Clinical and antioxidant efficacy of 4% mangosteen gel as a local drug delivery in the treatment of chronic periodontitis: A placebo-controlled, split-mouth trial

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Dental and Medical Problems, ISSN 1644-387X (print), ISSN 2300-9020 (online) *Dent Med Probl.* 2022;59(1):111–119

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Funding sources
None declared

Conflict of interest
None declared

Acknowledgements
The authors would like to acknowledge Professor Thimmasetty Jutur, the Head of the Department of Pharmaceutics at Bapuji Pharmacy College, Davangere, India, for his assistance in the preparation of the mangosteen gel, Mr. Varun Eranna from the Research Faculty of the University of Trans-Disciplinary Health Sciences and Technology, Bangalore, India, as well as the participants of the clinical trial.

Received on April 20, 2021
Reviewed on June 17, 2021
Accepted on June 21, 2021

Published online on March 31, 2022

Cite as
Manjunatha VA, Vemanaradhya GG, Gowda TM. Clinical and antioxidant efficacy of 4% mangosteen gel as a local drug delivery in the treatment of chronic periodontitis: A placebo-controlled, split-mouth trial. *Dent Med Probl.* 2022;59(1):111–119. doi:10.17219/dmp/139198

DOI
10.17219/dmp/139198

Abstract

Background. Currently, the knowledge on the clinical effect of 4% mangosteen gel as a local drug delivery, adjunctive to non-surgical periodontal therapy, on the gingival crevicular fluid (GCF) total antioxidant capacity (TAOC) levels in chronic periodontitis patients is limited.

Objectives. The aim of the study was to evaluate and compare the efficacy of 4% mangosteen gel and a placebo gel as an adjunct to scaling and root planing (SRP) on clinical and biochemical parameters in chronic periodontitis patients.

Material and methods. A total of 50 test sites from 25 patients with Stage II Grade B periodontitis were randomly divided into 2 groups. The experimental group was treated with SRP followed by a single subgingival application of 4% mangosteen gel, while the control group was treated with SRP followed by a single subgingival application of a placebo gel. Clinical parameters, including the plaque index (PI), the gingival bleeding index (GBI), the probing depth (PD), the relative attachment level (RAL), as well as biochemical parameters, i.e., the GCF TAOC levels, were evaluated using an ABTS (2,2'-Azino-bis-3-ethylbenzothiazoline-6-sulfonic acid) antioxidant assay kit at baseline (D0) and at 3 months (D3).

Results. The full-mouth PI and GBI values were significantly lower at D3 in comparison with D3. The experimental sites showed a significantly greater reduction in the PD and RAL scores as compared to control, and the GCF TAOC levels revealed a substantial rise throughout the study period, reversing from negative values at D0 to positive values at D3 in the experimental group.

Conclusions. Traditional SRP with the adjunctive local delivery of 4% mangosteen gel demonstrated an added benefit in improving clinical and biochemical parameters, and thereby encouraging the use of the mangosteen gel in clinical practice for the management of moderate chronic periodontitis.

Keywords: periodontitis, mangosteen, root planing, scaling

Introduction

One of the primary etiological factors for periodontitis is a microbial shift, which is always associated with a reduction in the number of beneficial symbionts and/or a rise in the number of pathogenic microorganisms in the ecosystem of the subgingival biofilm.[1] These pathogens disrupt the interaction between the host and the oral microbiome, eventually favoring the onset and progression of periodontal disease. Various cytokines, such as interleukin 8 (IL-8) and tumor necrosis factor alpha (TNF-α), are produced by pathogenic Gram-negative, anaerobic or facultative bacteria within the subgingival biofilm, further causing a surge in polymorphonucleocyte (PMN) activity as part of the primary immune response.[1,2]

Polymorphonucleocytes fight against microbes through the release of enzymes that are involved in the breakdown of proteins into smaller polypeptides or amino acids (proteolysis), as well as free radicals or reactive oxygen species (ROS) by an aerophilous surge. In order to maintain a homeostatic environment or to suppress the pathogenicity of microorganisms, ROS are detoxified and modified by the antioxidant system to form less reactive species.[1–3]

The traditional non-surgical periodontal therapy includes mechanical debridement by scaling and root planing (SRP). However, the efficacy of this treatment is limited due to inaccessibility in areas such as furcations, grooves, concavities, and deep periodontal pockets.[3–5]

To overcome this limitation, the local drug delivery (LDD) has been introduced. It has gained a lot of popularity due to certain advantages, such as a high and sustained local concentration of the drug without applying large doses, thus minimizing toxicity in comparison with systemic therapy.[6] Although various agents are being utilized as LDD, the need for more biocompatible and economical agents has consistently inspired clinicians to move toward herbal substances.

