



## Research Article

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### COMPARATIVE EVALUATION OF THE EFFICACY OF 4% MANGOSTEEN GEL AND 1% CHLORHEXIDINE DIGLUCONATE GEL IN MANAGEMENT OF PATIENTS WITH CHRONIC GINGIVITIS: A RANDOMIZED CLINICAL TRIAL

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#### ABSTRACT

**Aim:** To clinically evaluate & compare the efficacy of 4% Mangosteen Gel and 1% chlorhexidine digluconate gel in managing patients with chronic gingivitis. **Materials and Methods:** A total of 50 patients with an age group of 20-45 years diagnosed with generalized plaque-induced gingivitis were selected for this clinical trial once attaining their informed consent. A thorough case history was chronicled comprising plaque index (P.I.), gingival index (G.I.) and Sulcus bleeding index (SBI) at baseline; then full-mouth scaling and polishing (SAP) was performed by a solitary attuned examiner. Patients were then randomly assigned into two groups using a computer-generated random numbering sequence system. Patients in group A received 4% Mangosteen Gel, and group B received 1% chlorhexidine digluconate gel for home application. The post-treatment follow-up examination for P.I., G.I. and SBI changes were assessed after 14 days and 21 days and compared with baseline data. **Results:** In both the groups, the mean plaque index, gingival index and sulcus bleeding index scores were significantly decreased after the 14<sup>th</sup> and 21<sup>st</sup> day compared to baseline scores. There was no significant difference between the groups, but only in group B, there was a substantial difference in SBI scores observed on day 21. **Conclusion:** 4% Mangosteen Gel and 1% chlorhexidine digluconate gel were clinically effective when used as an adjunct to SAP in managing patients with gingivitis. Hence, 4% Mangosteen Gel can be considered an alternative to 1% chlorhexidine digluconate gel without any side effects in managing generalized plaque-induced gingivitis.

**Keywords:** Chlorhexidine, Gingivitis, Herbal, Mangosteen, Plant-based Gel

#### INTRODUCTION

The dualistic chief topographies of periodontal ailment exist gingival inflammation, i.e., gingivitis and the development of periodontal pockets leading to periodontitis. Gingivitis always precedes periodontitis but does not always progress to periodontitis. Gingivitis is a reversible condition with good oral hygiene; however, it can lead to periodontal disease if left untreated. Persistent inflammation of the gingiva can lead to more rapid and progressive tissue destruction of supporting tissues around the teeth & may eventually cause tooth loss. Hence the resolution of inflammation in the initial stage is crucial for the state of wellbeing of the periodontium.<sup>1</sup>

The management of gingivitis involves the mechanical removal of dental plaque aided by numerous chemical agents, such as mouth rinses with chlorhexidine<sup>1-3</sup> or essential oils<sup>1</sup> or dentifrices containing triclosan with 2.0% Gantrez copolymer<sup>1</sup>. In this vein, studies have evaluated the addition of these chemo-preventative agents to typical oral hygiene efforts and shown a statistically significant positive response to these products in controlling plaque and gingivitis.<sup>1</sup>

Chlorhexidine is considered the “gold standard” for the chemical plaque control<sup>2</sup>. However, long-term use still has some shortcomings, such as staining teeth, altered taste perception, metallic taste, burning sensation,<sup>2,3</sup>. These chlorhexidine limits have steered the evolution of naturally befalling oral hygiene goods. Which will be economical for routine oral hygiene

maintenance. Herbal interventions are a therapeutic strategy that warrants greater research attention in treating gingivitis and periodontitis.<sup>1,2</sup>

One such unique attempt is through *Garcinia mangostana* (MGA), more popularly known as Mangosteen, also called the “queen of fruits”, which belongs to the Guttiferae family. It contains various bioactive compounds, such as chrysanthemum; gartinones A, B, and C; sesquiterpenoids; gartinin; and tannins in its pericarp. The important characteristics of mangostana include anti-inflammatory, antimicrobial and antioxidant properties.<sup>4-8</sup> Other potential benefits of mangostana include inhibition of collagenolytic and gelatinolytic enzyme activity produced by the host tissues during inflammation by the activation of mediators like MMP-2, MMP-9.<sup>4-8</sup>

