

# Evaluation of anti-inflammatory effects of systemically administered curcumin, lycopene and piperine as an adjunct to scaling and root planing: A clinical study

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## Abstract

**Background:** The natural herbal extracts curcumin (*Curcuma longa*), lycopene and piperine demonstrated a very potent anti-inflammatory action and can be used as an antioxidant therapy in the management of inflammatory processes such as gingivitis and periodontitis. **Aim and Objective:** The aim of the present study is to evaluate the effects of systemically administered extracts curcumin, lycopene and piperine as an adjunct to scaling and root planing (SRP) in patients with moderate gingivitis. **Materials and Methods:** Sixty systemically healthy participants with moderate gingivitis were enrolled in a randomized clinical study. Participants were randomly distributed into two treatment groups: Group I (test group) (350 mg/day antioxidant therapy) along with SRP for 3 weeks and Group II (control group) SRP alone. Clinical parameters such as plaque index, gingival index and probing pocket depth were evaluated at baseline and after 21 days using paired *t*-test. **Results:** Both the treatment groups showed statistically significant reduction in clinical parameters, but the test group showed greater reduction as compared to control group ( $P < 0.05$ ). **Conclusion:** The results concluded that systemically administered antioxidants could cause better resolution of inflammation when used as an adjunct to SRP.

**Keywords:** Antioxidant therapy, curcumin, gingivitis, inflammation, lycopene, piperine

## Introduction

Periodontitis is an inflammatory process leading to periodontal attachment and bone loss initiated by plaque biofilm and products leading to tooth loss. Majority of the periodontal treatment modalities try to halt the advancement of periodontal destruction.<sup>[1]</sup> But even with application of appropriate periodontal modalities, there are some conditions or situations which remain unaffected. Although balanced nutrition and supplementation have emerged to be an important part of periodontal research, their role has not been thoroughly evaluated.<sup>[2]</sup> Hence, the factors which respond to the periodontal treatment therapy need to be recognized.

Various pro-inflammatory mediators such as interleukin-1 (IL-1), IL-6, PGE2 and tumor necrosis factor alpha, ions and reactive oxygen species (ROS) are produced from the inflamed periodontal tissues. The free radicals which have a very important role in diabetes, aging have led to a medical upheaval which includes antioxidants, that is, a rising new

standard of oral health care. These antioxidants scavenge the free radicals and prevent the damage caused by them hence acting as a remedial and prophylactic agents.<sup>[3]</sup>

Periodontal pathogens, despite having an important role in destroying periodontal tissue, also act as a risk factor for heart diseases, lung diseases and diabetes etc. Therefore, the antioxidant status should be evaluated to address the host resistance as these influences the extent of gingival and periodontal destruction. The nutritional counseling and supplementation should be an important part of periodontal protocol to enhance the outcome of conventional periodontal therapy.<sup>[2]</sup>

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Lycopene is one of the most effective antioxidants found in tomatoes and has a singlet oxygen quenching ability which provides prevention against various chronic disorders.<sup>[3]</sup> Rhizomes of the plant *Curcuma longa* Linn. contain curcumin which is a yellow colored phenolic pigment and has a very potent anti-inflammatory action due to oxygen radical scavenging activity and uncoupling of oxidative phosphorylation. Wide-ranging scientific research has confirmed a wide gamut of therapeutic effects such as anti-inflammatory, antifungal, antibacterial and antitumor in the dose range of 200 mg/kg body weight with negligible effects on human systems.<sup>[4]</sup> Similarly, *Piper nigrum* (black pepper) contains an alkaloid piperine which has a very high medicinal value due to its anti-inflammatory effect. Its main role is to enhance the bioavailability of various therapeutic agents such as curcumin and lycopene as it inhibits their hepatic and intestinal glucuronidation.<sup>[5]</sup> In humans, concomitant administration of piperine (20 mg) produces much higher concentrations of curcumin administered 1-h postdrug and its bioavailability increases by 2000%. Piperine enhances the serum concentrations, extent of absorption and bioavailability of curcumin in both rats and humans with no undesirable effects.<sup>[6]</sup>

The aim of the present study is to evaluate the effects of systemically administered curcumin, piperine and lycopene as an adjunct to scaling and root planing (SRP) in patients with moderate gingivitis.

