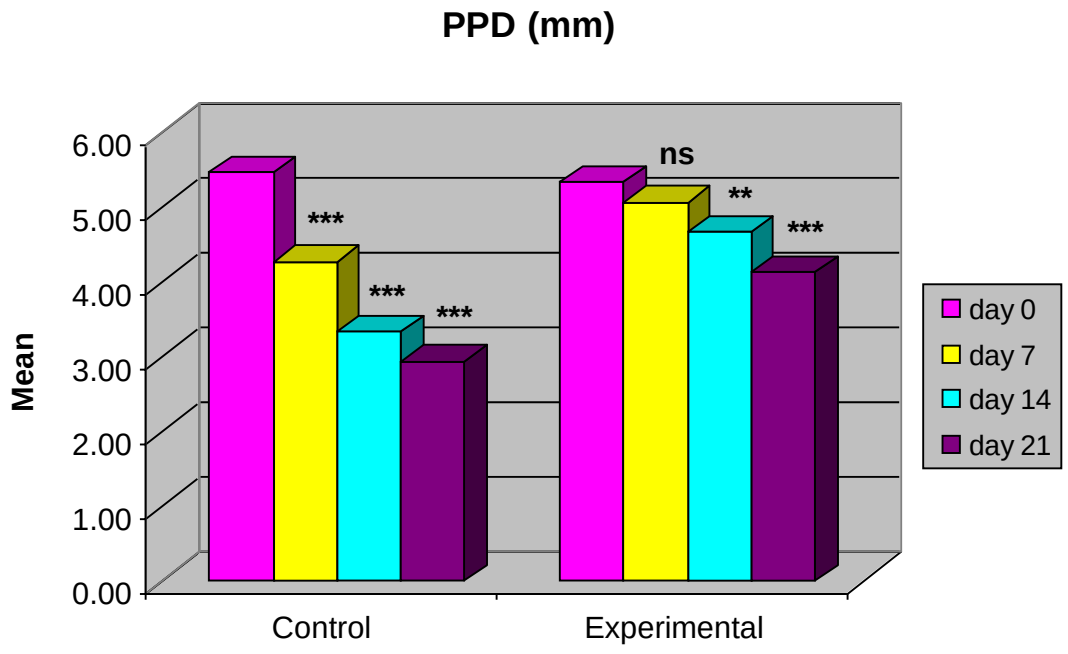


Fig. 7. Line graphs showing pre and post mean PPD score of two groups over the periods.

Table 8: For each group, comparison (*P* value) of difference in mean PPD score (mm) between the periods by Tukey test

Comparison	Control		Experimental	
	Mean difference	*P* Value	Mean difference	*P* value
day 0 vs. day 7	1.20	< 0.001	0.27	0.693
day 0 vs. day 14	2.13	< 0.001	0.67	0.002
day 0 vs. day 21	2.53	< 0.001	1.20	< 0.001
day 7 vs. day 14	0.93	< 0.001	0.40	0.195
day 7 vs. day 21	1.33	< 0.001	0.93	< 0.001
day 14 vs. day 21	0.40	0.195	0.53	0.023

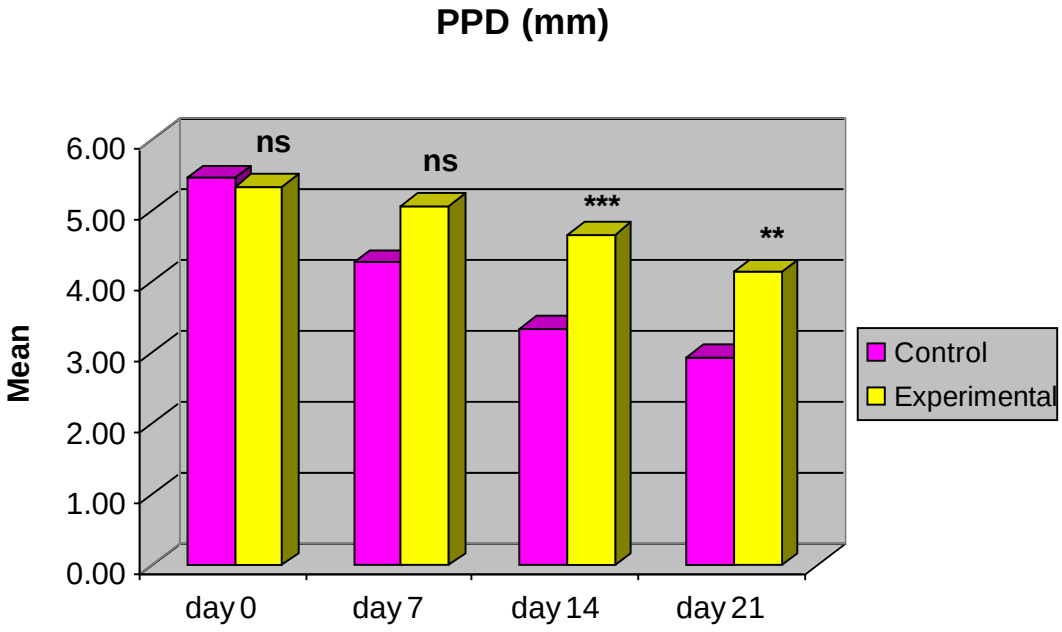


^{ns}P> 0.05 or $^{**}P$< 0.01 or $^{***}P$< 0.001- as compared to day 0

Fig. 8. For each group, bar graphs showing comparison of difference in mean PPD score between the periods.

