Triphala: A phytomedicine for local drug delivery – A strategic intervention

B. M. Shivaprasad, Padmavati Patil, Sruthi K. Nair, Navnita Singh, Shilpa Shivanand, Ume Sameera
Department of Periodontology, Raja Rajeswari Dental College and Hospital, Bengaluru, Karnataka, India

Abstract

Background: In the Indian system of medicine (ISM) *Triphala* is one of the oldest and longest used natural herbal remedy which consist of mixture of equal parts of the *Embilica officinalis* Gaertn. (Family- Euphorbiaceae), *Terminalia Chebula* Retz. (Family- Combretaceae) and Terminalia beleria [Gaertn.] Roxb. (Family- Combretaceae). Currently, *Triphala* is being extensively researched for its various therapeutic effects including its anti-caries, antioxidant, anti-collagenase and anti-microbial activities. This fruit extract is used in various forms in the treatment of periodontitis. **Aim:** The aim of the present study was to compare the clinical and microbiological benefits of routine scaling and root planing (SRP) with adjunctive use of *Triphala* (Hiora GA) as local drug delivery agent in the management of periodontitis. **Materials and Methods:** Thirteen patients diagnosed with chronic periodontitis were included in the present study. The control sites received SRP alone and the test sites received SRP with locally delivered *Triphala* (Hiora GA). The clinical parameters were evaluated at baseline, 15 days and 1 month. The plaque samples were cultured anaerobically for the keystone-periodontal pathogen *Porphyromonas gingivalis*, *Fusobacterium nucleatum* and *Prevotella intermedia*. The Mann–Whitney U-test and Wilcoxon signed-rank tests were performed to compare the results between the test and control groups. **Results:** Statistically significant improvement was observed in both groups. Intergroup comparison of prevalence of microorganisms also revealed a statistically significant difference ($P = 0.0007$) at 15 days and 1 month. **Conclusion:** Subgingivally delivered *Triphala* (Hiora GA) as an adjunct to SRP in the treatment of chronic periodontitis has shown anticipative results revealing slow and constant releasing property of *Triphala*.

Keywords: Periodontal disease, periodontal pathogen, targeted drug delivery

Introduction

Periodontal diseases are complex, multifactorial, polymicrobial infection characterized by the destruction of the tooth-supporting tissues. It has long been recognized that the interactions between the bacterial pathogenic microflora and the inflammatory responses of a susceptible host can produce the progressive destruction of periodontal tissues.[1]

Treatment of periodontal disease is focused towards the suppression of subgingival microflora. Root debridement performed by mechanical means, i.e., scaling and root planing (SRP), is most commonly used as initial treatment approach.[2] However, comprehensive mechanical debridement of sites with deep periodontal pockets is difficult to accomplish. It may fail to eliminate the pathogenic microflora because of their location within the gingiva or in areas inaccessible to periodontal instruments. In view of the complex ecosystem within the subgingival pocket, the adjunctive use of antimicrobial agents has been advocated along with mechanical instrumentation to reduce the need for surgical treatment of pockets.[3]

Local delivery therapeutic agents in the oral cavity avoid most of the problems associated with systemic therapy, limiting the drug to its target site and hence achieving a much higher concentration of the drug in the required region.[4] The clinical use of antibiotics and other antimicrobial agents, as adjuvants for the treatment of periodontitis, has been extensively investigated.[3,5,6] Alternative drugs have been used since ancient times to treat periodontal diseases. Among them, *Triphala* is an alternative drug which is highly valued for its various properties.

Address for correspondence: Dr. B. M. Shivaprasad, Department of Periodontology, RajaRajeswari Dental College and Hospital, Mysore Road, Bengaluru - 560 074, Karnataka, India.
E-mail: drspbmath@gmail.com

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Triphala composed of the fruits of three herbal plant trees, Indian gooseberry *Amalaki* (*Embilica officinalis* Gaertn.), *Bibhitaki* (*Terminalia beleria* [Gaertn.] Roxb.) and *Haritaki* (*Terminalia chebula* Retz.) have an ability to regulate the process of digestion and elimination. It possesses various biological activities such as anti-inflammatory, antibacterial, antifungal, antiviral, antimalarial, antimutagenic, radioprotective, antiallergic, anticancer, cardiotonic, hypocholesterolemic, capillary strengthening, hepatoprotective, immunomodulatory, adaptogenic, analgesic and anti-oxidant activities.[7] *Triphala* has been shown to have inhibitory activity against matrix metalloproteinase-9 (MMP-9) as it allows suppression of collagenase activity.[8]

There is little literature available on the beneficial effects of *Triphala* in preventing oral diseases. However, to the best of our knowledge, there are no available data comparing and evaluating the clinical effects of the adjunctive use of *Triphala* gel in the nonsurgical treatment of periodontitis. Based on these considerations, the aim of the present study was to investigate the clinical and antimicrobial effects of local application of *Triphala* gel as an adjunct to SRP in the treatment of chronic periodontitis.