Pharmacologically active phytochemicals obtained from plants have been widely identified as useful aids for the prevention, treatment and maintenance therapy of periodontal disease.[7] *Garcinia mangostana*, commonly referred to as mangosteen, also known as "the queen of fruits", belongs to the *Guttiferae* family. It contains diverse bioactive compounds, such as camphene, garcinones A, B and C, sesquiterpenoids, gartanin, and tannins. The significant characteristics of mangosteen include antioxidant, antimicrobial and anti-inflammatory properties.[8–12]

The LLD of the mangosteen gel following SRP has been shown to result in large decreases in the probing depth (PD), gingival index (GI) and gingival bleeding index (GBI) values, as well as improvement in clinical epithelial attachment in chronic periodontitis patients.[9–12]

Total antioxidant capacity (TAOC) is the degree of the magnitude of free radicals rummaged by a test solution, expressed as percentage and used to gauge the antioxidant capacity of a biological medium, like saliva, serum and gingival crevicular fluid (GCF).[1,2]

Gingival crevicular fluid is considered the most appropriate medium for investigating inflammatory biomarkers to evaluate oxidative stress in the supporting tissues of the periodontium.[1,2,13] Previous studies have shown improvement in the periodontal status and the GCF TAOC levels in adult periodontitis patients, following non-surgical periodontal therapy alone.[13] So far, only the antimicrobial potential of the mangosteen pericarp gel has been explicitly assessed, but its antioxidant impact in the treatment of chronic periodontitis has not been estimated. Hence, the aim of this study was to evaluate and compare the efficacy of the LDD of 4% mangosteen gel as an adjunct to non-surgical periodontal therapy on the GCF TAOC levels and clinical parameters in patients with chronic periodontitis.

Material and methods

Preliminary plan and moral statement

This clinico-biochemical study was carried out as a prospective, double-blinded, randomized, controlled, split-mouth trial. It was approved by the institutional review board (IRB) at Bapuji Dental College and Hospital, Davangere, India (No. BDCH/Exam 467/2018–2019). The study was performed in compliance with the ethical standards established by the World Medical Association (WMA) in the Declaration of Helsinki. Each patient was given a detailed verbal and written description of the study, and a signed consent form was obtained. The flow chart of the study design is presented in Fig. 1.

The split-mouth design and randomization were used in the present study to avoid inter-subject variability and bias. The selection of the test sites for both groups was also standardized at baseline to ensure reliable results.

Inclusion and exclusion criteria[13]

The patients were designated from the ambulatory care unit, Department of Periodontology, Bapuji Dental College and Hospital, according to the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. Patients within the age range of 35–60 years for both genders, with Stage II Grade B periodontitis (moderate periodontitis) were included. Patients having a minimum of 2 sites with PD ≤ 5 mm and clinical attachment loss (CAL) ≤4 mm with horizontal bone loss at 2 different quadrants, and requiring non-surgical treatment were considered as eligible for the study.

Patients with habits, like smoking, tobacco chewing or alcohol consumption, having uncontrolled diabetes, hypertension or immunocompromised conditions, pregnant women or lactating mothers, non-compliant or physically challenged people, and those who were not able to maintain oral hygiene or be followed up at a recall visit were excluded from the study.

