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Review Article

Review on drugs and drug delivery systems for the treatment of periodontitis

[1]Tanvi Phull, [2]Harmesh Sharma, [3]Kiran G M, [4]Himanshi Modi, [5]Sunidhi Gandhi

[1]Professor and Head of Department, [3,4,5]Post Graduate Student, Department of Periodontology, Pb. Government Dental College and Hospital, Amritsar, Punjab, India
[2]Senior lecturer, Department of Oral Surgery, Luxmi Bai Institute of Dental Sciences & Hospital, Patiala, Punjab, India

ABSTRACT:
There are many choices of antimicrobials that can be locally given into the mucosa to support non-surgical treatment for periodontitis, including metronidazole, chlorhexidine, minocycline, doxycycline and tetracycline. These medications are utilised in periodontal pockets and have the ability to reduce or completely eradicate periodonto-pathogenic microorganisms as well as control tissue inflammation. Selection of a right antimicrobial agent with appropriate route of drug administration is the key to successful periodontal therapy. Apart from antimicrobials, other drugs are also available for the treatment of periodontitis. Irrigating systems, fibers, gels, strips, films, microparticles, nanoparticles and low dose antimicrobial agents are some of the local drug delivery systems (LDDS) available in the field, which aims to deliver antimicrobial agents and other drugs to sub-gingival diseased sites with minimal or no side-effects on other body sites.
Key words: Periodontitis, Drugs, Drug Delivery systems

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Corresponding Author: Tanvi Phull, Professor and Head of Department, Department of Periodontology, Pb. Government Dental College and Hospital, Amritsar, Punjab, India

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INTRODUCTION

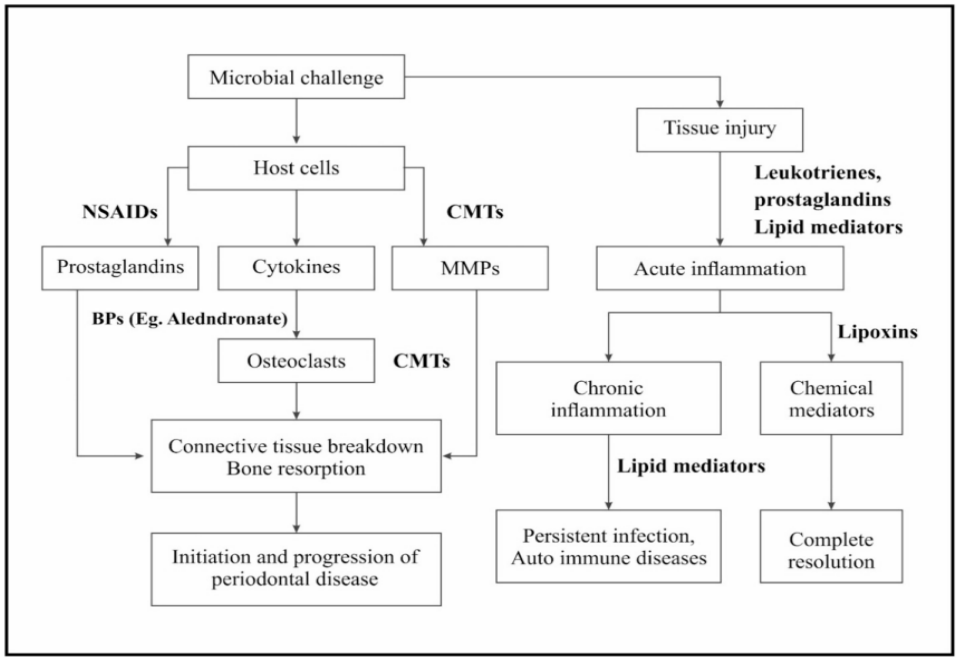
Periodontitis is one of the most common ailments affecting the teeth, leading to the destruction of the supporting and surrounding tooth structure. The term "periodontitis" is build-up of two words, i.e., "periodont-" meaning "structure surrounding the teeth" and "itis" means "inflammation." Periodontitis is originally a disease originating from the gingival tissue which if left untreated results in penetration of inflammation to the deeper tissues, altering the bone homeostasis causing tooth loss. Periodontal disease has a multifactorial origin. The main culprit identified in periodontitis is the bacterial biofilm growing on the tooth surfaces. While the host response determines the progression of the disease along with factors like local factors like plaque and calculus, genetics, environmental factors, systemic health of the patient, lifestyle habits and various social determinants also play a role. The deleterious effects of periodontopathogens are not limited to the periodontium, but they also exude their ill effects on the systemic health of the patients. [1,3,9]

