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Recent advances on novel periodontal drug delivery system

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Abstract

Periodontitis is an infectious disease resulting in inflammation the supporting within tissues of the teeth, progressive attachment loss and bone loss-carranza. Some of the etiology and risk factors are Microbial factors, local factors, systemic factors, genetic factors and behaviour factors. Periodontitis can occur at any age, most frequently observe in adults at the age of 30-35years. It involves the degeneration of periodontal ligaments, resorption of alveolar bone resulting in the disruption of the structure of the teeth. In global population nearly 10-15% of people are suffering with severe periodontitis according to WHO. In management of periodontal infection Antibacterial agents are most widely used. Widening of PDL space, generalised loss of alveolar bone are the radiographic feature. Treatment requires more aggressive surgical care. Because of abundant source, lack of toxicity and high tissue compatibility the Biodegradable polymers are extensively employed in periodontal drug delivery devices. In the last decades, the treatment has been optimized for the use of drug delivery systems to the periodontal pocket, with the advantage of delivering the drug in the specific site, sustaining and/or controlling the drug concentration. Recently, the use of new drug delivery systems has been receiving great interest. This review approaches the main delivery systems for the administration of drugs to the periodontal pocket, their usefulness as well as the advancement of these systems effectiveness in the periodontal therapy.

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Introduction

In 1998 FLEMMING identified that Periodontitis is an infectious disease resulting from inflammation within the supporting tissue of the teeth, progressive, attachment loss and bone loss [1]. The two major forms of inflammatory diseases affecting the periodontium are Gingivitis and Periodontitis. Gingivitis is the inflammation of the gingiva that does not result in clinical attachment loss .periodontitis is inflammation of the gingival and the adjacent attachment apparatus and is characterised by loss of connective tissue attachment and alveolar bone. Gingivitis is a reversible disease .Therapeutic approaches for periodontitis fall into two major categories are anti-infective treatment and regenerative therapy. According to the site it is classified into 2 types i.e. localized periodontitis and generalized periodontitis. The clinical features are colour: pale red to magenta, blunted or rolled gingival margin, low grade inflammation [2]. The aggressive periodontitis are: Age of the patient, Rate of progression, Familial nature of disease and Relative absence of local factors. The treatment of periodontitis are initial therapy, surgical therapy and maintenance phase. Periodontal disease can affect one tooth or many teeth [3].

Risk assessment for periodontitis

Heredity as determined by genetic testing and family history. Smoking including frequency, current use, and history. Hormonal Variations such as those seen in pregnancy and menopause. Systemic disease such as diabetes, osteoporosis, HIV. Stress as reported by the patient. Medications such as calcium channel blockers [4].

Treatment of periodontal disease

The key role in the treatment of periodontal disease lies in the reduction of inflammation, i.e. the removal of dental plaque and most of the periopathogens adhering to the tooth connective tissue and alveolar bone [5]. In order to deal with the invasion of microorganisms, we need a detailed plan of action

- Periodic examination and motivation of patients.
- Mechanical and professional plaque removal.
- Systemic or local use of antibiotics and antiseptics.
- Laser removal of narcotic and granulation tissue and disinfection of periodontal pockets.

All of the above methods are used to reduce or eliminate periopathogens and their by-products, and thus eliminate inflammation [6].

For treating of Periodontitis the various drug delivery systems are:

- Films,
- Strips,
- Fibbers
- Gels,
- Injectable Systems.

Films

Films are widely used in the form of intra pocket delivery system has been in the shape of film. The films are prepared by solvent casting or direct milling films are matrix delivery systems in which drugs are distributed throughout the polymer and release occurs by drug diffusion, or matrix dissolution or erosion. Films that release drugs by diffusion alone are prepared using water insoluble non-degradable polymers, whereas those that release by diffusion and matrix erosion, dissolution use soluble or biodegradable polymers. Bigger films are 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. Film can be rapidly inserted into the base of the pocket with minimal discomfort to the patient. If the thickness of the film does not exceed 400mm, and it has sufficient adhesiveness, it will remain submerged without any noticeable interference with the patient's oral hygiene habits [7]. The advantages of using this films are ease of insertion and minimum pain on insertion. Flims 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 [8].

Strips

Strips used are thin, elongated matrix bands in which the drug is distributed throughout the polymer and made up of of flexible polymers. Acrylic strips have been fabricated using a mixture of monomers, polymers and different concentrations of anti-microbial agents. Strips fabricated by using solvent casting for pressure melt method. Strips containing tetracycline, chlorhexidine demonstrated a decrease in number of motile rods, notably spirochetes. By using solvent casting technique the drug release was initially high on day one. By using agar diffusion test the antibacterial effect has been evaluated [9].