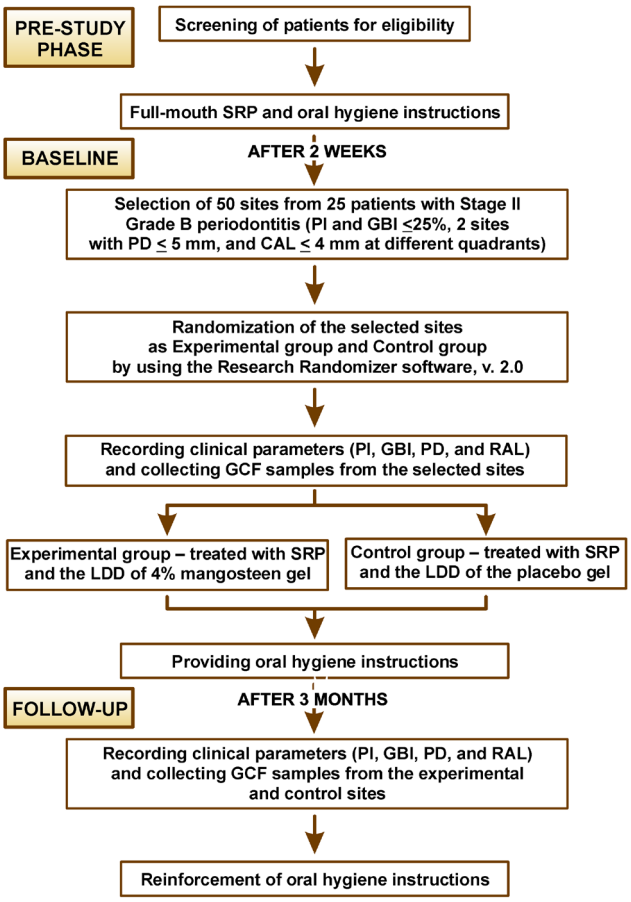

Fig. 1. Study design

SRP – scaling and root planing; PI – plaque index; GBI – gingival bleeding index; PD – probing depth; CAL – clinical attachment loss; RAL – relative attachment level; GCF – gingival crevicular fluid; LDD – local drug delivery.

Sample size calculation[14]

The sample size was calculated using the following equation (Equation 1):

$$N = \left[\frac{Z_1 - \alpha/2 + Z_1 - \beta}{\mu_A - \mu_B} \right]^2 \quad (1)$$

where:
N – sample size;
Z_1 – Z-value;
α – level of significance;
β – level of power;
$\mu_A - \mu_B$ – mean difference between the samples.

As per the calculation, at least 40 sites were needed to provide a power of 80% and to detect differences in the mean PD values between 2 study groups by the end of a 3-month period. A total of 50 sites were recruited to compensate for a 20% dropout rate.

Estimation of clinical parameters

Following the initial screening, supragingival full-mouth SRP was performed in all patients. After 2 weeks, only 25 patients who fulfilled the inclusion and exclusion criteria, with the full-mouth PI and GBI values ≤25% were selected. Both at baseline (D0) and at 3 months after treatment (D3), the PI,[15] GBI,[16] PD, and RAL values were recorded, and GCF samples were collected for the evaluation of the TAOC levels by a blinded examiner.

Randomization

The selected 50 sites from 25 patients were randomly assigned by means of the Research Randomizer software, v. 2.0 (https://www.randomizer.org/).

Groups

The selected sites for each group were managed with the allocated treatment plan by a qualified clinician. The control group sites were treated with SRP followed by a single application of the placebo gel. The experimental group sites were treated with SRP followed by a single application of 4% mangosteen gel.

Preparation of 4% *Garcinia mangostana* gel and the placebo gel

Pure mangosteen powder was obtained from Tamil Nadu Agricultural University, Coimbatore, India. The 4% mangosteen gel was made in the proportions presented by Rassameemasmaung et al.[11]

The concentration of the gel was adjusted according to the data obtained from a study by Mahendra et al.[9] A homogenizer was used for homogenizing all ingredients to produce the gel (Fig. 2). The placebo gel was prepared in the same manner, excluding the active ingredient (the mangosteen powder) and maintaining the same physical properties, such as color and taste (Fig. 3). Both 4% mangosteen gel and the placebo gel were preserved at 4°C during the course of the study.[9]

Collection of GCF samples[13]

After isolating the designated teeth, a standardized measure of 5 µL GCF from each test site was collected by placing calibrated, black color-coded 1–5-microliter volumetric microcapillary pipettes (Sigma-Aldrich, Burlington, USA) with the use of the extracrevicular (unstimulated) method. The collected GCF samples were moved to sterile Eppendorf tubes with 50 µL of alkaline phosphate buffered saline (PBS) and tagged according to the tooth number assigned to the chosen test group. Then, they were sealed firmly and immediately transported to the research laboratory, where they were stored at –80°C till the time of assay.