Table 9: For each period, comparison (*P* value) of difference in mean PPD score (mm) between the groups by Tukey test

Time period	Control vs. Experimental	
	Mean difference	***P* value**
day 0	0.13	1.000
day 7	0.80	0.059
day 14	1.33	< 0.001
day 21	1.20	0.001



$^{ns}P > 0.05$ or $^{**}P < 0.01$ or $^{***}P < 0.001$- as compared to control

Fig. 9. For each period, bar graphs showing comparison of difference in mean PPD score between the groups.

DISCUSSION

Periodontal diseases constitute a group of localized microbial-induced infections involving the gingival and supporting tissues of the teeth. There is considerable evidence implicating facultative and anaerobic bacteria as a primary cause of periodontal disease[67]. It is a multifactorial polymicrobial infection, induced by oral anerobic bacteria such as P.gingivalis and F. nucleatum. As P. gingivalis and F. nucleatum are strongly associated with Periodontitis[68].Majority of the treatment for elimination of pathogenic bacteria relies on mechanical debridement of bacterial deposits[69]. The control of prevalence and development of periodontal disease requires a reduction of subgingival microbial plaque mass or at least a suppression of periodontal pathogenic bacteria.

Systemic administration of antimicrobial agents required frequent dosing which is associated with the risk of developing resistant organisms and super infection as well as gastrointestinal disturbances and their inherent adverse drug effect[70 71].

However local drug delivery overcome these disadvantages and it can attain many folds higher concentration of an antimicrobial agent in sub gingival sites compared with a systemic drug regimen.

SRP disrupting and removing bacteria and calculus deposits, whereas LDD act like bacteriocidal and bacteriostatic, delivered in sub gingival pockets. So adjunctive use of local drug delivery along with SRP gives progressive effect in treatment of periodontitis[72].

Tetracycline offers a broad-spectrum antimicrobial properties and may be a useful adjunct to periodontal therapy. Tetracyclines are the most commonly prescribed antimicrobials in periodontal therapy. They imposes their antimicrobial effect by inhibiting protein synthesis.

The groups of tetracyclines are generally considered to be more effective against Gram-positive bacteria than Gram-negative bacteria and show good activity against most spirochetes as well as many anaerobic and facultative bacteria.

High drug concentrations have been reported in gingival crevicular fluid making them particularly suitable for periodontal applications[63].

Tetracycline is one of the most widely used antimicrobial in the treatment of periodontal discase. It has an anti- inflammatory properties[73] anti-collagenase action[74] and bone resorption[75]. It helps in periodontal regeneration by means of smear layer removal. Also when applied on dentin surface binding with fibroncetin increases. The absorbed fibronectin stimulates fibroblast attachment and growth[76]. while suppreising epithelial attachment and growth. Besides tetracyelme on the ability among antibioties to concentrate in the gingival crevicular fluid of the periodontal pricket a levels 2-10 times greater than those found in the serum[77]. Further, these antibiotics bind to the tooth surface and then be slowly released as a still active antimicrobial

As a model of local drug delivery, tetracycline is used in the form of tibers. strips, films. gels. In our study, commercially available tetracycline containing fibers (Periodontal AB Plus) was used as a control group. Its effectiveness has already been acknowledged as an adjunct to SRP[78].

Use of plant products is increasing in many segment of the population. At present; thousands of medicinal plants are being successfully used for the treatment of variety of diseases.. In the traditional Ayurvedic system of medicine, turmeric has been documented as an antiinflammatory, antimicrobial agent and also for its numerous other curative properties[79] (Ammon and Wahl, 1991). According to an estimate, 80% of the world's population relied upon plants for their medication[80]. The use of the medicinal plants is increasing in many countries where 35% of drugs contain natural products[81].

In our study we used Curcumin extract which encompasses curcuminoids and turmerones, the bioactive components that are already proven for the anti-inflammatory potential[82]. The desirable preventive or putative therapeutic properties of CU have also been considered to be associated with its antioxidant[13], anti-inflammatory[14],antimicrobial[16] and chemopreventive[15] properties. Curcumin, a hydrophobic polyphenolic compound derived from the rhizome of Curcuma longa and it has a wide spectrum of biological and pharmacological activities[83].

