Local drug delivery systems for treating periodontal diseases (A review of literature)

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ABSTRACT

In this review of literature, the light will be concentrated on the local drugs delivery systems for treating the periodontal diseases. Principles, types, advantages and indications of each type will be discussed in this paper. (J Bagh Coll Dentistry 2013; 25(4):79-85).

INTRODUCTION

The inflammatory periodontal diseases are widely accepted as being caused by bacteria associated with dental plaque. However, the nature of the periodontal disease resulting from dental plaque appears to depend to a large extent on the interaction among the bacterial agent, the environment, and the response of the host's defense mechanisms to the bacterial assault. Periodontal disease therapy has been directed at altering the periodontal environment to one which is less conducive to the retention of bacterial plaque in the vicinity of the gingival tissues, in particular, the marginal attachment apparatus. Classic therapeutic regimes to achieve this aim would include some or all of the following procedures:

1. instruction in oral hygiene techniques to achieve an adequate level of oral cleanliness,
2. scaling, correction of inadequate restorative dentistry, root planing, and the surgical elimination of pockets or other anatomical defects which aid bacterial retention and interfere with plaque removal.

Local delivery of chemotherapeutic agents into the pockets via a syringe or irrigating device has been shown to have an effect on the subgingival flora, but, clinically, it has not been effective in halting the progression of periodontal attachment loss [1,2] .The lack of clinical efficacy is probably because of the short time the irrigating solution remains in contact with the pocket environment [3].

The recent development of sophisticated, subgingivally placed delivery systems has provided the possibility of maintaining effective, intrapocket, levels of antibacterial agents for extended periods of time. These systems have provided the profession with a new tool which, in clinical trials, has been shown to alter the subgingival flora and influence the healing of the marginal attachment apparatus.

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Principle of Local Intrapocket Delivery of Antibacterial Drugs

1. The periodontal pocket provides a natural reservoir bathed by gingival crevicular fluid which is easily accessible for the insertion of a delivery device.
2. The gingival crevicular fluid provides a leaching medium for the release of a drug from the solid dosage form and for its distribution throughout the pocket.
3. These features, together with the fact that the periodontal diseases are localized to the immediate environment of the pocket, make the periodontal pocket a natural site for treatment with local sustained-release delivery systems.

The goal in using an intrapocket device for the delivery of an antibacterial agent is the achievement and maintenance of therapeutic levels of the drug for the required period of time.

Drug delivery systems for treating periodontitis

Various drug delivery system for treating periodontitis as Fibers, Film, Injectable systems, Gels, Strips and compacts, Vesicular systems etc. [4]

Fibers

Fibers, or thread-like devices, are reservoir-type systems, placed circumferentially into the pockets with an applicator and secured with cyanoacrylate adhesive for the sustained release of then trapped drug into the periodontal pocket. The release of the tetracycline from the cellulose acetate fibres as occurred by diffusion mechanism is rapid with approximately 95% of the drug released in the first two hours and, therefore, a single application of these fibres does not provide an effective drug concentration for long periods. Compared with the less effective tetracycline delivery from hollow fibres, fibres containing 20% (v/v) chlorhexidine, when placed into periodontal pockets, exhibited a prompt and marked reduction in signs and symptoms of periodontal disease. Fibers are used for the

treatment of periodontitis- **a- Hollow fiber** and **b- monolithic.**

In spite of the fact that the hollow fibres served as a good drug holding device, they permitted rapid evacuation of the drug. To retard drug release, drug-impregnated monolithic fibres were developed by adding drug to molten polymers, spinning at high temperature and subsequent cooling [5] .

Several polymers such as poly (e-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) fibres 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. [6] reported that EVA fibres containing 25% tetracycline hydrochloride maintained a constant drug level in the GCF above 600 mg/ml throughout ten days, showing zero-order release characteristics of EVA fibres . Tetracycline fibre treatment adjunctive to SRP showed significantly less periodontal disease recurrence (4%) compared with SRP alone (9%), tetracycline fibre alone for 10 days (10%) and tetracycline fibre alone for 20 days (12%). Studies that were wellconducted and well-controlled have demonstrated the clinical efficacy of these fibres but their actual value in patient therapy has been somewhat difficult to interpret because clinicians have found the fibre placement technique challenging include.

1- Patients experienced discomfort during fibre placement and at fibre removal
2- Various degrees of gingival redness were observed.
3- The complication of winding a fibre into place,
4- The need to retain the device within the pocket and then the removal of it after seven to ten days may limit its wide acceptance by patients and periodontists.

