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RESEARCH ARTICLE

COMPARATIVE CLINICAL EVALUATION OF EFFICACY OF SYSTEMICALLY ADMINISTERED ANTIOXIDANT LYCOPENE (STARMUNE®) AND HERBAL (OXITARD™) AS AN ADJUNCT TO SCALING AND ROOT PLANING IN PATIENTS WITH CHRONIC GINGIVITIS- A RANDOMIZED CLINICAL TRIAL

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Abstract

Background: It is a complex interaction between host-microbial interactions involving cellular and humoral factors and networks of cytokines, chemokine, and some growth factors. Reactive oxygen species (ROS) and the antioxidant defense systems that repair cell, and molecular. Some of the true major reactive oxygen species and free radicals are superoxide, hydroxyl, per hydroxyl, hydrogen peroxide, hypochlorous acid, ozone. There is an equilibrium between increases ROS and decreases antioxidant defense due to oxidative stress.

Materials and Method: Total thirty systemically healthy subjects were selected with age group 20±45years. Subjects were randomly assigned into 3 Groups. Group I: 10 patients receiving scaling and root planning alone, Group II: 10 patients receiving Starmune™ 5mg capsule with SRP twice a day for 2weeks, Group III: 10 patients receiving Oxitard™ manufactured by Himalaya Herbals® with SRP twice a day for 2 weeks. Clinical parameters such as Plaque index, gingival index and Sulcus bleeding index was evaluated at baseline after 2weeks.

Results: Plaque index on compare from baseline to after 2 weeks no significant difference was observed. While in Gingival index from baseline to 2 weeks more significant difference was observed in group II group III compare to group I. In Sulcus bleeding index from baseline to 2weeks no statistical significant difference were observed.

Conclusion: The antioxidant Lycopene and Herbal Oxitard™ have also shown an additional benefit as an adjunct to non-surgical periodontal therapy.

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Introduction:-

Periodontal disease is a multifactorial disease-causing inflammation of supporting tissue in periodontium which leads to periodontal tissue destruction and progression of diseases. Biofilm present on the tooth surface is mostly due to gram-negative bacteria. Bacteria that colonize the periodontal tissues in the inflammatory and immune response ultimately involved the systemic circulation of the body¹. There are a complex bi-directional series of host-microbial

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interactions involving cellular and humoral factors and networks of cytokines, chemokine, and some growth factors. More specifically, there is an imbalance between proteolysis enzymes and their inhibition. For examples: reactive oxygen species (ROS) and the antioxidant defense systems that repair tissue, cell, and molecular²

Free Radicals is a term as “any species capable of independent existence that contain one or more unpaired electrons” Reactive oxygen species are capable of oxidizing a various biomolecules cell and tissue function that include free radicals, chlorine and nitrogen which are highly reactive in nature³

Battino et al., (1999) reported that the term ROS is more popular as it encompasses other reactive species which are not true radicals but still them capable of formed intracellular and extracellular environment. Some of the true major reactive oxygen species and free radicals are superoxide, hydroxyl, per hydroxyl, hydrogen peroxide, hypochlorous acid, ozone etc⁴

The antioxidant is a lower concentration of oxidized substrate. The equilibrium between increases ROS and decreases antioxidant defense due to oxidative stress⁵ Sies et al., (1991) stated that oxidative stress has been defined “as a disturbance in the pro-oxidant–antioxidant balance in favor of the former, leading to potential damage”⁶

ROS may harm different types of cells and tissues through protein damage, lipid peroxidation and DNA damage. In chronic inflammation presence of periodontal pathogens may act against reactive oxygen species to damage the tissue of Periodontium. The antioxidants an important role in preserving the structural integrity of cells and tissues. It maintains the balance between oxidant and antioxidants⁷

The various classification system has been categorized⁸:

1. The mode of function
2. The location of action- intracellular and extracellular

Preventive antioxidants:

Examples: Enzymes: superoxide dismutase enzymes (1, 2 and 3), catalase, glutathione peroxidase, DNA repair enzymes.

