Periodontitis–Disease and Treatment – A Review

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ABSTRACT
Periodontal disease is a term that encompasses several pathological conditions affecting the tooth supporting structures. Periodontitis is an inflammatory disease of the supporting tissues of the teeth caused by groups of specific microorganisms. Aggressive forms of periodontitis can be localized or generalized. Various drug delivery systems are used to treat this condition. Intra pocket dental films could be easily placed into the periodontal pocket, and be capable of delivering therapeutic concentrations of drug for prolonged period of time at a much lower dose, hence obviating untoward side effects. The concept that localized problem sites may be treated by local drug delivery appears attractive as the antimicrobial agent is delivered within periodontal pockets and the therapy is targeted on specific pathogenic microorganisms. Local delivery of antimicrobial agents using controlled release systems should be considered as adjunctive to mechanical debridement for the treatment of localized forms of periodontal destruction.

Keywords: Periodontal diseases, Periodontitis, Antimicrobial agents.

INTRODUCTION
Periodontitis or pyorrhea is a set of inflammatory diseases affecting the periodontium, i.e., the tissues that surround and support the teeth. The word "periodontitis" comes from the Greek word peri, means "around" and odous (genitive odontos) means "tooth", and the suffix -itis, in medical terminology "inflammation". Periodontitis involves progressive loss of the alveolar bone around the teeth, and if left untreated, can lead to the loosening and subsequent loss of teeth. It is caused by microorganisms that adhere to and grow on the tooth's surfaces, along with an overly aggressive immune response against these microorganisms. Periodontal disease includes conditions such as chronic periodontitis, aggressive periodontitis, systemic disease associated periodontitis, and necrotizing periodontitis. These conditions are characterized by destruction of the periodontal ligament, resorption of the alveolar bone, and the migration of the junctional epithelium along with the tooth surface. The clinical signs of periodontitis are changes in the morphology of gingival tissues, bleeding as well as periodontal pocket formation. This pocket provides an ideal environment for the growth and proliferation of anaerobic pathogenic bacteria.

Periodontal pocket formed by pathogenic bacteria. Periodontitis is a localized inflammatory response caused by bacterial infection of a periodontal pocket associated with subgingival plaque. This periodontal pocket provides ideal conditions for the proliferation of microorganisms. The disease may then require extensive treatment, failing which the teeth may be lost. The therapeutic goal can be achieved by removing bacteria, by mechanical cleaning of plaque and topical application of
Periodontal diseases are a group of conditions that affect the supportive structures of the teeth, including the periodontium, which consists of the cementum, periodontal ligament, and gingiva. Periodontal disease is a term that includes a number of pathological conditions described by inflammation and degeneration of the gums (gingivitis) and the supporting structures of the teeth. Typically, periodontal diseases are gingivitis (inflammation of the gingival) and periodontitis (inflammation of the periodontal ligament). The primary etiology of gingivitis is poor or ineffective oral hygiene, which leads to the accumulation of a mycotic and bacterial matrix at the gum line, called dental plaque. Other contributors are poor nutrition and underlying medical issues such as diabetes. In some people, gingivitis progresses to periodontitis with the destruction of the supporting structures of the teeth.

**Clinical Features of Periodontitis**

Periodontitis are the group of conditions, which affect the supportive structures of the teeth. The development of periodontitis involves breakdown of the periodontal tissues, probably due to both direct effect of bacteria on the tissue and also the associated inflammatory response and the formation of the periodontal pocket between the surface of the tooth and the soft tissues. The periodontal pocket provides a diverse environment for the colonization of microorganisms. The bacteria accumulate in the periodontal pocket that develops between the roots of affected teeth and soft tissues. If the disease is allowed to progress, increased tooth mobility and possibly tooth loss may result. One of the clinical features of the periodontal disease is the formation of a periodontal pocket, which is pathologically deepened sulcus. In normal sulcus, the gap between the gingiva and the tooth is normally between 1 and 3 mm deep. However, during periodontitis, the depth of pocket usually exceeds 5 mm.