As tetracycline has ability to develop microbial resistance in the micro-organism. Hence to overcome these issues, curcumin could be used as local drug delievery in the form of collagen fibers administered to check its efficacy in periodontitis cases.

Therefore utilizing the beneficial properties of curcumin to treat periodontitis.

The split-mouth design has been the principal research tool in periodontal clinical trials to compare different treatment modalities. In this study to avoid mixing of curcumin and tetracycline which probably may leached out and bias the treatment effect specially in mandibular teeth, we chose whole mouth clinical design.

Inclusion and exclusion criteria were considered as per the previous studies.

The reduction in plaque score in our study is in accordance with study conducted by Lindhe J etal in 1979[84] assessing the effect of locally administered tetracycline via hollow fiber devices measuring clinical parameters and microbial analysis. Plaque score which was measured on baseline ,7th day, 14th day, 21th day and 37th day. The result showed significant reduction in plaque score in tetracycline group from 14th day till 37th day.

Heijl etal in 1991[85] examined the efficacy of periodontal treatment using tetracycline containing fibers and the result showed that plaque score remained similar to the baseline i.e it did not increase throughout the treatment.

Nagasri etal 2015[86] evaluated effect of curcumin as adjunct to SRP found significant reduction in microbial growth emphasizing antimicrobial property of curcumin.

Arunachalam etal 2017[87] evaluated anti plaque effect of curcumin in gingivitis by evaluating salivary reactive oxygen species and proposed that antioxidant property of curcumin can be responsible towards its anti-inflammatory action.

Curcumin due to its low solubility, rapid metabolism, and hence low bioavailability it suffers limitation that hold it back from clinical application[88]. So therefor curcumin have limited therapeutic success in various animal and clinical studies[89].

Various new technique have been taken in consideration to overcome the limitations of the use of curcumin including the incorporation in delivery systems[90].

By Using different drug delivery system such as nanotechnology, polymeric nanoparticles, solid lipid nanoparticles (SLN), liquid crystal systems, precursor systems for liquid crystals liposomes, and microemulsions, is an interesting approach to improve a formulation‘s most desirable properties.Furthermore, nanoscale particles may represent a future where activity is ensured, and the problems associated with using medicinal plants are overcome[91].

Gingival score

In our study results are showing similar reduction in gingival score with results presented by Lisgarten etal[92] in 1978 in which they treated 6 human subjects with advanced periodontal disease by tetracycline administration via systemic route, revealed change in gingival index score,gingival fluid flow and probing depth. In another study conducted by lindhe in 1979[93] showed that gingival index score reduced significantly over 37 days with local administration of tetracycline using hollow fibers. It proved that the treatment effects observed were obtained by administration of less than 1/1000 of the amount of tetracycline used in listgarten etal 1978.

On applying curcumin gel there was a significant improvement amongst the cases compared to the SRP group on Day 30. A significant decrease in gingival score was observed in 30th day compared to SRP group that was similar to the past researches done by Behal R etal[40], and Gopinath V et al that used 2% curcumin gel as a local application.

Thus, significant decrease in gingival index score in the experimental areas (curcumin) in our study can be because of the anti-inflammatory, antioxidant, antibacterial activities of curcumin.

Curcumin, the main bioactive component of turmeric, has posed to be a good anti-inflammatory agent because it cause down regulation of cyclo-oxygenase pathway via arachidonic acid inhibition. It was found that the anti-inflammatory properties of curcumin are also mediated through their effects on cytokines, lipid mediators, eicosanoids and proteolytic enzymes. It also acts as an anti-oxidant agent by scavenging the superoxide radicals, hydrogen peroxide and nitric oxide from activated macrophages and inhibits lipid peroxidation[94].

Pocket probing depth-

Moreover, at final evaluation, the net mean decrease (i.e. mean change from day 0 to day 21) in PPD score of tetracycline group (46.3%) was found 23.8% higher as compared to curcumin group (22.5%).

Newmann etal in 1994[95] reported that the statistically greater improvement in pocket probing depth at 1 month ($p<0.05$),3 month($p<0.05$) and 6 months ($p<0.01$) for tetracycline fiber treated sites as compared to SRP treated group.

Lindhe etal 1979[84] reported that the pocket probing depth measurments showed a significant improvement between the initial examination and examination carried out after 14 and 37 days in SRP+Tetracycline group.

Various other studies conducted using tetracycline fibers alone or as an adjunct to SRP showed significant reduction in pocket probing depth. Tetracyclines are semi-synthetic, broad spectrum chemotherapeutic agents which are bacteriostatic in action. As they are capable of achieving high concentration in the sulcular fluid hence they are effective against rapidly multiplying bacteria.

Merline etal[96] clinical study has shown that applications of Curcumin gel has reduced gingival inflammatory signs and promote healing with reduced pocket depth superior than the widely used metronidazole gel medicament.

