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A Review on Nano-Approaches Against Periodontitis Treatment

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Periodontitis is a provocative condition of the secretions that destroys the alveolar bone, the formation of periodontal pockets, and the degeneration of periodontal ligaments. WHO estimates that between 10 and 15 percent of people worldwide have severe periodontitis. The development of a wide variety of microflora, particularly anaerobes, in the compartments, the release of toxins and enzymes, and the stimulation of the body's immune system are the causes of the disease. Periodontitis was effectively treated using a variety of local or systemic methods. Currently, site-specific delivery, low dose requirements, bypassing first-pass metabolism, a reduction in gastrointestinal side effects, and other factors make the controlled local drug delivery approach preferable to the general approach because it primarily focuses on improving therapeutic outcomes. It offers a safe and efficient way of therapy overall, which improves patient compliance. Various surgical and mechanical procedures completely failed to eradicate the areas' germs. Numerous polymer-based delivery methods, including fibers, films, chips, strips, microparticles, nanoparticles, and nanofibers manufactured from various natural and synthetic materials, have been investigated to successfully transport various medications. These solutions have good mucoadhesion qualities, are Fill the pockets, have high retention at the target site, and are biocompatible and biodegradable. The study gives a general summary of all the different periodontitis targeted delivery systems that are now available and being created.

Keywords: Periodontitis, enzymes, microflora, biocompatible, microparticles, nanoparticles

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Introduction

Periodontitis, a chronic inflammatory disease brought on by an infection, is greatly influenced by the type of biofilms that develop. Dental plaque accumulation along the gingival margin of those who are susceptible causes an inflammatory response, which changes the microbial ecology and may have negative consequences on the periodontium.[1] Periodontitis, which frequently causes irreparable loss of attachment and alveolar bone, can develop from chronic inflammation of the gingival that affects the gingival. The majority of periodontitis cases are in populations of adults; however, it can also affect younger people and have adverse effects.[2] The main reason individuals lose teeth is an advanced illness, and other health issues that impact overall wellness are linked to periodontitis.[3]

The characteristic of periodontitis, an inflammatory disorder of the periodontium, is a progressive deterioration of the tissues supporting the tooth. Aetiology, a succession of microbial diseases with no clear cause, is currently known to include one or more than 300 species.[4] It is believed that the disease progresses in irregular, relatively brief bursts of fast tissue destruction followed by intervals of disease remission. Despite the seemingly random distribution of disease activity episodes, the resulting tissue breakdown displays a symmetrical pattern of alveolar bone loss and pocket formation that is common to several forms of periodontitis. However, the distribution of the most affected teeth and surfaces may differ among the diseases.[5]

According to several investigations, bacterial cells have been detected in the pocket wall of periodontitis lesions. Bacteraemia's, which frequently develop in patients with periodontitis after relatively basic actions like chewing and dental hygiene practices, are frequently translocated into the tissues.[6] Nevertheless, as the clinical implications may differ, it is critical to differentiate between the quiet invasion of periodontal tissues by bacteria and the direct invasion that may occur in an acute infection.[7]

Around 50% of adult populations worldwide have periodontal disease, particularly in its mild and moderate forms, while only 10% of adult populations worldwide have the severe type, Which is more common in the third and fourth decades of life.[8] Age, gender, ethnicity, and socioeconomic position are the demographic factors affecting periodontitis. Smoking, diabetes mellitus, metabolic syndrome, and obesity are additional serious risk factors. Notably, diabetes and smoking can expose people to severe periodontal disease as early as adolescence or adulthood. Additionally, smoking has a direct correlation with young people's tooth loss. The primary reason for adult tooth loss is severe periodontitis.[9]

About how gingivitis could develop into periodontitis in some people, there is still much to discover. Clinical and microbiological cross-sectional research may be helpful. Studies of natural history across time enable the study of prospective elements and circumstances that might affect disease development.[10] Age, gender, plaque, calculus, and pre-existing attachment loss are now some of the known risk factors for the development and progression of periodontitis; genetic predisposition for the onset of the disease appears to be a recurrent finding.[11] Numerous microorganisms have been recognized in terms of microbiology. The Actinobacillus actinimycetemcomitans bacteria is linked to the beginning of the disease, according to the Java project's finding on the natural progression of periodontal disease. Males are more prone to illness, which is consistent with the research. Since the presence of pockets less than 5mm was discovered to be a predictive indicator for disease progression, it appears to be a helpful tool. [12]