**Signs and Symptoms**

1. Total loss of attachment (clinical attachment loss, CAL)
2. Gingival recession, and
3. Probing depth

In the early stages, periodontitis has very few symptoms; and in many individuals the disease has progressed significantly before they seek treatment. Symptoms may include:

- Redness or bleeding of gums while brushing teeth, using dental floss or biting into hard food (e.g., apples) (though this may occur even in gingivitis, where there is no attachment loss)
- Gum swelling that recurs
- Spitting out blood after brushing teeth
- Halitosis, or bad breath, and a persistent metallic taste in the mouth
- Gingival recession, resulting in apparent lengthening of teeth. (This may also be caused by heavy-handed brushing or with a stiff tooth brush.)
- Deep pockets between the teeth and the gums (pockets are sites where the attachment has been gradually destroyed by collagen-destroying enzymes, known as collagenases)
- Loose teeth, in the later stages.

Patients should realize gingival inflammation and bone destruction are largely painless. Hence, people may wrongly assume painless bleeding after teeth cleaning is insignificant, although this may be a symptom of progressing periodontitis in that patient.

**CAUSES**

Periodontitis is an inflammation of the periodontium, i.e., the tissues that support the teeth. The periodontium consists of four tissues:

- gingiva, or gum tissue,
- cementum, or outer layer of the roots of teeth,
- alveolar bone, or the bony sockets into which the teeth are anchored, and
- Periodontal ligaments (PDLs), which are the connective tissue fibers that run between the cementum and the alveolar bone.

The primary etiology of gingivitis is poor or ineffective oral hygiene, which leads to the accumulation of a mycotic and bacterial matrix at the gum line, called dental plaque. Other contributors are poor nutrition and underlying medical issues such as diabetes. In some people, gingivitis progresses to periodontitis with the destruction of the supporting structures of the teeth.
of the gingival fibers, the gum tissues separate from the tooth and deepened sulcus, called a periodontal pocket. Subgingival microorganisms (those that exist under the gum line) colonize the periodontal pockets and cause further inflammation in the gum tissues and progressive bone loss. Examples of secondary etiology are those things that, by definition, cause microbial plaque accumulation, such as restoration overhangs and root proximity. The excess restorative material that exceeds the natural contours of restored teeth [these are termed “overhangs”] and serves to trap microbial plaque, potentially leading to localized periodontitis. Smoking is another factor that increases the occurrence of periodontitis, directly or indirectly and may interfere with or adversely affect its treatment. If left undisturbed, microbial plaque calcifies to form calculus, which is commonly called tartar. The primary cause of both gingivitis and periodontitis is the microbial plaque that adheres to the tooth surfaces; there are many other modifying factors. A very strong risk factor is one's genetic susceptibility. Several conditions and diseases, including Down syndrome, diabetes, and other diseases that affect one's resistance to infection, also increase susceptibility to periodontitis. According to some researchers periodontitis may be associated with higher stress.

Causative Organisms
The most commonly grown gram negative facultative or obligate anaerobic pathogenic bacteria are Actinobacillus actinomycetemcomitans, Bacteroides gingivalis, Bacteroides melaninogenicus sub species intermedius, Bacteroides forsythus, Porphyromonas gingivalis and Prevotella intermedia and Capnocytophaga species, Campylobacter rectus’ and Fusobacterium nucleatum.