At present, scaling and root planning (SRP) is the fundamental treatment for periodontitis. SRP mechanically removes the pathogenic biofilm and delays the repopulation of the microbes which are associated with periodontitis. However, due to limited access to the microbes which inhabit deep in the periodontal pocket and the anatomical complexities of the tooth, SRP alone cannot completely remove the pathogens. In addition, periodontitis, as an inflammation which is closely associated with bacterial infections, can lead to alveolar bone loss and tissue damage. Therefore, SRP can enhance the curative effect by combination with drugs, which are classified as antibacterial drugs, anti-inflammatory drugs, and drugs which promote bone regeneration and tissue regeneration. The success of the overall therapeutic process relies not only on the drug properties but also on the carrier system and route of administration. In this context, this review highlights

applications of various drugs and drug delivery system in the treatment of periodontitis. [20]

HOST MODULATION THERAPY (HMT)

Though microbial attack is the pre-requisite for the initiation of PD, Kornman in his classical model of periodontal pathogenesis has well explained the role of host in the severity of the disease. In this regard, to regulate the hyperactive host response to the microbial attack, Golub et al. introduced the concept of HMT in 1992. Bisphosphonates, non-steroidal anti-inflammatory drugs (NSAID's), tetracycline and their analogues are some of the key host modulating agents that have gained significant attention in periodontics. These agents, when administered acts at various levels of inflammatory process and inhibits productions of key mediators involved in tissue destruction. Currently, SDD also called as Periostat is the only commercially available USFDA approved host modulating agent which is prescribed as 20 mg doxycycline to be taken orally twice daily for 3 months and in some cases, it is continued for up to 9 months. Chemically modified tetracyclines (CMT) are a unique class of tetracyclines having inhibitory actions on collagenolytic activity and metalloproteinase – mediated alveolar bone loss. CMTs are distinct from conventional tetracyclines in that they are advantageous as they do not cause gastrointestinal upsets and its beneficial effects can be attained with decreased number of doses. A group of other anti-inflammatory agents namely lipoxins, resolvins and protectins have also been shown to reduce clinical signs of inflammation when used adjuvant to mechanical therapy. The main advantage of these resolving mediators is that these molecules are produced in response to the normal inflammatory response and are natural physiological resolution agonists. [16]



Role of bisphosphonates (BPs), NSAIDs, Chemically modified tetracycline (CMT) and agents for resolution of inflammation in host modulation [16]

IRRIGATING SYSTEMS

Oral irrigation (OI) is a generic term used to describe an irrigating system employed professionally in the dental clinic as well as personally applied by the patient at home to prevent and treat the PD. In 1962, a Colorado dentist Gerald Moyer in collaboration with an Engineer John Mattingly introduced the OI system as an alternative to dental flossing to enhance patients' oral hygiene. OI is therefore called as dental water jet and water flosser. Irrigation flushes away the bacteria from the tooth and periodontal tissue surface causing non-specific reduction of plaque bacteria. OI systems comprise two components, the device and the irrigating solution in which the effectiveness is governed by the irrigation pressure, stream characteristics, and jet type. Though, both end port and side port cannula achieve similar depth of penetration, the side port cannulas eject solution at a low pressure as the velocity of the irrigating agents are reduced by the resistance created at the closed end point as compared to the open-end port where there is patency to the irrigating solutions without any resistance. Water flossing action of the flosser includes an integration of pulsation and pressure with subsequent shear hydraulic force that disrupts the plaque and expels subgingival bacteria effectively. The compressive force causes steady water flow leading to constant pressure on the tissue promoting the escape of bacteria and its byproducts while the phase of decompression facilitates further displacement of debris and bacteria.[7,10,11,13,15]