Scavenging (chain breaking) antioxidants:

Examples: Vitamin C, carotenoids (including retinol – vitamin A), uric acid, a-tocopherol (vitamin E), polyphenols (flavonoids), bilirubin, albumin, ubiquinone (reduced form), reduced glutathione and other protein-bound)

Over 600 carotenoids have been identified to date. Carotenoids are recognized as substances that give color to vegetables and fruits, and their antioxidant effects as vitamin A precursors are well-known. Most important carotenoids are α -carotene, β -carotene, lycopene, crocetin, canthaxanthin, and fucoxanthin. B-carotene is a combination of two molecules of vitamin A (also known as retinol) and gets absorbed by the small intestinal mucosa⁹

Lycopene is known as the carotenoids. The greatest known source of lycopene is tomatoes, which are widely used for cooking. The inter-relationship between lycopene intake and risk of diseases due to free radicals may lead to cancer, cardiovascular diseases, asthma, arthritis, stroke, cataract genesis, hepatitis and also periodontitis. Lycopene is the most efficient biological antioxidizing agents due to this property¹⁰⁻¹¹

While the herbal product OxitardTM capsules (Himalaya Drug Company) has been reported to protect the free radical damages¹²

Material and Method:-

The study was conducted in Swargiya Dadasaheb Kalmegh Smruti Dental College and Hospital, Nagpur. Total thirty systemically healthy subjects were selected from the outpatient's Department of Periodontology. Patients with age (20±45 years) were involved in the randomized clinical trial. The patients were divided into three groups with a sign of mild to moderate gingivitis. The patients were randomly distributed between the three treatment groups: Group I (n=10), received only oral prophylaxis alone, Group II (n=10), received 5mg Lycopene/ day for 2 weeks with oral prophylaxis (full mouth scaling and root planing completed) commercially available as (Cap. StarmuneTM 5mg, Akumentis Healthcare Ltd, Mumbai, India contained natural Lycopene, Fig. 1)



Figure. 1:- Cap. Starmune™ 5mg.

Group III (n=10) received Herbal Antioxidant /day for 2 weeks with complete oral prophylaxis. Herbal Product-Capsule Oxitard™ (Himalaya Drug Company, Bengaluru, Karnataka, India. Fig.2)

Product Ingredients:

(Mangifera indica)- 94 mg, Ashwagandha (Withania somniferous) - 71 mg, Gajara (Daucus carota) - 47 mg, Yashtimadhu (Glycyrrhiza glabra) - 29 mg, Draksha (Vitis vinifera) - 12 mg. The powder comprise Amalaki (Embolia officinalis) - 141 mg, Lavanga (Syzygy aromaticum) -29 mg, Yashada brahma -2.5 mg, Oil Godhuma (Triticum aestivum) -6.5 mg



Figure.2:- Cap. Oxitard™

Inclusion and Exclusion criteria:

Patients showing clinical sign of mild to moderate gingivitis and probing depth <4mm with no evidence of clinical attachment loss. Patients who have not received any medication before such as antibiotics for past 6 months or counter an antioxidant like Vit C, Vit B, β -carotene within past 3 months and did not receive drug allergy will be included in the study.

Patients with the systemic condition, such as cardiovascular diseases, pregnant and lactating women, diabetes, and intake of smokers were excluded from the study.

All the patients instructed and motivated to maintain oral hygiene during the study period. Patients were randomly assigned in three groups 10 on each group based upon the coin toss method. All the patient received inform consent followed by deep scaling and root planing performed using ultrasonic scalers and universal curettes. All the clinical

parameters were evaluated at baseline and 2 weeks, such as Plaque Index by Silness and Loe, (1964)¹³, Gingival index by (Loe and Silness, (1963)¹⁴, Sulcus Bleeding Index by Mulhemann& Son (1971)¹⁴.

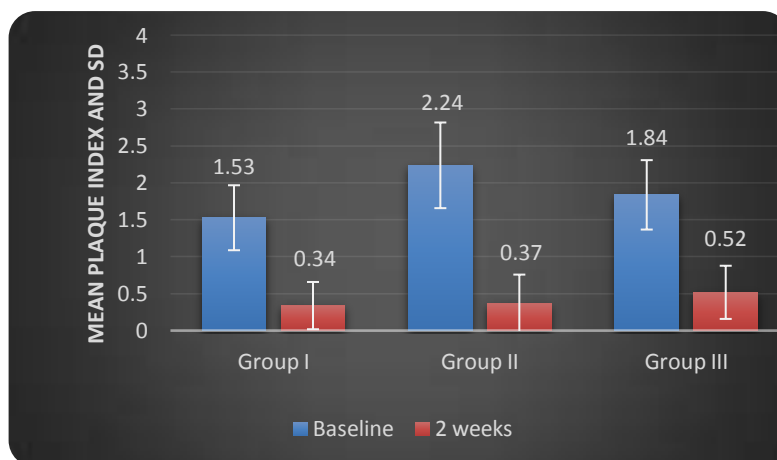
Statistical Analysis:

After the completion of the study, the analysis was carried out. The statistical analysis was done by using descriptive and inferential statistics using Student's paired t-test, one way ANOVA and Multiple Comparison: Tukey Test and software used in the analysis were SPSS 22.0 version and $p < 0.05$ is considered as the level of significance.

Results:-

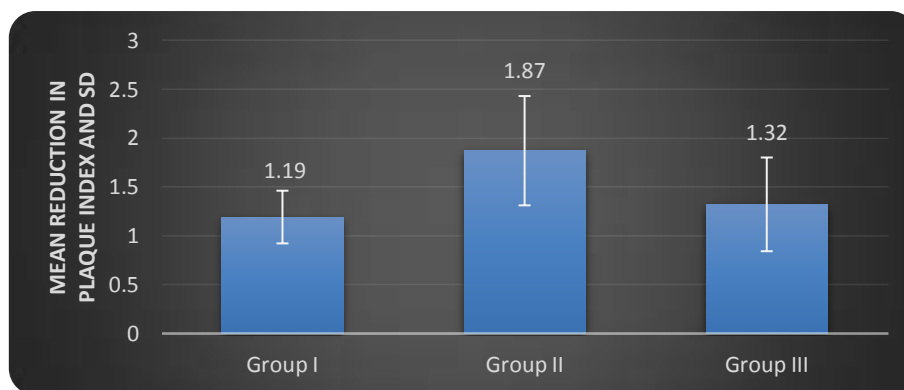
Plaque Index:

In mean plaque index in group I at baseline was 1.53 ± 0.44 and at 2 weeks it was 0.34 ± 0.32 . By using Student's paired t-test statistically significant difference was found in mean plaque index in group I ($t=13.60$, $p=0.0001$). In mean plaque index in group II at baseline was 2.24 ± 0.58 and at 2 weeks it was 0.37 ± 0.39 . By using Student's paired t-test statistically significant difference was found in mean plaque index in group II ($t=10.48$, $p=0.0001$). In mean plaque index in group III at baseline was 1.84 ± 0.47 and at 2 weeks it was 0.52 ± 0.36 . By using Student's paired t-test statistically significant difference was found in mean plaque index in group III ($t=8.56$, $p=0.0001$).



Graph 1:- Plaque index analysis in three groups from baseline to 2 weeks.

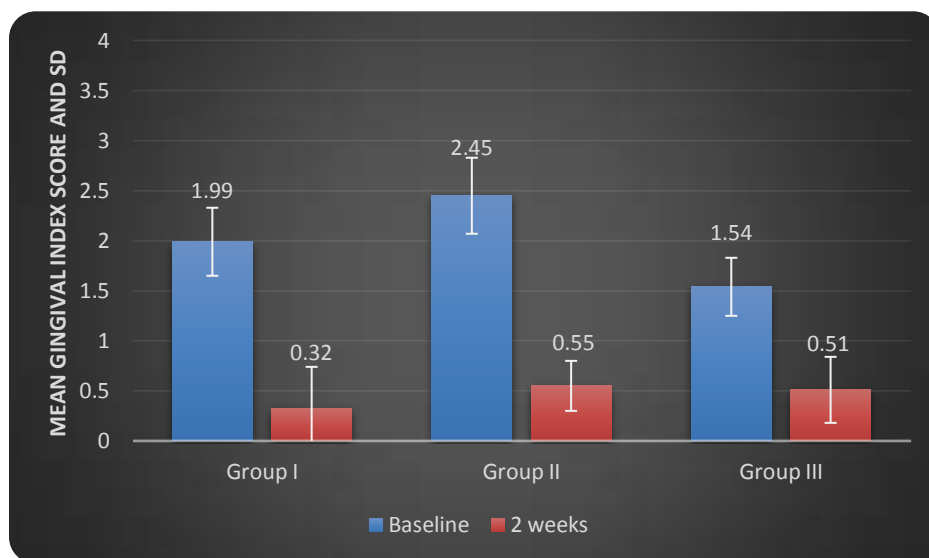
On comparison mean reduction in plaque index at 2 weeks in group I was 1.19 ± 0.27 , in group II it was 1.87 ± 0.56 and in group III it was 1.32 ± 0.48 . By using one way ANOVA statistically significant variation was found in a mean reduction in plaque index in three groups ($F=6.187$, $p=0.006$). By using multiple comparisons Turkey-Test statistically significant difference was found in mean reduction between group I and group II ($p=0.007$) and between-group II and group-III ($p=0.032$) and no significant difference was found between group I and group III ($p=0.803$).