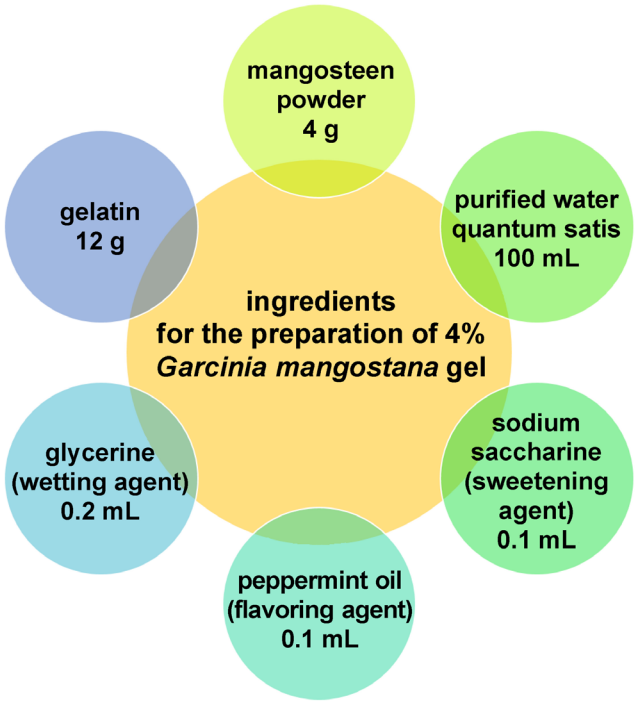

Fig. 2. Ingredients for the preparation of 4% mangosteen gel

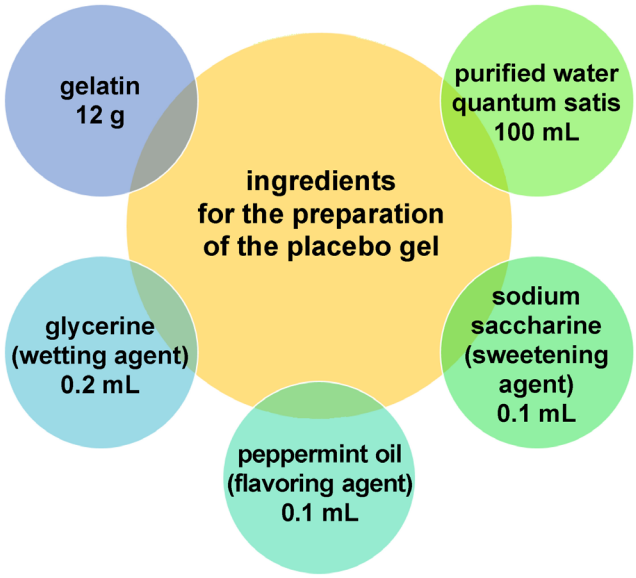

Fig. 3. Ingredients for the preparation of the placebo gel

Scaling and root planing protocol[13]

All the selected patients underwent thorough subgingival SRP with the use of ultrasonic scalers (Woodpecker India, New Delhi, India). Root planing was conducted using either 4R/4L or 2R/2L Columbia universal curettes (Hu-Friedy, Chicago, USA).

Intracrevicular administration of 4% mangosteen gel and the placebo gel

For standardization, both 4% mangosteen gel (4 g/100 mL) and the placebo gel were loaded into a hypodermic syringe with a 24-gauge angulated blunt needle and delivered to the experimental and control sites, respectively.

The tip of the needle was slowly slid over the tooth surface down to the base of the pocket, and the allocated gel was injected into the deepest part of the pocket at both experimental and control sites. While extruding the material, the needle was gradually withdrawn till it reached the upper portion of the pocket and the excess gel was removed. The selected sites were sealed with a periodontal dressing to prevent the ingress of oral fluids, which was then removed after 1 week.[13,17]

Biochemical evaluation

An ABTS (2,2'-Azino-bis-3-ethylbenzothiazoline-6-sulfonic acid) antioxidant assay kit (Zen-Bio Inc., Durham, USA) was used to determine the GCF TAOC levels at the selected sites. The collected GCF samples were added to the wells of microtiter-coated plates with a pipette. The plates were sealed and incubated for 2 h at room temperature (18–25°C). The reagents were added as per the manufacturer's instructions. Color development was monitored every 5 min. Positive wells turned blue in color. The determination of optical density in each well was performed using a microplate reader (Molecular Devices, San Jose, USA) at an absorbance of 405 nm.

Statistical analysis

The data obtained from the clinical and biochemical evaluation is presented as mean and standard deviation ($M \pm SD$). The PI, GBI, PD, and RAL parameters were analyzed using Student's t test, one-way analysis of variance (ANOVA) and Šidák's post hoc test for pairwise comparisons. The GCF TAOC levels were analyzed using the Mann–Whitney U test for pairwise comparisons, Student's t test and the Kruskal–Wallis test. For all tests, $p \leq 0.001$ was considered statistically significant.