Materials and Methods

This was a randomized split-mouth design for comparison of two treatments: the control site was treated with SRP alone and the test site was treated with *Triphala* gel (Hiora GA) after SRP. The trial was conducted at the Department of Periodontics. Thirteen patients, 7 males and 6 females, aged 25–50 years (mean age, 35.6 ± 12.2 years) were enrolled in the study. All participants were informed about the treatment procedure and its potential benefits. Informed consent was obtained from the patients.

Patients who presented with good health and were diagnosed with chronic periodontitis having minimum of 20 natural uncrowned teeth, with at least one pocket per quadrant with a probing pocket depth (PPD) minimum of 5 mm with persistent bleeding on probing and nonsurgical phase of therapy completed at least 3 months before baseline were included in the study. Patients allergic to *Triphala*, use of systemic antimicrobial therapy within 2 months, history of periodontal surgery, smokers, pregnant and lactating mothers, patients with any systemic disease like diabetes that can alter the course of periodontal disease progression and treatment were excluded from the study.

All the clinical measurements were performed. On their first visit, all patients were examined to register the gingival index (GI) (Silness and Loe, 1964), Sulcus bleeding index (BI) (Muhlemann and Son, 1971), probing pocket depth (PPD) and clinical attachment level (CAL) were measured at six sites per tooth.

Treatment procedures

At baseline, clinical parameters such as GI, sulcus BI and pocket probing depth were recorded. SRP of all teeth were performed under local anesthesia. Target sites were randomized at split mouth level (left side/right side) to one of the two treatment groups; SRP alone, SRP with *Triphala* gel (Hiora GA, Himalaya, Herbal Healthcare, India). Following debridement, test sites were irrigated gently with cold saline and then left for 10 min to achieve hemostasis before the placement of *Triphala* gel (Hiora GA). *Triphala* gel (Hiora GA) with an applicator was administered subgingivally into selected periodontal pockets and compared with the control site (SRP site). Patients were reexamined at 15 days and 1 month, but no further *Triphala* gel (Hiora GA) was placed irrespective of pocket depth.

Microbial sampling

Subgingival plaque was removed with sterile paper points and sample sites were isolated with cotton rolls and gently air-dried before sampling. At baseline (before SRP) and at 15 days and 1 month posttreatment, subgingival plaque samples were collected from the deepest site of the pocket with the help of sterile paper point which was removed after 20 s. Samples collected were then transferred to 1 ml thioglycollate broth (transport medium) and sealed tightly to avoid contamination. Once it was received in the laboratory, the sample was mixed thoroughly and 5 µl each was inoculated using sterile loop onto the following medium: enriched blood agar (*Porphyromonas gingivalis* [Pg]), Brewer's anaerobic agar (*Fusobacterium nucleatum* [Fn]) and blood agar (*Prevotella intermedia* [Pi]).

Statistical analysis

The intragroup comparison was done using the Wilcoxon signed-rank test to evaluate the difference between two treatments or conditions where the samples were correlated, and the intergroup comparison was made using the Mann–Whitney U-test to determine if a difference exists between two groups. In the present study, value of $P < 0.05$ was considered as statistically significant.

Results

Intragroup evaluation at different time intervals in the test group showed that all the changes were statistically significant at all the time intervals ($P < 0.05$). Evaluation of change at different time intervals in the control group also showed that the changes were statistically significant at all the time intervals ($P < 0.05$) as shown in Table 1. A comparison of the mean change in clinical parameters between baseline and 1 month revealed a statistically significant intergroup difference for all the parameters by means of the test group showing significantly higher change when compared to that of the control group ($P < 0.05$) as shown in Table 1. Table 1 shows the mean GI, BI, PPD and CAL scores in both test and control sites at different points of time, i.e., baseline, 15 days and 1 month.

Statistically significant difference was not seen in relation to GI, BI, PPD, and CAL between test and control groups at baseline and 15 days.

Table 2 and Figure 1 depict the changes in the mean value of PPD at various points of time.