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. Sustained release devices composed of cross-linked fish gelatin (bycoprotein) containing chlorhexidine diacetate or chlorhexidine hydrochloride have been developed by Steinberg .In vitro release profile of chlorhexidine from such degradable films is dependent on the amount of chlorhexidine incorporated into the film, by the cross-link density of the polymer and by the chlorhexidine salt used. The time of total drug release is short and varies from 4 to 80 h. Films based on synthetic biodegradable polymers such as poly (lactide-co-glycolide) (PLGA) containing tetracycline have been developed for modulated-release of drug in the periodontal pocket as slab like device. In vitro release study showed that insoluble films release drug by diffusion and soluble release drug by dissolution of the carrier.

The advantages of such a device include

1- Ease of insertion.
2- Dimensions that confirms well with the dimensions of the pocket.
3- Minimum pain on insertion [7].

Non-biodegradable ethyl cellulose based films for the delivery of chlorhexidine diacetate; metronidazole, tetracycline and minocycline have been developed by solvent evaporation method and clinically tested. Ethyl cellulose films showed sustained drug release and release rates were dependent on the casting solvent and drug load. The use of chloroform as the casting solvent significantly retarded the release rate of the drug compared to ethanol as the casting solvent. The incorporation of polyethylene glycol in the films, however, enhanced the release rate of the drugs. Published clinical findings also confirmed that the treatment with drug-loaded ethyl cellulose films produced significantly greater improvements in the incidence of bleeding on probing, probing depths and attachment levels when compared to the conventional maintenance treatment. In contrast to the non-degradable systems discussed above, the films made up of degradable polymers erode or dissolve in the gingival crevice so that removal after treatment is not required. Natural and synthetic biopolymers play a pivotal part in drug delivery to periodontal pocket. More recently, a film composed of cross-linked hydrolysed gelatin and glycerine for local delivery of chlorhexidine digluconate has been developed and commercialised under the tradename Periochip. The system showed an initial burst effect, whereby 40% of chlorhexidine was released in the first 24 hours, followed by a constant slower release over about seven days. This film has the advantage over other

biodegradable films in which it remains inside the pocket with no additional aids for retention because of the adhesive nature of the Periochip components.

Synthetic biodegradable polymers have also been evaluated for sustained release of drug in the periodontal pocket. The combination of amoxycillin and metronidazole in the carrier polymer PLGA showed not only an extended spectrum of antimicrobial activity but also a synergistic effect against E. limosum, which had been reported to be resistant to metronidazole in earlier studies. The films showed a sustained in vitro release for a period of 16 days and the in vivo drug concentrations were maintained above the MIC value for the entire period of the release studies. By contrast, PLGA films containing tetracycline hydrochloride showed poor retention in the periodontal pockets with incomplete release of tetracycline. This effect could be attributed to the hydrophobic nature of PLGA matrix and the difference in physicochemical properties of the drugs.

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. These systems allow easy application of therapeutic agent using a syringe. They are also cost saving.

Gels

Mucoadhesive, metronidazole containing gel systems based on hydroxyethyl cellulose, corbopol 974, and polycarbophil have been made. Gel is applied sublingually with the help of blunt cannula and syringe. The gel is only marginally affective in decreasing the anaerobic bacterial count. This may be due to low number of bacteria susceptible to metronidazole or due to presence of bacterial biofilms. Locally applied controlled release doxycycline gel may partly counteract the negative effect of smoking on periodontal healing following no surgical therapy[8] The first was tetracycline base loaded into the microtubular excepient halloysite, which was coated with chitosan to further retard drug release. The syringeability of this formulation at various temperatures was evaluated to ensure ease of delivery to periodontal pocket. A stability study was performed to examine change in thermoresponsivity over time [9] In addition, lidocaine release from gels was evaluated using a release apparatus stimulating buccal condition .The results indicated that an increase in carbopol concentration significantly increased gel compressibility, hardness and adhesiveness factors that affect ease of gel removal from container, ease of gel application onto mucosal membrane, and gel bioadhesion . Characterization of tetracycline containing bioadhesive polymer network designed for the treatment of periodontal disease and result shows that effect of increasing drug concentrations on the rheological and textural properties was dependent on PVP(polyvinylpyrrolidone) concentration. Locally applied controlled release DOX gel may partly counteract the negative effect of smoking on periodontal healing. The safety profile, longer-term retention, antimicrobial activity suggests that tetracycline containing copolymer gels represents a safe and effective bioerodible therapy for periodontitis. Growing interest in developing absorbable pharmaceutical surgical products that degrade in biologic environment to safe by products and leaves the residual mass at application site justified the search fir novel absorbable gels. Comparative analysis of tetracycline containing dental gels: poloxamer and monoglyceride based formulations have been done which shows that poloxamer and monoglyceride gels, when applied subgingivally, produce a significant improved outcome in moderate to deep periodontal pockets[10].