Results

Clinical parameters

A significant reduction ($p \leq 0.001$) was observed in the PI, GBI (Fig. 4 and Fig. 5, respectively), PD, and RAL (Tables 1,2) scores in both groups at D3 as compared to D0.

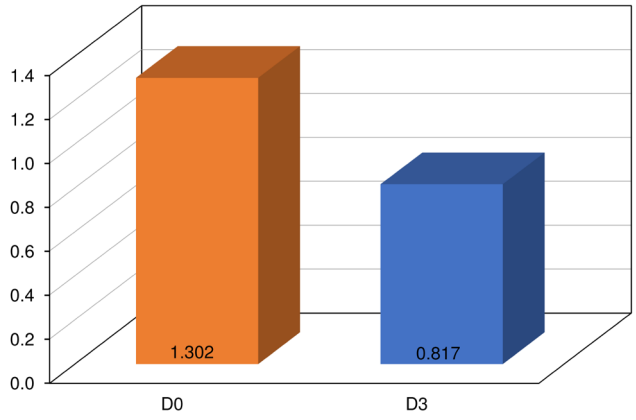

Fig. 4. Comparison of the mean plaque index (PI) scores at baseline (D0) and at 3 months post-treatment (D3)

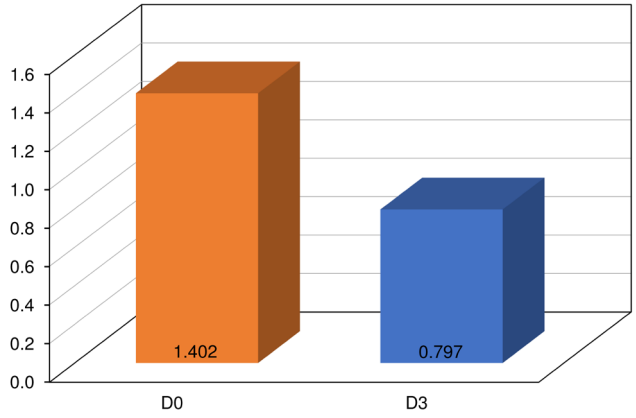

Fig. 5. Comparison of the mean gingival bleeding index (GBI) scores at baseline (D0) and at 3 months post-treatment (D3)

Probing depth (PD)

Intragroup comparison of the PD scores at D0 and D3 in the control and experimental groups

In the control group, the mean PD score at D0 was 5.630 ±0.928 mm, and then it decreased to 4.200 ±0.887 mm at D3. The difference between the pre- and post-treatment mean PD scores was 1.430 ±0.041 mm ($p < 0.001$; $f = 0.790$).

In the experimental group, the mean PD score at D0 was 5.730 ±0.828 mm, which was reduced to 2.870 ±0.900 mm after treatment at D3. The difference between the pre- and post-treatment mean PD scores was 2.860 ±0.072 mm ($p < 0.001$; $f = 1.350$) (Table 1).

Intergroup comparison of the PD scores at D0 and D3 in the control and experimental groups

At D0, the mean PD score was lower in the control group (5.630 ±0.928 mm) than in the experimental group (5.730 ±0.828 mm). The difference in the mean PD scores between the control and experimental sites was –0.100 ±0.100 mm, which was not statistically significant. At D3, the mean PD score was higher in the control group (4.200 ±0.887 mm) as compared to the experimental group (2.870 ±0.900 mm). The difference in the mean PD scores between the control and experimental sites was 1.330 ±0.013 mm ($p < 0.001$) (Table 2).

Table 1. Comparison of the probing depth (PD), the relative attachment level (RAL) and the gingival crevicular fluid (GCF) total antioxidant capacity (TAOC) levels between baseline (D0) and 3 months (D3) for both the control and experimental sites

Parameter	Control sites					Experimental sites				
	D0	D3	D3 vs. D0‡	*p*-value#	*f*-value†	D0	D3	D3 vs. D0‡‡	*p*-value#	*f*-value††
PD [mm]	5.630 ±0.928	4.200 ±0.887	1.430 ±0.041	<0.001*	0.790	5.730 ±0.828	2.870 ±0.900	2.860 ±0.072	<0.001*	1.350
RAL [mm]	7.630 ±1.351	6.730 ±1.112	0.900 ±0.239	<0.001*	1.000	8.030 ±1.098	5.930 ±1.230	2.100 ±0.132	<0.001*	2.340
GCF TAOC level [μM]	–0.294 ±0.901	–0.178 ±0.145	–0.116 ±0.756	>0.001	41.261	–0.374 ±0.215	0.041 ±0.200	–0.415 ±0.015	<0.001*	41.641

Data presented as mean ± standard deviation (*M* ±*SD*). ‡ Šidák's post hoc test; ‡‡ Mann–Whitney *U* test; # Student's *t* test; † ANOVA; †† Kruskal–Wallis test; * statistically significant.

