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Systematic Review on Effectiveness of Curcumin in Treatment of Periodontitis

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Abstract

Background: Curcumin is a herbal agent with a multitude of medicinal properties. It is known to aid in proper digestion, enhancing blood circulation, anti-microbial and anti-inflammatory properties and so on. Periodontitis is one of the most prevalent diseases affecting the human race. Many current studies are focused on establishing the potency of curcumin against periodontitis and its other uses in dentistry as it is a natural substance with minimal adverse effects and powerful medicinal value.

Aim: To determine the effectiveness of curcumin in the treatment of periodontitis.

Study Design: A systematic review of clinical trials done using curcumin as an effective agent against periodontitis. Electronic databases were searched and obtained a total of 460 articles, among which 9 studies where included in this study.

Results: Nine studies were included in the systematic review of which all are clinical trials. Among which, eight studies showed that curcumin, when used as an adjunct to scaling and root planing, had a crucial role in reducing the inflammation and improving the periodontal status.

Conclusion: Curcumin being a natural anti-microbial agent having equal or potency as that of other synthetic agents, makes it a better alternative as an adjunct to scaling and root planing for the treatment of periodontitis.

Keywords: Curcumin, Periodontitis, Dentistry, Herbal medicine and clinical trial.

INTRODUCTION:

Periodontitis is one of the most commonly encountered persistent infectious states constituting inflammatory reaction in the host induced by various infectious agents eventually leading to apical migration of the junctional epithelium, obliteration of connective tissue and supporting bony structure, tooth mobility and tooth loss[1]. It can manifest in various forms like.

- Aggressive periodontitis(common in childhood),
- Chronic periodontitis,
- Periodontitis due to any systemic condition[2].

Risk factors of periodontitis can be broadly classified as modifiable and non-modifiable factors[3]. These include smoking, bad oral hygiene, diabetes mellitus, periodontal pathogens, psychological stress, cardiovascular diseases, drug-induced, obesity, genetic factors, haematological disorders, hormonal imbalance, pregnancy, host immune response, age, sex and socio-economic status[1]. Based on recent researches they are trying to enact a relationship between different systemic diseases with periodontitis. Diabetes being a proven risk factor for periodontitis, it is said to be detrimental to serum glycaemic levels[4, 5]. This research also shows the negative impact of periodontal conditions on glucose metabolism and that it could be controlled significantly by non-surgical treatments[6].

Treatment for periodontitis can be of two types: non-surgical and surgical (can include orthodontic treatment procedures also).The treatment can be divided into 4 phases – Nonsurgical – surgical – restorative – maintenance phase[8]. The main motive of periodontal treatment modalities is infection control and reduction in periodontal inflammation. Various methods of treatments are as follows-

- Surgical intervention
- Mechanical therapy – Scaling and root planing
- Pharmacological agents –
    - Antimicrobials
    - Host response modulating agents – doxycycline, tetracycline, bisphosphonates
    - Localized drug delivery system –chlorhexidine, tetracycline, metronidazole etc.,
    - Periodontal dressing
- Maintenance of oral hygiene - flossing, brushing, supragingival/ subgingival irrigation
- Recent advancements – laser therapy, photodynamic therapy, platelet-rich plasma, herbal products like curcumin, probiotics etc.[7]

Among this, many recent researches are concentrated on the effectiveness of curcumin as an adjunct to scaling and root planing. Since ancient times medicinal plants were used successfully for the treatment of multiple diseases in humans. Curcumin also known as Turmeric or Curcuma longais well known for its ayurvedic properties, to improve blood circulation, to improve digestion and reduce gas and bloating and improving bile production [10]. In dentistry, curcumin is used as

- Pit and fissure sealant
- Dental pain
- Subgingival irrigant
- Against pre-cancerous lesions
- Local drug delivery system and periodontal problems[9].

Taking account of the fact that curcumin is an herbal product with good anti-inflammatory and anti-microbial properties with very few adverse effects of usage, this study is aimed at the review of its effectiveness on controlling periodontitis.

MATERIALS AND METHOD

STUDY DESIGN:

A systematic review about clinical trials was done using curcumin as an effective agent against periodontitis.