## Study design

### Subjects

This study was conducted on 60 participants with chronic generalized gingivitis aged between 18 and 55 years attending the Department of Periodontics, Sri Guru Ram Das Institute of Dental Sciences and Research, Amritsar, Punjab. The participants included in the study were in good general health and met the following criteria:

- Systemically healthy participants
- Minimum of 20 natural teeth
- Age group between 18 to 55 years
- Moderately/severely inflamed gingiva with swollen gums which bleed on probing.

### Exclusion criteria

1. Any systemic disease such as diabetes, cardiovascular diseases and renal diseases
2. Pregnant or lactating women
3. Individuals with history of consumption of antibiotic therapy within previous 6 months
4. History of consumption of anti-inflammatory drugs within the previous 3 months.

### Design

The selected participants were divided into two groups:

- Group I: 30 participants having chronic generalized gingivitis treated with SRP alone
- Group II: 30 participants having chronic generalized gingivitis treated with SRP along with 350 mg (curcumin

300 mg, piperine 5 mg and lycopene 10 mg) given for 21 days twice a day.

The antioxidant therapy was given systemically in the dosage of 350 mg over 3 weeks. Each capsule was composed of curcumin, piperine and lycopene.

### Clinical parameters

The clinical parameters evaluated were:

1. Plaque index (PI) (Silness and Loe, 1964)
2. Gingival index (GI) (Loe and Silness, 1963) and
3. Probing pocket depth (PPD).

PPD was measured with Williams probe and acrylic stent as a guide for reproducibility from the gingival margin to base of the pocket.

The proposed study was reviewed by the ethic committee of the institution and clearance was obtained. Informed consent was obtained from each participant before conducting the trial. The procedures followed were in accordance with the Helsinki Declaration of 2000.

### Statistical analysis

Statistical analysis for the post treatment changes in various clinical parameters was performed at baseline and by paired *t*-test and *P* < 0.05 was considered as statistical significant difference.

## Results

Sixty participants with chronic generalized gingivitis were included in this study. Intergroup comparison of clinical parameters at baseline and 21 days was recorded using paired *t*-test.

The mean score of PI for patients of Group I (gingivitis patients treated with SRP alone) was  $1.52 \pm 0.20$  at baseline and  $0.93 \pm 0.21$  at 3<sup>rd</sup> week and for GI, it was  $1.71 \pm 0.25$  at baseline and  $0.95 \pm 0.20$  at 3 weeks. Probing depth (PPD) mean score at baseline was  $1.84 \pm 0.22$  and it reduced to  $1.50 \pm 0.15$  at 3<sup>rd</sup> week [Tables 1 and 2].

The mean score of PI for patients of Group II (gingivitis patients treated with SRP and antioxidant therapy) was

**Table 1: Comparison of plaque index, gingival index, probing depth of test and control group**

Parameter	Test group	Control group	<i>t</i>	<i>P</i>
Baseline	Mean±SD	Mean±SD		
Age	25.76±6.57	29.86±8.04	2.161	0.035
PI-0	1.38±0.27	1.52±0.20	2.282	0.026
GI-0	1.73±0.28	1.71±0.25	0.292	0.771
PD-0	1.74±0.22	1.84±0.22	1.742	0.087
After 3 <sup>rd</sup> week				
PI-3	0.74±0.17	0.93±0.21	3.867	0.000
GI-3	0.77±0.23	0.95±0.20	3.109	0.003
PD-3	1.25±0.15	1.50±0.15	6.394	0.000

*P* < 0.05 (significant), PI: Plaque index, GI: Gingival index, PD: Probing depth. Paired *t* test

**Table 2: Comparison of percentage between test and control group reduction in plaque index, gingival index, and probing depth at baseline and 3 weeks**