Table 2. Comparison of the probing depth (PD), the relative attachment level (RAL) and the gingival crevicular fluid (GCF) total antioxidant capacity (TAOC) levels between the control and experimental sites at both baseline (D0) and 3 months (D3)

Time of assessment	PD [mm]				RAL [mm]				GCF TAOC level [μM]			
	control sites	experimental sites	D3 vs. D0‡	*p*-value#	control sites	experimental sites	D3 vs. D0‡	*p*-value#	control sites	experimental sites	D3 vs. D0‡‡	*p*-value#
D0	5.630 ±0.928	5.730 ±0.828	–0.100 ±0.100	>0.001	7.630 ±1.351	8.030 ±1.098	–0.400 ±0.253	>0.001	–0.294 ±0.901	–0.374 ±0.215	0.080 ±0.686	<0.001*
D3	4.200 ±0.887	2.870 ±0.900	1.330 ±0.013	<0.001*	6.730 ±1.112	5.930 ±1.230	0.800 ±0.118	<0.001*	–0.178 ±0.145	0.041 ±0.200	–0.219 ±0.055	<0.001*

Data presented as *M* ±*SD*. ‡ Šidák's post hoc test; ‡‡ Mann–Whitney U test; # Student's t test; * statistically significant.

Relative attachment level (RAL)

Intragroup comparison of the RAL scores at D0 and D3 in the control and experimental groups

In the control group, the mean RAL score at D0 was 7.630 ±1.351 mm, and then it decreased to 6.730 ±1.112 mm at D3. The difference between the pre- and post-treatment mean RAL scores was 0.900 ±0.239 mm ($p < 0.001$; $f = 1.000$).

In the experimental group, the mean RAL score at D0 was 8.030 ±1.098 mm, which was reduced to 5.930 ±1.230 mm after treatment at D3. The difference between the pre- and post-treatment mean RAL scores was 2.100 ±0.132 mm ($p < 0.001$; $f = 2.340$) (Table 1).

Intergroup comparison of the RAL scores at D0 and D3 in the control and experimental groups

At D0, the mean RAL score was lower in the control group (7.630 ±1.351 mm) than in the experimental group (8.030 ±1.098 mm). The difference in the mean RAL scores between the control and experimental sites was −0.400 ±0.253 mm, which was not statistically significant. At D3, the mean RAL score was higher in the control group (6.730 ±1.112 mm) as compared to the experimental group (5.930 ±1.230 mm). The difference in the mean RAL scores between the control and experimental sites was 0.800 ±0.118 ($p < 0.001$) (Table 2).

The intra-examiner reliability was checked using Cohen's kappa coefficient, which amounted to 0.82, indicating good precision and agreement.

Biochemical parameters

Gingival crevicular fluid (GCF) total antioxidant capacity (TAOC) level

Intragroup comparison of the GCF TAOC levels at D0 and D3 in the control and experimental groups

In the control group, the mean GCF TAOC level at D0 was −0.294 ±0.901 μM, and then it increased to −0.178 ±0.145 μM at D3. The difference between the pre- and post-treatment mean GCF TAOC levels was −0.116 ±0.756 μM, which was not statistically significant.

In the experimental group, the mean GCF TAOC level at D0 was −0.374 ±0.215 μM, which rose to 0.041 ±0.200 μM after treatment at D3. The difference between the pre- and post-treatment mean GCF TAOC levels was −0.415 ±0.015 μM ($p < 0.001$; $f = 41.641$) (Table 1).

Intergroup comparison of the GCF TAOC levels at D0 and D3 in the control and experimental groups

At D0, the mean GCF TAOC level was found to be higher in the control group (−0.294 ±0.901 μM) than in the experimental group (−0.374 ±0.215 μM). The difference in the mean GCF TAOC levels between the control and experimental sites was 0.080 ±0.686 μM ($p < 0.001$). At D3, the mean GCF TAOC level was lower in the control group (−0.178 ±0.145 μM) as compared to the experimental group (0.041 ±0.200 μM). The difference in the mean GCF TAOC levels between the control and experimental sites was −0.219 ±0.055 μM ($p < 0.001$) (Table 2).