For thousands of years and in various cultures, medicinal plants have been utilized to treat various human ailments portions of the globe. They still serve as the primary source of medication in rural areas of developing nations, and traditional medicines are used to treat about 80% of the population.[13] Medicinal plants' natural components are rich sources of physiologically active substances. Many are the foundation for creating novel lead compounds for use in medications. In terms of illness brought on by microbes, the rise in resistance of numerous common pathogens to therapeutics already in use, such as antibiotics and antiviral medicines, has rekindled interest in the synthesis of novel anti-infective substances. There is a lot of potential for finding novel bioactive compounds because over 500,000 plant species exist worldwide, only 1% of which have been studied phytochemically.[14]

Several botanicals have been reported to stop the growth of Streptococcus mutans and other oral microorganisms, hence preventing caries. To combat the high prevalence of oral disorders, researchers are looking for molecules from natural sources, such as plants, that are inexpensive, efficient, and non-toxic. Natural products have been employed in folk medicine for 100 years and are thought to be the new source of antibacterial agents. There are several reports of conventional plants and natural products used to cure oral problems.[15]

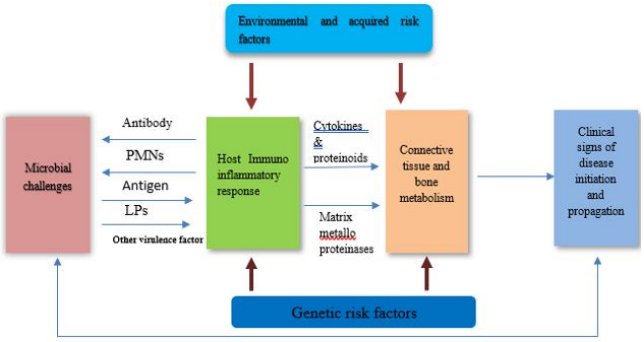
Modern drug delivery systems are built for targeted, controlled, delayed drug release. So far, polymer- or microparticle-based hydrogels have been used in dentistry, which could be due to their structure, and rate of release In-depth study has recently been conducted globally to increase the efficacy of delivery systems.[16] In comparison to microspheres, microparticles, and emulsion-based delivery systems, the nanoparticulate system offers several benefits, including high dispersibility in an aqueous medium, regulated release rate, and excellent stability. Due to their small size, nanoparticles can reach locations inaccessible to other delivery methods, like the periodontal pocket areas below the gum line. These methods enable a consistent dispersion of the active agent over a long period while reducing the administration frequency. [17]

Periodontites: An inflammatory condition of the periodontal tissues called periodontitis causes the periodontal ligament fibres and the bone into which they are embedded to stop supporting the teeth that are impacted. Gingivitis, which spreads to the underlying tissues, might start as periodontitis. Lesions from gingivitis do not always turn into periodontitis, though.[18]

Clinically, variable gingival redness and swelling levels may be present in periodontitis lesions. The gingiva may display minimal oedema and redness and appear clinically normal in cases of chronic illness.[19] The gingival surface may be stippled and have a solid consistency. Damage to the periodontal ligament and alveolar bone may result from a periodontal disease that affects deeper tissues. The main reason for adult tooth loss is the breakdown of these supporting tissues, ultimately leading to tooth loss.[20]

Periodontitis is currently thought to be caused mainly by chronic bacterial infections, the makeup of which can vary from person to person and, to a lesser extent, from site to site on the teeth of the same subject.[21] Although there are presently more than 300 species of bacteria in the oral cavity, just 5% are thought to be closely linked to periodontitis, with 1% being present in more than 90% of all cases (Slots, personal communication). Unfortunately, it has been challenging to identify the illness-causing organisms in humans due to the complexity of the flora, the intermittent nature of disease activity periods, and the relatively substantial variations in the data obtained within and between people.[22]

Pathogenesis of Periodontities



Application of Nano-Formulation on Periodontites

Table – 1

Sl no	Nature of nanoparticles used	Choices of drugs	Study design	Target cell/tissue/organisms	Applications	References
1	Polymersomes	Metronidazole or doxycycline	In vitro	Organotypic oral mucosal model and intracellular P. gingivalis inside keratinocyte monolayers.	Antibiotics that normally cannot enter host cells can be effectively delivered by polymersomes.	23
2	Nano DOX/chitosan particulate system incorporated in PVA based films	Doxycycline	In vitro+clinical	Periodontal tissue cells.	Compared to the control and placebo groups, both DOX and nanostructured films significantly improved the periodontal metrics.	24
3	Functionalized ROS-responsive drug delivery device based on PDA	Minocycline hydrochloride	In vivo+ In vitro	Macrophages	Potential for reprogramming the inflammatory microenvironment in periodontitis by polarizing	25
4	pH-responsive PLGA/chitosan nanospheres	Metronidazole and N-PTB, a host modulator.	In vivo	cells from periodontal tissue of the rat maxilla.	Metronidazole or N-PTB-encapsulated PLGA/chitosan nanospheres demonstrated the potential to control the course of periodontitis.	26