Microbiological analysis

Sub-gingival plaque samples for microbiological analysis were taken from the test and control sites at baseline, 15 days and 1 month. The data were derived from a total of 72 obtained subgingival plaque samples obtained. Microbiological parameters included the assessment of reduction of the three periodontal pathogens at baseline, 15 days and 1-month follow-up visits. The quantities of colonies are expressed as colony-forming units per ml.

The mean and standard deviation at different time intervals (baseline, 15 days and 1 month) with respect to Pg, Pi and Fn in test and control groups is shown in Table 2. At the follow-up intervals, an intragroup comparison revealed a statistically significant ($P < 0.05$) reduction in both the groups. The percentage change of prevalence of Pg, Pi and Fn at baseline, 15 days, and 1 month is shown in Table 3 for both test and control groups. Overall, in both the groups, there was statistically significant reduction in relation to the clinical parameters. Furthermore, the groups showed a reduction in the microbial count of Pg, Pi and Fn.

In Figures 2-4, the comparison of test and control groups with respect to Pg, Pi and Fn at various point of time, i.e., at baseline, 15 days and 1 month is seen.

Discussion

Advances in understanding the etiology and pathogenesis have led to the development and subsequent acceptance of the use of pharmacological agents in the management of periodontal diseases. However, the use of chemical compounds has exposed the patients to its different side effects. A lot of interest is undertaken by researchers to find effective remedies of diseases by harmless herbal drugs.

The present study was undertaken to evaluate the efficacy of subgingivally placed *Triphala* gel (Hiora GA) as an adjunct to SRP in the management of chronic periodontitis. The severity of chronic periodontal disease was similar in both

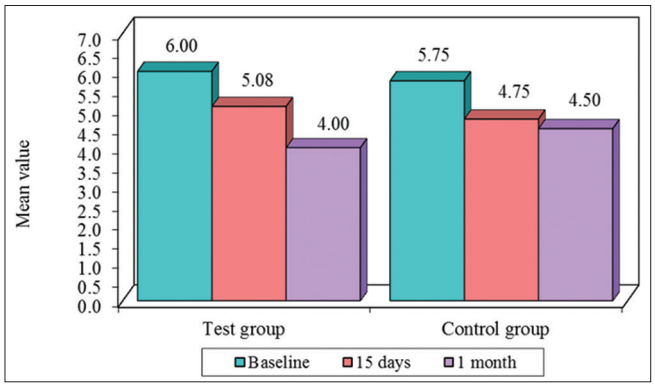

Figure 1: Comparison of test and control groups with respect to probing pocket depth scores

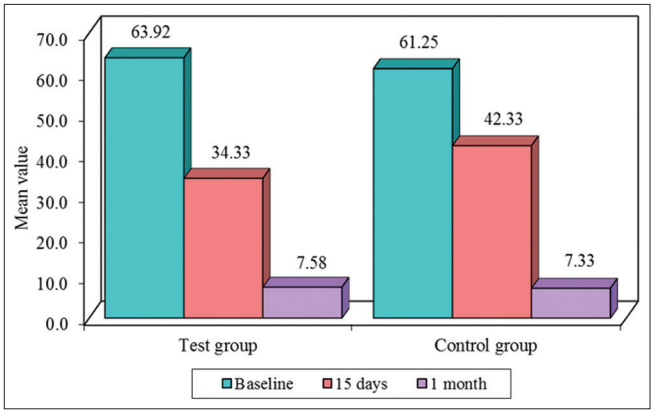

Figure 2: Comparison of test and control groups with respect to *Porphyromonas gingivalis* scores

Table 1: Comparison of clinical parameters in control and test sites at different time period

Pathogens	Control site (SRP), mean±SD			Test site (SRP and *Triphala* gel)		
	Baseline	15 days	1 month	Baseline	15 days	1 month
Mean GI	1.92±0.67	1.29±0.54	0.69±0.17	1.91±0.66	1.29±0.53	0.45±0.21
Mean BI	2.50±0.52	1.50±0.52	0.78±0.11	2.50±0.52	1.33±0.49	0.50±0.17
Mean PPD	5.75±1.06	4.75±0.97	4.50±0.90	6.0±0.95	5.08±0.90	4.00±0.73
Mean CAL	4.08±1.0	2.92±1.08	2.50±0.80	4.0±0.95	3.17±0.94	2.08±0.79

SRP: Scaling and root planning, SD: Standard deviation, GI: Gingival index, BI: Bleeding index, PPD: Pocket probing depth, CAL: Clinical attachment level

Table 2: Comparison of prevalence of *Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum* different time period in test and control sites