Correlation between clinical parameters and GCF TAOC levels

At 3-month follow-up, a significant positive correlation was observed between the GCF TAOC levels and one of the clinical parameters (RAL) in the experimental group (the 4% mangosteen gel group) when compared to the control group (the placebo gel group) (Fig. 6).

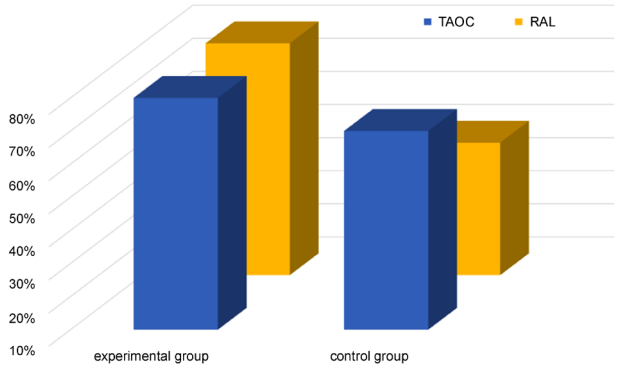

Fig. 6. Positive correlation between relative attachment level (RAL) and the gingival crevicular fluid (GCF) total antioxidant capacity (TAOC) level

Discussion

The authors of the present study hypothesized that the LDD of 4% mangosteen gel as an adjunct to SRP would show superior outcomes as compared to SRP with the placebo gel in terms of clinical efficacy and antioxidant potential, which is essential in the management of periodontitis patients. Differences in the study outcomes between the experimental and control groups were found to be statistically significant, with the 4% mangosteen gel group exhibiting better performance. Thus, the formulated hypothesis was confirmed. The adjunctive use of a subgingival LDD with gel formulations for the management of periodontitis have been highly popularized due to their less invasiveness and their ability to access deep-seated sites, such as furcations and invaginations.[13,18]

Recently, different vegetative antimicrobials have acquired extraordinary significance in the arena of preventive periodontics, as they have no aftereffects.[9–11] Thus, they are being extensively used as an unconventional

alternative to systemic antimicrobials, which have disadvantages, like hypersensitivity reactions, gastrointestinal intolerance and the development of bacterial resistance.[19,20] These downsides can be evaded with the local application of antimicrobial medications in the subgingival environment, achieving an adequate concentration of the drug for a longer duration of time.[21] The adjunctive use of an antimicrobial LDD has been observed to produce a superior effect, with a decrease in PD and gingival inflammation.[18]

Mangosteen is a marvelous fruit; its pericarp is commonly utilized in the Middle East for the therapy of diarrhea, and skin and chronic wound infections.[7] Since ancient times, this natural product has been a fundamental element in Chinese medicine and Ayurveda.[22] It appears to have antifungal, anticytotoxic, antiviral, antibacterial, antihistamine, antioxidant, and anti-inflammatory properties.[8–10] The leaves and bark of the mangosteen tree are utilized to produce chewing sticks as an astringent in oral care in some African nations.[23] The mangosteen pericarp extract has exhibited antibacterial properties against numerous pathogenic microbes.[24–27] Previous studies have indicated that the mangosteen pericarp extract is effective against *Streptococcus mutans* at a minimum inhibitory concentration (MIC) – the lowest concentration of a chemical substance (usually a drug) that prevents bacteria from growing significantly – of 0.625 μg/mL.[11]

Its active components are xanthone derivatives, such as α-, β- and γ-mangostin, gartinin, and 1- and 3-isomangostin. Among these, α-mangostin has the strongest antibacterial effect.[28] Studies have also demonstrated that the mangosteen extract has low toxicity when applied topically.[29,30] Alpha-mangostin, when administered orally to rats at a high dose (1.5 g/kg body weight) to test its hepatotoxicity, demonstrated a lowered serum glutamate pyruvate transferase activity for a period of 12 h, indicative of its safety with a topical application.[31]

The ethanolic extract (80%) from the pericarp of mangosteen inhibited the growth of *Porphyromonas gingivalis (P. gingivalis)*, the main periodontopathic bacteria, at a MIC of 3.91 mg/mL[8,9] and showed positive results in the reduction of clinical inflammation in chronic periodontitis patients with a dosage of 4% mangosteen gel.[10] Hence, the preparation of 4% mangosteen gel preparation was considered in the present study.