Classification of periodontitis
The classification system for periodontal diseases and conditions are listed below:
1) Chronic Periodontitis
   A. Localized
   B. Generalized
2) Aggressive Periodontitis
   A. Localized
   B. Generalized
3) Periodontitis as a Manifestation of Systemic Diseases
   A. Associated with hematological disorders
      1. Acquired neutropenia
   B. Associated with genetic disorders
      1. Familial and cyclic neutropenia
      2. Down syndrome
      3. Leukocyte adhesion deficiency syndrome
      4. Papillon-Lefèvre syndrome
      5. Chediak-Higashi syndrome
      6. Histiocytosis syndromes
      7. Glycogen storage disease
      8. Infantile genetic agranulocytosis
      9. Cohen syndrome
     10. Ehlers-Danlos syndrome
        (Types IV and VIII)
     11. Hypophosphatasia
     12. Other
4) Necrotizing Periodontal Diseases
   A. Necrotizing ulcerative gingivitis (NUG)
   B. Necrotizing ulcerative periodontitis (NUP)
5) Abscesses of the Periodontium
   A. Gingival abscess
   B. Periodontal abscess
   C. Pericoronal abscess
6) Periodontitis Associated With Endodontic Lesions
   Combined periodontic-endodontic lesions
7) Developmental or Acquired Deformities and Conditions
   A. Localized tooth-related factors that modify or predispose to plaque-induced gingival diseases/periodontitis
      1. Tooth anatomic factors
      2. Dental restorations/appliances
      3. Root fractures
      4. Cervical root resorption and cemental tears
   B. Mucogingival deformities and conditions around teeth
      1. Gingival/soft tissue recession
         a. facial or lingual surfaces
         b. interproximal (papillary)
      2. Lack of keratinized gingival
      3. Decreased vestibular depth
      4. Aberrant frenum/muscle position
      5. Gingival excess
         a. pseudopocket
         b. inconsistent gingival margin
         c. excessive gingival display
         d. gingival enlargement
6. Abnormal color
C. Mucogingival deformities and conditions on edentulous ridges
   1. Vertical and/or horizontal ridge deficiency
   2. Lack of gingiva/keratinized tissue
3. Gingival/soft tissue enlargement
4. Aberrant frenum/muscle
5. Decreased vestibular depth
6. Abnormal color

D. Occlusal trauma
1. Primary occlusal trauma
2. Secondary occlusal trauma

Diagnosis of Periodontitis
A diagnosis of periodontitis is established by inspecting the soft gum tissues around the teeth with a probe (i.e., a clinical examination) and by evaluating the patient's X-ray films (i.e., a radiographic examination), to determine the amount of bone loss around the teeth. In 1976, Page & Schroeder introduced an innovative new analysis of periodontal disease based on histopathologic and ultrastructural features of the diseased gingival tissue. Plaque-induced periodontal lesions are divided into four stages:

1. Initial lesion
2. Early lesion
3. Established lesion
4. Advanced lesion

1. Initial lesion
The oral cavity is perpetually populated by pathogenic microorganisms; because there is a constant challenge to the mucosa in the form of these microorganisms and their harmful products, it is difficult to truly characterize the boundary between health and disease activity in the periodontal tissues. The oral cavity contains over 500 different microorganisms. It is very hard to distinguish exactly which periodontal pathogen is causing the breakdown of tissues and bone. As such, the initial lesion is said to merely reflect "enhanced levels of activity" of host response mechanisms "normally operative within the gingival tissues." Features of the Initial Lesion
- Vasculitis of vessels subjacent to junctional epithelium
- Increased migration of leukocytes into junctional epithelium
- Extravascular presence of serum proteins, especially fibrin
- Alteration of the most coronal portion of junctional epithelium
- Loss of perivascular collagen

2. Early lesion
While the early lesion is not entirely distinct from the initial lesion, it is said to encompass the inflammatory changes that occur from days four to seven after plaque accumulation has commenced. It is characterized by a matured leukocytic infiltrate that features mainly lymphocytes. Immunoblasts are quite common in the area of infiltration, while plasma cells, if present, are only at the edges of the area. The early lesion can occupy up to 15% of the connective tissue of the marginal gingiva and up to 60-70% of collagen may be dissolved. Features of the Early Lesion
- Accentuation of features of the initial lesion, such as the considerably greater loss of collagen
- Accumulation of lymphocytes subjacent to junctional epithelium
- Cytopathic alterations in resident fibroblasts
- Preliminary proliferation of basal cells of junctional epithelium

