

**HERBS IN PERIODONTOLOGY – LOCAL DRUG DELIVERY**

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Article Received on  
26 November 2013  
Revised on 21 December  
2013,  
Accepted on 18 January  
2014

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**ABSTRACT**

Gingival diseases are the most prevalent dental conditions affecting the adult population. Periodontal disease may appear in a generalized form or in localized areas and highly organized bacterial populations form the advancing front of periodontal pockets. Local delivery controlled release antimicrobials have some advantages over the systemic route, including the high local drug levels in the periodontal pockets, reducing the adverse effects associated with systemic delivery of antibiotics and the drug compliance issues. Local delivery increase the concentration of antimicrobial agent in the pocket and in the GCF where patient compliance is not required. By means of controlled local delivery of agents in the periodontal pocket, a single administration of a limited volume of such agents can maintain therapeutic

concentrations within the crevicular fluid for a longer period of time than any other mode of delivery.

**Keywords:** Herbs, Local Drug Delivery, Periodontitis.

## INTRODUCTION

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.<sup>[1]</sup>

### 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 .<sup>[1]</sup>

### Rationale for use of locally delivered drugs

The use of systemic antimicrobials as a part of the therapy in the management of periodontal diseases has been accepted as an adjunctive therapy for decades.<sup>[2]</sup> Several studies have concluded that in specific clinical situations, such as with patients with deep pockets, patient with progressive or active diseases or with specific microbiological profiles, antimicrobial therapy adjunctive to scaling and root planing could be clinically relevant. However, there is a lack of clear protocol for the use of antibiotics which may be due to specific properties of biofilm, which make subgingival periodontal pathogens more difficult to target, and, therefore, the development of strategies specifically designed to treat the subgingival microflora, as a biofilm, is highly desirable.

Current periodontal therapy strongly emphasizes suppressing or eradicating specific periodontal pathogens. However, present treatment modalities differ in their ability to eliminate periodontal pathogens. Non-surgical scaling and root planing may remove subgingival *Campylobacter rectus* but is frequently ineffective against *Porphyromonas gingivalis*, *Prevotella intermedia*, *Bacteroides forsythus* and enteric rods and may not significantly reduce *Actinobacillus actinomycetemcomitans* or *peptostreptococcus*. Microbial debridement may fail to remove pathogenic organism because of their location in subepithelial gingival tissues, crevicular epithelial cells, altered cementum, radicular dentinal tubuli or furcation or other anatomic features complicating adequate instrumentation. Moreover, periodontal pathogens frequently colonize oral mucosa, tongue dorsum, tonsils and may translocate from non-periodontal sites to periodontal crevices. Systemic antibiotics enter the periodontal tissues and periodontal pocket via serum and can affect microorganisms outside the reach of cleaning by instrument or topical antiinfective chemotherapeutics. Systemic antibiotic therapy can also potentially suppress periodontal pathogens residing on the tongue or other oral surfaces, thereby delaying subgingival recolonization of pathogens.<sup>[3]</sup> But the adverse side effects of antibiotics are minimized if they can be used at the lowest effective doses. This is the rationale for topically applied antibiotics. This approach theoretically utilize locally applied antibiotics at doses far below those used systematically. The initial results are encouraging; however, further experiments are needed to determine whether effective antibiotic levels can be achieved at the depths of the periodontal pockets where the flora is most difficult to irradiate.<sup>[4]</sup>

## ALOE VERA

Aloe, native to Africa, is also known as “lily of the desert” (as shown in Fig I), the “plant of immortality”, and the “medicine plant”. Aloe, the name was derived from the Arabic *alloe* meaning “bitter” because of the bitter liquid found in the leaves, while *vera* in latin means “true”. There are many species of Aloe but the main medicinal one is *Aloe Vera Barbadosensis*.<sup>[5]</sup>

## PART OF PLANT USED

The Aloe vera leaf consists of 2 different parts: central mucilaginous part and peripheral bundle sheath cells (as shown in Fig I). The parenchymal tissue makes up the inner portion of the aloe leaves and produces a clear, thin tasteless jelly-like material called Aloe vera gel.<sup>[6]</sup>



**Figure – I : - Aloe Vera plant**

### **USES**

Dental uses of Aloe vera are multiple. It is extremely helpful in the treatment of gum diseases like gingivitis, periodontitis. It reduces bleeding, inflammation and swelling of the gums. 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.<sup>[7]</sup>

### **VARIOUS FORMS OF ALOE VERA USED**

Toothpaste: The jelly for healing promotion, which can also be used for burns, stings, insect bites and many skin lesions; such as “AloeDent”, “Aloe tooth gel”, “Forever bright”, ”Kingfisher aloe vera tooth paste”.