SEARCH STRATEGY:

The following electronic databases were used to find published articles on the effectiveness of curcumin in the treatment of periodontitis PubMed, Ovid Medline,
Elsevier science direct, Wiley online library, Grey literature, Cochrane Library, Cinahl, Prospero, OSF, Scopus. Each database was searched to obtain the articles using Mesh representations. The mesh term used was "periodontitis/periodontal diseases" AND "curcumin". After the search, a total of 460 articles were obtained among which 9 articles were finalized for further studies.

ELIGIBILITY CRITERIA

Inclusion criteria:

1) Studies published in English
2) Articles on the effectiveness of curcumin in periodontitis
3) Clinical trial studies
4) Full-text articles
5) Publications over the years

Exclusion criteria:

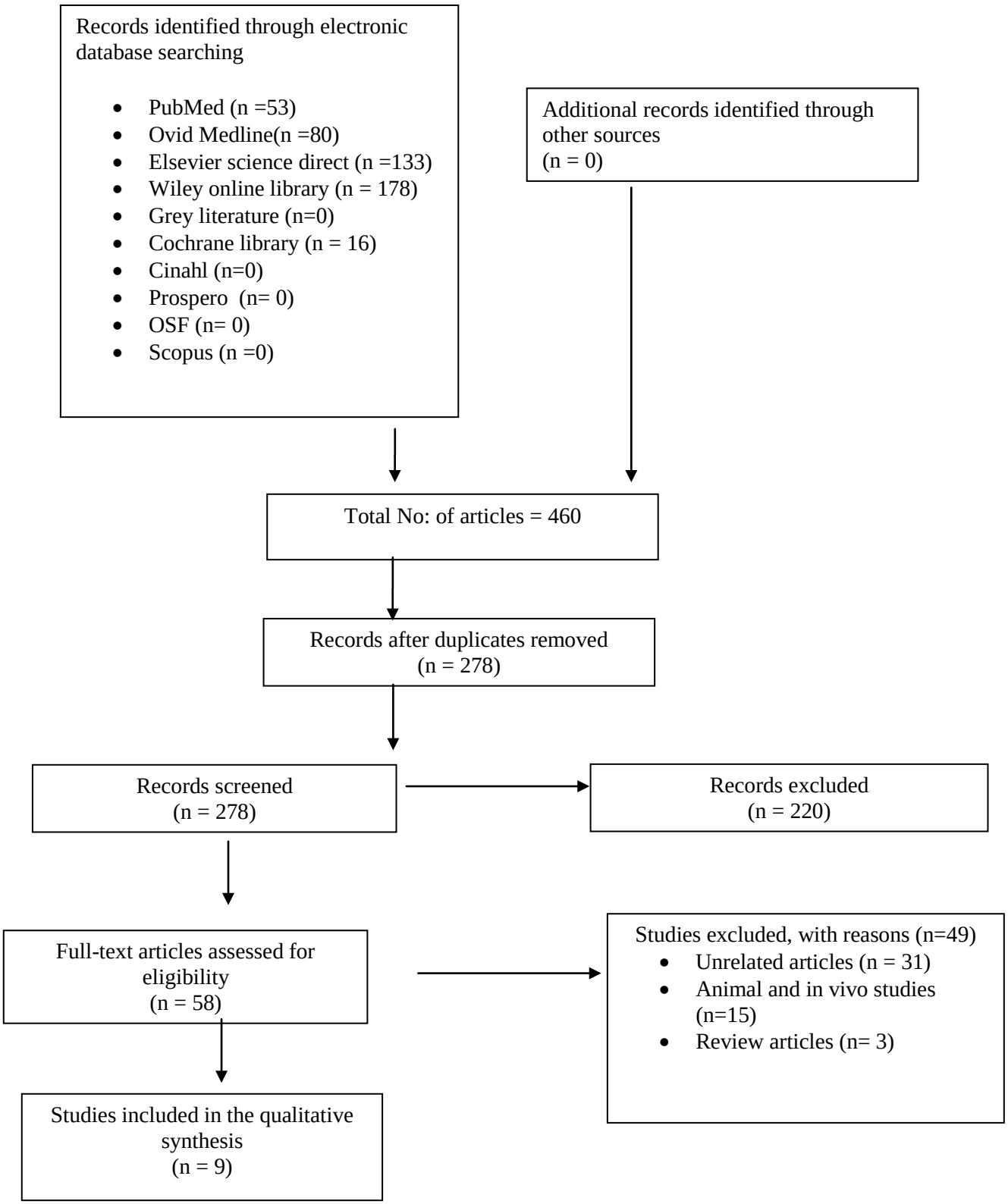
1) Articles published in other languages
2) Only abstracts available
3) Unrelated articles
4) Animal studies
5) In-vitro studies