Pathogens	Control site (SRP), mean±SD			Test site (SRP + *Triphala* gel), mean±SD		
	Baseline	15 days	1 month	Base line	15 days	1 month
Pg	61.25±23.46	42.33±12.00	7.33±4.25	63.92±26.00	34.33±9.19	7.58±5.25
Pi	68.33±25.61	39.92±15.70	20.83±10.42	71.67±24.53	45.92±10.92	21.25±8.52
Fn	79.17±31.97	46.33±16.85	23.67±12.52	82.75±40.03	48.33±10.52	21.58±11.25

Pg: *Porphyromonas gingivalis*; Pi: *Prevotella intermedia*; Fn: *Fusobacterium nucleatum*, SRP: Scaling and root planning, SD: Standard deviation

Table 3: The percentage of change of prevalence of *Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum* at different time period in test and control sites

Clinical data	Percentage change at control sites (SRP)			Percentage change at test sites (SRP + *Triphala* gel)		
	Base line-15 days and *p*	Base line-30 days and *P*	15 days 30 days and *P*	Base line-15 days and *P*	Base line-30 days and *P*	15 days-30 days and *P*
Pg	30.88	88.03	82.68	46.28	88.14	77.91
	0.0342*	0.0029*	0.0281*	0.0135*	0.0029*	0.0042*
Pi	41.59	69.51	47.81	35.93	70.35	53.72
	0.0033*	0.0029*	0.0096*	0.0135*	0.0029*	0.0022*
Fn	41.47	70.11	48.92	41.59	73.92	55.34
	0.0033*	0.00338	0.0121*	0.0150*	0.0037*	0.0022*

*P<0.05. Pg: *Porphyromonas gingivalis*; Pi: *Prevotella intermedia*; Fn: *Fusobacterium nucleatum*, SRP: Scaling and root planning

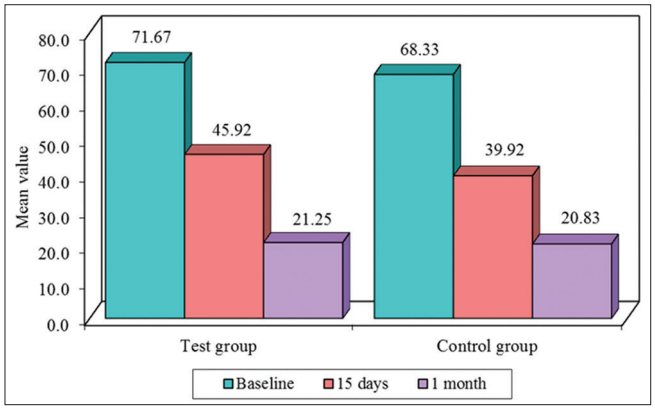

Figure 3: Comparison of test and control groups with respect to *Provetella intermedia* scores

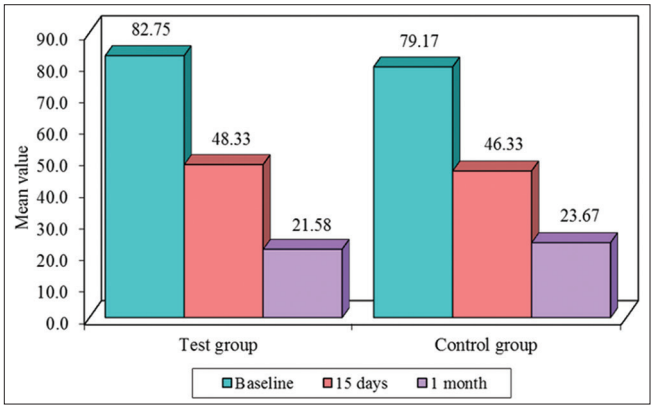

Figure 4: Comparison of test and control groups with respect to *Fusobacterium nucleatum* scores

the SRP group alone and SRP with *Triphala* gel (Hiora GA) group. During the active treatment, *Triphala* gel (Hiora GA) was well tolerated with no side effects observed in any of the patients. The clinical findings were evaluated at baseline, 15 days and after 1 month. To evaluate the efficacy of the treatments in suppressing the pathogenic flora, microbiological analysis of the subgingival samples was carried out along with clinical evaluation. Hence, the present study evaluated both clinical and microbiological parameters at baseline as well as after the placement of *Triphala* gel (Hiora GA) in the periodontal pockets and thus permitted correlation of the results. *Triphala* is also used as a blood purifier and possess anti-inflammatory, analgesic, anti-arthritic, hypoglycemic and anti-aging properties.[9]