Fibers

Fibbers are thread like devices or 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. Several polymer like polyecaprolactone (PCL), polyurethane, polypropylene cellulose acetate propionate and ethylvinyl acetate (EVA) has been investigated as matrices for the delivery of drug to the periodontal pocket. Examples of fibers are chlorhexidine fibers and tetracycline fibers. fibers Containing 20% (v/v) chlorhexidine, when placed into periodontal pockets, exhibited a prompt and marked reduction in Signs, and Symptoms of Periodontal disease. Single application of these fibers does not provide an effective drug concentration for long periods [10].

Gels

Gels are applied sublingually with the help of blunt Cannula and Syringe. Mucoadhesive, metronidazde Containing gel Systems, based hydroxyethyl cellulose, Corbopol 974, and polycarbophil have been made. The gel is only marginally

Affective in decreasing the anaerobic bacterial Count. This is due to that the bacteria is susceptible to MTZ or due to presence of biofilms. First the tetracycline base was loaded into the micro tubular excipient halloysite, which was coated with chitosan to further retard drug release. A stability study was performed to examine change in the thermos responsivity over time. If the carbopol concentration increases the gel compressibility, hardness and adhesiveness factors that affect the ease of gel removal from container, ease of gel application onto the mucosal membrane and gel bio adhesion. The tetracycline containing the antimicrobial activity, safety profile and long-term retention that helps in the effective therapy of periodontitis [11].

Injectable Systems

Injectable Systems are particularly attractive for the delivery of antibiotic agents into the periodontal pocket. The drug is introduced into the periodontal pockets by using syringes without causing any pain. The cost of this therapy is considerably reduced to when compared to devices that need time to be placed and secured. Moreover, an injectable delivery Systems should be able to fill the pocket, thus reaching a large proportion of pathogens [12].

Vesicular Systems

Vesicular liposomal systems are designed to mimic the bio – membranes in terms of structure and bio- behaviour. These are investigated intensively for targeting periodontal biofilms. A bearing liposomes have been found to be effective for the delivery of triclosan to periodontal biofilms. Robinson and co-workers reported further on the affinity and specificity of immunoliposomes to reduce dental plaque. 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 .vesicular systems are deliberate to parodist the bio membranes in positions edifice. Invitro and In vivo revisions have publicized that, even after a very short exposure. Even though the courtesy towards giving bacterial infection has generated many efficacious delivery devices. The anti oralis immunoliposomes showed the greatest affinity by net charge on lipid bilayer [13].

Nano particulate system

Nano periodontics involves the analysis of matter at sub atomic and microscopic level, which has progressed in the field of periodontics. Nanoparticles because of their surface area, dimensions and quantum effects exhibit enhanced rigidity, stability and gas penetrability. Modern drug delivery systems are designed for targeted controlled slow drug release. Recently, intensive research is being performed all over the world to improve the effectiveness of delivery systems. Nanoparticles remaining to the small size infiltrate regions that may be inaccessible to other delivery systems. The multicomponent release systems can be merged into any decorous oral hygine product encompassing gels, chewing gums and toothpaste. These systems condense the frequency of administration and uniform distribution active agent over a prolonged period of time. Antisense oligonucleotide loaded chitosan-tripolyphosphate (TPP) nanoparticles were structured and accessed [14]. The bio adhesive assets of the

Nanoparticles are indorsed to the certainly stimulating surfactants on the particle surface. The Nano particulate System provides several advantages as compared with microspheres, microparticles and emulsion based delivery systems [15].

Micro particulate system

Micro particles based system of biodegradable poly alpha hydroxyl acids such as poly lactide (PLA) or poly lactide-co-glycolide (PLGA) comprehending tetracycline has been considered for periodontal disease therapy. PLGA microspheres comprehending minocycline have been formulated and have been used for the purging of Porphyramonas gingivalis from the pocket. Microparticles of poly (dl-lactic-co-glycolic acid) (PLOA) encompassing periodontal pe chlorhexidine free base, chlorhexidine digluconate, and their reminder or enclosure complex with methylated-beta-cyclodextrin (MBCD) were organized with unassuming emulsion and solvent evaporation procedure [16,17].