Injectable Gels

Together with the solid devices, semisolid formulations also receive reasonable attention for the localized delivery of antibiotics. Semisolid or gel formulations can 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. Various oleogels and hydrogels for the delivery of tetracycline (2.5%), metronidazole (25%), metronidazole benzoate (40%), as well as a combination of tetracycline (2.5%) and metronidazole benzoate (40%), have been tested and satisfactory results have been achieved. The gels composed of cellulose derivatives such as hydroxypropylmethyl cellulose and hydroxyethyl

cellulose do not appear to have sustained release properties. Surprisingly, despite the rapid drug release and poor retention of these gels, positive clinical results in moderate to deep periodontitis were obtained. Bioadhesion or mucoadhesion is a preliminary requirement for prolonged release of the drug at the site [11].

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. Chitosan, a novel biodegradable natural polymer, in a gel form (1%, w/w) with or without 15% metronidazole, had demonstrated effectiveness in the treatment of chronic periodontitis. 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 therapeutic 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 8C. Tetracycline-loaded bioadhesive semisolid, polymeric system based upon hydroxyethyl cellulose- and polyvinylpyrrolidone- and metronidazole-loaded systems based upon Carbopol 974P, hydroxyethyl cellulose and polycarbophil are reported. Another such system composed of Poloxamer 407 and Carbopol 934P and containing propolis extract were designed for the treatment of periodontal disease. The release of the propolis was controlled by the relaxation of polymer chains and the greatest mucoadhesion was noted for the formulation containing 60:1 ratio of Poloxamer 407:Carbopol 934P. Another injectable biodegradable gel based on poly(DL-lactide) dissolved in a biocompatible solvent N-methyl-2-pyrrolidone (NMP) (Atrigel1) was widely studied . The Atrigel1 loaded with 10% doxycycline hyclate showed high levels of doxycycline (250 mg/ml) in the GCF for a period of seven days. Interestingly, levels of 10–20 mg/ml were still present for three to five days after the polymer had been removed. It is possibly because of minute particles of polymer remaining within the pockets or because of the substantive effects of tetracyclines within the periodontal pocket-adjacent-tooth-surface environment. In another study, Atrigel1 containing 5% sanguinarine was found to be superior to the control in the treatment of adult periodontitis and the findings have been recently confirmed in a human clinical trial. The semisolid system based on water-free mixtures of lipids, such as glycerol monooleate (monoglyceride) and sesame oil (triglyceride), is characterised 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 hexagonals on contact with water. The reverse hexagonal form has more favourable sustained release properties, compared with the initial cubic form. The matrix is degraded by neutrophils and bacterial lipase in the GCF. Biodegradable gels are other useful prospects for the delivery of therapeutic agents into periodontal pockets. Bioerodible lactic– glycolic acid gels were found to be safe and tetracycline levels observed at days 3 and 8 probably represent significant antimicrobial efficacy.

Strips and Compacts

Strips are thin and elongated matrix bands in which drugs are distributed throughout the polymer. Generally, strips are made up of flexible polymers having a position securing mechanism, and accommodate a wide range of interproximal spacing .Acrylic strips have been fabricated using a mixture of polymers, monomers and different concentrations of anti microbial agents. Strips were fabricated either by solvent casting or pressure melt method. Strips containing tetracycline, metronidazole or chlorhexidine demonstrated a decrease in number of motile rods, notably spirochetes. In a later development, the evaluation of amoxycillin-clavulainic acid loaded acrylic strips is reported. 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. Tissue adhesive implants were made using n-butyl-2-cyanoacrylate as a drug trapping material and slowly release drug when used in the structure of a biodegradable local drug delivery device [12]. Ornidazole dental implants containing ethyl cellulose, hydroxy propyl cellulose, hydroxy propyl methyl cellulose and dibutyl phthalate by solvent casting technique result showed that drug release was initially high on day one to achieve immediate therapeutic level of drug in pocket, followed by marked fall in release by day two[13] Chlorhexidine slow release devise has been made and it is antibacterial effect has been evaluated by agar diffusion test.