In our study there is significant decrease in pocket probig depth can be seen in curcumin group at day 21th, but due to its rapid metabolism properties means its retaintivity is low, gives compromising results on pocket probing depth as compared to tetracycline group.

CONCLUSION

Based on the clinical parameters, the following can be concluded from this study:

1. Gingival score showed significant decrease in (P value< 0.001) curcumin group at 14th day as compared to both 0 and day 7.

2. Plaque score showed significant decrease (P<0.01) or (P<0.001) in tetracycline group at both day 14th and 21st as compared to baseline and day 7.

3. PPD reduced significant decrease in tetracycline group (P<0.001) at both day 14 and 21as compared to both day 0 and day7. It further reduce significant at day 7 as compared to base line.

4. Incurcumin group PPD also reduced significant (P<0.05 or P<0.001) at day 21st as compared to day 0,7,14.

5. Curcumin group prove to be more efficacious when compared to tetracycline group in Gingival parameter i.ecurcumin has higher mean %variation from baseline to 21st day due to its anti-inflammatory activity.

6. Tetracycline group proves to be more efficacious when compared to curcumin group in plaque score and pocket probing depth parameter.

With in the limitations of present study it can be concluded that treatment with tetracycline improves clinical parameters in periodontitis patients as compared to curcumin group.

Curcumin incorporated fiber can be effectively used in the treatment gingivitis, as it has potent anti inflammatory and anti plaque action. The fiber was well tolerated and had good patient acceptance with no side effect. Further research has to be done at improving curcumin formulation and delivery systems, that may be beneficial in the treatment of periodontal disease.

More longitudinal study with large sample size can be considered in future to strength the result of this study.

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APPENDICES

ANNEXURE -1

BABU BANARASI DAS COLLEGE OF DENTAL SCIENCES (FACULTY OF BBD UNIVERSITY), LUCKNOW

INSTITUTIONAL RESEARCH COMMITTEE APPROVAL

The project titled **"Comparative Clinical Evaluation of Tetracycline Fibers With Curcumin Incorporated Collagen Fibers – A Randomised Clinical Study."** submitted by **Dr Aditi Raj** Post graduate student from the **Department of Periodontology** as part of MDS Curriculum for the academic year 2018-2021 with the accompanying proforma was reviewed by the Institutional Research Committee present on **27th November 2018** at BBDCODS.

The Committee has granted approval on the scientific content of the project. The proposal may now be reviewed by the Institutional Ethics Committee for granting ethical approval.

Prof. Vandana A Pant
Co-Chairperson

Prof. B. Rajkumar
Chairperson

ANNEXURE -2

Babu Banarasi Das University
Babu Banarasi Das College of Dental Sciences,
BBD City, Faizabad Road, Lucknow – 226028 (INDIA)

Dr. Lakshmi Bala
Professor and Head Biochemistry and
Member-Secretary, Institutional Ethics Committee

Communication of the Decision of the VIIth Institutional Ethics Sub-Committee

IEC Code: 27 **BBDCODS/01/2019**

Title of the Project: Comparative Clinical Evaluation of Tetracycline Fibers With Curcumin Incorporated Collagen Fibers – A Randomised Clinical Study.

Principal Investigator: Dr. Aditi Raj **Department:** Periodontology

Name and Address of the Institution: BBD College of Dental Sciences Lucknow.

Type of Submission: New, MDS Project Protocol

Dear Dr. Aditi Raj,

The Institutional Ethics Sub-Committee meeting comprising following four members was held on 10th January 2019.

1.	Dr. Lakshmi Bala Member Secretary	Prof. and Head, Department of Biochemistry, BBDCODS, Lucknow
2.	Dr. Amrit Tandan Member	Prof. & Head, Department of Prosthodontics and Crown & Bridge, BBDCODS, Lucknow
3.	Dr. Rana Pratap Maurya Member	Reader, Department of Orthodontics & Dentofacial Orthopedics, BBDCODS, Lucknow
4.	Dr. Sumalatha M.N. Member	Reader, Department of Oral Medicine & Radiology, BBDCODS, Lucknow

The committee reviewed and discussed your submitted documents of the current MDS Project Protocol in the meeting.
The comments were communicated to PI thereafter it was revised.

Decisions: The committee approved the above protocol from ethics point of view.

