Original Article

# Anti-Inflammatory Effect of Local Application of Curcuma Gel in Patients of Chronic Periodontitis



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## ABSTRACT

**Objective:** To determine the anti-inflammatory effects of oral curcuma gel on salivary calprotectin level in patients of chronic periodontitis.

**Study Design:** Randomized controlled clinical trial study.

**Place and Duration of Study:** This study was conducted at the Department of Periodontology, de' Montmorency College of Dentistry (Punjab Dental Hospital) Lahore from February 2019 to August 2019.

**Materials and Methods:** In this experimental study 15 patients were selected having chronic periodontitis and pocket depth 3-7mm. Subgingival ultrasonic scaling was done of patients at day 0 after collection of saliva and Pocket depth (PD) measurement. Patients were instructed to apply c*urcuma* oral gel (each gram containing 10 mg of curcuma longa extract and glycerol is used as a vehicle), twice a day for three weeks after brushing. Pocket depth (PD) measured and saliva was collected 3 times during the study – Day 0, Day 10 and at day 21 with ±2 days of arrival. The calprotectin levels will be measured in saliva and compared each time by ELISA technique according to manufacturer's instructions.

**Results:** In this study, curcuma oral gel treatment proves to be effective in terms of PD measured and calprotectin levels in saliva. Marked reduction in PD from 5.27±0.78 at day 0 to 3.17±0.41 at day 21 has been measured having p-value < 0.001. Mean calprotectin level at day 0 is 3.75±0.64 and at day 21 is 1.67±0.32.

**Conclusion:** This study shows effectiveness of curcumin in curing periodontitis by reducing proteomes present in saliva. The anti-inflammatory action of Curcuma gel topical application is proved clinically by the values of PD measured and biochemically by reduction in salivary calprotectin level.


**Key Words:** Saliva, Calprotectin level, Periodontitis, Curcuma gel

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## INTRODUCTION

The periodontium means supporting tissues of teeth and inflammation of these tissues is called periodontitis.[1] Periodontitis is a bacterially induced inflammation of periodontal tissues which leads to shrinkage of gums and loosening of teeth.[2]

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Chronic periodontitis (CP) is the most common periodontal disease consisting of chronic inflammation of periodontal tissues. It leads to the destruction of connective tissue (ginigivae, periodontal ligaments) and loss of the adjacent supporting bone.[3]Clinical attachment loss (CAL) of ≥5 mm is characterized as severe chronic periodontitis (SP).[4]

The major categories of saliva available are whole saliva and cell free saliva.[5] Whole saliva can be stimulated or unstimulated. The salivary flow of unstimulated saliva ranges from 0.3 to 0.4 mL/min.[6]Saliva is said as "the mirror image of blood" for diagnosing various diseases.[7] Numerous studies have emphasized on role of salivary biomarkers for diagnosing and foretelling periodontal disease advancement.[8,9]

The proteome is the protein complement of the genome, and proteomics is the study of its analysis.[10] Calprotectin is a 36-kDa glycoprotein of lipocalin family. Hetrodimercal protect in is formed by S100A8 and S100A9.[11]Calprotectin is found in the cytoplasm of neutrophils (representing 60% of cytosolic proteins) and macrophages.[12] and is a protein secreted from neutrophils during cell death and is linked with

innumerable autoimmune and inflammatory diseases like periodontitis.[13]

Turmeric (haldi) is a rhizome of Curcuma longa. Curcuminoids are a leading chemical element of turmeric including bisdemethoxycurcumin, demethoxycurcumin, and CUR.[14]Curcumin has prominent pleiotropic effects e.g. anti-inflammatory, anti-oxidation, and anti-tumor effects.[15]Curcumin is analogous to phenylbutazone, a well-known anti-inflammatory agent.[12] Curcumin causes inhibition of COX-1 and COX-2 to prevent production of prostaglandin E2 and 5-Hydroxyeicosatetrainoic acid (5-HETE).[16]

In 1937, first article was published on the use of curcumin in human disease.[17] The acceptable daily intake of curcuminoids by WHO and food and drug administration (FDA) is 0-3 mg/kg.[18]Turmeric has wide span of pharmacological actions such as antioxidant, anti-protozoal, anti-venom activities, anti-microbial, anti- fungal, anti-malarial, anti-viral, wound healing, anti-inflammatory, anti-proliferative, anti-dysenteric for children, anti-angiogenic, anti-tumor and anti-aging properties.[19]