Mangosteen extract is bactericidal against Periodontopathic microorganisms like *Porphyromonas gingivalis* and *Actinobacillus actinomycetemcomitans*.<sup>5</sup> An experimental study was carried out to compare the 12.5% and 25% mangosteen peel extract during the healing process of gingivitis in mice. 12.5% mangosteen peel extract showed the highest anti-inflammatory potential.<sup>6</sup>

Following scaling and root planning, local drug delivery (LDD) of 4% mangosteen gel revealed a significant reduction in plaque index, gingival index and sulcus bleeding index scores and upsurge of clinical epithelial attachment in chronic periodontitis patients.<sup>9,10</sup>

There is a lack of literature regarding the evaluation of therapeutic benefits of mangosteen gel for the management of chronic gingivitis. Hence, this study evaluated the effect of mangosteen pericarp extract incorporated gel formulation for managing patients diagnosed with gingivitis compared to an established chemical plaque agent chlorhexidine.

## MATERIALS AND METHODS

### Sampling method and size calculation

The sample size was calculated via the following formula.<sup>11</sup>

$$n = \left[ \frac{Z_{1-\alpha/2} + Z_{1-\beta}}{\mu_A - \mu_B} \right]^2$$

As per the calculation, at least 40 patients were needed to provide 80 % power and detect a difference in the means of bleeding index between two study groups by the end of 21 days. Fifty patients were recruited to compensate for the 20% dropout of patients who might fail to follow up.

Ethical clearance for research was obtained from the Bapuji Dental College and Hospital (Ref.No. BDC/Exam/506/2020-21), Davanagere, Karnataka, India. During the conduct of the study, all human ethical principles as per the World Medical Association's Declaration of Helsinki (2013) and the guidelines of Good Clinical Practice (Indian Council of Medical Research) were followed.

### Sampling criteria

The study included patients with an age range between 20 and 45 years having at least 20 permanent natural teeth, except for the third molar, who was diagnosed with generalized plaque-induced gingivitis (according to the 2017 world workshop guideline for periodontal and peri-implant disease classification)<sup>12</sup> & intact periodontium with bleeding on probing (BOP)  $\geq 30\%$ .

The patients with a history of using antibiotics or other drugs in the past three months, having actual periodontal pockets, wearing removable or fixed prosthetic devices, and having habits like smoking, chewing tobacco, medically compromised, pregnant & lactating women were excluded from the study.

### Methods

Signed informed consent was obtained from all the selected patients before the commencement of the study. A single calibrated assessor conceded out the scrutiny. Following the recording of comprehensive case history at baseline, patients underwent full mouth gingival inspection for recording plaque index (P.I.) by Silness and Loe in 1964,<sup>9</sup> gingival index (G.I.) by Loe & Silness in (1967)<sup>9</sup> and sulcus bleeding index (SBI) by Muhlemann and Son, 1971.<sup>10</sup>

Following full-mouth, ultrasonic scaling, group A patients received 4% Mangosteen Gel and group B received 1% chlorhexidine digluconate gel (Hexigel, ICPA Health Products, Mumbai, India) for home application. Patients were tutored to take a pea-size portion of the therapeutic gel on the index finger and smoothly massage all over the gingiva for 1 minute, twice a day for 21 days. Subjective and objective criteria were assessed after the 14th day and 21st day.<sup>13</sup>

### Subjective criteria<sup>13</sup>

- (1) Taste acceptability: 0-acceptable; 1-tolerable; 2- unacceptable.
- (2) Burning sensation: 0-absent; 1-present;
- (3) Dryness/soreness: 0-absent; 1-present.

### Objective criteria<sup>13</sup>

- (1) Ulcer formation: 0-absent; 1-present;
- (2) Staining of teeth: 0 - absent; 1-present;
- (3) Staining of tongue: 0-absent; 1-present;
- (4) Allergy: 0-absent; 1-present.

