Review Article

Local Delivery Systems for Periodontal Therapy: An Overview

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ABSTRACT

Periodontal disease is an infection of periodontium causing destruction of soft tissue that supports the bone. This condition is treated by using antibacterial agents by oral route. It has been observed that drug administration by this route caused adverse reactions due to high dose. The concept of delivering the drug directly into the periodontal pocket led to the development of local drug delivery systems. This concept gained attention as it requires low dose, produces sustained/controlled action and delivers the drug near to or onto the target site. This review attempts to comprehensively present various local drug delivery systems for treatment of periodontal disease. Various local delivery systems such as fibers, strips, films, vesicular systems, injectables, microparticles and nanoparticulate systems. Antibacterial agents such as tetracycline and Metranidazole are commonly used in periodontal therapy and extensive research led to design and formulation of these drugs as strips, gels, injectables and inserts. These and other such systems were designed and the outcome with respect to patient compliance and therapeutic effect is quite encouraging. This review attempts to present some periodontal local drug delivery systems.

Keywords: Periodontal disease, periodontal pocket, local devices.

INTRODUCTION

India has vast geographic area divided into states, which differ with regard to their socioeconomic, educational, cultural and behavioral tradition. These factors may affect oral health status. Under the Government of India and World Health Organization collaborative program on oral health, a multicentre oral health survey was envisaged in the year 2004. Age groups of 35-44 years and 65-74 high prevalence (100%) of periodontal disease were reported from few of the states (Orissa, Rajasthan) in this study. The prevalence of loss of attachment was significantly higher in the 65-74 years group as compared to the 35-44 years group. The rest of the centers had prevalence ranging between 15% and 33%. The highest prevalence in 65-74 years group was recorded in Maharashtra (96%), followed by Orissa (90%), Delhi (85.5%), Rajasthan (75%), Uttar Pradesh (68%) and Pondicherry (55%). Arunachal Pradesh recorded the lowest prevalence, viz., 20%. The general trend observed for loss of attachment was that it was higher in the rural areas than in the urban population and was higher in males as compared to females. But in the geriatric age group, the prevalence of loss of attachment was higher among females[1].

Periodontitis is indicated by signs and symptoms ranging from simple gum inflammation to damage of tissue and bone that support the teeth. Periodontitis can be categorized as chronic periodontitis, aggressive periodontitis and necrotizing periodontitis depending upon the progression of disease.[2] Bacteria and their by-products, directly or indirectly are responsible for triggering host-mediated responses causing injury to gum.[3] Periodontitis progresses from gingivitis or gingival swelling, bleeding and bad breath and later leads to the formation of periodontal pocket thereby causing infection.

Mode of treatment: [4]

I. Oral hygiene

Brushing twice a day

Flossing regularly to remove plaque

Dental visit for regular check up and professional cleaning

Avoid smoking

II. Mechanical debridement

Scaling and root planning (SRP)

Mechanical debridement aimed at removing the subgingival micro flora.

III. Antibacterials

Antibacterials are used as adjunct with mechanical debridement in the management of periodontal infection. They are administered both systemically and locally. Few antibacterials recommended in this condition are tetracycline, minocycline, doxycycline, erythromycin, Clindamycin, ampicillin, amoxicillin, Metranidazole and are available in the form of tablets, capsules, oral suspensions etc. Systemic administration of drugs leads to several adverse effects such as GIT disturbances, hypersensitivity reactions and bacterial resistance. The objective of this review is to comprehensively present recent research in developing local drug delivery devices to treat periodontitis

Goodson et al in 1979 first proposed the concept of controlled delivery in the treatment of periodontitis. Local drug delivery of antimicrobial agents can cause a 100-fold increase in its concentration at subgingival sites as compared to systemic administration, this can reduce total patient dose by over 400 fold avoiding development of drug resistant at non oral body sites.

This lead to extreme research aimed to design formulations suitable for delivery the drug into the periodontal pocket.

Local delivery systems for periodontitis

1. Fibers
2. Strips
3. Films
4. Gels
5. Vesicular systems
6. Microparticulate system
7. Nanoparticulate system

1. Fibers

Fibers are reservoir-type systems, placed circumferentially into the pocket with an applicator and secured with an adhesive. Fibers are formulated either as hollow fibers (reservoirs without rate controlled systems-drug release-diffusion) or monolithic fibers (reservoirs with rate controlled drug release). These delivery systems posses certain limitations such as difficulty in placing the fiber in the pocket, patient discomfort and sometimes may cause allergic reactions[5].

2. Strips

Thin, elongated matrix bands in which drugs are distributed throughout the polymer is called strip. These are having advantages of flexibility and easy placement. These strips brought significant improvement in effective microbial eradication from the pockets than other delivery systems[6]

3. Films

Films are drug delivery device where matrix either non-biodegradable or biodegradable in which drug is distributed throughout the matrix and drug release occurs by erosion, matrix dissolution or drug diffusion. Bigger films could be applied within the cavity onto the cheek mucosa or gingival surface. This system has several advantages than other intra pocket drug delivery devices such as thickness of films is less than 400µm will remain immersed into the periodontal pocket such that it does not interfere with regular healing process, can be punched into different sizes, easily inserted into pocket, more patient compliance[7,8].

