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Original Article

In-Situ Gel of Statins for Periodontitis Diseases

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ABSTRACT

Periodontitis is a chronic inflammatory disease affecting the teeth' supporting structure, leading to tissue destruction and loss of teeth. Conventional treatment strategies like mechanical debridement and systemic antibiotic therapy have limitations due to bacterial resistance and patient compliance challenges. Therefore, in situ gels have emerged as a promising local drug delivery system for effectively managing periodontitis. This review explores the role of HMG-CoA inhibitors (statins), in in situ gel formulations for periodontal therapy. Statins exhibit pleiotropic effects, including anti-inflammatory and bone-regenerative properties, which make them an attractive adjunct in periodontitis treatment. The review discusses various fabrication methods for in-situ gels, including temperature-sensitive, pH-responsive, and ion-activated systems that sustain and control drug release. Compared to conventional drug delivery methods, in-situ gels enhance drug retention within the periodontal pocket, improve therapeutic efficacy, and minimize systemic side effects. This review underscores the potential of atorvastatin-loaded in situ gels as an innovative and effective approach for managing periodontitis, paving the way for future advancements in periodontal therapy.

Keywords: Periodontitis, In-situ gel, HMG-CoA inhibitors, Statins, Drug

INTRODUCTION

Periodontitis is a leading cause of tooth loss. It is a chronic, multifactorial infectious disease that affects the supporting tissues of the teeth, caused by periodontopathogens that accumulate in dental plaque, leading to infection. [1] It is characterized by inflammation of the periodontal ligament, associated with microbial activity and the host's immune response. This inflammation results in the loss of periodontal attachment and subsequently alveolar bone.[2, 3] It is relatively common worldwide, impacting nearly 60% of the elderly and 50% of adults.[4] The 2022 global report by the World Health Organization (WHO) on oral health status estimated that oral diseases affect nearly 3.5 billion people worldwide. Among these, two billion individuals have dental caries in their permanent teeth. Additionally, periodontal diseases impact about 19% of the global adult population, accounting for over one billion cases. In European countries, the report indicates that more than 50% of the population may experience some form of periodontitis, with over 10% suffering from its severe form. The prevalence of periodontitis increases significantly in older adults, reaching 70–85% among those aged 60 to 65 years.[5] The primary cause that drives toward periodontal destruction are the poor oral hygiene and the host's defence against the microbial infection along with the composition of the periodontal microflora. Various associated risk factors are smoking and diabetes mellitus, modulate the onset and progression of the disease.[6] Once diagnosed individual with periodontitis, the treatment aims to resolve inflammation and infection that to reduce further tissue damage and regenerate lost bone structures to restore health and normal function of teeth. The routine treatment options for periodontitis are use of surgical and non-surgical methods based on harshness of the disease. The various non-surgical method includes scaling, root planning and obeying of best oral hygiene practices from qualified dentistry whereas surgical options are grafting of bone at the diseased site of mouth cavity, removing the diseased tissue and cleaning of tooth roots (flap surgery).[7] However, following a mechanical debridement of periodontitis either surgical and non-surgical treatment approach, as an adjunct systemic antimicrobial therapy help to cure periodontitis