3. Established lesion
The hallmark of the established lesion is the overwhelming presence of plasma cells in relation to the prior stages of inflammation. Beginning two to three weeks after first plaque formation, the established lesion is widespread in both human and animals populations and can be seen commonly associated with the placement of orthodontic bands on molars. Features of the Established Lesion
- Predominance of plasma cells without bone loss
- Presence of extravascular immunoglobulins in the connective tissue and junctional epithelium
- Continuing loss of collagen
- Proliferation, apical migration and lateral extension of the junctional epithelium, with or without pocket formation
4. Advanced lesion
Many of the features of the advanced lesion are described clinically rather than histologically.23
- Periodontal pocket formation
- Gingival ulceration and suppuration
- Destruction of the alveolar bone and periodontal ligament
- Tooth mobility, drifting and eventual loss

Features of the Advanced Lesion17
- Extension of the lesion into alveolar bone, periodontal ligament with significant bone loss
- Continued loss of collagen
- Cytopathic alterations in plasma cells in the absence of altered fibroblasts
- Formation of periodontal pocketing
- Conversion of bone marrow into fibrous connective tissue

TREATMENT
The treatment of periodontal disease begins with the removal of sub-gingival calculus (tartar) and biofilm deposits. A dental hygienist procedure called scaling and root planing is the common first step in addressing periodontal problems, which seeks to remove calculus by mechanically scraping it from tooth surfaces. Another method for treatment of periodontal disease involves the use of an orally administered antibiotic, Periostat (Doxycycline). Periostat has been clinically proven to decrease alveolar bone loss and improve the conditions of periodontal disease with minimal side-effects. However, Periostat does not kill the bacteria, as it only inhibits the body's host response to destroy the tissue. There are two possible approaches to improve the drug action
  i. Sustained and controlled drug release to reduce or eliminate side effects by improving the therapeutic index;
  ii. Site-specific drug delivery to minimize systemic effects.

These two strategies have been explored by the association of drugs with different vehicles, either naturals or synthetics.41

Periodontal diseases are treated by antibiotics given by systemic route or by the local delivery system. The choice of the antimicrobial agents in periodontal diseases must be based on the bacterial etiology of the infection.12 Several antibiotics have been tested for their clinical and microbiological efficacy in periodontal diseases. Antibiotics are usually given to supplement the beneficial effects of scaling and root canaling, a common treatment for periodontal disease. Systemic administration has been useful in treating periodontal pockets, but repeated and long term use of systemic drugs is fraught with potential danger including resistant strains and superimposed infections. These drawbacks can be markedly reduced if antimicrobial agent to be used is applied locally. Concentration of drug in tissues can be enhanced by incorporating the active agent into controlled release delivery system and placing them directly in to periodontal pocket. A local drug delivery system delivering the therapeutic agent at sufficient levels inside the pocket and at the same time minimizing the side effects associated with systemic drug administration.

Various approaches to treat Periodontitis
Gingivitis can usually be treated simply. Plaque and tartar are removed from teeth; the inflamed tissues around a tooth usually heal quickly and completely. More serious cases of periodontitis cannot be treated by routine dental procedures. Dental surgery may be necessary to remove plaque, tartar, and infected gums tissue. Surgical access to facilitate mechanical instrumentation of the roots has been utilized to treat chronic periodontitis for decades.10 Appropriate therapy for patients with periodontitis varies considerably with the extent and pattern of attachment loss, local anatomical variations, type of periodontal disease, and therapeutic objectives.11

The primary objectives of therapy for patients with chronic periodontitis are to halt disease progression and to resolve inflammation.12 Therapy at diseased site is aimed at reducing etiologic factors below the threshold capable of producing breakdown, thereby allowing repair of the affected region. Local application into periodontal pocket could be very advantageous, both in terms of rising drug concentration directly in the action site, and in preventing systemic side effects such as gastrointestinal complaints, depression, and tachycardia. Controlled delivery of chemotherapeutic agents within periodontal pockets can alter the pathogenic flora and improve clinical signs of periodontitis.11