Forwarded by:

Lakshmi Bala 22/01/19

(Dr. Lakshmi Bala)
Member-Secretary
IEC

Member-Secretary
Institutional Ethic Committee
BBD College of Dental Sciences
BBD University
Faizabad Road, Lucknow-226028

(Dr. B. Rajkumar)
Principal
BBDCODS

PRINCIPAL
Babu Banarasi Das College of Dental Sciences
(Babu Banarasi Das University)
BBD City, Faizabad Road, Lucknow-226028

ANNEXURE -3

सीएसआईआर - राष्ट्रीय विज्ञान संचार एवं सूचना स्रोत संस्थान
CSIR - National Institute of Science Communication and Information Resources
वैज्ञानिक एवं औद्योगिक अनुसंधान परिषद् Council of Scientific & Industrial Research
(विज्ञान एवं प्रौद्योगिकी मंत्रालय, भारत सरकार Ministry of Science & Technology, Govt. of India)

RAW MATERIAL HERBARIUM AND MUSEUM, DELHI (RHMD)

Ref. No.-NISCAIR/RHMD/Consult/2020/3721-22 22/12/2020

CERTIFICATE FOR CRUDE DRUGS AUTHENTICATION

This is to certify that rhizome, stolon sample of *Curcuma longa*, received from Ms. Aditi Raj, vide letter No. Nil, Dated 10th December 2020 has been **found correct as rhizomes of *Curcuma longa* L. which is commonly known as Haldi, Haridra, Turmeric.** The identification has been done on the basis of macroscopic studies of the sample followed by detailed scrutiny of literature and matching the sample with authentic samples deposited in the Raw Material Herbarium and Museum, Delhi (RHMD).

Identification pertains to the quantity/quality of specimen/sample(s) received in RHMD. This certificate is not issued for any judicial purpose.

(Dr. Sunita Garg)
Emeritus Scientist, CSIR-NISCAIR
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Ph.: +91-11-25846001; 25846301, Ext. 263

(Mr. R S. Jayasomu)
Chief Scientist
Head, RHMD

Ms. Aditi Raj
BBD University
BBD City, Faizabad Road
Lucknow-226 028, UP
Mob.- 9839278227, 9560520244
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विज्ञान संचार भवन, डॉ. के.एस. कृष्णन मार्ग, पूसा, नई दिल्ली-110012, भारत Vigyan Sanchar Bhawan, Dr. K.S. Krishnan Marg, Pusa, New Delhi-110012, India
फोन Phone: +91-11-25846301,25842303; 25846304-7, 25842990, 25840602, 25847544, 25847566 फैक्स Fax: +91-11-25847062, 25849949
विज्ञान सूचना भवन, 14, सत्संग विहार मार्ग, नई दिल्ली-110067 Vigyan Suchna Bhawan, Satsang Vihar Marg, New Delhi-110067
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ANNEXURE -4

Babu Banarasi Das College of Dental Sciences
(Babu Banarasi Das University)
BBD City, Faizabad Road, Lucknow – 227105 (INDIA)

सहमति पत्र

अध्ययन शीर्षक.....
अध्ययन संख्या.....
प्रतिभागी के पूर्ण नाम.....
जन्म तिथि / आयु.....
प्रतिभागी का पता .....
फोन नं. और ई-मेल पता .....
योग्यता .....
व्यवसाय: छात्र / स्व कार्यरत / सेवा / ग्रहिणी .....
अन्य (उचित रुप मे टिक करें) .....
प्रतिभागी की वार्षिक आय .....
प्रत्याशीयो के नाम और प्रतिभागी से संबंध...(परीक्षण से संबंधित मौत के मामले मे मुआवजे के प्रयोजन के लिए)

1. मेरी पुष्टि है कि मैने अध्ययन हेतु सुचना पत्र दिनांक ..... को पढ व समझ लिया तथा मुझे प्रश्न पुछने या मुझे अध्ययन अन्वेषक ने सभी तथ्यों को समझा दिया है तथा मुझे प्रश्न पुछने के समान अवसर प्रदान किए गये।

2. मैंने यहॉ समझ लिया कि अध्ययन में मेरी भागीदारी पूर्णतः स्वैच्छिक है और किसी भी दबाव के बिना स्वतंत्र इच्छा के साथ दिया है किसी भी समय किसी भी कारण के बिना , मेरे इलाज या कानूनी अधिकारो को प्रभावित किए बिना , अध्ययन में भाग न लेने के लिए स्वतंत्र हुँ ।

3. मैंने यह समझ लिया है कि अध्ययन के प्रायोजक , प्रायोजक की तरफ से काम करने वाले लोग, आचार समिति और नियामक अधिकारियों को मेरे स्वास्थ्य रिकार्ड को वर्तमान अध्ययन या आगे के अध्ययन के सन्दर्भ देखने के लिए मेरी अनुमति की जरूरत नही है, चाहे मैने इस अध्ययन से नाम वापस ले लिया है। हॉलाकि मै यह समझता हुँ कि मेरी पहचान को किसी भी तीसरे पक्ष या प्रकाशित माध्यम में नही दी जायेगी।

4. मै इससे सहमत हूँ कि कोई भी डेटा या परिणाम जो इस अध्ययन से प्राप्त होता है उसका वैज्ञानिक उद्देश्य (ओं) के उपयोग के लिए मेरी तरफ से कोई प्रतिबंध नही है।
5. भविष्य के अनुसंधान के लिए भंडारित नमूना (ऊतक/रक्त) पर अध्ययन के लिए अपनी सहमति देता हुँ।

हॉ [ ] नही [ ] अनउपयुक्त [ ]

6. मै परीक्षण की अनुमति देता हुॅ। मुझे इसके द्वारा यदि कोई परेशानी होती है, इसके बारे में जानकारी दे दी गई है। मैने रोगी जानकारी सूचना पत्र को पढ तथा समझ लिया है।

प्रतिभागी / कानूनी तौर पर स्वीकार्य प्रतिनिधि का हस्ताक्षर (या अंगूठे का निशान.....