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completely. Several antibiotics based on proper microbial diagnosis and sensitivity testing are prescribed for the management of periodontitis diseases are likely tetracyclines, doxycycline, minocycline, clavulanic acids, amoxicillin etc. The effective concentration of the antibiotic may not achievable at the periodontal disease site (gingival crevicular fluid) leading to poor therapeutic response. Further, the repeated or long past use of the antibiotics (for some other infections/diseases) may lead to the development antimicrobial resistance by producing resistant strains of microorganisms and other side effects.[8, 9]. So some alternatives to antibiotics are much required. Various literatures stated that statins may be used for the management of periodontitis other than antibiotics. Statins, a class of drugs that inhibit 3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase introduced in 1987 [10], commonly used to lower blood cholesterol levels in patients with hyperlipidaemia and atherosclerosis, thereby reducing the risk of cardiovascular events. Statins are exhibiting, which include anti-inflammatory, antioxidant properties, and their potential effects pleiotropic effects on epithelization and wound healing. Additionally, they possess antimicrobial, antiviral, and fungicidal properties actions beyond their lipid-lowering capabilities, may contribute to the management of periodontal disease. As stated by Tahamtan S. et al. (2020) Statins have notable effects in the management of oral health including chronic periodontitis, alveolar bone loss due to either extraction or chronic periodontitis, osseointegration of implants, dental pulp cells, orthodontic tooth movement, and orthodontic relapse, wound and/or bone healing, salivary gland function. Henceforth, the statins may be considered as novel, safe, inexpensive, and widely-accessible therapeutic moiety in dentistry and dental treatments. The statins like simvastatin, rosuvastatin, atorvastatin is reported to use adjunct in the periodontal diseases. The Statins, helps to control periodontal inflammation through inhibition of proinflammatory cytokines and promotion of anti-inflammatory and/or proresolution molecule release, mainly, through the ERK, MAPK, PI3-Akt, and NF-κB pathways. Moreover, they are able to modulate the host response activated by bacterial challenge, to prevent inflammation-mediated bone resorption and to promote bone formation. Furthermore, they reduce bacterial growth, disrupt bacterial membrane stability, and increase bacterial clearance, thus averting the exacerbation of infection. Local statin delivery as adjunct to both nonsurgical and surgical periodontal therapies results in better periodontal treatment outcomes compared to systemic delivery. Moreover, combination of statin therapy with other regenerative agents improves periodontal healing response. Therefore, statins could be proposed as a potential adjuvant to periodontal therapy, alternative to antibiotics. It is also requiring alternative way to treat the periodontitis other that oral route of administration locally to increase the drug concentration at the periodontal disease site. The local drug delivery has been emerged as a significant strategy of periodontal treatment, allowing for applying the drug locally and directly to the periodontal pocket of the oral cavity.[11] This method increases exposure to the medication and kill periodontal pathogens more effectively with reduced dose resulting in improved therapeutic outcomes than orally administered tablets or capsules. The local drug delivery for the periodontitis disease solves different issues like drug distribution (reduce systemic exposure), drug concentration (increase drug concentration), therapeutic potential (may act better locally), frequeny (reduce frequency of administration), Super infection (limited in compare to systemic therapy) etc. Thus, the local drug delivery addresses the issues and complications associated with systemic antibiotics.[9] The various local rug delivery usually are fibers, strips, films, and microparticulate systems, are available for treating periodontitis. However, the various local drug delivery for the treatment of periodontitis For instance, patients have reported discomfort and varying degrees of gingival redness when removing fibers.[12] Using non-biodegradable polymers in strips poses another significant disadvantage, as they offer only temporary clinical improvements after treatment completion. Additionally, preparing films presents challenges related to their thickness and adhesiveness, while microparticulate systems struggle with poor retention within the periodontal pocket. The strategic disadvantages of local drug delivery may be overcome by delivering drugs, including statins, to treat periodontal diseases by administering the drug in in-situ mucoadhesive gel form. In-situ gels are a drug delivery system where the formulation is initially liquid or solution. Still, upon contact with the body, it

undergoes a sol-to-gel transition by change of temperature, pH, or ionic concentration, allowing for targeted and sustained drug delivery. Using biodegradable and water-soluble polymers in these formulations enhances their acceptance and effectiveness for drug delivery.[13] In situ mucoadhesive gels, thus, when applied to the periodontal pockets, due to muco-adhesiveness, produce local and sustained delivery of the incorporated drug. Thus, in situ mucoadhesive gels may be a promising local drug delivery method because they can maintain high drug levels in the gingival crevicular fluid for extended periods, resulting in desired clinical benefits.[14] These gels are administered as precursors that transform into a gel at the action sites.[15] Numerous in situ gels, including temperature-sensitive, light-responsive, and pH-dependent gels, have demonstrated potential in managing periodontal diseases.[16] Here in this review, we have focused on insights into periodontitis treatment, the pathophysiology of periodontitis, and the research and/or clinical trials status of statins in the treatment of periodontal diseases, an insight of in situ gel in the management, particularly periodontitis.

