

Nature Itself Is The Best Medicine – Herbal Local Drug Delivery In Periodontitis

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Abstract: Periodontal disease is a chronic inflammatory disease affecting the supporting structures of the teeth. It is multifactorial in origin which leads to many therapeutic modalities for its management. The use of natural therapies for all kinds of diseases is now being considered for the treatment of many chronic diseases. Herbal drugs in a suitable vehicle such as in the form of a local drug delivery system can be a good adjunct and alternative to conventional periodontal treatment. [Karanjkar A NJIRM 2015; 6(6):83-88]

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Introduction: Microbial plaque accumulation in gingival crevices induces an inflammatory response which progresses into a chronic destructive condition of the supporting tissues of the teeth termed as periodontitis. Periodontitis, one of the common causes of tooth loss, is the outcome of mainly poor oral hygiene, poor nutrition or any underlying systemic conditions. Microbial and other environmental factors are believed to initiate and modulate periodontal disease and genetic predisposition leads to its progression.

Until now the treatment was mainly on the basis of microbial etiology. Current research is focused on host modulatory therapy (HMT) which uses immunomodulatory intervention strategies which help in tuning of the host response to maximize the protective and minimize the destructive aspects of periodontal host response (HMT). The present scenario of periodontal treatment consists of combination of mechanical, antimicrobial and host modulation therapy.¹

Available host modulatory agents are either collagenase inhibitors, bisphosphonates, or agents restricting the production of MMP's, cytokines or prostanoids. But HMT is also meant to disrupt the cell signaling pathways. When there is a microbial challenge, the virulence factors acts as inducing stimulus for signal transduction which ultimately results in cytokine production and other secondary mediators like MMP's and PGE2. Side effects and increased cost of production of synthetic agents have prompted researchers to think about naturally available agents for HMT. Many natural products have been tried for periodontal host modulation therapy which include turmeric, clove, neem, green tea, honey,

Triphala etc. Antimicrobial, anti-inflammatory, antiplaque, antioxidant and astringent actions of these agents have been confirmed in several studies. Natural agents for periodontal therapy must be effective, affordable and acceptable to the patient.¹

Medicinal plants have been used as traditional treatments for numerous human diseases for thousands of years and in many parts of the world. In rural areas of the developing countries, they continue to be used as the primary source of medicine. About 80% of the people in developing countries use traditional medicines for their health care. The natural products derived from medicinal plants have proven to be an abundant source of biologically active compounds, many of which have been the basis for the development of new lead chemicals for pharmaceuticals. With respect to diseases caused by microorganisms, the increasing resistance in many common pathogens to currently used therapeutic agents, such as antibiotics and antiviral agents, has led to renewed interest in the discovery of novel anti-infective compounds. As there are approximately 500,000 plant species occurring worldwide, of which only 1% has been phytochemically investigated, there is great potential for discovering novel bioactive compounds.²

Benefits of herbal drugs: Herbal drugs have long era of use and better patient tolerance as well as public acceptance.

Herbal drugs acts as a renewable source, which is our only hope for sustainable supplies of cheaper medicines for the worlds growing population. Availability of medicinal plants is not a problem

especially in developing countries like India having rich agro-climatic, cultural and ethnic biodiversity.

The cultivation and processing of medicinal herbs and herbal products is environment-friendly.

Throughout the world, herbal medicine has provided many of the most useful and vast variety of drugs to the modern medical science.²

Local drug delivery: The choice of the antimicrobial agents in periodontal diseases must be based on the bacterial etiology of the infection. Several antibiotics have been tested for their clinical and microbiological efficacy in periodontal diseases. It can be noted that only a limited number of antimicrobial agents have been used so far in formulations of local delivery systems. There are distinct phases in a periodontal treatment plan where a dental practitioner can use a sustained release device. It can be used as an adjunct to scaling and root planing and for periodontal maintenance therapy and can be safely used in medically compromised patients.³In recent times novel drugs are been tried in local drug delivery such as herbal products, growth factors and some drugs to rectify the osseous defects.⁴

The various herbal drugs that have been used in the treatment of periodontal disease are aloe vera, Green tea, neem, turmeric, curcumin, honey. They have been used as gels, mouthrinses, ointments, as a component of capsules that can be ingested and even as local drug delivery systems.