Aloe and Propolis hand cream which helps to counteract frequent hand washing and the wearing of latex gloves; e.g “Aloe vera cream with propolis”. Aloe activator spray which is excellent for throat infections, painful erupting wisdom teeth and joint pains is available as “Aloe activator”. Aloe vera juice, which is taken systemically as a drink for irritable bowel syndrome and as a strong detoxifying agent. It also acts as neuro-sedative and an immune enhancer As powerful nutritional supplement and antioxidant.<sup>[5]</sup>

Fujita *et al* , stated that carboxypeptidase in Aloe vera inactivates bradykinin by about 67% and relieves pain.<sup>[8]</sup> Hegger *et al* , showed its antibacterial properties against *Candida albicans*, *Streptococcus pyogenes*, *Streptococcus fecalis*.<sup>[9]</sup> Heggens and Robson showed that barbolin and aloe emodin in aloe vera block prostaglandin (PG) synthesis. The decrease in gingival index can be attributed to presence of sterols as anti-inflammatory agents and lupeol as an antiseptic analgesic.<sup>[10]</sup> Payne et al, reported Aloe vera gel used in wound site lessened

inflammation with less pain. <sup>[11]</sup> Vazquez *et al*, stated Aloe vera decreases edema and number of neutrophils and also prevents migration of Poly morpho nuclear leucocytes (PMNL). <sup>[12]</sup> Barrantes *et al* stated Aloe vera inhibits the stimulated granulocyte Matrix metallo proteinases (MMPs) inhibiting cyclo-oxygenase and lipo-oxygenase pathways. <sup>[13]</sup> Rocio Bautsta *et al* showed that carboxypeptidase in Aloe vera had good anti-prostaglandin synthesis properties and compounds inhibiting oxidation of arachidonic acid, which might decrease inflammation. <sup>[14]</sup> Geeta Bhat *et al* in her study concluded that its use in local drug delivery results in significant reduction in pocket depth and resulted in reduction in the gingival index. <sup>[15]</sup>

### TURMERIC GEL

It is an antiseptic used in the traditional system of Indian Medicine , as a component of local drug delivery. <sup>[16]</sup> Turmeric (Haldi) is a rhizome of *Curcuma longa* and may be a more acceptable and viable option for the common man (Fig - II). It has proven properties like anti-inflammatory, anti-oxidant , antimicrobial , hepatoprotective , immune-stimulant , antiseptic , anti-mutagenic and also accelerates wound healing.

Drake <sup>[16]</sup> and Han <sup>[17]</sup> *et al*, observed anti-microbial activity of turmeric . Roobal Bahal *et al* stated that on use of 2% turmeric gel , significant reduction in the mean plaque index , gingival index , sulcus bleeding index , probing pocket depth and significant reduction in trypsin like enzymes activity of “Red-Complex” microorganisms. <sup>[15]</sup>



**Figure – II : - Turmeric powder**

### CENTELLA ASIATICA

It is a small herb belonging to the family Apiaceae . it is commonly used in the Ayurvedic medicine for both internal and external application to treat various diseases (Fig - III). The

chemical structure of active compound from the plant was found to be a glycosidic terpene and was termed as Asiaticiside.<sup>[18]</sup>

Maghart et al reported better results that may be postulated as a result of the stimulatory property of centell extract on collagen synthesis and therefore resulting in improved attachment gain.<sup>[19]</sup> Suguna et al reported that the alcoholic extract of centella increased cellular proliferation and collagen synthesis at the wound site as marked by increase in protein and collagen content of granulation tissue.<sup>[20]</sup> Grindwit et al showed that the treatment of periodontal pockets with a newly formulated herbal medicament from extracts of centella resulted in greater improvement in probing depth.<sup>[21]</sup>



**Figure – III : - *Centella Asiatica***

#### **Azadirachta indica (Neem)**

Neem has been used in India for thousands of years as the preferred tool for maintaining healthy gums and teeth. Brushing with neem twigs and chewing neem leaves and seeds after a meal has been the traditional dental care practice. It has been considered to have various therapeutic activities such as astringent, antiseptic, insecticidal, antiulcer and for cleaning the teeth in gingivitis and periodontitis.<sup>[21]</sup>

Family - *Meliaceae*

Leaves of the neem (as shown in Fig -IV) 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 has also shown good in vitro, broad range antibacterial activity.

Neem extracts contains Azadiractin – the active principle, glycosides – antimicrobial, sterols, luminols-anti-inflammatory and flavenoids.<sup>[21]</sup>





**Figure – IV : - *Neem***

### HERBAL COMBINATION

Along with individual herbs, herbal combinations can combat periodontitis.