### Preparation of 4% *Garcinia mangostana* gel

The pure extract of mangostana powder was obtained from Tamil Nadu Agricultural University, Coimbatore, India. The 4% mangosteen gel was prepared in the following proportions using the formulation presented by Rassameemasmaung *et al.*<sup>14</sup>. The concentration of the gel was adjusted according to the data obtained from the study done by Mahendra J *et al.*<sup>7</sup>. A homogenizer is used to equalize all ingredients to form a gel depicted in Figure 1. 4% mangosteen gel was preserved at 4°C during the study.<sup>6</sup>

To assess compliance, the test patients received a home maintenance card. Patients who missed the application of gel were excluded from the study. The patients were re-evaluated under P.I., G.I., SBI and Home Maintenance was evaluated by using the Home Maintenance card on Day 14 and Day 21, two patients in Group A, three patients in Group B were withdrawn from the study, as they were unable to come for follow-up due to personal circumstances.

### Statistical Analysis

Clinical measurements were manually recorded during the investigation and transferred to a data table created in a Microsoft Excel spreadsheet. The data were analyzed using statistical software package R (4.1.0 / 18 May 2021). Then use the t-test or Mann test-Whitney U test to match normality. P < 0.05 was set to obtain statistical significance.

## RESULTS

There was no statistically significant difference in the average gingival score between patients in different intervention groups at baseline and different time intervals. However, between baseline and after the intervention, the gingival score of each group decreased, as shown in Graph 1. In group A, the average G.I. value at the beginning of the study fell after 21 days. After 21 days, group B obtained the same results; the p-value on both sides was 0.95, and no statistically significant difference was observed in the middle panel. The subject scores of various parameters at the beginning of the study and at different time intervals in the two groups. Graph 2 shows the patients' plaque score decreases between groups A and B from baseline and after the intervention. The double-sided P-value is 0.43.

In addition, there was no significant difference in the sulcus bleeding index at different time intervals. Still, as shown in Table 1, it decreased from the first visit to the third visit (from 0.29±0.7 to 0.19±0.16 in group A, from 0.29 ± 0.10 to 0.12 ± 0.04 in Group B). The double-sided p-value is 0.43. P-value (P= 0.033) is <0.05 at 21 days, and the SBI score reduction is statistically significant in group B.