Waterpik®, is one such OI device with a reservoir and a handle with replaceable tips. Studies have shown that Waterpik® is effective in removing the bacterial biofilm from the crest of marginal gingiva to a distance of approximately 50% at a moderate to high pressure setting of 50–90 psi and pulsation rate of 1200–1400 per min. Success of the locally delivered antimicrobial agents in irrigation system depends on its depth of penetration, complexity of infection, GCF flow, drug concentration, and available amount of drug for sufficient duration of time at the pocket region. Diffusion of the drug into deeper levels of the pocket and the duration of exposure to the antimicrobial agent also determines the proficiency of irrigation devices. In supragingival irrigation devices, the irrigating agent penetrates to the depth of 29–71% of shallow pockets and 44–68% in case of moderately deep and deep pockets, whereas subgingival irrigation has better penetrability with the range of 75–93% into the deep pocket. [2,4,6,14,21]

Effectiveness also depends on the ecosystem of bacteria in the pocket, for example, planktonic Streptococcus sanguis is inhibited by 0.2% of chlorhexidine (CHX) and 0.05% cetylpyridinium within 5 min, whereas a complex bacterial biofilm structure resists and survives for > 4 h of exposure to the same. The antimicrobial activity of the drug is also hampered by the presence of blood components, serum proteins and pus in the pocket. In addition, the rate of GCF flow is also one of the key factors that determines the contact time between antimicrobial agents and subgingival bacteria. Several clinical studies have been done till date in which 0.2% CHX, saline solution, sterile water, and SRP were used as controls in comparison to 10 mg/mL of tetracycline, povidone iodine (2–10%), ozonated water, 0.25% sodium hypochlorite, essential oils, mixture of 1% povidone and 3% hydrogen peroxide. These irrigating agents showed comparatively better therapeutic results than the standard controls when used as an adjunctive therapy to SRP. Results of the study were assessed based on significant reduction in clinical variables such as BOP, PPD scores and CAL gain.

In another study, povidone iodine (10%) was used as an irrigating agent adjuvant to full mouth ultrasonic debridement (FMUD) as compared to FMUD with saline irrigation in generalized aggressive periodontitis patients. The two groups presented reduction of full mouth bleeding score, plaque score and had statistically significant PD reduction, CAL gain and improvement in level of gingival recession ($p < .05$) from baseline. Both therapies reduced the microbial count of Pg levels in deep pockets ($p < .05$). However, inter-group comparison in terms of clinical, immunological and microbiological parameters demonstrated nonsignificant difference ($p > .05$).

In a clinical scenario, it is important to note that soon after the SRP, the microbial adhesion on tooth surface starts within the nanoseconds and it generally takes 12 h for the bacteria to repopulate in the pocket area and initiate disease process in the oral cavity. Irrigating agents have transient action but when used on a regular basis helps to prevent re-population of the bacterial flora in the periodontal pocket. Hence, it is suggested that the irrigating system when used as an adjuvant to mechanical plaque control, plays an important role to prevent the occurrence of PD. Though irrigating systems are effective in clearing the bacteria from subgingival sites, the results are not long lasting due to limitations such as restricted penetration into the deepest point of the pocket, requirement of high manual dexterity in personally applied devices, lack of sustained release of drug and rapid clearance by GCF. [2,4,6,8,14]

LOCAL DRUG DELIVERY (LDD)

The most important step in treating periodontitis is eradicating pathogenic microbes from the periodontal pocket. Development of local drug delivery occurs due to reducing the limitation of mouth washes and subgingival irrigation. [19]

LDDS, which are directly placed in the periodontal pocket, can provide a high enough concentration of active drugs for a long enough period of time. LDDS can bring more advantages compared with systemic administration, which include avoidance of gastro-intestinal issues and first pass metabolism by direct application at a specific site, higher efficacy, and fewer side effects by controlling drug release, and improved patient compliance by reducing dosing frequency. In view of these advantages, LDDS has been explored as strategies for periodontitis treatments in recent decades. In addition, LDDS exerts its curative effect mainly by loading three types of drugs including anti-bacterial, inflammation modulating, alveolar bone and tissue repairing agent for the treatment of periodontitis. [20]

Table 1: Some typical anti-bacterial LDDS for periodontitis [20]