Mixture of peppermint oil , menthol , sage oil , chamomile , clove oil , caraway oil can reduce periodontitis symptoms .<sup>[21]</sup> Centella extract has the property of promoting collagen synthesis. Along with Punica extract it shows synergism. As tannins have affinity for proteins, they form bonds with collagen fibres.<sup>[22]</sup>

Triphala, the combination of fruits of three medicinal plants, *Terminalia chebula* (family name: Combretaceae), *Terminalia bellirica* (family name: Combretaceae), and *Phyllanthus emblica* (family name: Euphorbiaceae), has been used extensively as a drug against a number of diseases. These three medicinal plants were all shown separately to reduce hypercholesterolemia and atherosclerotic changes in rabbits fed a high-cholesterol diet for 16 weeks. *T. chebula* demonstrated the most potent effect in this study. Ayurveda purportedly strengthens all tissues of the body, prevents aging, promotes intellect, and prevents disease. It possesses various biological activities such as anti-inflammatory, antibacterial, antifungal, antiviral, antimalarial, antimutagenic, radioprotective, antiallergic, anticancer, cardiogenic, hypocholesterolaemic, capillary strengthening, hepatoprotective, immunomodulatory, adaptogenic, analgesic, and antioxidant activities. Thus, the present study was carried out to evaluate the inhibitory effect of triphala on PMN-type MMP activity, compared with another ayurvedic medicine, kamillosan liquid. These were compared with doxycycline, which has known anticollagenase activity.<sup>[21]</sup>

## CONCLUSION

Local delivery may be an adjunct to conventional therapy. The sites most likely to be responsive to this adjunctive treatment method may have refractory or recurrent Periodontitis, or specific locations where it is difficult to instrument root surfaces. However, the data are limited to support this concept. At present, there is insufficient data to indicate that one local drug delivery device is clearly superior to all the other systems. However, desired characteristics include ease of placement, controlled release of drugs and resorbability. In conjunction with conventional treatment, systemically administered drugs appear to be as effective as local drug delivery. To date, results from studies assessing local drug delivery systems have not justified extending the time interval between supportive periodontal maintenance visits. There are preliminary, but very limited data, regarding the ability of local delivery to help suppress future disease progression. There is insufficient data to indicate that local drug delivery induces bacterial resistance to antimicrobial agents. Long-term studies are needed to address this important issue. There is limited long term data evaluating the efficacy of local drug delivery, in terms of reducing the need for periodontal surgery more than scaling and root planing alone.

Prudent administration of antimicrobial agents following judicious pharmacologic principles will preclude the abuse of chemotherapeutic agents and reduce the potential of developing or selecting drug resistant bacterial strains. Local drug delivery systems with controlled release properties have the potential to be used as a therapeutic component in the management of periodontal diseases. However, additional randomized, controlled studies are needed to help delineate the types of lesions, periodontal diseases, or specific situations where local delivery systems would be most beneficial.

When locally delivered herbs are used as an adjunct to scaling and root planing, it helps in reduction of pocket depth and gain of clinical attachment. It is a beneficial antimicrobial, anti-inflammatory and anti-plaque agent. It also shows favorable reduction of trypsin-like enzyme activity of microorganisms associated with periodontal disease. The experimental material was biologically well accepted by the oral tissues and showed good acceptability. It was easy to use, noninvasive technique requiring less chair side time, with no side effects. The adjunctive use of local drug delivery may provide a defined, but limited, beneficial response.



## FUTURE PERSPECTIVE

To elucidate the use of local drug-delivery system in future, a long-term studies should be carried out on a large sample of subjects. Further studies are needed to evaluate the long-term clinical advantages of this adjunctive therapy to determine which types of patients and lesions will benefit most from the incorporation of locally delivered agents. Furthermore, microbiological studies are also required to corroborate with the clinical findings.

In the future several approaches could be attempted to increase the efficacy of locally delivered drugs against biofilm bacteria, avoiding the adverse effects associated with mechanical instrumentation of the root surface. These approaches include the simultaneous delivery of surface acting agents, enzymes, electric fields, or ultrasounds.

Timed-release, serially-delivered, or combination of local delivery drugs, such as metronidazole plus amoxicillin and ketoprofen, may be beneficial for certain refractory subjects. Incorporation of anti-infectives with anti-inflammatory products, as well as growth factors to enhance cell attachment, would, of course, be ideal. Future products should consider incorporation of antimicrobials and other agents into the membranes and guided tissue devices that can enhance regenerative outcomes.

**Conflicting Interest:** Nil

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