Test group	Baseline	3 weeks	Reduction	Percentage reduction	<i>t</i>	<i>P</i>
PI	1.38±0.27	0.74±0.17	0.64±0.20	45.99±9.58	17.743	0.000
GI	1.73±0.28	0.77±0.23	0.95±0.13	55.77±6.89	41.702	0.000
PD	1.74±0.22	1.25±0.15	0.49±0.10	27.95±3.43	26.978	0.000
Control group	Baseline	3 weeks	Reduction	Percentage reduction	<i>t</i>	<i>P</i>
PI	1.52±0.20	0.93±0.21	0.59±0.14	39.09±9.49	22.337	0.000
GI	1.71±0.25	0.95±0.20	0.76±0.10	44.70±5.95	42.663	0.000
PD	1.84±0.22	1.50±0.15	0.34±0.10	18.36±3.91	18.082	0.000

*P*<0.05 (significant). PI: Plaque index, GI: Gingival index, PD: Probing depth

1.38 ± 0.27 at baseline and 0.74 ± 0.17 at 3<sup>rd</sup> week. For GI, the values for mean score were 1.73 ± 0.28 at baseline and 0.77 ± 23 at 3 weeks. In this group, PPD score reduced from 1.74 ± 0.22 to 1.25 ± 0.15 at 3<sup>rd</sup> week [Tables 1 and 2].

On comparison between Group I and II using paired *t*-test, statistically significant difference was observed in all the parameters with highly significant reduction in GI (*P* < 0.003) at 3<sup>rd</sup> week.

## Discussion

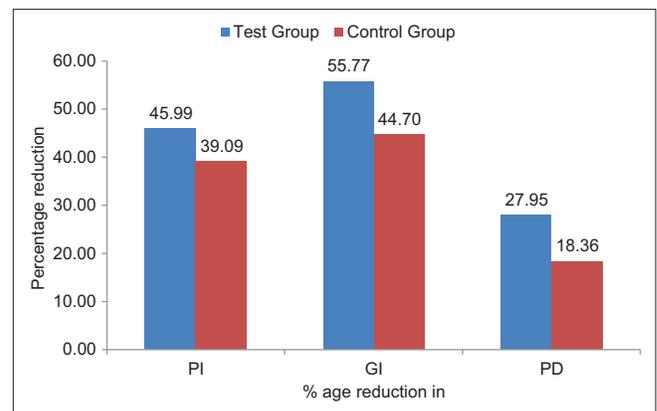
The effect of metabolic ROS cannot be overlooked in the multitude of various mechanisms which lead to the destruction of gingival and periodontal tissues.<sup>[7]</sup> The healthy gingival connective tissue and epithelium demonstrate polymorphonuclear leukocytes (PMNLs) as predominant cells (96%) and the presence of periodontopathic bacteria functionally activates PMNLs leading to increased production of ROS. Chronic inflammation subjects the nearby cells to increased levels of ROS due to extracellular release from phagocytic cells.<sup>[8]</sup> In order to study the damaging effect of ROS and the antioxidant protection against bacterial action, the periodontal and gingival tissues provide the principle environment.<sup>[7]</sup> Hence, the periodontal diseases can be treated by various researchers by including antioxidant therapy as a part of periodontal protocol.

In this context, the present study has evaluated the effects of systemically administered extracts of curcumin, piperine and lycopene as an adjunct to SRP in patients with moderate gingivitis.

In the current study, on intergroup comparison, PI, GI and bleeding scores between the test and the control groups showed statistically significant results at 21<sup>st</sup> day interval. Furthermore, mean significant percentage reduction of scores was found in both the groups with greater reduction in test group [Graph 1].