हस्ताक्षरकर्ता का नाम..... दिनांक .....अन्वेषक के हस्ताक्षर ..... दिनांक .....

अध्ययन अन्वेषक का नाम .....

गवाह के हस्ताक्षर ..... दिनांक .....गवाह के नाम .....

मैनें पीआईडी और विधिवत भरे सहमति फार्म का एक हस्ताक्षर की नकल प्राप्त की.

प्रतिभागी कानूनी तौर पर प्रतिनिधि का हस्ताक्षर/ अंगूठे का निशान ..... दिनांक.....

Babu Banarasi Das College of Dental Sciences

(Babu Banarasi Das University)
BBD City, Faizabad Road, Lucknow – 227105 (INDIA)

Consent Form (English)

Title of the Study ……..

Study Number……..
Subject's Full Name…….
Date of Birth/Age ……
Address of the Subject…….
Phone no. and e-mail address……
Qualification ……
Occupation: Student / Self Employed / Service / Housewife/
Other (Please tick as appropriate)
Annual income of the Subject……
Name and of the nominees(s) and his relation to the subject…… (For the purpose of compensation in case of trial related death).

1. I confirm that I have read and understood the Participant Information Document dated ……..for the above study and have had the opportunity to ask questions. **OR** I have been explained the nature of the study by the Investigator and had the opportunity to ask questions.
2. I understand that my participation in the study is voluntary and given with free will without any duress and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
5. I permit the use of stored sample (tooth/tissue/blood) for future research. **Yes [ ] No [ ] Not Applicable [ ]**
6. I agree to participate in the above study. I have been explained about the complications and side effects, if any, and have fully understood them. I have also read and understood the participant/volunteer's Information document given to me.

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:……..
Signatory's Name……. Date …….
Signature of the Investigator…… Date……..
Study Investigator's Name..... Date……..
Signature of the witness…… Date……..
Name of the witness……
Received a signed copy of the PID and duly filled consent form
Signature/thumb impression of the subject or legally Date……..

Acceptable representative

ANNEXURE -5

BabuBanarasi Das College of Dental Sciences

(A constituent institution of BabuBanarasi Das University)

BBD City, Faizabad Road, Lucknow – 227105 (INDIA)

Participant Information Document (PID)

1. Study title

Comparative Clinical Evaluation of Tetracycline fibers with Curcumin Incorporated collagen fibers- A Randomised Clinical Study.

2. Invitation paragraph

You are being invited to take part in a research study, it is therefore important for you to understand why the study is being done and what it will involve. Please take time to read the following information carefully. Ask us for any clarifications or further information. Whether or not you wish to take part is your decision.

3. What is the purpose of the study?

The purpose of this study is to evaluate the clinical parameters regarding the efficacy and time release pattern of the *Curcuma longa* (curcumin) placed in chronic periodontitis patients compared with tetracycline fibers.

4. Why have I been chosen?

You have been chosen for this study as you are fulfilling the required criteria for this study.

5. Do I have to take part?

Your participation in the research is entirely voluntary. If you do, you will be given this information sheet to keep and will be asked to sign a consent form. During the study you still are free to withdraw at any time and without giving a reason.

6. What will happen to me if I take part?

You will be one of 30 sites in 30 patients enrolled in the study. These sites will be divided into 2 groups –SRP+TTC and SRP + Curcumin .Now, collagen fibers will be incorporated with *curcuma longa* in 15 sites and on other 15 sites collagen fibers will be

incorporated with Tetracycline fibres in patients with Chronic Periondontitis with >5mm pocket probing depth.

7. What do I have to do?

You do not have to change your regular lifestyles for the investigation of the study.

8. What is the procedure that is being tested?

The procedure will involve evaluating and comparing the effectiveness and time release pattern of curcumin incorporated fiber with tetracycline fibers.

9. What are the interventions for the study?

Patient with chronic periodontitis with pocket probing depth more than 5 mm and with radiographic evidence of bone loss will be included. Now, we will divide the sites into 2 groups of 15 sites each. IN one group we will insert the collagen fibers incorporated with *curcuma longa*and in other group we will insert the collagen fibers incorporated with Tetracycline fibers. Now we will evaluate the efficacy and time release pattern of *curcuma longa*incorporated fibers as local drug delivery system in periodontitis and to compare the effectiveness and time release pattern of curcumin incorporated fibre with tetracycline fibers.