SEARCH ENGINES

- PubMed
- Ovid Medline
- Elsevier science direct
- Wiley online library
- Grey literature
- Cochrane library
- Cinahl
- Prospero
- OSF
- Scopus

After the search using the appropriate mesh terms a total of 460 articles where found from the online databases. After duplicates removal 278 articles were screened and 58 full-text articles were available. Inclusion-exclusion criteria were applied and the final 9 related articles were selected for further assessment. Figure 1shows the flow diagram of a number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review.

Figure 1: Flow diagram showing the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic



RESULT

TABLE 1: CHARACTERISTICS OF THE INTERVENTIONS IN THE INCLUDED STUDIES.

SL No:	AUTHOR	YEAR	PATIENT SELECTION	DURATION	PREPARATION USED	INTERVENTION
1	M. Nagasri P Mohankumar	2015	30 patients of the age group 35-60 with 2 sites in contralateral quadrant having PPD of >5mm.	4 weeks	• Curenext oral gel 10g containing C.longa	2 sites in each patient. • Group, I control: only scaling and root planing at baseline. • Group II test: scaling and root planing followed by local application of curcumin.
2	PL Ravishankar	2017	14- males 6- females between 27-53 years with chronic periodontitis and PPD >5mm bilaterally.	3 month	• Curcumin gel • Ornidazole gel	60 pockets in 20 patients were randomized and test gel was injected into the periodontal pocket and the periodontal dressing was done. • Group I: curcumin gel • Group II: ornidazole gel
3	Roobal Behal, Amita M. Mali, SUhit S. Gilda	2011	30 patients with chronic periodontitis with PPD of 5-7mm in at least 2 sites in different quadrants.	45 days	• 2% Whole turmeric gel.	• 30 control sites scaling and root planing • 30 experimental sites scaling and root planing followed by placement of turmeric gel
4	Merline K. Varghese	2014	15 subjects of both sexes having at least 3 sites with PPD 4-6 mm with moderately or severely inflamed gingiva that bleeds on probing.	30 days	• Metronidazole gel 10mg • Curcumin gel 10mg	• Group A: 15 subjects were treated with scaling and root planing followed by placement of metronidazole. • Group B: 15 subjects were treated with scaling and root planing by placement of curcumin
5	V Anitha	2015	20 males 10 females with chronic periodontitis 20-50 years of age with PPD 4-6mm.	30 days	• Curcumin solution • 0.1% chlorhexidine gel	Full mouth scaling and root planing • Group I: 30 sites SRP followed by subgingival curcumin • Group II: 30 sites SRP and subgingival chlorhexidine. Periodontal dressing over the site.
6	Sruthima N.V.S. Gottumukkala, Sabitha Sudarshan	2014	120 sites from 60 patients of age group 25-55 of both sexes (2 sites in contralateral quadrants) with PPD >5mm with radiographic evidence of bilateral bone loss.	6 months	• Indigenous curcumin • Chlorhexidine chips	120 sites from 60 patients were randomly treated with curcumin or chlorhexidine chips after scaling and root planing • Group I: curcumin in collagen • Group II: chlorhexidine chips
7	Madhu Bhatia	2014	15- males 10 females of age 21-45 having chronic periodontitis with .5mm PPD bilaterally.	6 months	• 1% Curcumin gel	50 sites from 25 patients were selected • Test group: scaling and root planing along with 1% curcumin gel • Control group: only scaling and root planing
8	Shweta S Hugar Suvarna Patil	2016	30 patients of age 25-50 having chronic periodontitis and PPD of <5mm bilaterally.	45 days	• 0.2% chlorhexidine gel • 2% curcumin gel	30 patients were randomly divided into two groups • Group 1: control group 30 sites on the left side treated by scaling and root planing and chlorhexidine gel placement • Group 2: experimental group right side treated by scaling and root planing and curcumin gel
9	Maha M A Nasra Heba M Khiri	2017	20 patients of age 35-55 of both sexes with periodontitis with isolated pockets of >5mm.	1 month	• Carbopol-poloxamer gel of curcumin	20 patients were divided into two groups randomly • Group I: Control group of 10 received SRP • Group II: an experimental group of 10 received SRP and pockets were overfilled with curcumin gel and process was repeated once a week for three weeks

Table 1: shows the characteristics of the intervention in the included studies. In all the above studies the effectiveness of curcumin over other medicinal preparations against periodontitis was reviewed and compared. Trials were conducted in patients with chronic periodontitis and PPD more than 3.5mm. Trial duration (1-6 months) and preparations used varied in each study.