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. Jones and Kaszuba reported interactions between

liposomes made up of phosphatidylinositol (PI) and bacterial 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. Succinylated Concanavalin-A (lectin)-bearing liposomes (proteoliposomes) have been found to be effective for the delivery of triclosan to periodontal biofilms. In vitro and in vivo studies have revealed that, even after a very short exposure, the proteoliposomes are retained by the bacteria eventually delivering triclosan into the cellular interiors. The potential of lectin-bearing liposome systems as a targeting system for the control of gingivitis and dental plaque has been extensively studied by Vyas *et al.* [14]. The delivery of triclosan and chlorhexidine was studied for several liposomal compositions involving cationic as well as anionic lipids [15] 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. PLGA microspheres containing minocycline have been formulated and have been used for the elimination of Porphyromonas gingivalis from the periodontal pocket. Microparticles of poly (dl-lactic-co-glycolic acid) (PLGA) containing chlorhexidine free base, chlorhexidine di gluconate and their association or inclusion complex with methylated-beta-cyclodextrin (HPBCD) were prepared with single emulsion, solvent evaporation technique[16] Non-biodegradable as well as biodegradable materials have beeninvestigated 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. Tetracycline-containing microcapsules in Pluronic F127were reported to formgel at body temperature and hold the microcapsules in the periodontal pocket for the duration of treatment. PLGA microcapsules and microspheres have been proposed for the delivery of tetracycline and histatins. These microparticulate systems provide stability to the encapsulated drug. The in vitro drug release from such systems depends upon the polymer (lactide: glycolide) ratio, molecular weight, crystallinity and pH of the medium. Some questions, however, related to the retention of such formulations in the periodontal pocket need clarification.

Nanoparticulate System

Modern drug delivery systems are designed for targeted controlled slow drug release. Nanomaterials are of interest from a fundamental point of view because the properties of a material (e.g. melting point, electronic properties, optical properties) change when the size of the particles that make up the material becomes nanoscopic. With new properties, come new opportunities for technological and commercial development and applications of nanoparticles have been demonstrated or proposed in areas as diverse as microelectronics, coatings and paints, and biotechnology [17]. From these applications has come the development of nanopharmaceuticals, nanosensors, nanoswitches, and nanodelivery systems. Each of these has considerable significance in the field of local, or targeted, drug delivery. 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 gingival line[5] These systems reduce the frequency of administration and further provide a uniform distribution of the active agent over an extended period of time. Biocompatible nanoparticles composed of 2-hydroxyethyl methacrylate (HEMA) and polyethyleneglycol dimethacrylate (PEGDMA) could be used as a drug delivery system for dental applications. The polymer-based nanoparticles were prepared via micellar polymerisation, which resulted in a well dispersible white powder material with particle size in the range of 50–180 nm. These nanoparticles are suitable for incorporation into a hydrogel matrix and to design new drug delivery devices for dental applications. Moulari investigated the in vitro bactericidal activity of the

Harungana madagascariensis leaf extract (HLE) on the oral bacterial strains largely implicated in dental caries and gingivitis infections. HLE-loaded PLGA nanoparticles were prepared using interfacial polymer deposition following the solvent diffusion method. Incorporation of the HLE into a colloidal carrier improved its antibacterial performance and diminution of the bactericidal concentration was observed. Shefer and Shefer patented a controlled release system useful for site-specific delivery of biologically active ingredients over an extended period of time. This system is a multi-component release system comprising biodegradable nanoparticles having bioadhesive properties encapsulated within a moisture sensitive microparticle. The bioadhesive properties of the nanoparticles are attributed to the positively charged surfactant entrapped on the particle surface. The multi-component release system can be incorporated into any suitable oral hygiene product including gels, chewing gums, toothpaste and mouthwash for the treatment and prevention of periodontal disease. Antisense oligonucleotide- loaded chitosan-tripolyphosphate (TPP) nanoparticles were prepared and evaluated. Chitosan/oligonucleotide-TPP nanoparticles, which were prepared by adding TPP after the formation of chitosan/oligonucleotide complex, showed the sustained release of oligonucleotides and are suitable for the local therapeutic application in periodontal diseases[18]. In an attempt to obtain a novel delivery system adequate for the treatment of periodontal disease, triclosan-loaded polymeric (PLGA, PLA and cellulose acetate phthalate) nanoparticles were prepared by emulsification–diffusion process. A preliminary in vivo study in dogs with induced periodontal defects suggested that triclosan-loaded nanoparticles penetrate through the junctional epithelium [19].