Various herbal substances used for local drug delivery in periodontitis:

ALOE VERA



Aloe Vera has been used medicinally for a few thousand years. Its history of health benefits was first recorded in Egyptian medical writings in 1500BC. Even Cleopatra was said to have pampered her skin with Aloe gel. History reports that Alexander the Great captured the island of Socotra in the Red Sea, which had abundant Aloe fields, to help heal the battle

wounds of his troops. Aloe was applied to cuts, infections, blisters, insect bites and used for internal maladies. The initial credible research on Aloe Vera was done by Dr. C.E. Collins in 1934, where several cases of Roentgen Dermatitis, the ulcerated skin lesions were treated with Aloe Vera leaves split and wrapped around the wounds. A markedly improved rate of healing was observed.

The constituents of aloe vera are related to biological effects, which are as follows:⁵

- Healing properties
- Protective effects
- Anti-inflammatory action
- Effects on immune system
- Antibacterial
- Antioxidant
- Antiviral
- Antitumor activity
- Moisturizing and anti-ageing effect
- Antiseptic effect

Aloe vera is a handy home remedy that can be used as a moisturizing agent. Aloe vera has been used for various skin conditions, including radiodermatitis, frostbite, psoriasis and genital herpes infection with good results.

Dental uses of Aloe vera are multiple. It is extremely helpful in the treatment of gingivitis, periodontitis and reduces bleeding and inflammation. It is a powerful antiseptic in pockets where normal cleaning is difficult, and its antifungal properties help greatly in the problem of denture stomatitis, aphthous ulcers, cracked and split corners of the mouth. It is a powerful healing promoter and can be used following extractions. It has been used in root canal treatment as a sedative dressing and file lubrication during biomechanical preparation.⁶

Subgingival administration of aloe vera gel results in improvement of periodontal condition. Aloe Vera can be used as a local drug delivery system because of its various benefits such as:

1. It is easily available.
2. It is cheap
3. Easily applicable with minimal equipments

Aloe latex contains anthraquinones, which are chemical compounds that are used in healing and arresting pain because they are anti-inflammatory in

nature. But, because aloe vera tooth gel tends to be less harsh on teeth, as it does not contain the abrasive elements typically found in commercial toothpaste, it is a great alternative for people with sensitive teeth or gums.⁷

A study was done by Virdietto evaluate the effect of **aloe vera gel** as an adjunct to scaling and root planing (SRP) in the management of chronic periodontitis. On one side, SRP was done and on the contra lateral side along with SRP pure aloe vera gel was applied in the periodontal pockets at the baseline. Aloe vera gel was applied by a syringe inserted up to the base of the pocket. Aloe vera gel used in this study was CURAGEL prepared by Cure Pharma. It is the pure aloe vera extract obtained from the centre of the leaf, processed to eliminate the toxins and having 2% sodium benzoate as a preservative. Aloe vera gel was reapplied after the first week and second week in the selected site just at the entrance of the periodontal pocket. Probing pocket depth, gingival index and plaque index were noted at the baseline and after 6 weeks. There was a significant improvement in the periodontal parameters after 6 weeks in both the groups. On comparing, the SRP with aloe vera group showed significantly better results than SRP alone ($P < 0.0001$). This study shows that the use of aloe vera can indeed be used in the management of periodontal disease.⁷

GREEN TEA



Green tea is widely consumed in China, Japan, Korea, and Morocco. It has been considered as a healthy beverage since ancient times. The traditional Chinese medicine has recommended this plant for headaches, body aches, general pain, digestion, depression, as an energizer, and in general to prolong life. Green tea also has many oral health benefits. It has cognitive function and positive impact on bone density, caries, periodontal disease, and diabetes. Numerous epidemiological and clinical studies have revealed several physiological responses to green tea that may be relevant in promoting health and preventing or treating some chronic diseases.

The main components in green tea responsible for its use in periodontal disease are the catechins. They have the following biological actions: antioxidative property, capacity to modulate the physical structure of cell membranes, antimicrobial property and also anticariogenic activity. These have led to an interest in green tea for the benefit of oral health and in particular periodontal health.