Antimicrobial choice for treatment
The choice of the antimicrobial agents in periodontal diseases must be based on the bacterial etiology of the infection.12 Some antimicrobial agents have been selected because of their substantivity which refers to the property of some medications that have an intrinsic ability to bind to the soft and/or hard tissue walls of the pocket. Commonly used antimicrobials are the following
1. Chlorhexidine
The use of chlorhexidine as an antifungal and antibacterial agent in dentistry is well documented. Its major application has been for the control of dental plaque. However, a number of studies have indicated that chlorhexidine is also effective in periodontitis. Chlorhexidine was primarily used in mouthrinses and was recommended in the hygiene phase of treatment as an adjunct to toothbrushing. Most attention, however, has been focused on the use of chlorhexidine during the operative and immediate post-operative phases of non-surgical and surgical periodontal treatment. Chlorhexidine’s potential effects at these times are: (i) a surface bacteriostatic action; (ii) improved wound healing and patient preference to dressings in the immediate-post-surgical phase; (iii) optimum plaque control immediately post-treatment when discomfort may compromise tooth-cleaning.

2. Sanguinarine
Sanguinarine is a benzophenanthridine alkaloid with a wide-spectrum antiseptic activity. The proposed mechanism of action is an alteration of the bacterial wall, so that aggregation and attachment are reduced. The product may be cationic and the degree of substantivity is unclear. Adverse effects include a burning sensation of the mouth.

3. Histatins
The histatins are a group of small, cationic histidine-rich peptides secreted by human parotid and submandibular salivary glands. These endogenous peptides have been shown to bind to hydroxyapatite, suggesting a role in the formation of the acquired enamel pellicle. The histatins play a major role in protecting the host oral cavity from etiologic pathogens. In particular, the histatins are antifungal and also demonstrate bactericidal and bacteriostatic effect against periodontal pathogens such as Porphyromonas gingivalis, Prevotella intermedia and Bacteroides forsythus.

4. Tetracycline
Tetracyclines are a group of broad-spectrum antimicrobial agents that were introduced into clinical practice in the late 1940s. There are now numerous compounds on the market, all based on the congeneric derivatives of the polycyclic naphthacene carboxamide. Tetracycline, doxycycline and minocycline are used extensively in the management of periodontal diseases. They are bacteriostatic antibiotics which interfere with bacterial protein synthesis and also inhibit tissue collagenase activity. They have a broad spectrum of activity inhibiting both Gram negative and Gram positive organisms.

5. Metronidazole
Among the antibiotics that have been considered for periodontal treatment, metronidazole has often been chosen because of its selective efficacy against obligate anaerobes. Metronidazole acts by inhibiting DNA synthesis. It is known to convert into a reactive reduced form and affects specifically anaerobic rods and spirochetes in the subgingival microflora.

6. Ofloxacin
Ofloxacin is a newly developed synthetic pyridine carboxylic acid (PCA) derivative. Although the earlier PCA derivatives were not active against Gram positive bacteria and anaerobes, ofloxacin can kill Gram positive bacteria and anaerobic bacteria. Local delivery systems have potential limitations and benefits. If used as a monotherapy, problems associated with local delivery can include allergic reaction, possible inability to disrupt biofilms, and failure to remove calculus. The benefits include the ease of application, selectively targeting a limited number of diseased sites that were unresponsive to conventional therapy, and possibly enhanced treatment results at specific locations. Local drug delivery systems provide several benefits; the drug can be delivered to the site of disease activity at a bactericidal concentration and it can facilitate prolonged drug delivery.

Conventional drug formulations for the mouth, such as toothpaste and mouthwash, have very low penetration into periodontal pocket. Films appear to be a suitable dosage form to deliver drugs into periodontal pocket, because the anatomic construction of the pocket allows for relatively easy insertion of such a delivery device. Moreover, the use of biodegradable polymers can increase patient compliance, as the inserted film does not need to be removed.

Existing approaches for local drug delivery in periodontal pocket are often unsatisfactory due to their rapid drug release or poor biodegradability of polymeric carrier. Adverse drug reactions are a greater concern and more likely to occur if drugs are distributed via systemic route. An ideal formulation should exhibit ease of delivery, good retention at application site, and controlled release of drug. Treatment with antibiotic may be necessary if infection is present and introduction of locally delivered antibiotics is especially for the
treatment of localized disease. Disadvantages of systemic antibiotic therapy relate to the fact that the drug is dissolved by dispersal over whole body and a small portion of total dose actually reaches the subgingival microflora in periodontal pockets. Various drug delivery systems for treating periodontitis are Fibers, Film, Injectable systems, Gels, Strips and compacts Vesicular systems etc.