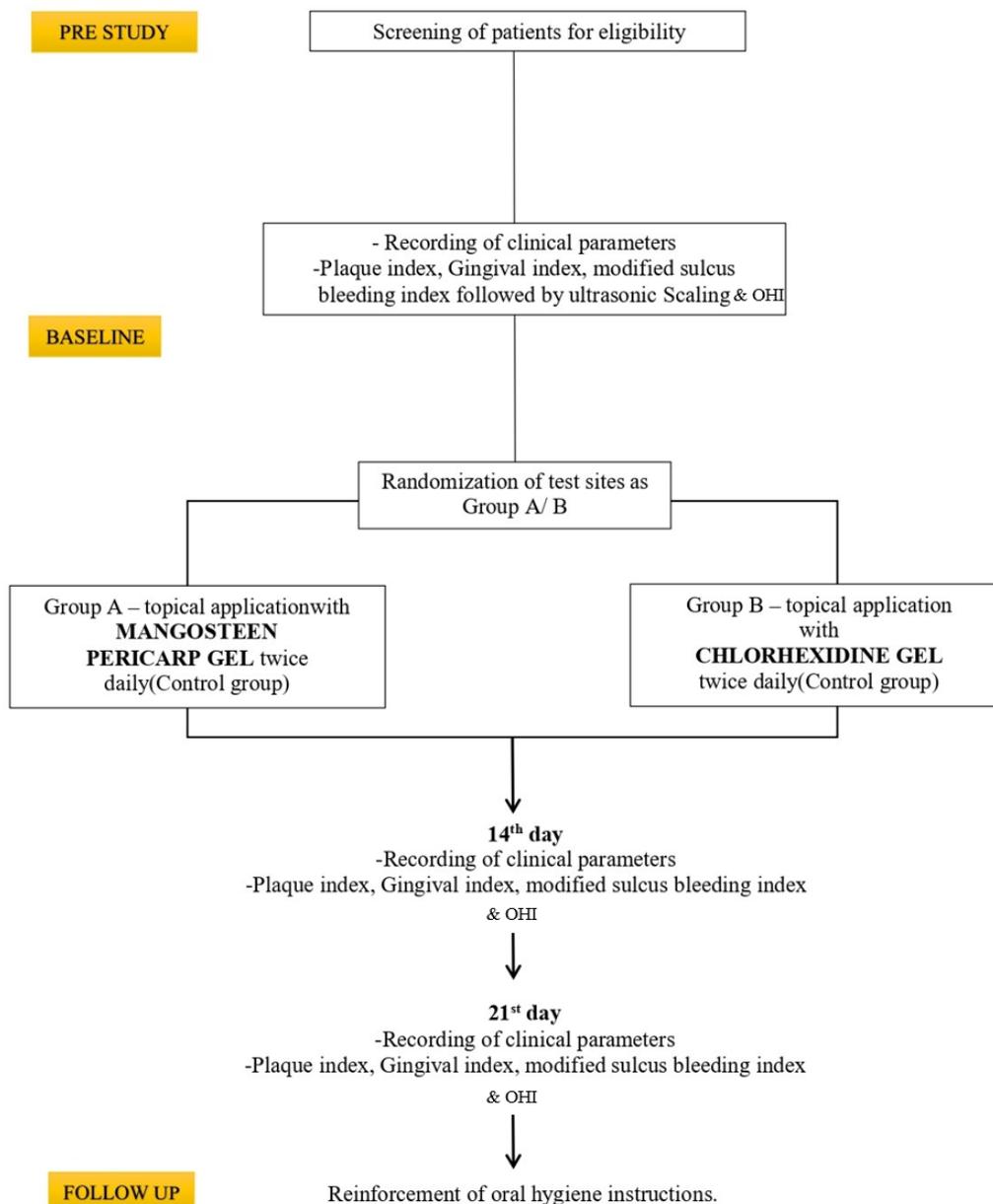


Figure 1: Study Design

Table 1: Comparison of the sulcus bleeding index scores at baseline, day 14, and day 21 in group A and group B using Mann–Whitney U test

Groups	Mean ± SD		
	Baseline	14 days	21 days
Group A	0.29 ± 0.7	0.23 ± 0.16	0.19 ± 0.16
Group B	0.29 ± 0.10	0.19 ± 0.06	0.12 ± 0.04
Statistical inference	P = 0.623	P = 0.468	P = 0.033**

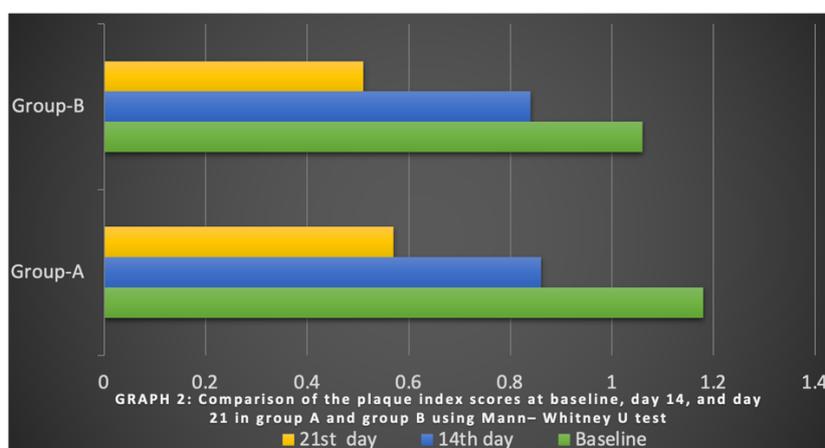
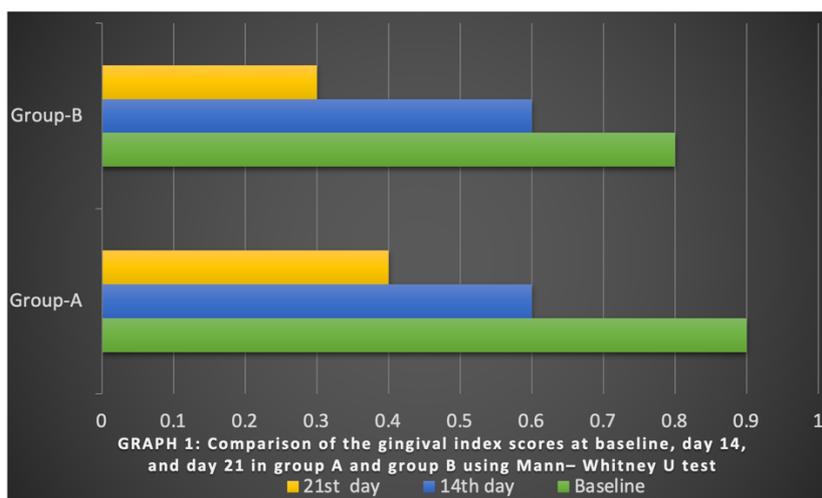
\*\*P ≤ 0.05 (As P-value is <0.05 at 21 days, the sulcus bleeding index score reduction is statistically significant in group B)