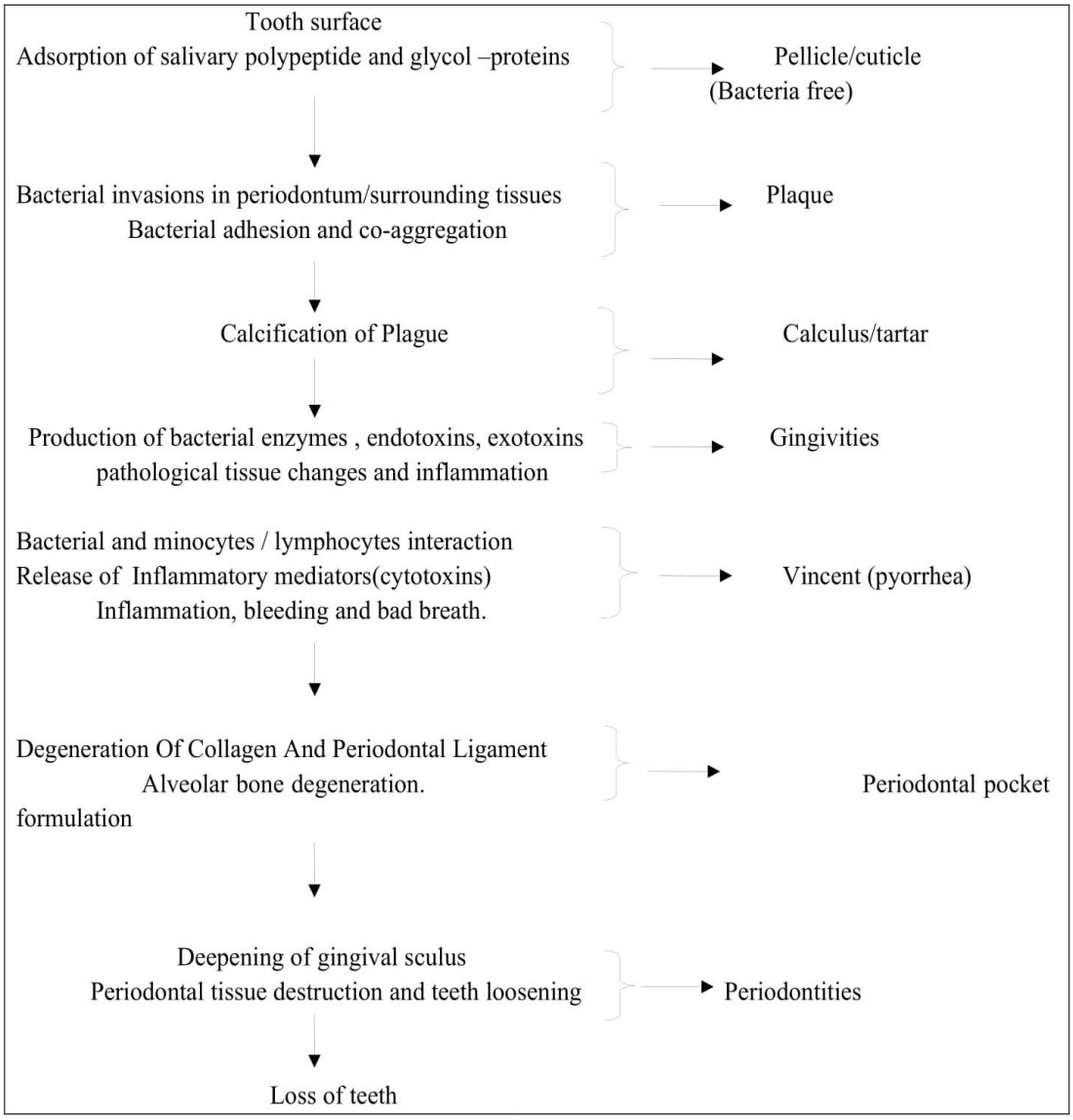

Fig: 01 Flow chart representing pathogenesis of periodontal diseases. Formation of bacterial plaque: calcification of plaque: pathological and immunological manifestation resulting in gingivitis and periodontitis

Conclusion

Periodontitis results in the loss of periodontal attachment structures. If left untreated, tooth loss eventually may result. The currently available scientific evidence supports consistent plaque control at home and the routine use of SRP along with locally-delivered sustained-release antimicrobials and sub-antimicrobial systemic dosing of doxycycline in the professional treatment of chronic periodontitis. This article details about the different types of periodontal drug delivery systems like films, fibers, gels, Nano-particulate systems, micro-particles, and injectable systems. A shift from nonbiodegradable polymers to a variety of biodegradable polymers have helped in Achieving biocompatible sustained-release formulations, reduced the dosage frequency, and thus minimized the chances of bacterial resistance. It has to be designed to contribute to the systemic eradication of side effects of antibiotics.

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