Fibers
These are thread-like devices, are reservoir-type systems, placed circumferentially into the pockets with an applicator and secured with cyanoacrylate adhesive for the sustained release, then trapped drug into the periodontal pocket. In spite of the fact that the hollow fibers served as a good drug holding device, they permitted rapid evacuation of the drug. To retard drug release, drug-impregnated monolithic fibers were developed by adding drug to molten polymers, spinning at high temperature and subsequent cooling. Several polymers such as poly (ε-caprolactone) (PCL), polyurethane, polypropylene, cellulose acetate propionate and ethyl vinyl acetate (EVA) have been investigated as matrices for the delivery of drug to the periodontal pocket. In this respect, monolithic EVA fibers were found to be effective in controlling the release of encapsulated drug, and the same has been demonstrated by several in vitro and in vivo studies. Some patients experienced discomfort during fiber placement and removal, like various degrees of gingival redness were observed.

Films
A far more widely used form of intra-pocket delivery device has been in the shape of film, prepared either by solvent casting or direct milling. Bigger films either could be applied within the cavity onto the cheek mucosa or gingival surface or could be cut or punched into appropriate sizes so as to be inserted into the site of action. Films are matrix delivery systems in which drugs are distributed throughout the polymer and release occurs by drug diffusion and/or matrix dissolution or erosion. Films of various polymers have been made for the controlled release of therapeutic agents. The advantages of such a device include ease of insertion, dimensions that conforms well with the dimensions of the pocket and minimum pain on insertion. Intraperiodontal pocket drug delivery has emerged as a novel paradigm for the future research. Some natural biodegradable polymers have been used for controlled release of antibacterial agents in the treatment of periodontitis.

Injectable System
Injectable systems are particularly attractive for the delivery of antibiotic agents into the periodontal pocket. The application can be easily and rapidly carried out, without pain, by using a syringe. Thus, the cost of the therapy is considerably reduced compared to devices that need time to be placed and secured. Moreover, an injectable delivery system should be able to fill the pocket, thus reaching a large proportion of pathogens. They are also cost saving.

Gels
The gel is only marginally effective in decreasing the anaerobic bacterial count. Locally applied controlled release DOX gel may partly counteract the negative effect of smoking on periodontal healing following surgical therapy.

Injectable Gels
Together with the solid devices, semisolid formulations also receive reasonable attention for the localised delivery of antibiotics. Semisolid gel formulations have indeed have some advantages. In spite of the relatively faster release of the incorporated drug, gels can be more easily prepared and administered. Moreover, they possess a higher biocompatibility and bioadhesivity, allowing adhesion to the mucosa in the dental pocket and, finally, they can be rapidly eliminated through normal catabolic pathways, decreasing the risk of irritative or allergic host reactions at the application site. Bioadhesion or mucoadhesion is a preliminary requirement for prolonged release of the drug at the site. The retention time, as determined by fluorescein release, was found to be significantly higher for chitosan gel as compared to xanthan gum and poly(ethylene oxide) gel. Bioadhesive semisolid, polymeric system can be utilised as an important intra-pocket delivery vehicle because it can easily pass through a cannula into a periodontal pocket where it solidifies in situ to deliver the therapeautic agent for a prolonged period. These systems exhibit a pseudoplastic flow and thermoresponsive behaviour, existing as a liquid at room temperature and gel at 34–37°C. The semisolid system based on water-free mixtures of lipids, such as glycerol monooleate (monoglyceride) and sesame oil (triglyceride), is characterized by a solid–gel transition and become semisolid on contact with gingival fluid in the periodontal pocket. The system is based
on the ability of glycerides to form liquid crystals, that is, reverse hexagonalons on contact with water. The reverse hexagonal form has more favourable sustained release properties, compared with the initial cubic form.