Systems	Polymer matrix	Drug incorporated	Study design	Results
Fibers	Cellulose acetate	Tetracycline	Clinical trials (patients)	The formulation showed a burst (approximately 95%) within the first 2 h and reduced gingival index values. Spirochetes were successfully eliminated from the gingival sulcus by providing less than 1/1000 of the amount of tetracycline that was required for systemic therapy.
	Ethylene vinyl acetate	Tetracycline	Clinical trials (patients)	The formulation could maintain a constant drug level in the gingival crevicular fluid above 600 mg/mL throughout 10 days. Furthermore, Significant decrease in probing depth and increase in attachment level were observed at the one-, three-, and six-month clinical visits.
	Ethylene vinyl acetate	Tetracycline	Approved for marketing (patients): Actisite®	Clinical trials indicated that this formulation had good antibacterial potential, maintaining a sustained drug level in gingival crevicular fluid (above 1000 μg/mL) throughout 10 days.
Strips and films	Polyethyl methacrylate	Tetracycline/ Metronidazole	Clinical trials (patients)	Both formulations showed sustained release over 4 to 5 days with a significant burst release on the first day. Significant antibacterial activities against gram-negative rods, fusiforms and spirochetes were observed in tetracycline strips. But Metronidazole strips tended not to be as effective as expected.
	PLGA	Tetracycline	Clinical trials (patients)	PLGA-SF containing 25% tetracycline demonstrated sustained release for 10 days. Compared with traditional maintenance treatment, the application of PLGA-SF was confirmed to significantly reduce the incidence of bleeding on probing and probing pocket depths.
	Gelatin	Chlorhexidine	Approved for marketing (patients): Periochip®	Periochip® is a rectangular chip, containing chlorhexidine gluconate embedded in a biodegradable polymer-gelatin matrix. The drug release was lasted for 7 days after administration, however, the burst release on the first day was also observed. Clinical trials demonstrated that it can improve the clinical symptoms of periodontitis.
Microspheres	PLGA/PCL	Doxycycline	Clinical trials (patients)	Microspheres with a particle size of 90 to 200 μm showed an entrapment efficiency of 24% and in-vitro release up to 11 days. The formulation has been shown to be remarkably effective both in microbiological experiments and clinical trials for up to three months.
	PLGA	Doxycycline	Preclinical studies: in vitro	The doxycycline-loaded microspheres were formulated to have a size <10 μm and low polydispersity, maintaining drug release behavior for up to 21 days. In vitro studies revealed concentration-dependent toxicity and antibacterial properties against P. gingivalis and Fusobacterium nucleatum.
	PLGA	Minocycline	Approved for marketing (patients): Arestin®	Arestin is a PGLA microsphere loaded with minocycline, which has been approved by the US FDA for marketing. Microbiological outcomes indicated that minocycline concentrations could be maintained up to 14 day and effectively inhibited bacterial activity.
Nanosystems	MPEG-PLA *(nanoparticles)*	Minocycline	Preclinical studies: in vitro/in vivo (beagle dogs)	Minocycline-NPs was round with a mean diameter of about 100 nm. The release profile showed that approximate 96% of the minocycline was released after 12 days. A preliminary in vivo work demonstrated that minocycline-NPs could significantly improve periodontitis symptoms by penetrating the junctional epithelium.
	Chitosan *(nanoparticles)*	Doxycycline	Preclinical studies: in vitro	Doxycycline-loaded nanoparticles with a mean particle size of 50 nm showed approximately 75% entrapment efficiency and 28% loading capacity. And it had an orderly morphology with an excellent cytocompatibility, preferable antibacterial properties for P. gingivalis and effective downregulation of inflammatory factors in human gingival fibroblasts.
	N, N, N-trimethyl chitosan/ Lecithin *(nanoliposomes)*	Doxycycline	Preclinical studies: in vitro/in vivo (SD rats)	Obtained nanoliposomes with mean particle size of around 176.0 nm and zeta-potential of around +12.31 mV presented distinct inhibitory effects for periodontal biofilms by delivering doxycycline to the target location. Histological examination and pharmacodynamics indicated elimination of inflammation and bone reconstruction compared to the control group.
Gels	Chitosan/ β-glycerophosphate	Minocycline	Preclinical studies: in vitro/in vivo (SD rats)	The formulation displayed a desirable gelling behavior (liquid-like at room temperature and gel-like at 37 °C). In vivo studies showed that rats' liver and kidney tissue sections were normal, with no structural damage. Pharmacodynamic experiments showed that the gel could significantly decrease the probing depth and gingival index, confirming a good therapeutic effect.
	Phytantriol/Propylene glycol/Water	Minocycline	Preclinical studies: in vitro/in vivo (SD rats)	The injectable formulation was developed for local administration of minocycline hydrochloride, which could form a cubic phase gel in excess water in 6.97 ± 0.10 s. The results of in vitro drug release suggested the minocycline presented a sustained release for 4 days. The gel significantly reduced gingival index, probing depth and alveolar bone loss compared to the model group. Besides, the pathological characteristics of model rats were improved.
	PLGA/Poloxamer 407	Moxifloxacin		