4. Injectable systems

Injectable systems are most suitable drug delivery device for the delivery of antibiotic agents into the periodontal pocket. It is a simple to use with little or no discomfort to the patient with help of the syringe and forms a gel that helps in retaining the drug for required time within the pocket thus reaching a large proportion of pathogens

Semi solid or gel formulations change into sticky semisolid or solid phase so as, to prevent it from being washed out. The release rate of the drug from the gel is faster as compared to other formulations. It can be easily prepared and administered· Bio adhesive semisolid, polymeric system can be utilized 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 pseudo plastic flow and thermo-responsive behavior, existing as a liquid at room temperature and gel at 34–37°C[9].

5. Vesicular systems

Liposomal systems are bilayered vesicles resembles the bio-membranes in terms of structure and behavior and hence investigated intensively for targeting periodontal pathogen. Liposomes are made up of phosphotidylinositol and biofilms. The targeting of liposomes was thought to be because of the interaction of the polyhydroxy groups of liposomes with the surface polymers of bacterial glycol-calyx. The potential of lecithin bearing liposome (proteoliposomes) as a targeting system for the control of gingivitis and dental plaque are used[10].

6. Microparticulate system

Micro particles formulated using both biodegradable and non-biodegradable polymeric materials were investigated for the preparation of microspheres. They were formulated as chips, dental pastes, and injectable systems. These microparticluate systems provide stability of the encapsulated drug. The in vitro drug release of microparticular system depends upon the polymer (Lactide: Glycoside) ratio, molecular weight, crystallinity and pH of the medium[11,12].

7. Nano particulate system

A Nano-particulate system developed to improve the effectiveness of the delivery system. Various advantages of a nano-particulate system compared to micro particle, microsphere and emulsion based delivery system includes increased stability, controlled release rate, high dispersibility in an aqueous medium. Nanoparticles penetrate deeper regions because of their small size that may be inaccessible to other delivery system, such as the periodontal pocket area below the gum line[13].

Table 1: Some of the examples drug delivery devices in the treatment of periodontitis[14, 15]

Devices	Fibers	Strips	Films	Injectable systems	Vesicular systems	Microparticluate	Nanoparticular
Polymer used	Ethylene or vinyl acetate, cellulose acetate, poly(e-caprolactone)	Polymeth-acrylate, HPMC, HP+ meth acrylic acid Polyhydroxy butyric acid polylactide-co-glycolic acid (PLGA) ethyl cellulose	Ethyl cellulose cross-linked ate collagen gelatin cross-linked gelatin+ glycerin chitosan chitosan+ PLGA Chitosan + PCL PLGA Poly(ortho ester) Eudragit L+ Eudragit S PCL	Chitosan HEC+ Polyvinylpyrrolidone HEC+ Poly carbophil Poloxamer 407+ Carbopol 934P Glycerol monooleate+ sesame oil PLGA	Phosphotidylinositol Immunoliposomes	Pluronic F 127 PLGA PLGA + PCL	PLGA Chitosan Cellulose acetate phthalate PLGA
Drug	Tetracycline HCL Chlorhexidine	Tetracycline Metranidazole Chlorhexidine Doxycycline	Metranidazole Minocycline Tetracycline Chlorhexidine Taurin Iproflavone Metranidazole Clindamycin	Metranidazole Tetracycline Propolis	Triclosan Anti orals	Tetracycline Histatin peptides	Harungana madagascariensis leaf extract Antisense oligonucleotide Triclosan

Table 2: List of Marketed formulations of various dosage forms[16]

Brand name	Drug	Dosage form	Manufacturer
Actinide®	Tetracycline	Non resorbale fiber	Alzacorp
Arestin®	Minocycline	Biodegradable powder in syringe	Oropharma corp. Warminster
Atridox®	Doxycycline	Biodegradable mix in syringe	Atrix Labs,Ft,Collins, Co
Dentamycin®	Minocycline	Biodegradable mix in syringe	Sun star Corp., Tokyo, Japan
Elyzol®	Metranidazole	Biodegradable mix in syringe	Dumex Corp. Co Denmark
Periochip®	Chlorohexidine	Biodegradable device	Dexcel Pharma Inc Jerusalem
Periochip®	Chlorohexidine/Tetracycline	Films	Perioproducts Ltd.
Periochip®	Gluconate	Inserts	Perioproducts Ltd.
Gluconate®	Metranidazole	Inserts	Perioproducts Ltd.
Elyzol®	Minocycline	Gels	Dumex pharma
Atrigel®	Doxycycline	Gels	Atridox (atrid lab)

CONCLUSION

Periodontal disease is common in all age groups affects about 20-50% of global population and makes it a public health concern. Risk of cardiovascular disease, cause 19% to 44% increase among individuals aged 65 years. Type 2 diabetic individuals with severe form of periodontal disease have 3 fold greater mortality risk compared with individuals with no or mild periodontitis. Oral use of antibiotics in periodontitis has limitations, as it requires high dose to reach the target site, and also cause other adverse reactions. This has led to extensive research aimed in developing local periodontal systems overcomes those adverse effects. However, local drug delivery systems have been used most widely nowadays in the form of fibers, strips and films, injectable gel systems, vesicular systems, microparticluate systems and nanoparticulate systems. The recent advances in the development of local drug delivery systems into the periodontal pocket have promised to improve patient compliance with improved periodontal therapy.

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