10. What are the side effects of taking part?

There are no side effects on patients of this study.

11. What are the possible disadvantages and risks of taking part?

There are no risk or disadvantages of taking part in this study.

12. What are the possible benefits of taking part?

This study will help us to know to evaluate the efficacy and time release pattern of *Curcuma longa* (curcumin) incorporated fibers as local drug delivery system in periodontitis. It also compare the effectiveness and time release pattern of curcumin incorporated fibers with tetracycline fibers.

13. What if new information becomes available?

If additional information becomes available during the course of the research you will be told about these and you are free to discuss it with your researcher, your researcher

will tell you whether you want to continue in the study. If you decide to withdraw, your researcher will make arrangements for your withdrawal. If you decide to continue in the study, you may be asked to sign an updated consent form.

14. What happens when the research study stops?

If the study stops/finishes before the stipulated time, this will be explained to the patient/volunteer.

15. What if something goes wrong?

If any severe adverse event occurs, or something goes wrong during the study, the complaints will be handled by reporting to the institution (s), and Institutional ethical community.

16. Will my taking part in this study be kept confidential?

Yes it will be kept confidential.

17. What will happen to the results of the research study?

The results of the study will be used to compare clinical evaluation of tetracycline fibers with curcumin incorporated collagen fibers.Your identity will be kept confidential in case of any report/publications.

18. Who is organizing the research?

This research study is organized by the academic institution (BBDCODS).

19. Will the results of the study be made available after study is over?

Yes.

20. Who has reviewed the study?

The study has been reviewed and approved by the Head of the Dept, and the IEC/IRC of the institution.

21. Contact for further information

Dr. ADITI RAJ

Department of Periodontology and Implantology

BabuBanarasi College of Dental Sciences.

Lucknow-227105

Mob- 9560520244

Dr. Vandana A Pant (HOD)

Department of Periodontology and Implantology

BabuBanarasi College of Dental Sciences.

Lucknow-227105

Mob-9935957775

Dr. LaxmiBala,

Member Secretary,

Babu Banarasi College of Dental Sciences.

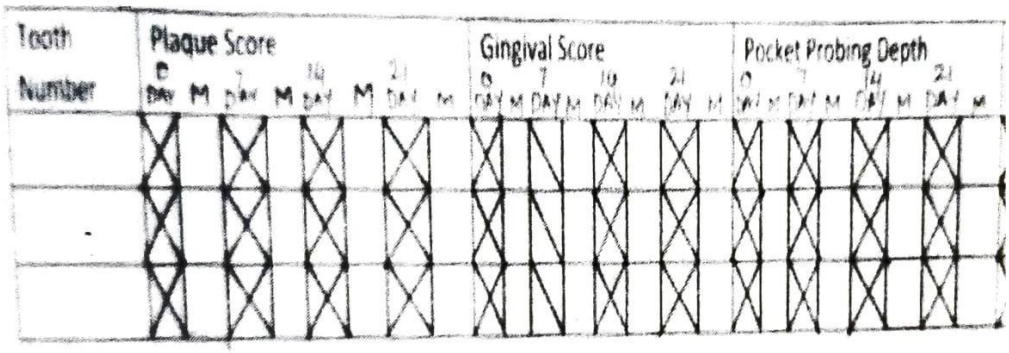
Lucknow

bbdcods.iec@gmail.com

ANNEXURE -6

Name of the Patient:

Tetracycline/Neem incorporated Fibers



ANNEXURE -7

Formula used for the analysis

Arithmetic Mean

The most widely used measure of central tendency is arithmetic mean, usually referred to simply as the mean, calculated as

$$\bar{X} = \frac{\sum_{i=1}^{n} X_i}{n}$$

Standard deviation and standard error

The standard deviation (SD) is the positive square root of the variance, and calculated as

$$SD = \sqrt{\frac{\sum X_i^2 - \frac{(\sum X_i)^2}{n}}{n-1}}$$

and SE (standard error of the mean) is calculated as

$$SE = \frac{SD}{\sqrt{n}}$$

where, n= no. of observations

Analysis of Variance

Analysis of variance (ANOVA) is used when we compare more than two groups simultaneously. The purpose of one-way ANOVA is to find out whether data from several groups have a common mean. That is, to determine whether the groups are actually different in the measured characteristic. One way ANOVA is a simple special case of the linear model. For more than two independent groups, simple parametric ANOVA is used when variables under consideration follows Continuous exercise group distribution and groups variances are homogeneous otherwise non parametric alternative Kruskal-Wallis (H) ANOVA by ranks is used. The one way ANOVA form of the model is

$$Y_{ij} = \alpha_{.j} + \varepsilon_{ij}$$

where;

- Y_{ij} is a matrix of observations in which each column represents a different group.
- $\alpha_{.j}$ is a matrix whose columns are the group means (the "dot j" notation means that α applies to all rows of the j^{th} column i.e. the value α_{ij} is the same for all i).
- ε_{ij} is a matrix of random disturbances.