Systems	Polymer matrix	Drug incorporated	Study design	Results
			Formulation under investigation: in vitro/in vivo (SD rats)	A dual-barrier temperature sensitive gel system based on poloxamer 407 containing moxifloxacin loaded PLGA nanoparticles was applied to against periodontitis. In vitro release results showed continuous release of moxifloxacin for 7 days without burst release. And the γ-scintigraphy imaging indicated an enhanced retention ability and prolonged drug release at the periodontal pocket. Treatment with this dual delivery system for 1 week obtained superior efficacy than treatment with a commercial gel formulation for 3 weeks.
	PLA	Doxycycline	Approved for marketing (patients): Atridox®	The viscous gel was approved for delivering doxycycline to the subgingival area. Clinical studies showed that doxycycline levels in gingival crevicular fluid maintained a 7-days effective antimicrobial concentration. The results of clinical trials demonstrated that the subgingival delivery of Atridox® achieved a favorable efficacy in reducing the clinical signs of adult periodontitis.
	hydroxyethyl cellulose/ eudragit/triacetine	Minocycline	Approved for marketing (patients): Periocline®	This Minocycline was incorporated in a matrix composed of hydroxyethyl cellulose, eudragit, triacetine and magnesium chloride. The minocycline concentration in gingival crevicular fluid reached 1300 μg/mL at 1 h, however, decreased to 90 μg/mL after 7 h. This study demonstrated that Periocline® could remove the periodontal pathogen and reduce the depth of probing.

HCl represents hydrochloride.
PLGA represents poly lactic-*co*-glycolic acid.
PCL represents poly (ε-caprolactone).
MPEG-PLA represents Methoxy-poly (ethylene glycol) poly (lactic acid).
NMP represents *N*-methyl-pyrrolidone.

Table 2: Some typical inflammation modulating LDDS for periodontitis [20]

Systems	Polymer matrix	Drug incorporated	Study design	Results
Films	Gelatin	Curcumin	Preclinical studies: in vitro	The biodegradable crosslinked gelatin film loaded with curcumin could provide proper mucoadhesive properties and mechanical strength. Experiments demonstrated that curcumin could be wrapped inside a smooth and uniform film in an amorphous form, and could be effectively and continuously delivered up to 7 days.
Nanosystems	PLA/PGA *(nanoparticles)*	Curcumin	Preclinical studies: in vivo (SD rats)	The curcumin-NPs produced by emulsion-solvent evaporation technique abrogated inflammatory bone resorption in the LPS-induced model of periodontal disease. And it was found that both the number of osteoclast and infiltrating inflammatory cells were significantly reduced.
	Phosphatidylcholine/ Cholesterol *(nanoliposomes)*	Atorvastatin	Preclinical studies: in vitro	The atorvastatin nanoliposomes with mean diameter of 178 nm and encapsulation efficiency of 87.3% was successfully prepared by thin film hydration method. Compared with free drugs, the formulation had a higher inhibition of lipopolysaccharide-induced pro-inflammatory cytokine release.
Gels	Pluronic F127/Carbopol P934	Curcumin	Clinical trials (patients)	The curcumin-loaded in situ gelling formulation showed in-vitro release for 7 days and accepted gelation temperature ranging from 28 to 34 °C. Clinical research verified the 2% curcumin gel could significantly reduce probing depth, improve bleeding index, and inhibit the extent of plaque.
	Chitosan/β-GP/Gelatin	Aspirin/EPO	Preclinical studies: in vitro/in vivo (Wistar rats)	The injectable and thermosensitive hydrogel loaded with aspirin and erythropoietin had an excellent biocompatibility and could continuously release the active substance for at least 21 days. HE-staining and micro-CT results further confirmed the abilities of the hydrogels to stimulate periodontium regeneration and improve anti-inflammatory effect.
	Chitosan	Atorvastatin	Preclinical studies: in vitro	The bioadhesive gel with suitable viscosity and injectability released atorvastatin for 6 days. Subsequent in vitro anti-inflammatory studies exhibited a decrease in cytokine levels after the application of the formulation. The anti-inflammatory activity was observed to increase with the aid of chitosan.
	PCL/Chitosan	Triclosan/ Flurbiprofen	Preclinical studies: in vitro/in vivo (SD rats)	Nanoparticles containing triclosan were distributed in hydrogel, while flurbiprofen was directly loaded into the hydrogel. The characterization data displayed that the dual nanogel system consists of nanosized spherical structures and exhibited pH-dependent swelling/erosion and temperature-responsiveness. Besides, the in-vivo study confirmed the dual antibacterial and anti-inflammatory effects.
	PLGA	Chlorhexidine/ Ibuprofen	Preclinical studies: in vitro/in vivo (mice)	ISFI loading of 1.5% chlorhexidine and ibuprofen was non-toxic and significantly reduce the P. gingivalis growth. The in-vivo results showed that 1.5% chlorhexidine-ibuprofen loaded ISFI could be used to control infection and inflammation as an effective adjunct for periodontal treatment.