Curcumin exerts a very potent anti-inflammatory,<sup>[9,10]</sup> antibacterial<sup>[11]</sup> and antioxidant<sup>[12]</sup> effect which leads to reduction in bleeding on probing and redness via:

- Reduction of the inflammatory mediators generated through arachidonic acid metabolite pathway. It causes nuclear factor kappa B (NF-κB) activation<sup>[13-15]</sup> inhibition



**Graph 1:** Comparison of percentage reduction in plaque index, gingival index, and probing depth in Group 1 and 2. *P* < 0.05 (significant)

and pro-inflammatory enzyme cyclooxygenase-2<sup>[14,15]</sup> downregulation

- The vascularization by fibrosis of the connective tissue<sup>[16]</sup> occurs by promotion of migration of various cells including fibroblasts in wound bed. This enhances wound healing by causing an increase in the number of fibroblasts<sup>[17]</sup> leading to greater reduction in PPD in test group.

Behal *et al.*<sup>[18]</sup> concluded that the experimental local drug-delivery system containing 2% whole turmeric gel can be used as an adjunct to SRP as it helps in reduction of pocket depth and gain of clinical attachment.

Gottumukkala *et al.*<sup>[19]</sup> studied the effectiveness of subgingival irrigation of indigenous 1% curcumin solution and concluded mild-to-moderate beneficiary effect of curcumin irrigation when used as an adjunct to SRP.

Muglikar *et al.*<sup>[20]</sup> studied the efficacy of curcumin mouthwash as an adjunct to SRP in the treatment of chronic gingivitis and to compare chlorhexidine in terms of its anti-inflammatory and antimicrobial properties. They concluded that curcumin is comparable to chlorhexidine as an anti-inflammatory mouthwash and it is an effective adjunct to mechanical periodontal therapy.

Curcumin has shown to effectively inhibit cytokine gene expression at mRNA and protein levels and NF-κB is inhibited

only with the lower dose of curcumin with significant reduction of the inflammatory infiltrate and increased collagen content and fibroblastic cell numbers which could explain the reduction in PPD along with bleeding on probing in the participants.<sup>[21]</sup>

Elburki *et al.*<sup>[21]</sup> have shown that a novel chemically modified curcumin reduces the severity of experimental periodontal disease in rats.

Lycopene is one of the most effective antioxidants found in tomatoes and has a singlet oxygen quenching ability which provides prevention against various chronic disorders.<sup>[3]</sup> It has been classified to the class of compounds known as carotenoids which are the yellow, orange and red pigments produced by plants.<sup>[22]</sup>

Lycopene has the exceptional feature of binding to chemical species that react with oxygen, thus being the most competent biological antioxidantizing agent.<sup>[23]</sup>

Di Mascio *et al.*<sup>[24]</sup> showed that lycopene is the most efficient biological carotenoid singlet oxygen quencher.

Chandra *et al.*<sup>[7]</sup> and Arora *et al.*<sup>[25]</sup> concluded in their studies that systemic lycopene and oral prophylaxis showed statistically significant reduction in GI, compared to placebo oral prophylaxis group. In both the studies, patients were followed up for 2 weeks in gingivitis patients and 2 months in chronic periodontitis patients respectively.

Piperine acts by inhibiting or quenching free radicals and ROS. It also enhances the bioavailability of various therapeutic agents such as curcumin and lycopene as it inhibits their hepatic and intestinal glucuronidation.<sup>[5]</sup>

Shoba *et al.*<sup>[6]</sup> evaluated the bioavailability of curcumin in rats and healthy human volunteers. When curcumin was given alone, in the dose 2 g/kg to rats, moderate serum concentrations were achieved over a period of 4 h. Concomitant administration of piperine 20 mg/kg increased the serum concentration of curcumin for a short period of 1–2 h postdrug without any undesirable effect. Hence, the synergistic effect of curcumin and piperine enhances the reduction in clinical parameters.

## Conclusion

The antioxidant therapy has emerged as an important part of conventional periodontal therapy. Diet low in antioxidants predispose an individual at increased risk of developing gum disease as well as destruction of periodontal tissue. Hence, the antioxidant status needs to be evaluated along with the periodontal protocols. Nutritional supplementation and balanced diet should be an integral part of periodontal research as well as treatment protocol to enhance the outcome of conventional periodontal therapy.

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## Conflicts of interest

There are no conflicts of interest.

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