Kaneko et al found that a four-week regimen of mouth washing with a dilute catechin solution reduced the halitosis associated with periodontal disease. Tea catechins especially EGCG deodorizes methyl mercaptain, the main cause of halitosis. EGCG inhibited growth and adhesion of *Porphyromonasgingivalis* to buccal epithelial cells. Hirasawa et al demonstrated bactericidal activity of green tea catechins against prevotella and *P. gingivalis* at concentration of 1 mg/ml. They found significant reduction in markers of gingivitis after the use of slow release buccal delivery system applied over a period of 8 weeks. More recent studies have shown that some virulence factors (toxic metabolites, protein tyrosine phosphatase, and gingipains) and aetiological agents of periodontal disease are neutralised by EGCG and green tea polyphenols inhibit the collagenase activity of oral bacteria. Among the tea catechins ECG and EGCG with galloyl radical, showed the most potent inhibition effect on collagenase activity when an optimal concentration of tea catechins (100 µg/ml) was added to reaction mixture containing collagenase and collagen.⁸

Kudva et al did a study to evaluate the adjunctive use of locally delivered green tea catechin with scaling and root planing, as compared to scaling and root planing alone in the management of chronic periodontitis. Test sites received scaling and root planing along with green tea catechin strips and control sites received scaling and root planning alone. Green tea catechin strips were manufactured by Department of Pharmaceutics, KLES College of pharmacy, Hubli, Karnataka. Strips are transparent rectangular shaped (size- 2 mm in width, length- 4 mm and 0.3 mm in thickness) with catechin used from green tea powder and hydroxypropyl cellulose (HPC) as the carrier. Green tea catechin chip was grasped with tweezer and inserted deep in the periodontal pocket so that the chip rested subgingivally at the base of the pocket, and not exposed. Intercomparison between microbial

results demonstrated a considerable reduction of occurrence of *Aggregatibacter actinomycetemcomitans*, *Prevotella intermedia*, *Fusobacterium* species and *Campylobacter* in test. It was concluded that green tea catechin local delivery along with scaling and root planing is more effective than scaling and root planing alone.⁹

Hattarki et al did a study to assess the effect of green tea catechins on the red complex organisms using Polymerase Chain Reaction for microbiological analysis. The Hydroxy propylcellulose strips (HPC), containing catechin, were rectangular measuring 2 mm in width, 4 mm in length, and 0.3 mm in thickness and were placed into the selected study sites and covered by Coe-pack to keep the strip in place. Clinical and microbiological parameters were recorded at baseline, 1st, and 5th week after treatment. The results showed statistically significant difference in clinical parameters and significant reduction of red complex organisms from baseline to 1st week and baseline to 5th week in both study and control groups. Hence green tea catechin can be used as an effective local drug delivery along with scaling and root planing in treatment of chronic periodontitis.¹⁰

NEEM



Neem has been used in India and South Asia for thousands of years as the preferred tool for maintaining healthy teeth and gums. Brushing with neem twigs and chewing neem leaves and seeds after a meal has been the traditional dental care practice in this area. With available modern preparations many people are now using commercial products that contain the same basic neem components.

The antibacterial activity of neem has been evaluated and known from ancient times. Neem has been considered to have various activities such as astringent, antiseptic, insecticidal, anti ulcer and for cleaning the teeth in pyorrhoea and other dental

diseases. Other than this leaf extract of the neem showed superior antiviral and antihyperglycemic activity *in vitro* and *in vivo* on animals.

Leaves of the neem have been used in the treatment of gingivitis and periodontitis. Neem has also showed better efficacy in the treatment of oral infections and plaque growth inhibition in treating periodontal disorders. Neem had showed good *in vitro* broad range antibacterial activity.

Pai et al did a study to evaluate the effectiveness of neem (*Azadirachta indica* A. Juss) leaf extract against plaque formation. This was assessed in males between the age group of 20–30 years over a period of 6 weeks. The study included formulation of mucoadhesive dental gel containing *Azadirachta indica* leaf extract (25 mg/g). Neem extract was prepared from the dried leaves of neem collected from the medicinal garden of College of Pharmaceutical Sciences, Manipal, India and dried under controlled parameters. The concentration of the neem extract in the gel formulation was restricted to 25 mg/g of the gel to fulfill the organoleptic properties of the final formulation, as neem is bitter drug. A 6-week clinical study was conducted to evaluate the efficacy of neem extract dental gel with commercially available chlorhexidine gluconate (0.2% w/v) mouthwash as positive control. Microbial evaluation of *Streptococcus mutans* and *Lactobacilli* species was carried out to determine the total decrease in the salivary bacterial count over a period of treatment using a semi-quantitative four quadrant streaking method. The results of the study suggested that the dental gel containing neem extract has significantly reduced the plaque index and bacterial count than that of the control group.¹¹