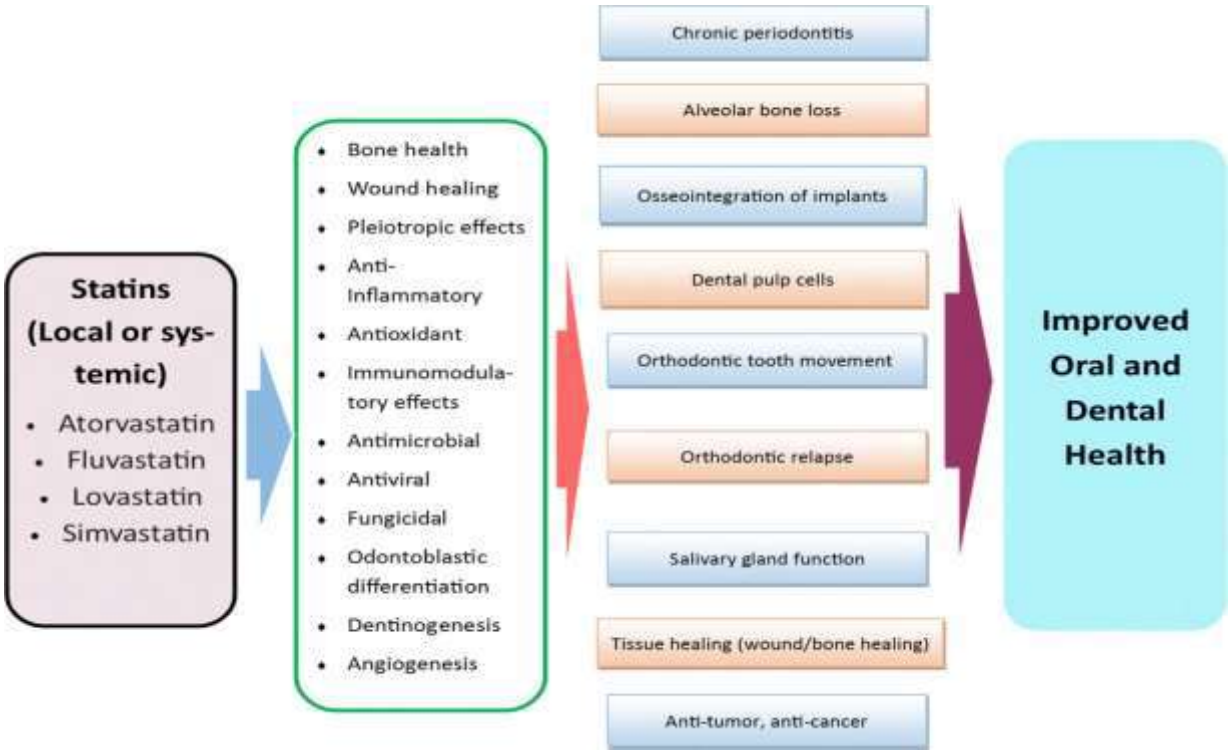

Figure 1: Multifaceted Roles of Statins in Enhancing Oral Health Outcomes

Insight of periodontitis treatment

The management of periodontitis can be done broadly by using either non-surgical or surgical methods, or sometimes both, depending on the severity of the disease. The non-surgical method is scaling and root planning (SRP) for chronic periodontitis. Scaling involves the removal of plaque and tartar (calculus) from the tooth surfaces, both above and below the gum line. After scaling, root planning is performed to smooth the rough surfaces of the tooth roots. This smoothing process helps facilitate the reattachment of the gums to the teeth, promoting healing and reducing pocket depths. It may involve removing cementum or dentin contaminated with bacteria or toxins.[17] The antibiotic therapy after SRP involves monotherapy with β-lactams (such as amoxicillin with or without clavulanic acid), metronidazole, tetracyclines (including tetracycline, doxycycline, and minocycline), clindamycin, and ciprofloxacin.[18] with their reported disadvantages during the therapy to strengthen the requirement of statins The **β-lactams**, especially amoxicillin, periodontists commonly prescribe broad-spectrum antibiotics for treating periodontal abscesses. These antibiotics demonstrate excellent tissue distribution but tend to have relatively low concentrations in the crevicular fluid, a biological fluid derived from the gingival tissues (the gums). Since some periodontal pathogens can produce β-lactamases that inactivate β-lactams, the combination of amoxicillin and clavulanic acid