5	AuNPs were treated with Justicia glauca (aqueous leaf extract).	Azithromycin and Clarithromycin	In vitro	Escherichia coli, Candida albicans, Lactobacillus acidophilus, Bacillus subtilis, Staphylococcus aureus, Streptococcus mutans, Micrococcus luteus, and Pseudomonas aeruginosa.	It is possible to use the biogenic drug delivery system for azithromycin and clarithromycin as a potential antibacterial treatment.	27
6	A mucoadhesive drug delivery chip made from sodium alginate, gelatin, glycerol, and AgNPs	Glutaraldehyde	In vitro	pseudomonas aeruginosa (for MIC) and Murine macrophages (for cell viability).	The unique AgNPs chip demonstrated strong antibacterial action against P. aeruginosa, dimensional stability, and little impact on the survival of murine macrophage cells.	28
7	Composite membrane made from a polymeric blend and 20nm SiO2 and functionalized with drug	Zinc or doxycycline	In vitro	Osteoblast like cell	Doxycycline-doped membranes could potentially be used in GBR treatments for a number of difficult illnesses, such as periodontal infections.	29
8	Lyophilized HESc plant extract (seed/flower) mixed with AgNPs	Flowers and seeds of Syzygium cumini	In vitro	S. aureus, S. epidermidis, S. mutans, S. oralis, C. albicans, F. nucleatum, A. naeslundii, and V. dispar	S.cumini seeds and flowers hydroalcoholic extracts have species-dependent MIC antibacterial activity against medical/dental infections. The MIC was dramatically decreased when AgNPs were added to HESc.	30
9	Composite PG nanofibers of PLGA and GT were blended by electrospinning and coaxial electrospinning	Tetracycline hydrochloride	In vitro	S. aureus, S. epidermidis, S. mutans, S. oralis, C. albicans, F. nucleatum, A. naeslundii, and V. dispar	The drug-loaded core shell nanofibers have an ideal burst release followed by a sustained drug release, making them a viable drug delivery technology for periodontal disorders.	31
10	Poly(d,l-lactide-coglycolideacid)(PLGA) and chitosan NPs	Tetracycline +Lovastatin	In vitro + In vivo	Osteo blastcell cultures (ALP activity and cyto toxicity assay),A. actinomycetemcomitans and P.nigrescens(MICassay), and beagle dogs (periodontal defect regeneration)	PLGA-lovastatin-chitosan tetracycline nanoparticles showed good antibacterial activity,biocompatibility and increased alkaline phosphatase activity.	32
11	PLGA nanospheres	Doxycycline	Clinical experiment that is concurrent, randomised, and placebo-controlled	Periodontal tissue cells	Locally applied PLGA/DOX nanospheres are a complementary therapeutic strategy for the management of periodontal disease in people with type 2 diabetes. Deep pockets may also aid in the local control of pro- and anti-inflammatory cytokines, microbial decrease, and the improvement of clinical indices.	33
12	nDOX gel in chitosan polymer matrix polymer and dispersed in PVA	Doxycycline	Clinical	Periodontal tissue cells	Within three months, treatment with nDOX gel as an adjuvant to SRP improves clinical metrics and inflammatory markers.	34
13	Calcium deficient hydroxyapatite nano carrierspreparedfromCa(OH2)and (NH4)2HPO4solutions, of different Ca/Pratios CDHA1.55/1.61/1.64	Tetracycline	In vitro	S. aureus and E. coli bacteria in human fibroblasts from the periodontal ligament (hPDLF)	In addition to being excellent for medication administration, CDHA nano carriers have the ability to regenerate bone in local periodontal applications.	35

Table 2 – Different forms of periodontal nanoparticles based on investigated intra pocket delivery system

Sl no	Delivery system	Polymer matrix	Drug incorporated	References
1	Strip	Ethyl cellulose	Chlorhexidine	36
2	Strip	Hydroxypropyl cellulose +methacrylic acid	Ofloxacin	37
3	Strip	PLGA	Tetracycline HCl	38
4	Fibers	Poly (e-caprolactone) (PCL)	Tetracycline HCl	39
5	Fibers	Cellulose acetate	Tetracycline HCl	40

Conclusion

Numerous targeted delivery systems have been developed to help eradicate the systemic adverse effects of antibiotics as our understanding of periodontal disease and medication administration techniques has grown. These consist of microparticles, nanoparticles, nanofibers, strips, films, chips, and fibers. Reduction in dosage frequency, creation of biocompatible sustained-release formulations, and the prevention of bacterial resistance have all been made possible by the switch from nonbiodegradable polymers to a range of biodegradable polymers. These tools and root planking and scaling techniques offer a potent cure for the ailment. However, nanoscale intra-pocket devices are still developing as a promising opportunity for cutting-edge, effective treatment at low doses.

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