The nanoparticles were prepared using poly(D,L-lactide-coglycolide), poly(D,L-lactide) and cellulose acetate phthalate. Poly (vinyl alcohol) was used as stabilizer. Batches were prepared with different amounts of triclosan in order to evaluate the influence of the drug on nanoparticle properties. Solid nanoparticles of less than 500 nm in diameter were obtained. These triclosan nanoparticles behave as a homogeneous polymer matrix-type delivery system, with the drug (triclosan) molecularly dispersed. Release kinetics indicates that the depletion zone moves to the center of the device as the drug is released. This behavior suggests that the diffusion is the controlling factor of the release.

A preliminary in vivo study using these nanoparticles has been performed in dogs with only the gingival index (GI) and bleeding on probing (bleeding on probing) being determined [19]. With respect to the gingival index (GI), at days 1 and 8, it was found that a severe inflammation was detected in control and experimental sites (GI ¼ 3). It was concluded that triclosan nanoparticles were able to effect a reduction of the inflammation of the experimental sites.

Nano drug delivery carriers periodontal future aspects Various nano materials that can be used are **Liposomes.** Their exterior lipid bilayer is very chemically reactive, thereby providing a means to conveniently couple “tags” on a covalent basis. Such “tags” can be antibodies, antigens, cell receptors, nucleic acid probes, etc. This provides significant versatility in assay formats (i.e., immunoassay, receptor- based, nucleic acid probe, etc.) possible. With diameters ranging in size from approximately 50 nm to 800 nm, their aqueous core encapsulates up to millions of molecules of signal generating “markers” that can be detected in a variety of different way. A variety of different encapsulants are possible including visually detectable dyes (since the lipid bilayer is transparent), optically and fluorometrically detectable dyes, enzymes, and electroactive compounds.

C60

C60 are spherical molecules about 1nm in diameter, comprising 60 carbon atoms arranged as 20 hexagons and 12 pentagons: the configuration of a football. Hence they find application as Nano Pharmaceuticals with large drug payload in their cage like structure. On the other hand with development of various chemical substitutes for C60, it is possible to develop functionalized C60 with better drug targeting properties Carbon nanotubes are adept at entering the nuclei of cells and may one day be used to deliver drugs and vaccines. The modified nanotubes have so far only been used to ferry a small peptide into the nuclei of fibroblast cells. [20] developed injectable periodontal drug delivery systems and showed that erythromycin had increased adsorption by nano HA microspheres in periodontal infected site [19] produced triclosan-loaded nanoparticles by the emulsification diffusion process, in an attempt to deliver drugs for the treatment of periodontal disease. The nanoparticles were prepared using poly (D,L- lactide-coglycolide), poly(D,L-lactide) and cellulose acetate phthalate. Poly (vinyl alcohol) was used as stabilizer.It was found that triclosan was released in controlled

manner in specific sites and found to be quite effective

Miscellaneous: low-dose antibiotic

Recently, there has been interest in the use of low-dose antibiotics. The dose is so low that the drug does not act to kill bacteria, but rather to change the way the body responds to infection. Production of the enzyme collagenase is essential because older gingival tissues are replaced with new tissues. In periodontal disease there is an overproduction of collagenase, causing the destruction of healthy gum tissue. An interesting effect of low-dose antibiotics is that they not only kill the bacteria that may cause periodontal disease but also reduce the body's production of collagenase, an enzyme that destroys gingival tissues. The antibiotic doxycycline was found to combat these enzymes, even in doses so small that there was no antibiotic effect. The advantages of smaller doses are that there is a great reduction in the chances of formation of resistant bacterial strains and side effects. Periostat is a capsule of 20 mg of doxycycline, and clinical studies have shown that patients who take two capsules daily have a reduction in clinical inflammation. The daily 40-mg dose is so low as not to qualify as an antibiotic, and there is no known effect on the pocket bacteria. Thus, Periostat must be used in conjunction with other therapies that address bacterial removal [(5)]

As conclusions; eradication of microorganisms from the periodontal pocket is the most important step in treating periodontitis. The limitations of mouth rinsing and irrigation have prompted research for the development of alternative delivery system. Recently, advances in delivery technology have resulted in the controlled release of drugs. The requirements for treating periodontal disease include a means for targeting an anti-infective agent to infection sites and sustaining its localized concentration at effective levels for a sufficient time while concurrently evoking minimal or no side effects. This research has discussed local drug delivery devices used in treating periodontitis. From that following conclusions can be made: local drug delivery system is used effectively in controlling tissue associated bacteria, it eradicates the periodontal pathogens for several weeks.

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