PLA represents poly lactic acid.
PGA represents co-glycolic acid.
PLGA represents poly lactic-*co*-glycolic acid.
EPO represents erythropoietin.
β-GP represents β-sodium glycerophosphate.

Table 3: Some typical alveolar bone repairing and tissue repairing LDDS for periodontitis [20]

Systems	Polymer matrix	Drug incorporated	Study design	Results
Membranes	PLLA	Platelet-derived growth factor-BB	Preclinical studies: in vitro/in vivo (SD rats)	PDGF-BB loaded PLLA membranes with proper degradation property was able to release the active agent for 28 days. It could potentially enhance the regenerative efficacy of alveolar bone after 2 weeks of treatment.
	PEG-b-PCL	SP600125/BMP-2	Preclinical studies: in vitro/in vivo (beagle dogs)	The nanofiber membranes showed a good degradation performance and a prolonged release profile up to one month. In vivo study further confirmed that the nanofiber membrane markedly avoided alveolar destruction and recovered bone defects.
Scaffolds	Chitosan/ Hydroxyapatite	Doxycycline	Preclinical studies: in vitro	Doxycycline loaded scaffolds displayed a compressive strength of 14 MPa/cm^3 and an elastic response of 0.34. And formulation showed an initial burst (6–8 h) followed by sustained release for the remaining 64 h. The non-toxicity and effective cell adhesion of the preparation were verified. In addition, the scaffold can promote the survival of pre-osteoblasts.
Microspheres	PLGA	PDGF/Simvastatin	Clinical trials (patients)	The microsphere could facilitate the sequential delivery of platelet-derived growth factor and simvastatin to repair periodontal tissue defects. And they demonstrated good biocompatibility in vivo, with reduced apoptosis and inflammation. The pharmacodynamic results showed that the microspheres could increase the bone volume fraction and reduce trabecular separation in the process of dentoalveolar regeneration.
Gels	Gelatin methacrylate	Periodontal ligament stem cells	Preclinical studies: in vitro/in vivo (beagle dogs)	The gel with proper microarchitecture, mechanical strength and surface roughness facilitated proliferation and osteogenic differentiation of human periodontal ligament stem cells and further promoted new bone formation.
Nanoparticles	PLGA/Chitosan	Lovastatin/ Tetracycline	Preclinical studies: in vitro/in vivo (beagle dogs)	The nanoparticles with mean particle size of 111.5 nm could control the sequential release of tetracycline and lovastatin for 21 days and enhance their biological functions in bone regeneration. The compound preparation provided several advantages, including good biocompatibility and increased anti-bacterial activity. Micro-CT results showed significant new bone formation at the alveolar bone defect site filled with nanoparticles.

Notes: PLLA represents porous poly (L-lactide) (PLLA).
PEG-b-PCL represents polyethylene glycol-b-poly (ε-caprolactone).
PDGF-BB represents Platelet-derived growth factor-BB.
BMP-2 represents bone morphogenetic protein-2.
PLGA represents poly lactic-*co*-glycolic acid.
PDGF represents platelet-derived growth factor.
rhFGF-2 represents recombinant human fibroblast growth factor type 2.