should be used judiciously.[19] **Metronidazole**, which has a narrow spectrum of activity primarily targeting strictly anaerobic bacteria, effectively treats refractory periodontitis associated with P. gingivitis and/or P. intermedia. It achieves effective antibacterial concentrations in gingival tissues and crevicular fluid, and its oral administration has minimal impact on the indigenous microflora of the oral cavity and intestines.[20] **Tetracyclines**, including doxycycline and minocycline, are effective against significant periodontal pathogens such as A. actinomycetemcomitans. They also possess anti-collagenase properties, which help reduce tissue destruction and bone loss. Clindamycin is effective against gram-positive cocci and gram-negative anaerobic rods, though it has limited impact on A. actinomycetemcomitans. This antibiotic is also beneficial for treating refractory periodontitis.[20] **Ciprofloxacin** targets several periodontal pathogens, including A. actinomycetemcomitans, effectively penetrating affected periodontal tissues and achieving higher concentrations in the crevicular fluid than serum. Given the variety of periodontal pathogenic bacteria present in periodontal lesions, treating aggressive periodontitis with a combination of antibiotics is increasingly common. [21] Sometimes it is recommended to use combination antibiotic thrapy and he primary advantage of using antibiotic mixtures is the broader spectrum of activity and potential synergistic effects. Common combinations include metronidazole and amoxicillin for infections caused by A. actinomycetemcomitans, metronidazole, and ciprofloxacin for mixed periodontal infections or for patients allergic to amoxicillin.[22] However, when non-surgical treatments are insufficient to manage periodontitis or if the condition has progressed to an advanced stage, surgical interventions may be necessary. These procedures aim to eliminate bacterial deposits, reduce pocket depths, and regenerate lost bone and tissue.[23] Common surgical treatments for periodontitis include Flap Surgery (Pocket Reduction Surgery), Soft Tissue Grafts and bone grafting. In Flap Surgery, the gums are folded back to expose the tooth roots and underlying bone. Plaque, tartar, and infected tissue are removed through scaling and root planning. The bone may be reshaped to create a more favourable environment for healing, and the gums are then sutured back into place tightly against the teeth.[24] On the other hand, the soft tissue grafting involves grafting gum tissue from the patient's palate or a donor source to reinforce damaged gum tissue and cover exposed tooth roots. This procedure improves aesthetics and reduces tooth sensitivity caused by gum recession.[25] Bone Grafting: This procedure replaces bone lost due to periodontitis with the patient's own bone or artificial/donated bone material. It promotes bone regeneration and provides a stable foundation for the teeth. Tissue-Stimulating Proteins: A gel or solution containing proteins is applied to the tooth root to stimulate the growth of new bone and tissue around the tooth. [26]

Pathophysiology of Periodontitis

Periodontitis is an inflammatory disease caused by gram-negative anaerobic bacteria, which affects the supporting tissues of the teeth.[27] Periodontal diseases are divided into two main categories: gingivitis and periodontitis.[28] Gingivitis is the initial and mildest form of the disease. However, if it is neglected and left untreated, it can progress and lead to more severe degenerative changes in the tissues, ultimately resulting in periodontitis.[29] The primary causes of periodontitis include poor oral hygiene, alcohol consumption, stress, tobacco use, diet, immune disorders, and systemic diseases. Gram-negative and gram-positive bacteria form a plaque on the teeth' supporting tissues, accumulating over time. These bacteria release collagenase enzymes, antigens, bacterial lipopolysaccharides, endotoxins, ammonia, and hydrogen sulphide.[15] As a response to this bacterial presence, the flow of gingival crevicular fluid increases in the gingival crevice. This fluid contains significant amounts of β-glucuronidase, elastase, prostaglandins, neutrophils, and proteoglycans, all contributing to gingival inflammation.[15] Research has shown that bacteria such as Abiotrophic spp. and Capnocytophaga spp. may play a crucial role in developing plaque biofilms. While the formation of these biofilms has a strong immunological and inflammatory basis, various risk factors also contribute significantly.[30] These include congenital factors (such as genetic predispositions and sex) and acquired factors (such as smoking, stress, obesity, and coexisting systemic diseases).[31] The damage to gum tissue, ligaments, and bone in the mouth is a result of two main processes: the direct, destructive effects of virulence