Total antioxidant capacity is an important biochemical marker in determining the cumulative action of antioxidants present in body fluids.[1,2,18] The extracrevicular (unstimulated) method with the aid of microcapillary pipettes was used for GCF sampling in an attempt to minimize trauma to the gingival tissues,[13,32] preventing bleeding and the contamination of the GCF sample.

At the end of the 3-month study, both groups showed a statistically significant reduction in PI, GBI, PD, and RAL. This may be attributed to the thorough removal of local factors during the pre-study phase, and the selection of patients with PI and GBI <25%, along with the reinforcement of oral hygiene instructions at baseline.

The full-mouth PI scores reflect the oral hygiene status of individual patients. The significant reduction in the PI scores from D0 to D3 in the present study was similar to that observed by Mahendra et al.[9]

Bleeding associated with inflammation may be due to structural alterations in the vessel walls and environs, which results in increased capillary fragility and permeability, predisposing to bleeding upon probing.[16] In our study, significant improvement in the GBI scores occurred at the end of the 3-month period. This improvement confirms the better oral hygiene status of the patients, prolonging the effect of the therapy, which is attributed to the Hawthorne effect.[8–10] The obtained results are in accordance with those of Rassameemasmaung et al., who showed a similar reduction in the GBI scores upon the application of 4% mangosteen gel.[11]

Similar to other studies,[8–10] the experimental sites (the 4% mangosteen gel group) showed a greater reduction in the PD and RAL scores as compared to the control sites (the placebo gel group). The obtained results may be due to the resolution of gingival inflammation, causing the shrinkage and reattachment of the connective tissue fibers, along with the downregulation of inflammatory mediators, given the short duration of this study.[13]

Periodontal pathogens, such as *Aggregatibacter actinomycetemcomitans* or *P. gingivalis*, implicate oxidative stress, thus launching the production of free radicals and ROS in higher concentrations, which results in the destruction of the periodontal tissues, either by degrading the ground substance or by releasing collagenases and various inflammatory mediators.[2,4,5]

It is noteworthy that although both the study groups showed statistically significant increases in the GCF TAOC levels, a slightly greater increase in the mean GCF TAOC level was observed in the experimental group (the 4% mangosteen gel group) in comparison with the control group after 3 months. This may be due to the antioxidant effect of mangosteen, along with the scavenging of free radicals by the enzymatic mechanism of superoxide dismutase.[33]

At baseline, both groups demonstrated a statistically significant association between the GCF TAOC levels and changes in clinical parameters. This substantiates the assumption that cases of periodontal disease are associated with low GCF TAOC levels due to an increase in the level of ROS.[12]

A statistically significant positive correlation between RAL and the GCF TAOC levels was also observed in the experimental group (the 4% mangosteen gel group) at a 3-month follow-up. This is attributed to the direct effect of mangosteen on the upregulation of the GCF TAOC levels, which brought improvement in clinical parameters, hence proving its antioxidant potential.[12]

This is the first clinical trial to compare the efficacy of both 4% mangosteen gel and a placebo gel as adjuncts to SRP by evaluating changes in clinical parameters and the GCF TAOC levels upon their subgingival LDD. However, the present study recruited a small number of patients who were followed up for only 3 months. Hence, further randomized, controlled clinical trials need to be considered with larger sample sizes and longer follow-up periods, employing different modes of LDD and greater concentrations of mangosteen, with various antioxidant biomarkers to obtain stronger outcomes.

Conclusions

This clinic-biochemical trial demonstrated that the local delivery of 4% mangosteen gel into the periodontal pockets of chronic periodontitis patients significantly reduced the mean PI, GBI and PD scores, and gain in the RAL scores. It also demonstrated a significant increase in the GCF TAOC levels at the end of the 3-month period, proving the antioxidant efficacy of 4% mangosteen gel. This can provide a new direction in the field of periodontal therapy. However, long-term, multicenter, randomized, controlled clinical trials are required in order to further understand the clinical and microbiological profile of patients with chronic periodontitis after the application of mangosteen gel as LDD, and also to compare this treatment protocol with other established and clinically proven standard drugs.

Ethics approval and consent to participate

The study was approved by the institutional review board (IRB) at Bapuji Dental College and Hospital, Davangere, India (No. BDCH/Exam 467/2018–2019). It was performed in compliance with the ethical standards established by the World Medical Association (WMA) in the Declaration of Helsinki. All participants provided written informed consent prior to the investigations.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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