NOVEL TRENDS IN LOCAL DRUG DELIVERY

Many studies have been conducted for newer agents other than what we discussed earlier, in the field of local drug delivery with maximum benefit. Newer agents include simvastatin, atrovastatin, azithromycine, metformine alendronate, clarithromycin and herbal products like aloevera, neem, tulsi, tea tree oil, lemon grass, pomogranate etc. Kuduva et al had been observed that green tea catechin local delivery along with scaling and root planing is more effective than scaling and root planing alone.

Bhat et al concluded that sub gingival administration of Aloe Vera gel results in improvement of periodontal condition. Aloe Vera gel can be used as a local drug delivery system in periodontal pockets.

Agarwal et al did a study to investigate the adjunctive effects of subgingivally delivered 0.5% clarithromycin (CLM) as an adjunct to scaling and root planing for treating chronic periodontitis in smokers. They concluded that although both treatment strategies seemed to benefit the individuals, the adjunctive use of 0.5% clarythromycin as a controlled drug delivery system enhanced the clinical outcome.

Kumari et al concluded that the atrovastatin local drug delivery as an adjunct to SRP can be used in the treatment of intrabony defect in chronic periodontitis among smokers.

Pradeep et al observed that local delivery of metformin into the periodontal pocket stimulated significant increase in the probing pocket depth reduction, clinical attachment level gain, and improved intrabony defect depth reduction compared to placebo in adjunct to scaling and root planning. This can provide a new direction in the field of periodontal healing. Rao et al concluded that, there was greater decrease in modified sulcus bleeding index and probing pocket depth and more clinical attachment loss gain with significant intrabony defect fill at vertical defect sites treated with scaling and root planning plus locally delivered metformin, versus SRP plus placebo, in smokers with generalized chronic periodontitis.

Elgendy et al reported that the local delivery of tea tree oil gel in case of chronic periodontitis may have some beneficial effects to augment the results of the conventional periodontal therapy. Moreover, it places a focus on the value of monitoring GCF levels of pentraxin-3 as a marker of periodontal tissue healing.

Shivaraj et al proposed that locally delivered 2% lemongrass essential oil gel offers a new choice of safe and effective adjunct to scaling and root planing in periodontal therapy.

Hosadurga et al proposed the use of 2% curcumin gel and 2% tulsi (O. Sanctum) gel in the treatment of experimental periodontitis. [19]

Melatonin by virtue of its effects, could be used as a novel non- pharmacological support to modulate host response in patients affected by chronic periodontitis. [12] As the degree of periodontal disease increases, the salivary melatonin levels are depressed, indicating that melatonin may act to protect from external bacterial insults. melatonin may have effect a favorable effect in slowing osteoclastogenesis, improving the quality of alveolar bone and preventing the progression of periodontal disease. melatonin-mediated rise in OPG may have therapeutic utility in conditions associated with accelerated bone resorption such as periodontal disease. [5] Montero et al proposed that 1% topical melatonin for 20 days significantly decreased IL-1β, IL-6 and PGE2 in GCF of pts with diabetes and periodontitis. Tinto et al in their study concluded that oral administration of melatonin (1 mg per day for 30 days) after one-stage full mouth NSPT determined a greater change from baseline PD if compared to NSPT alone, in untreated stage III periodontitis.

Coenzyme Q10 serves as an endogenous antioxidant and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation. The effects and mechanisms of action of CoQ10 include stabilization of calcium-dependent channels, inhibition of intracellular phospholipases, prostaglandin metabolism, free radical scavenging and direct membrane stabilization. [18] It was also found that, long-term regular intake of nutritional dietary supplement of CoQ10 is more beneficial in nonsurgical treatment outcome of periodontal disease. [17] Sale et al conducted a study were they used Co Q10 topically and intrasulcularly as an adjunct to SRP in the management of periodontitis and found a significant improvement in clinical parameters.

CONCLUSION

Owing to the advanced knowledge gained regarding the etiopathogenesis of periodontitis, there is a continuous search for the development of new and novel treatment strategy to prevent disease progression and also to combat the tissue destruction caused by the intricate interaction between the pathogenic micro-organisms and the host defence mechanisms.Due to the tissue invasive nature of periodontopathogens,mechanical debridement of the root surface and the diseased soft and hard tissue surfaces alone will not be sufficient to prevent further tissue loss and facilitate regeneration of the lost tissue. Therefore, appropriate pharmacological agents and delivery systems has to be incorporated as an adjuvant to conventional periodontal therapy to achieve best clinical results.

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