factors secreted by the bacteria in dental plaque and the indirect effects stemming from the body's intensified, non-specific inflammatory response to periodontal pathogens. As a result, inflammation progresses, increasing damage in these oral structures. [32]

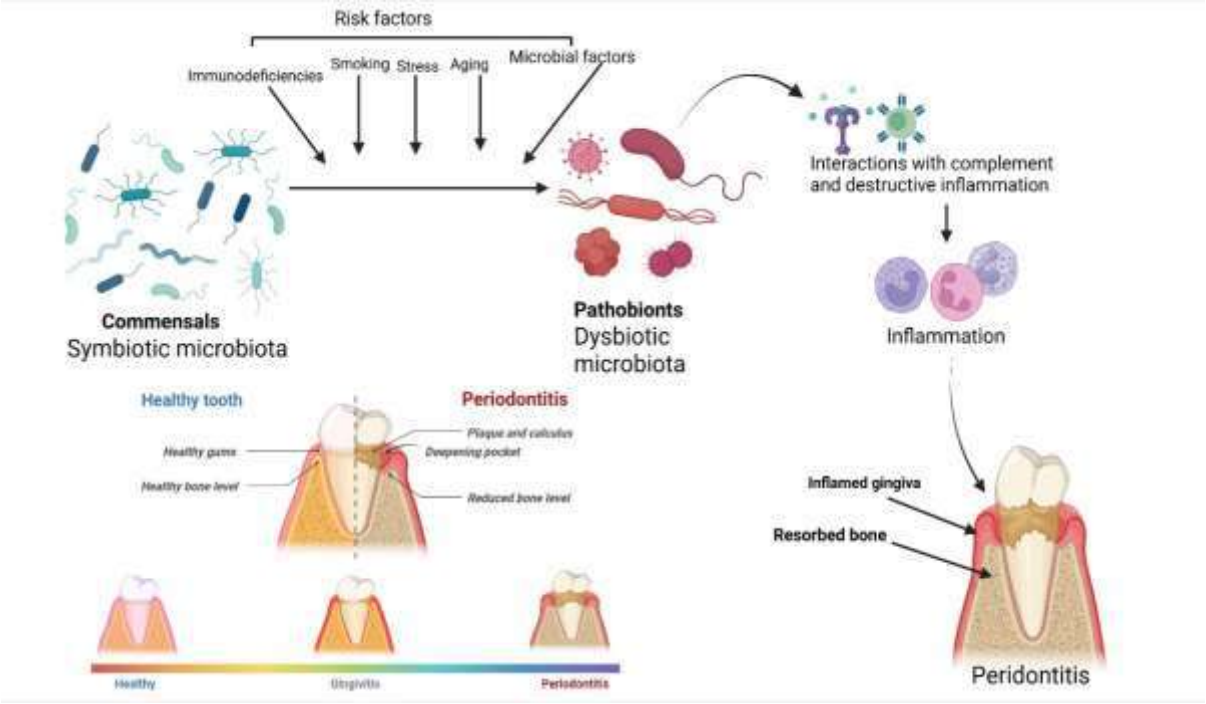

Figure 2: - Pathophysiology of Periodontitis

Methods of fabrication of situ gel:

In situ drug delivery systems present a promising solution to overcome existing challenges in treatment. These liquid preparations can be swiftly injected into the periodontal pocket and, after solvent replacement, solidify into a gel with a customized shape.[33] The in-situ gel remains in a liquid state under non-physiological conditions. Still, it transforms into a gel in physiological conditions, responding to stimuli such as pH, temperature, ions, and solvents in the oral cavity.[34] This gel allows for controlled drug release directly at the target site, which helps reduce side effects and enhances patient compliance. The main advantages of the implants of formation in situ are as follows: they can quickly be injected into periodontal pockets, harden to form a solid implant with customized geometry, the time-controlled release of drugs, and no need to remove the empty remnants.[35]

Various mechanisms for ISG (In-situ gel)

ISG formation due to physiological stimuli:

Temperature-triggered ISG systems consist of injectable liquids that can be administered minimally invasively into the body, solidifying within the targeted tissue, organ, or body cavity. The concept focuses on creating mucoadhesive formulations with a temperature-activated polymer solution, which transitions to a gel state within a 25^0C to 37°C. Polymers with a low critical solution temperature of approximately 32°C undergo a phase transition at body temperature. [36]

pH-triggered ISG systems A polymer with either a basic or an acid group is classified as a pH-sensitive polymer. These polymers undergo polymerization in response to varying physiological or environmental pH levels as they either accept or release protons. The transition from solution to gel occurs when there is a change in physiological pH, resulting in the formation of a gel in situ.[37]

Ionic Strength ISG the presence of specific ions, such as calcium ions, can induce gelation by promoting ionic interactions that encourage cross-linking between polymer chains. For example, gellan gum forms gels with calcium ions, facilitating stable cross-linking and gel formation. This mechanism is especially advantageous for ocular drug delivery

systems, as the ionic composition of tear fluid can trigger gelation when it comes into contact with the polymer solution.[38]

ISG formation due to ion-activated system:

A change in the ionic strength of the instilled solution triggers gelation. The gelation rate is influenced by the osmotic gradient surrounding the surface of the gel. Specifically, alterations in the ionic strength of the instilled solution induce this gelation process. Key electrolytes, such as Ca^{2+}, Mg^{2+}, and Na^{+} cations, are present in the fluids found in the oral cavity and play a crucial role in initiating gel formation when the solution is introduced into body cavities. Polymers exhibiting this behaviour include alginates, hyaluronic acid, and gellan gum (often called Gelrite).[39]

ISG formation due to solvent exchange: The gel solidifies due to the solvent exchange with the surrounding aqueous environment.

Swelling, a critical mechanism for forming in situ gel, involves water absorption from the surrounding environment, causing the material to expand and occupy the desired space. Such material includes glycol monooleate (Myverol 18-99), lipidic and polar. When the polar lipids swell, they form lyotropic liquid crystalline phase structures. This material also possesses bio-adhesive properties and can be degraded by enzymatic action in vivo.[40]

DIFFUSION

Drug release from the system occurs through two primary mechanisms: diffusion and erosion, with diffusion being the more reliable and accurate process. Diffusion is the movement of atoms, ions, and molecules from an area of higher concentration to one of lower concentration, driven by a concentration gradient.[16] In situ gel formation, which relies on the diffusion mechanism, involves the precipitation of a polymer matrix as the solvent diffuses from the polymer into the surrounding tissue.[41] A useful solvent for this process is N-methyl pyrrolidine. The diffusion rate is influenced by the porosity of the polymer matrix, which, in turn, depends on the pore formation process that occurs during phase inversion. [42]Drug release from a solid implant can occur through three main pathways: the diffusion of the drug through water-filled pores, the erosion of the implant, or osmosis. The sudden drug release observed during the preliminary lag period—between the formulation's administration and the implant's subsequent solidification—is called burst release.[43]