Table 2: shows the outcome and result of the effectiveness of curcumin against periodontitis in the above-mentioned studies. The outcome and results were positive in the above studies showing curcumin as a potent adjunct of scaling and root planing in reducing the pocket and improving periodontal status except for one where chlorhexidine concentrations proved to be more effective.

Table 3 shows the bias analysis of all the included studies. It is categorized as high risk bias "-", low risk bias "++" and unclear "?". Categorization was done according to the Cochrane risk of bias tools for randomized controlled trials .

TABLE 2: OUTCOME DATA AS REPORTED IN INCLUDED STUDIES

SL No.	AUTHOR	YEAR	OUTCOME	RESULT
1	M. Nagasri	2015	Major reduction in plaque index, gingival index, probing depth, Cal and a significant decrease in pathogenic bacterial strains	The outcome suggests that local application of curcumin along with scaling and root planing is effective in improving periodontal parameters.
2	PL Ravishankar	2017	Clinical parameters after 3 months showed that better reduction in PI, CI, CAL, PD in the group under curcumin treatment than ornidazole group	The outcome shows more effectiveness for curcumin than ornidazole as an adjunct to nonsurgical periodontal therapy
3	Roobal Behal, Amita M. Mali, Suhit S. Gilda	2011	After 45 days of observation, no allergic reactions where observed, a significant reduction in PI, GI, PPD, bleeding index were observed along with gain in clinical attachment in both groups.	The outcome proves that local drug delivery system of 2% whole turmeric gel can be used as an adjunct to scaling and root planing in the treatment of periodontitis.
4	Merline K. Varghese	2014	On recording clinical parameters after 30 days reduction in modified sulcular beeling index, GI, PPD was observed in both groups but better results were observed in group B.	Better results were shown by curcumin treatment in the reduction of gingival inflammation and improvement of periodontal pocket depth compared to metronidazole
5	V Anitha	2015	In the intra-group comparison between PPD, CAL and microbiological evaluation after 30 days, a significant reduction was seen in the values of both groups treated with curcumin and chlorhexidine.	The outcome shows that the efficiency of curcumin is equivalent to that of chlorhexidine but being a natural ayurvedic herb gives it the upper hand of being the better alternative.
6	Sruthima N.V.S. Gottumukkala, Sabitha Sudarshan	2014	After 6 months of observation, the chlorhexidine group showed better improvements in clinical – PPD, CAL and biological parameters than the curcumin group.	The comparison showed that chlorhexidine chips were more potent than the indigenous curcumin in controlling periodontitis but both groups showed significant improvement in periodontal status.
7	Madhu Bhatia	2014	After an analysis over 1, 3 and 6 months there was a greater reduction in CAL, PPD, PI, GI, and microbiological count also had a drastic reduction in the curcumin group than the control group.	The study shows that locally delivered 1% curcumin is effective in inhibiting the growth of oral bacteria and can be used as an adjunct to scaling and root planing in the treatment of periodontitis, even though at this concentration the effects where short term.
8	Shweta S Hugar Suvarna Patil	2016	Analysis done after 30 and 45 days showed a significant reduction in PPD, PI, GI, and sulcular bleeding index. In comparison, greater results were observed in the experimental group.	The comparison between the two results shows that curcumin can be used as an adjunct to scaling and root planing effectively in mind to moderate periodontal pockets with an evident reduction in indices scores.
9	Maha M A Nasra Heba M Khiri	2017	Records of clinical parameters after 30 days showed significant improvements in PI, Bleeding index and PPD. Also, the new gel formulation was stable with no significant side effects or irritation.	Clinical studies on periodontitisusing the formulated gel form of curcumin have shown promising results in the reduction of PPD, BI, GI making it a suitable agent against periodontitis.