**Strips and Compacts**
Acrylic strips have been fabricated using a mixture of polymers, monomers and different concentrations of antimicrobial agents. Strips were fabricated either by solvent casting or pressure melt method. Highest level of antibacterial agent was released during the first 24 hours period followed by release of therapeutic level of drugs for a subsequent 9 days period. Effect persisted even after 3 week of removal of acrylic strips.

**Vesicular Systems**
Vesicular liposomal systems are designed to mimic the bio-membranes in terms of structure and bio-behaviour, and hence are investigated intensively for targeting periodontal biofilms. The targeting of liposomes was thought to be because of the interaction of the polyhydroxy groups of liposomes with surface polymers of the bacterial glycol-calyx. Robinson and co-workers reported further on the affinity and specificity of immunoliposomes to reduce dental plaque. The anti-oralis immunoliposomes showed the greatest affinity for S. oralis and affinity was unaffected by net charge on the lipid bilayer or by the number of antibodies conjugated to the liposomal surface.

**Microparticle System**
Microparticles based system of biodegradable poly alpha hydroxy acids such as poly lactide (PLA) or poly (lactide – co-glycolide) PLGA containing tetracycline has been designed for periodontal disease therapy. Non-biodegradable as well as biodegradable materials have been investigated for the preparation of microspheres. These materials include the polymers of natural origin, modified natural substances and synthetic polymers. They could preferably be formulated as a chip or could be part of a dental paste formulation, or otherwise be directly injected into the periodontal cavity.

**Nanoparticulate System**
Modern drug delivery systems are designed for targeted controlled slow drug release. Up to now polymer or microparticle-based hydrogels have been applied in dentistry, which can affect the rate of release because of their structure. Recently, intensive research is being performed all over the world to improve the effectiveness of delivery systems. The nanoparticulate system provides several advantages as compared with microspheres, microparticles and emulsion-based delivery systems, including high dispersibility in an aqueous medium, controlled release rate and increased stability. Nanoparticles, owing to their small size, penetrate regions that may be inaccessible to other delivery systems, such as the periodontal pocket areas below the gum line. These systems reduce the frequency of administration and further provide a uniform distribution of the active agent over an extended period of time. Another approach is antimicrobial enzymes covalently attached to nanoparticles to generate antibiotic-free treatment for microbial infections. Satishkumar et al. developed a system in which hen-egg lysozyme. Antimicrobial enzyme was covalently attached to two types of polystyrene latex nanoparticles: positively charged, containing aliphatic amines surface group; and negatively charged, containing sulphate and chloromethyl surface group. These particles were showing lower activity compared to free enzyme, but can be explored for targeted antimicrobial activity.

**Surgical treatment for periodontal diseases**

**Bone/Tissue grafts**
It is the method employed mostly to replace or speed up the formation of new cells of bone or gingiva, which is destroyed in periodontitis. The grafting also helps to prevent the gum tissue from growing into the area of the bone, allowing the gum and the bone to grow again. This technique is known as Guided Tissue Regeneration (GTR).

**Flap Surgery**
This is the next step of tissue grafting and is used when the periodontal pockets are still seen even after the use of medications and tooth-cleaning techniques. This involves removal of the calculus and lifting back the gums. The gums are sutured back in place so that the tissue can re-grow and fit around the tooth. The success rate is very low in this type of surgery, because the gums have lost the stiffness and very rarely gain it again.

**CONCLUSION**
From the preceding review of the recent advances in periodontal drug delivery systems it can be said that the antibiotic-free, mucoadhesive, biodegradable nanoparticles technology has an immense opportunity for the designing of a novel, low-dose and effective treatment method by the use of the...
intra-pocket controlled device. These devices are proving to be more convenient, easy-to-use and more effective than the regular drugs and medicines which act systemically. These devices also do not probe the risk of overdose or systemic overload, simple for formulation, affordable and easily available.11

REFERENCES
10. www.spindlerperiodonticspecialist.com