Graph 2:- Comparison of mean reduction in Plaque index in three groups.

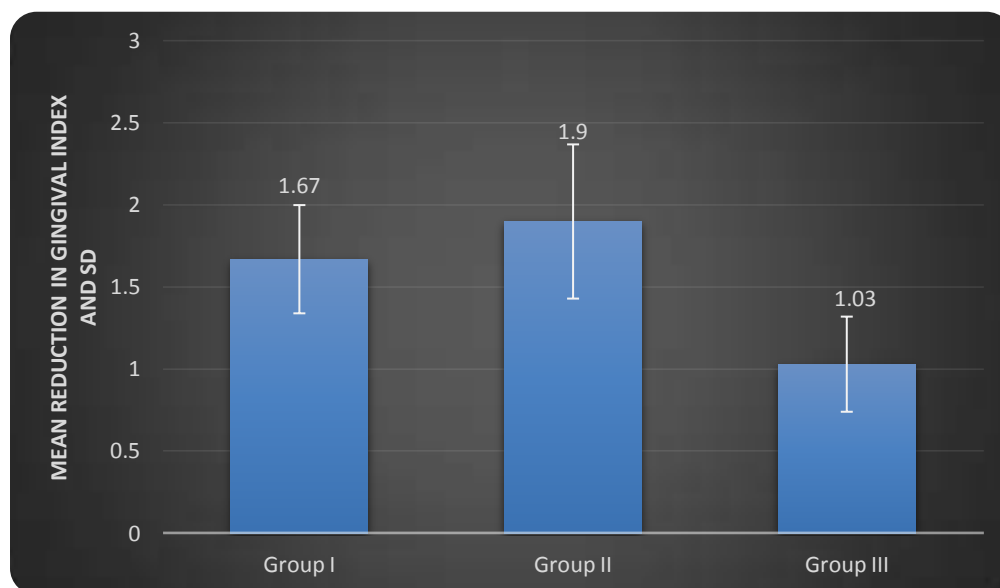
Gingival Index:

In mean gingival index in group I at baseline was 1.99 ± 0.34 and at 2 weeks it was 0.34 ± 0.42 . By using Student's paired t-test statistically significant difference was found in the mean gingival index in group I ($t=15.67$, $p=0.0001$). In mean gingival index in group II at baseline was 2.45 ± 0.38 and at 2 weeks it was 0.55 ± 0.25 . By using Student's paired t-test statistically significant difference was found in the mean gingival index in group II ($t=12.74$, $p=0.0001$). In mean gingival index in group III at baseline was 1.54 ± 0.29 and at 2 weeks it was 0.51 ± 0.33 . By using Student's paired t-test statistically significant difference was found in the mean gingival index in group III ($t=8.56$, $p=0.0001$).



Graph 3:- Gingival index analysis in three groups from baseline to 2 weeks.