TABLE 3: BIAS ANALYSIS OF INCLUDED STUDIES

Sl No.	AUTHOR AND YEAR	RANDON SEQUENCE GENERATION	ALLOCATION CONCEALMENT	SELECTIVE REPORTING	INCOMPLETE COUTCOME DATA	BLINDING OF OUTCOME ASSESSMENT	BLINDING PARTICIPANTS AND PERSONALS
1	M. Nagasri, 2015	++	-	++	++	?	++
2	PL Ravishankar, 2017	++	-	++	++	-	++
3	Roobal Behal, 2011	++	-	++	++	++	++
4	Merline K Varghese, 2014	++	-	++	++	?	?
5	V Anitha, 2015	++	-	++	++	?	++
6	Sruthima NVS Gottumukala, 2014	++	-	-	-	++	++
7	Madhu Bhatia, 2014	++	-	++	++	?	?
8	Shwetha S Hugar, 2016	++	-	++	++	?	?
9	Maha MA Nasra, 2017	++	-	++	++	?	?

DISCUSSION

Periodontitis being one of the most prevalent diseases in the world, finding an appropriate and compelling treatment for it, which has the least adverse effect to the user is of at most importance. Conventional drugs have various adverse reactions, on the contrary, curcumin/ turmeric is a herb which is abundantly available t at affordable rates which have copious medicinal value and least side effects. On that account multiple studies were conducted to determine the capability of curcumin to improve the periodontal status.

Application of curcumin is wide. It have been used as and an anti-inflammatory and anti-microbial agent, hepato-protective, anti-platelet aggregatory factor, anti-mutagenic agent, cardio-protectant and gastric treatments[10]. In dentistry, curcumin is known to have a wide range of uses, it is used as a pit and fissure sealant, plaque detecting agent, an analgesic agent, mouthwash, onco-protective and last but not the least in periodontal therapy[9, 10].

In this study, a total of 460 articles were obtained. After careful assessment 9 clinical trials were selected for further evaluation and discussion. Among the 9 articles, 8 articles backed the study.

Nagasri and Mohankumar[10] in 2015 did a randomized split-mouth study in 30 patients with a periodontal pocket depth of 5mm and above. Treatment was done in two groups a control group and the experimental group. Plaque index, Gingival Index, pocket depth and clinical attachment level were recorded. Subgingival plaque was also collected using Gracey curette and the microbial sample was stored in Tris- EDTA medium and PCR was performed later on. The results showed a superior improvement in the experimental group than that in the control group and on PCR a decrease in microbial growth count. Henceforth the study shows the therapeutic effect of turmeric in periodontitis.

In the study done by RL Ravishankar[13] conducted a single-blind randomized study to the contrast between potency of curcumin and ornidazole in its activity against periodontitis for 1 month. 20 patients were selected who were having chronic periodontitis and a pocket depth of more than 5 mm. drug placement was done by using customized acrylic stents. Both of the commercially available test gels were injected into the study site and dressing was done. Group one had curcumin treatment and groups two was treated with ornidazole. Specific instructions were given to the patients after treatment. Clinical parameters were recorded on day 1, day 30 and after 3 months. At the end of three months, a better result was shown by the curcumin group than the ornidazole group as a local drug delivery agent to improve periodontal status.

Roobal Behal and colleagues conducted a study on the potency of 2% curcumin gel as a local drug delivery agent[11] against periodontitis. 30 patients with chronic periodontitis and a pocket depth of 5-7mm were selected. Studies were done in two groups after scaling and root planing, control and experimental groups in which the latter received curcumin treatment and the pocket opening were covered by Coe-Pak to retain the material and to prevent contamination. Clinical parameters were recorded on day 1, 30 and 45. Microbiological studies were done by the collection of subgingival plaque using a sterile curette and were assessed for the presence of trypsin-like protease activity. Effective healing was observed in the experimental group at 45 days. It also showed a reduction in the trypsin-like activity of microorganisms and the material was biologically accepted with no irritation or side effects.

In the study conducted by Merline K Varghese[14], she compared and contrasted the efficiency of commercially available curcumin and metronidazole gel in treating periodontitis. A split-mouth study was conducted in 30 subjects in 2 groups of 15 with a pocket depth of 4-6mm and inflamed gingiva with bleeding on probing. One was treated with curcumin and the other with metronidazole after scaling and root planing. The drug was delivered by injection and periodontal dressing was done to prevent contamination. All clinical parameters were analyzed on day 1 and 30 and results were compared. A significant result was observed in both the groups but superior results were seen in the curcumin group. Hence curcumin being a natural agent is the better alternative.