The model posits that the columns of Y are a constant plus a random disturbance. We want to know if the constants are all the same.

Tukey multiple comparison Test

After performing ANOVA, Tukey HSD (honestly significant difference) post hoc test is generally used to calculate differences between group means as

$$q = \frac{\bar{X}_1 - \bar{X}_2}{SE}$$

where,

$$SE = \sqrt{\frac{S^2}{2}\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}$$

S^2 is the error mean square from the analysis of variance and n_1 and n_2 are number of data in group 1 and 2 respectively.

Level of significance "*P*" is the probability signifies level of significance. The mentioned p in the text indicates the following:

P > 0.05- Not significant (ns)

P < 0.05- Just significant (*)

P < 0.01- Moderate significant (**)

P < 0.001- Highly significant (***)

ANNEXURE -8

Observation

Group A: Control group (SRP + TTC)

Pt. no.	Tooth no.	Gingival index score				Plaque index score				Pocket probing depth (mm)			
		0 days	7 days	14 days	21 days	0 days	7 days	14 days	21 days	0 days	7 days	14 days	21 days
1	43	0.8	0.6	0.6	0.6	1.4	1.39	1.32	1.26	5	4	3	3
2	42	1.52	1.52	1.52	1.52	1.6	1.58	1.51	1.47	5	4	3	3
3	45	1.32	1.32	1.3	1.3	1.5	1.48	1.51	1.47	5	4	3	3
4	42	1.25	1.25	1.23	1.23	1.2	1.18	1.11	1.06	5	5	3	2
5	43	1.41	1.39	1.39	1.39	1.4	1.38	1.31	1.27	5	5	3	2
6	44	1.31	1.29	1.29	1.29	1.5	1.48	1.41	1.37	5	4	3	3
7	16	1.26	1.26	1.24	1.24	1.4	1.38	1.31	1.27	6	6	5	5
8	17	1.32	1.29	1.29	1.23	1.5	1.48	1.41	1.37	5	4	3	3
9	25	1.41	1.41	1.39	1.39	1.6	1.58	1.51	1.47	7	5	4	4
10	12	0.9	0.9	0.5	0.5	1.4	1.38	1.31	1.27	7	5	4	4
11	42	1.27	1.27	1.25	1.25	1.5	1.45	1.41	1.37	5	4	2	2
12	37	1.4	1.38	1.38	1.38	1.3	1.28	1.21	1.17	5	3	3	2
13	25	1.25	1.25	1.23	1.23	1.5	1.48	1.41	1.37	5	3	3	2
14	26	1.25	1.25	1.23	1.23	1.3	1.28	1.21	1.17	6	5	5	3
15	35	1.4	1.4	1.4	1.38	1.3	1.28	1.21	1.17	6	3	3	3

Group B: Experimental group (SRP + Curcumin)

Pt. no	Tooth no.	Gingival index score				Plaque index score				Pocket probing depth (mm)			
		0 days	7 days	14 days	21 days	0 days	7 days	14 days	21 days	0 days	7 days	14 days	21 days
1	43	1.26	1.24	1.2	1.15	1.4	1.39	1.39	1.32	5	5	5	4
2	42	0.9	0.7	0.5	0.2	1.5	1.39	1.48	1.48	6	6	5	5
3	45	1.3	1.28	1.22	1.18	1.3	1.5	1.28	1.28	5	5	5	4
4	42	1.3	1.28	1.22	1.18	1.6	1.28	1.58	1.51	6	5	5	4
5	43	1.4	1.38	1.34	1.28	1.4	1.58	1.48	1.32	5	5	5	4
6	44	1.52	1.49	1.46	1.4	1.5	1.48	1.48	1.48	6	6	5	4
7	16	1.26	1.24	1.2	1.15	1.6	1.6	1.58	1.58	5	5	4	4
8	17	1.32	1.3	1.24	1.2	1.3	1.3	1.3	1.3	5	5	4	4
9	25	1.31	1.29	1.23	1.19	1.4	1.39	1.39	1.39	5	5	5	4
10	12	1.25	1.23	1.19	1.14	1.3	1.3	1.28	1.28	5	4	4	3
11	42	1.31	1.29	1.23	1.19	1.6	1.6	1.58	1.58	6	5	5	5
12	37	1.13	1.12	1.06	1.02	1.6	1.58	1.58	1.51	6	6	6	5
13	25	1.4	1.38	1.34	1.28	1.4	1.39	1.39	1.39	5	4	4	4
14	26	1.3	1.28	1.22	1.18	1.4	1.39	1.39	1.32	5	5	4	4
15	35	1.41	1.39	1.35	1.3	1.5	1.48	1.48	1.48	5	5	4	4

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