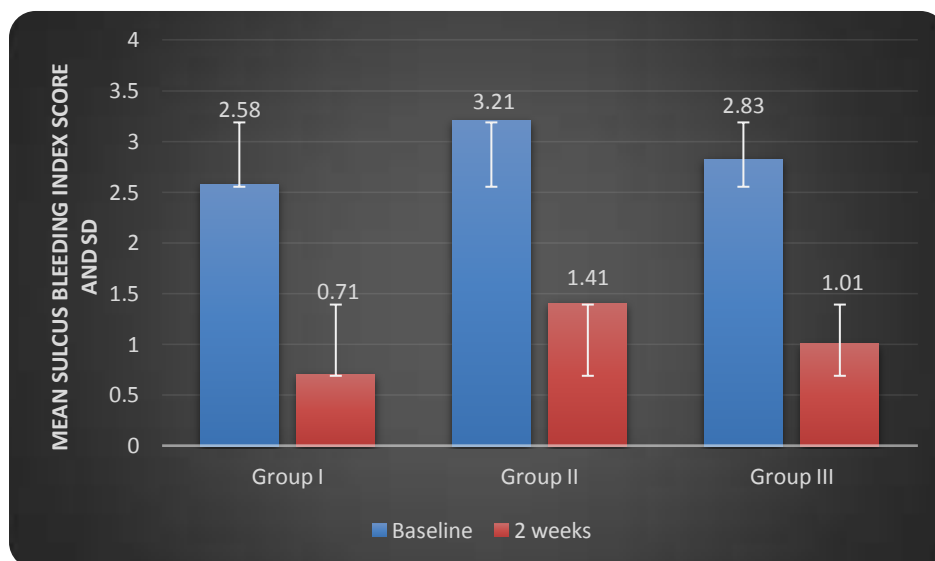
On comparison of mean reduction in the gingival index at 2 weeks in group I was 1.67 ± 0.33 , in group II it was 1.90 ± 0.47 and in group III it was 1.03 ± 0.29 . By using one way ANOVA statistically significant variation was found in a mean reduction in the gingival index in three groups ($F=14.35$, $p=0.006$). By using multiple comparisons Turkey-Test no statistically significant difference was found in mean reduction between group I and group II ($p=0.372$) and significant difference between group II and group-III ($p=0.0001$) and no significant difference was found between group I and group III ($p=0.002$).



Graph 4: Comparison of mean reduction in the gingival index in three groups.

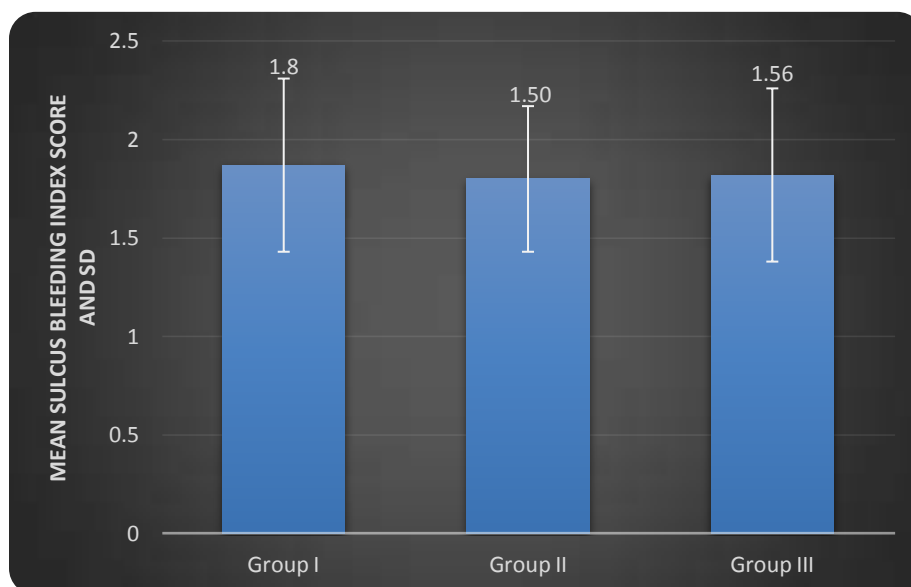
Sulcus Bleeding Index:

In mean sulcus bleeding index in group I at baseline was 2.58 ± 0.56 and at 2 weeks it was 0.71 ± 0.68 . By using Student's paired t-test statistically significant difference was found in mean sulcus bleeding index in group I ($t=13.14$, $p=0.0001$). In mean sulcus, bleeding index in group II at baseline was 3.21 ± 0.34 and at 2 weeks it was 1.41 ± 0.55 . By using Student's paired t-test statistically significant difference was found in mean sulcus bleeding index in group II ($t=15.09$, $p=0.0001$). In mean sulcus, bleeding index in group III at baseline was 2.83 ± 0.34 and at 2 weeks it was 1.01 ± 0.52 . By using Student's paired t-test statistically significant difference was found in mean sulcus bleeding index in group III ($t=12.88$, $p=0.0001$).