An intergroup comparison done at baseline, 15 days and 1 month showed statistically significant ($P = 0.011$) reduction in gingivitis at the end of 1 month in group B, suggesting the efficacy of *Triphala* gel when used over a long period. In test group B, a reduction in bleeding scores was observed from baseline 2.50 ± 0.52 to 0.50 ± 0.17 at the end of 1 month which was statistically significant ($P = 0.0007$) when compared to that of control group A. In both groups, an initial reduction in pocket depth was observed, but at the end of 1 month, a statistically significant ($P = 0.16$) reduction in pocket depth was observed when *Triphala* gel was used, suggesting that the efficacy of *Triphala* gel over SRP alone. Intergroup comparison at 1 month revealed a statistically significant ($P = 0.18$) gain in CAL when *Triphala* gel was used.

Acharya Sushruta mentioned that *Triphala* pacifies *Kapha* and *Pitta Dosha*, which are the main causative factors of the periodontal diseases. It is also well acknowledged in classical Ayurvedic texts, *Triphala* has hemostatic, anti-inflammatory, analgesic and wound healing properties. *Haritaki* use in the mouth has shown effective results in treating bleeding gums and gingival ulcers and carious teeth. *Amalaki* contains enormous vitamin 'C' which is very essential to treat the bleeding gums.[10]

In the present study, there was significant inhibitory effect both the groups on Pg at baseline, 15 days and 1 month intervals, but no statistically significant ($P = 0.707$) differences were observed between both the groups. Intergroup comparison at 1 month revealed no statistically significant differences ($P = 0.686$) in the inhibition of Pi in both the groups. However, both the groups at baseline, 15 days and 1-month interval showed a statistically significant reduction in Fn, but at the end of 1 month, there were no statistically significant differences ($P = 0.506$) observed between both the groups.

Jagadish *et al.* conducted a study to determine the effect of *Triphala* on dental biofilm and concluded that *Triphala* has a potent anti-oxidant and antimicrobial activity and it inhibited the growth of *Streptococcus mutans* and Gram-positive cocci

which are involved in plaque formation when it was adsorbed onto the tooth surface.[11] The herbal extract effectively inhibited the biofilm formation and better anti-oxidant activity was exhibited by this extract which might be useful in protecting the gum cells effectively from released free radicals. *Terminalia bellerica* was shown to have the most active antioxidant, followed by *Phyllanthus embelica* and *T. chebula*. The major ingredients of *T. bellerica* are ellagic and gallic acid. *P. embelica* has several gallic acid derivatives, including epigallocatechin gallate and gallic acid, which is the major ingredient in *T. chebula*. The presence of these active ingredients, which are phenolic nature, might be responsible for scavenging of the free radicals. Studies showed that *T. chebula* which acts as anticaries agent, strongly inhibits the sucrose- or glucan-induced aggregations of *S. mutans*[12] and strengthens the gums, prevents and treats several diseases of mouth such as dental caries, spongy and bleeding gums gingivitis, and stomatitis.[13] Tannic acid is one of the major ingredients of the ripe fruit of *T. chebula, T. belerica*, and *P. embelica*. The tannic acid (in *Triphala*), has shown to be adsorbed well to the hydroxyapatite of the tooth or the salivary mucins. Alternately, it can also bind to anionic groups on the surface of the bacterial cells, which results in protein denaturation and ultimately lead to bacterial cell death.[11] Earlier studies have reported that tannic acid can be both bacteriostatic or bactericidal to some gram-positive and gram-negative pathogens.

Triphala has also shown to have inhibitory activity against MMP-9.[8] It allows suppression of collagenase activity well within the safety profile of toxicological studies. In addition, property other biological activities of *Triphala* which are well known to make it a potential Ayurvedic drug for the treatment of periodontal disease. Since Ayurvedic System of Medicine has a long history of therapeutic potential, it can be used as a logical approach to drug discovery, to screen the traditional natural products such as *Triphala* which shows a scientific proof of its superior antimicrobial potential.

Conclusion

The present study demonstrated a significant reduction of the GI, BI, probing pocket depth (PPD), CAL in the test group treated with SRP and *Triphala* (Hiora GA) when compared to the control sites treated with SRP alone. It is to conclude that subgingivally delivered *Triphala* (Hiora GA) as an adjunct to scaling and root planning (SRP) in the treatment of chronic periodontitis has shown promising results. Therefore, dosage form of *Triphala* are likely to replace the chemical compounds soon as it has intense antimicrobial, less side effects, and its cost-effective preventive strategies. However, more scientific work needs to be carried out to prove the efficacy.

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Conflicts of interest

There are no conflicts of interest.

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