Curcumin solution has a role as a sub gingival irrigation[20], as an ointment for oral submucous fibrosis, leukoplakia, and lichen planus.[21] Turmeric extract along with polymerizable resin can be applied as a pit and fissure sealant. Turmeric in mouthwash form was used by Bhandari and Shankwalkar, 1980.[22]Antimicrobial activity of turmeric was observed by Hamedet al.[23] and Munet al.[24]

The purpose of this study is to investigate the anti-inflammatory effect of oral curcuma gel in patients of chronic periodontitis by focusing on (MRP)8/14 (calprotectin) as an inflammatory marker and to co-relate the change in the level of this marker and that of PD (a known inflammatory clinical indicator).

# MATERIALS AND METHODS

In this randomized controlled clinical trial was carried out at Department of Periodontology, de' Montmorency College of Dentistry (Punjab Dental Hospital) Lahore from 2nd February 2019 to 5th August 2019. A total of 15 subjects of either sex with age range 20-40 years were selected.

**Pre-treatment assessment:** Patients were examined using a mouth mirror, explorer, William's graduated periodontal probe, tweezers and the related data was recorded in a patient Performa sheet.[25] At day 0 before starting ultrasonic scaling whole unstimulated salivary sample was collected in 15 ml test tube from both study and control groups. Subjects were asked not to eat, drink or smoke for at least 1 hour before saliva collection. Salivary calprotectin levels were measured by enzyme-linked-immunosorbent using a commercial Cal ELISA kit of GLORY Science USA. The ELISA procedure was performed according to the manufacturer's instructions. After undergoing ultrasonic scaling at day 0, patients were instructed to apply oral curcuma gel (each gram containing 10 mg of curcuma longa extract) with cotton buds on their gingivae in the whole oral cavity, twice a day for three weeks after brushing.[26] They were asked to leave the gel in place for at least 10 minutes and then rinse with water. Saliva was processed and PD was measured by William's graduated periodontal probe 3 times during the study – Day 0, Day 10 and at day 21 with ±2 days of arrival. The calprotectin levels were measured and compared each time by ELISA technique according to manufacturer's instructions.

**Post–treatment assessment:** Patients were examined using a mouth mirror and William's graduated periodontal probe to record PD at day 10 and day 21 in department of Periodontology, Punjab Dental Hospital Lahore. About 5ml of unstimulated saliva sample was collected in test tubes for assessment of calprotectin level by ELISA technique (Figs. 1-2). The data was entered and analyzed through SPSS-22.

# RESULTS

Repeated measures analysis of variance test revealed that mean Calprotectin levels differed statistically significant among different days (Table 1). Post hoc test using Bonferroni correction showed that the mean Calprotectin level at day 0 was significantly higher as compared to day 10 and 21. Similarly there was significant difference between day 10 and day 21 levels (Table 2).

**Table No.1: Comparison of Calprotectin levels (µg/L) among different days**

| Day | Mean±SD | Minimum | Maximum | p-value* |
|---|---|---|---|---|
| 0 | 3.75±0.64 | 2.47 | 4.72 | < 0.001 |
| 10 | 2.18±0.41 | 1.53 | 2.90 | |
| 21 | 1.67±0.32 | 1.17 | 2.15 | |

*Repeated measures ANOVA

**Table No.2: Pair wise comparison among days**

| Days | | Mean difference (µg/L) | Std. Error | P value |
|---|---|---|---|---|
| 0 | 10 | 1.577* | 0.139 | < 0.001 |
| | 21 | 2.081* | 0.145 | < 0.001 |
| 10 | 21 | 0.504* | 0.087 | < 0.001 |

**Table No.3: Showing comparison of the pocket depth levels among different days**

| Day | Mean±SD | Minimum | Maximum | p-value* |
|---|---|---|---|---|
| 0 | 5.27±0.78 | 4.00 | 6.50 | < 0.001 |
| 10 | 4.30±0.59 | 3.50 | 5.00 | |
| 21 | 3.17±0.41 | 2.50 | 4.00 | |