Graph 5:- Sulcus bleeding index analysis in three groups from baseline to 2 weeks.

On comparison mean reduction in sulcus bleeding index at 2 weeks in group I was 1.87 ± 0.44 , in group II it was 1.80 ± 0.37 and in group III it was 1.82 ± 0.44 . By using one way ANOVA no statistically significant variation was found in a mean reduction in sulcus bleeding index in three groups ($F=0.072$, $p=0.931$). By using multiple comparisons Turkey-Test statistically, no significant difference was found in mean reduction between group I and group II ($p=0.928$) and between-group II and group-III ($p=0.994$) and no significant difference was found between group I and group III ($p=0.963$).



Graph 6:- Comparison of mean sulcus bleeding index score in three groups.

Discussion:-

Periodontitis is an inflammatory condition representing the tissue response from the gram-negative bacteria. There is evidence that reactive oxygen species in the periodontal pathogen of inflammatory disorders¹⁵ A variety of ROS (e.g. Hydrogen peroxide, Hypochlorous acid, singlet oxygen) which can cause tissue damage by initiating a free radicals chain reaction¹⁶⁻¹⁷ This modulation of the free radical production seems to be essential for the inhibition of tissue destruction, and treatment with drugs that block the production of free ROS may be valuable.¹⁸⁻¹⁹ However chemotherapeutic agents used in periodontal therapy in addition to their antiseptic and antimicrobial effects are known to have an ant oxidative activity against oxidation²⁰ Among all the carotenoid, lycopene stands as the most potent antioxidant and immunomodulation agents. Various ingredients of it act as immunomodulation, free radical scavenger, and sources of Vit. A & Vit. C, they stimulate antioxidant enzyme activity, they repair oxidative damage, and they stimulate repair enzyme activity. However, the synergistic effect is known due to the combination of lower concentration of retinoid with other antioxidant agents like Lycopene and α -tocopherol Vit. E, Vit. C²¹

In the present study patients with chronic gingivitis were selected and administered antioxidant lycopene (StarmuneTM) and herbal (OxitarTM) as an adjunct to SRP. The patients enrolled in this study were given the regimen with no adverse effects of any rashes or allergic reaction. In this study, the plaque index, the gingival index shows statistically significant mean reduction in group II and group III, However similar results also reported by Chandra et al., 2007²², Shetty NA et al., 2012²³ who evaluated the effect of systemically administered lycopene as monotherapy as an adjunct to chronic gingivitis and found a statistically significant mean reduction in the gingival index and also in salivary uric acid levels.

S. Kaur et al., (2017)²⁴ conducted a study to evaluate anti-inflammatory effects of systemically administered curcumin, lycopene, piperine as an adjunct to scaling and root in terms of changes in plaque index, gingival index, probing pocket depth at baseline and 21 days and the author concludes that the orally administered antioxidants Lycopene could cause significant resolution of inflammation when used as an adjunct to SRP.

However, Herbal Antioxidants OxitarTM the present study also shows statistical significant mean reduction in gingival index, and sulcus bleeding index. It's found to be effective in the reduction of gingival lesion such as desquamative gingivitis and in the study Patil et al., (2014)²¹ for the treatment of oral submucous fibrosis because of its antioxidant & anti-inflammatory properties.

Similar results reported by Sravya et al., (2019)²⁵ who evaluated as smokers are more prone to tissue injury due to excessive release of ROS. Total 40 smokers with chronic periodontitis were randomly divided into groups. In the intragroup assessment statistically significant improvement in clinical and biochemical parameters observed from baseline to 3 months. Thus the author concluded that the OxitarTM is a powerful herbal antioxidant that can counteract the action of free radicals.

Future research need to focus on the mixture of antioxidants are more synergistic effect in the treatment of periodontal disease. Therefore long term studies needed.

Conclusion:-

Thus to understand, the study shows no adverse effects on systemically administered Drugs while, comparing a gold standard scaling and root planing, the antioxidant Lycopene and Herbal OxitarTM have also shown an additional benefit as an adjunct to non-surgical periodontal therapy.

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Nil

Conflicts of interest:

There are no conflicts of interest.

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