Table 2: Subjective criteria

Subjective criteria for (50 patients)	Taste acceptability			Burning		Dryness/soreness	
	Acceptable	Tolerable	Unacceptable	Present	Absent	Present	Absent
Group A (25 patients)	25	0	0	0	25	0	25
Group B (25 patients)	20	0	5	0	25	0	25

Table 3: Objective criteria

Objective criteria for (50 patients) dvf	Ulcer formation		Staining of teeth		Staining of tongue		Allergy	
	Present	Absent	Present	Absent	Present	Absent	Present	Absent
Group A (25 patients)	0	25	0	25	0	25	0	25
Group B (25 patients)	0	25	0	25	0	25	0	25



## DISCUSSION

Mechanical plaque debridement is a standard method of maintaining good oral hygiene. However, for most people, the enthusiasm of upholding the same standard of oral hygiene maintenance is one of the complex tasks. For this reason, many chemotherapeutic antiplaque drugs have been developed. Many antiplaque chemotherapeutic agents have been developed and employed successfully to overcome this. Among these agents' chlorhexidine is one of the most successful ones due to its broad-spectrum activity and substantivity.<sup>1-3</sup>

A systematic review by Raul et al. concluded that Mouth rinses containing 0.12 % chlorhexidine have significant antigingivitic effects in adults<sup>1</sup>. Nittayananta et al.<sup>15</sup> found that there was a decrease in gingivitis and the number of *Candida* species after brushing with chlorhexidine gel twice a day for two weeks in patients infected with the human immunodeficiency virus. The recent randomized clinical trial was also suggestive of great benefit in improving the indices (P.I., SBI) in chronic periodontitis Via LDD of chlorhexidine in adjunct to complete mouth disinfection.<sup>2</sup>

The long-term use of chlorhexidine agents revealed side effects like loss of Taste sensation,<sup>2,13</sup> stain formation,<sup>13</sup> ulcer development<sup>2</sup> and growth of resistant microorganisms.<sup>2,13</sup> This has attracted the clinicians & researchers to use antibacterial and anti-inflammatory herbs for the treatment of oral diseases to overcome the side effects associated with the widespread abuse of chlorhexidine.

A review conducted by Safiaghdam et al.<sup>16</sup> on medicinal plants for gingivitis supported the efficacy and safety of several medicinal plants like *Azadirachta indica* extract (Neem Leaf), *Garcinia mangostana* (Mangosteen), *Aloe barbadensis* (*Aloe Vera* extract), *Sanguinaria Canadensis* (BloodRoot) for gingivitis.<sup>16</sup>

The phytochemicals such as chrysanthemum; gartinones A, B, and C; sesquiterpenoids; gartinin; and tannins, present in Mangosteen, illustrated its antibacterial effect.<sup>6-8</sup> In an in-vitro investigation, the phenol compounds in mangosteen rind extract expressed their capability in inhibiting the growth of both gram-positive and gram-negative bacteria<sup>17</sup>