*Repeated measures ANOVA

**Table No.4: Detailed pair wise comparison among days**

| Days | | Mean difference (µg/L) | Std. Error | P value |
|---|---|---|---|---|
| 0 | 10 | 0.967* | 0.114 | < 0.001 |
| | 21 | 2.100* | 0.131 | < 0.001 |
| 10 | 21 | 1.133* | 0.103 | < 0.001 |

**Table No.5: Correlation of Calprotectin with Pocket depth**

| | |
|---|---|
| **Correlation at day 0** | |
| Correlation Coefficient | 0.629 |
| p-value | 0.012 ***** |
| **Correlation at day 10** | |
| Correlation Coefficient | 0.392 |
| p-value | 0.148 |
| **Correlation at day 21** | |
| Correlation Coefficient | 0.513 |
| p-value | 0.050* |

*p-value ≤ 0.05 is considered statistically significant.

Repeated measures analysis of variance test revealed that mean pocket depth differed statistically significant among different days, p <0.05 (Table 3). The results showed statistically significant reduction in pocket depths at day 10 and 21 compared to baseline values at day 0 (p <0.05). There was also significant improvement in pocket depths at day 21 compared to day 10 (p <0.05) [Table 4]. Table 5 shows correlation of Calprotectin levels with pocket depth. The correlation between Calprotectin levels and pocket depth was strong positive at day 0 and day 21 and they were significant.

# DISCUSSION

The current study was a multi-center, randomized, controlled clinical study. The results depicted the effects of curcumin on inflammatory marker (Calprotectin) and clinical marker (PD) in chronic periodontitis patients.

Study by Panov et al[13] reported that salivary calprotectin level and gingival inflammation both were decreased after azithromycin treatment 500mg/day for 4 days in chronic periodontitis patients. In the present study significant reduction in calprotectin level from 3.75±0.64 at day 0 to 1.67±0.32 at day 21 (Table 1) was observed after application of curcuma gel for 21 days consecutively.

Ravi Shankar et al[25] compared topical application of curcuma gel and reduction in PD (3.35±0.70 mm) to ornidazole group (5.07±1.003 mm). Curcumin has both antimicrobial and anti-inflammatory effects. It is in accordance with the present study where there is marked reduction in PD from 0 to 21 days i.e. 5.27 to 3.17 mm after curcuma gel therapy (Table 3).

Behal et al[26] evaluated the effects of LDD system containing 2% turmeric gel as an adjunct to scaling and root planning in chronic periodontitis. The study concluded that investigational drug used along with SRP was effective in removing the local irritants, reducing gingival inflammation, reducing PD and gain in clinical attachment level. PD was reduced from 5.72 at day 0 to 4.317 mm at day 45. Similar study conducted by Farjana et al.[24] to evaluate the anti-inflammatory effects of topical application of curcuma gel in gingivitis management. There was reported significant reduction in bleeding on probing on day 21. In the present study that reduction in inflammation was recorded as reduction in calprotectin levels in saliva. The salivary calprotectin level lowered and PD reduced as inflammation was reduced by application of oral curcuma gel (Table 5).

In the study by Kido et al.[27] there is a marked correlation in the GCF calprotectin levels and the concentrations of other biochemical markers (IL-1b and PGE2). Calprotectin was also found related with clinical indicators of periodontal inflammation. It was reported that calprotectin is present in dental calculus and inflammatory exudate of chronic periodontitis patients.[28] Porphyromonas gingival lipopolysaccharide is found to encourage the release of calprotectin from neutrophils and monocytes.[26]Currentlywe are investigating calprotectin as a marker of extent and progression of disease activity in patients of chronic periodontitis.

# CONCLUSION

This study shows effectiveness of curcumin in curing periodontitis by reducing proteomes present in saliva. The anti-inflammatory action of Curcuma gel topical application is proved clinically by the values of PD measured and biochemically by reduction in salivary calprotectin level. The use of curcumin topical application could be beneficial in the treatment of chronic periodontitis patients. Further long term clinical trials are needed to evaluate the effect of curcumin on periodontitis patients.

**Author's Contribution:**

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|---|---|
| Concept & Design of Study: | Iqra Amin |
| Drafting: | Asrar Ahmed, Amna Amanat |
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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