V Anita[15] in her study of the efficacy of curcumin (250mg in 5ml of ethanol) and chlorhexidine (0.1% gel) in periodontitis, choose 30 patients with chronic periodontitis and a pocket depth of 4-6mm. A split-mouth randomized study was done in 2 groups. Both received scaling and root planing. Group 1 received subgingival curcumin and group 2 subgingival chlorhexidine over which a periodontal dressing was placed. Clinical parameters were recorded on day 1, 15 and 30. Plaque sample was collected using a Gracey curette and microbiological analysis for colony forming units was done. A notable difference was observed in both the groups showing that both the groups are equally potent. But the preference is for curcumin as it is a natural agent. A similar study was done by Shweta S Hugar[19] using 0.2% chlorhexidine gel and 2%curcumin gel in 15 patients each in 2 groups. And results were also similar to the study done by V Anita and that curcumin is better than chlorhexidine in treating mild to moderate periodontal pockets.

While Sruthima et al [16] in their study in 2014 evaluated the effectiveness of chlorhexidine chips and indigenous curcumin. 60 patients with chronic periodontitis, more than 5 mm pocket depth, and bilateral bone loss were selected and a split-mouth design study was done. Curcumin collagen sponges were prepared for this purpose. A study was done in two groups who underwent scaling and root planing. One group got curcumin treatment and the other chlorhexidine. After placement of the agent periodontal dressing was provided for a week and special instructions were given. Subgingival plaque was collected using Gracey curette for microbiological studies. Clinical parameters and the microbiological parameter for colony count in Mueller Hinton Agar, BANA were recorded at day 1, 3rd month and 6th month. Both the agents have potent anti-microbial and anti-inflammatory effects but superior effects were observed in the case of chlorhexidine. It can be due to the variations in

concentrations of both the agents used and further studies are to be done for more appropriate results.

In the study conducted by Madhu Bhatia[18] in 2014, 25 patients with chronic periodontitis with a pocket depth of more than 5 mm bilaterally and a split-mouth study was done. Scaling and root planing was done for all patients. The test sites were injected with 1% curcumin gel was given to group 1 and group 2 was a control group. Clinical parameters were measured at day 1, 3rd and 6th month. Periodontal dressing using Coe-Pak was done. Gingival plaque samples were taken for microbiological studies. On comparing the results between the two groups there was a drastic reduction in the microbial count and inflammation. Periodontal status and clinical parameters improved drastically in the curcumin group compared to the control group showing the potency of curcumin as an anti-inflammatory and anti-microbial agent and prevent recolonization of periodontal pathogens.

In 2017 Maha et al[20] did a study by formulating a curcumin gel for the treatment of periodontitis. They chose 20 patients with periodontitis having isolated pockets of more than 5mm. Carbopol-poloxamer gel of curcumin was prepared and in-vitro studies of its gelation temperature, pH, viscosity, syringeability, chemical stability, and release reactions were studied in-vitro. All the patients received scaling and root planing. The control group had only SRP while the experimental group received the curcumin preparation after SRP. Special instructions were given to them after the procedure. Clinical variables were recorded on day 1 and after 1 month. The results after a month showed notable improvement in the periodontal status and that curcumin in gel form have superior properties.

Multiple animal studies and in-vitro studies were also conducted by multiple researches to prove the efficacy of curcumin as an antimicrobial and anti-inflammatory agent and its role in inhibiting bone resorption and its role in the treatment of multiple systemic disorders. But as these articles do not come under the inclusion criteria and henceforth not discussed in detail.

CONCLUSION

Curcumin being a naturally occurring anti-microbial and anti-inflammatory agent with diverse medicinal properties. Its role in improving periodontal status was proved by various in-vitro and in-vivo studies. Its properties were found to be equally potent as that of many commercially available agents. But as curcumin is a natural substance with a few chances adverse reactions is a superior adjunct to scaling and root planing as a treatment for periodontitis.

CONFLICT OF INTEREST**:** No Conflict of interest

SOURCE OF FUNDING: Self

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