TURMERIC



India has a rich history of using plants for medicinal purposes. Turmeric (*Curcuma longa* L.) is a medicinal

plant extensively used in Ayurveda, Unani and Siddha medicine as home remedy for various diseases. Turmeric is used as a food additive, preservative and colouring agent in Asian countries, including China and South East Asia. It is also considered as auspicious and is a part of religious rituals. In recent times, traditional Indian medicine uses turmeric powder for the treatment of biliary disorders, anorexia, coryza, cough, diabetic wounds, hepatic disorders, rheumatism and sinusitis. In China, *C. longa* is used for diseases associated with abdominal pains. The colouring principle of turmeric is the main component of this plant and is responsible for the anti-inflammatory property.¹²

Therapeutic effects of turmeric in turn depend on the therapeutic actions of curcumin:

It protects against free radical damage because it is a strong antioxidant.

It lowers the histamine level and stimulates the production of natural cortisone from adrenal glands. Thus it has a major role in reducing inflammation.

It protects the liver from a number of toxic compounds such as carbon tetrachloride, galactosamine, acetaminophen and Aspergillus aflatoxin.

It prevents clumping of platelets, which in turn improves blood circulation and may also help protect against atherosclerosis.

Turmeric also acts as an anti mutagenic, as it potentially helps prevent new cancers that are caused by chemotherapy or radiation used to treat existing cancers. It effectively inhibits metastasis of melanoma cells.

Curcumin which is the major constituent in turmeric has the ability to inhibit HIV in test tubes, though human trials are to be done to determine if there exist any usefulness for treating humans with this condition. Turmeric in the diet may prevent pain from arthritis, bursitis, and tendonitis.

Intake of turmeric increases the production of enzymes that digest fats and sugars and also stop cholesterol from forming gallstones, thus helpful for people with indigestion but not as effective as antacids.

Turmeric is exceedingly useful in the treatment of some urinary disorders such as diabetes mellitus.

When applied to the skin and exposed to sunlight, turmeric is strongly anti-bacterial and it can be used to treat parasitic infections as well.

In case of smallpox and chickenpox, turmeric is applied as a powder or as a paste to facilitate the process of scabbing.¹³

A study done by Behal et al compared the effect of experimental local-drug delivery system containing 2% whole turmeric (gel form) as an adjunct to scaling and root planing (SRP) with the effect achieved using SRP alone by assessing their respective effects on plaque, gingival inflammation, bleeding on probing pocket depth, relative attachment levels and trypsin-like enzyme activity of *Bacteroides forsythus*, *Porphromonas gingivalis* and *Treponema denticola*. The experimental local drug-delivery system was in liquid form (under refrigeration) and was carried in a syringe with a needle attached to it. With increasing temperature as in oral cavity, gel formation occurred, which could be used as a local drug to be delivered to the periodontal pocket. Clinical parameters and microbiological study by BANA assay were the parameters recorded on day 0, 30 days and 45 days. Both groups demonstrated statistically significant improvement in clinical parameters. Significant reduction in BANA values was observed for both the groups when compared to the baseline activity. Greater reduction was seen in all the parameters in the experimental group in comparison to the control group. The experimental local drug-delivery system containing 2% whole turmeric gel can be effectively used as an adjunct to scaling and root planing and is more effective than scaling and root planing alone in the treatment of periodontal pockets.¹⁴

Discussion & Conclusion: With the interest in more natural drug substitutes for allopathic medicine in all fields of health care, the use of herbal drugs in periodontal disease is a huge step forward. The advantages of herbal drugs are that they are more easily available, they are cheaper and are known to have less adverse side effects because they are essential natural products. They can be used in patients who are medically compromised and they have relatively fewer contraindications. Patient compliance for these products is also known to be

more satisfactory. Hence the use of herbal drugs in the local drug delivery approach can open up novel treatment modalities for periodontal disease.

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