The *Garcinia mangosteen*-Polyvinylpyrrolidone (GM-PVP) complex with a minimum inhibitory concentration of 10 mg revealed an inhibitory zone of 12 mm for *Porphyromonas gingivalis* and 10 mm for *Actinobacteria*.<sup>18</sup> Nguyen et al.<sup>19</sup> showed an effective way for inhibiting *Streptococcus* bacteria in the oral cavity by using the extracts of alpha mangostin, which is an effective glycolytic inhibitor. The xanthenes found in Mangosteen are used in mouthwash formulations to keep the mouth clean.<sup>20</sup>

The LDD is delivered at an optimal concentration that can last long enough to achieve the desired outcome without side effects. As a part of self-care at home, patients can use LDD in topical gel preparations. The reason for using is to remove any infectious/inflammatory components that remain in the periodontal tissue and cannot be removed mechanically by hand or electric equipment.<sup>21</sup>

This study evaluated the efficacy of the herbal gum astringent (i.e. 4% mangosteen gel) and 1% chlorhexidine digluconate for 21 days. Intraexaminer variation for interpretation of recording of clinical parameters at different intervals of the study period was calibrated with Cronbach's alfa levels of 0.9. We have tried to eliminate assessment bias as soon as possible.<sup>22</sup>

The decrease in the number of P.I., G.I. & SBI scores in both the groups indicates the antibacterial effect of the gels, especially when combined with mechanical debridement performed after the baseline examination. Similar results were obtained by the study done by Ambhore et al.<sup>23</sup>, where patients who received Triphala gel and Hexigel in group A & B respectively for home application, discovered that the mean P.I., G.I. & SBI scores significantly decreased after 14- and 28-day intervals as compared to baseline scores.

Bleeding associated with inflammation may be due to structural alterations of the vessel walls and environs, which results in increased capillary fragility and permeability, which predisposes to bleeding upon probing. In our study, a significant improvement in SBI scores occurred at the end of 21 days in group A with 4% mangosteen gel.

Inflammation-related bleeding can be caused by morphological changes in the blood vessel wall & its surrounding areas, directing enhanced penetrability & frangibility, which can easily trail to bleeding while probing.<sup>6,7</sup> In our study, group A with 4% mangosteen gel had a significant improvement in the SBI score at the end of 21 days. This can be attributed to tissue shrinkage due to the anti-inflammatory & vasoconstrictive effect of 4% mangosteen gel.<sup>6-8</sup>

The improvement in oral hygiene status of the patients may be attributed to, short term study period & reinforcement of oral hygiene instructions between the study intervals. This confirms the Hawthorne effect.<sup>23</sup>

The 4% mangosteen gel was acceptable in taste and biocompatible from the subjective and objective criteria evaluation. In contrast, the bitter taste was experienced by five patients for 1% chlorhexidine digluconate gel. (Table 2 & 3) In many other studies, specific side effects of using chlorhexidine mouthwashes similar to ours have been observed.<sup>13,24</sup>

The limitations of our study included small sample size, a short study period, and the trial was strictly confined only to the evaluation of the clinical effect of therapeutic gels on the gingiva. To overcome the limitations further, a multicentre longitudinal clinical trial having a longer follow up with a larger sample size using a controlled drug delivery of drugs mentioned above along with microbial or biochemical marker evaluation. Pre and post-operatively may throw more light on the possible benefits and problems associated with therapeutic gels.

This study highlighted the clinical benefits of 4% Mangosteen over 1% CHX gluconate gel in managing generalized plaque-induced gingivitis. The anti-inflammatory potential of Mangosteen's superiority over other established chemotherapeutic agents in the management of different clinical scenarios like advanced periodontal disease, implant mucositis and peri-implantitis also need to be explored.

## CONCLUSION

4% mangosteen gel and 1% chlorhexidine digluconate gel are equally effective in treating gingivitis. Since chlorhexidine gluconate gel has many side effects, 4% mangosteen gel can be

substituted for 1% chlorhexidine gluconate gel in patients with gingivitis without side effects.

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