Erosion-Controlled Release In erosion-controlled systems, the gel matrix degrades due to environmental factors such as pH, temperature, or enzymatic activity. As the gel erodes, it creates pathways for the drug to diffuse into the surrounding medium. The drug release rate is directly linked to the rate of gel erosion. A slower erosion rate can lead to a prolonged drug release, which is beneficial for maintaining therapeutic levels over an extended period.[37]This is especially useful in situations where frequent dosing is undesirable. Erosion-controlled release systems are particularly advantageous in ophthalmic formulations and localized therapies, where prolonged drug action is required without frequent re-administration. Formulations can achieve optimal release profiles that meet specific therapeutic needs by tailoring the gel's composition and responsiveness to environmental conditions.[44] In the table, some clinical studies show how HMG-CoA reductase effective in periodontitis, ATV, Atorvastatin; CP, Chronic Periodontitis; IBD, Infrabony depth; AL, Alendronate, DM2, Diabetes Mellitus 2, SBI, Sulcus Bleeding Index; PPD, Periodontal Probing Depth; CAL, Clinical Attachment Level; mSBI, modified Sulcus Bleeding Index; SS, Statistical significance.

Author name	Drugs name	Percentage of drugs	Duration of the study	Number of people that participate in the study	Significance of the study	Conclusion of the clinical study
Kumari et al., 2016 Journal of Investigative and	Assess the effectiveness of a 1.2% ATV local drug delivery as	Atorvastatin 1.2%	9 months	71 smokers 30–50 years old	There were no significant differences in the primary index between groups regarding acceptable statin toleration. The	Significant improvement in clinical parameters compared to placebo gel as

Clinical Dentistry [45]	an addition to scaling and root planning (SRP) for treating intrabody defects (IBD) in smokers with chronic periodontitis (CP) compared to a placebo gel.				ALD and ATV groups showed significant differences in all parameters. The ALN group demonstrated significant differences in pharmacodynamics, clinical acceptance level, and drug dosage response percentage when compared to the ATV group.	an adjunct to SRP.
Wiench, R. et al (2025) A Systematic Review. Biomedicines [46]	Atorvastatin (ATV) & Rosuvastatin (RSV)	1.2%	6 months	60	RSV showed better outcomes.	RSV gel is more effective than ATV in some parameters
Pradeep et al. (2015) J Periodontol .[47]	Rosuvastatin	1.2%	6 months	65	Compared to placebo, there was a significant decrease in mSBI scores, PD reduction, CAL gain, and IBD reduction.	1.2% Rosuvastatin in situ gel shows greater probing depth, gingival index reduction, and increased gain in clinical attachment level.
Ali et al. (2021) The Journal of Drug Delivery Science and Technology [48]	Simvastatin (SV), Microspongs in 2% Chitosan Gel	2%	N/A	24	Chitosan gels containing SV microsponges significantly reduced pocket depth and clinical attachment loss compared to those prepared with free SV.	Simvastatin microsponges in a Chitosan gel show promise as a local treatment for chronic periodontitis. The use of microsponges enhances Simvastatin's dissolution and penetration.
Kanoriya et al. (2019) Journal of Advanced Clinical & Research Insights[49]	Rosuvastatin	1.2%	9 months	60	Significant greater mean probing depth reduction and greater mean gain in clinical attachment level were seen in the RSV group at different time periods. Moreover, a	Smokers with CP patients showed significant improvement in evaluated clinical parameters in

					greater mean defect depth reduction was found in the RSV group (23.91 ± 1.03, 29.24 ± 0.834) after 6 and 9 months, respectively. Significant defect depth reduction (radiographic) and clinical parameters improvement compared to placebo.	RSV group with greater percentage of defect depth reduction as compared to placebo group.
Pradeep et al., 2016 Journal of Investigative and Clinical Dentistry[50]	Evaluate and compare the efficacy of 1% ALN and 1.2% ATV gel as local drug delivery systems in conjunction with scaling and root planning (SRP) for treating intrabony defects in chronic periodontitis patients.	Atorvastatin 1.2% Alendronate 1%	9 months	104 30–50 years old 53 males and 51 females	No statistically significant differences in the Plaque Index (PI) between the groups regarding statin toleration. The Alendronate (ALD) and Atorvastatin (ATV) groups showed statistically significant differences in all parameters. The ALN group displayed statistically significant differences in probing depth (PD), clinical attachment level (CAL), and percentage of defect reduction (DDR%) when compared to ATV.	Both ATV and ALN can be used as an effective mode of treatment for CP patients. However, ALN was comparatively better than ATV.
Kumari et al., 2016 Journal of Periodontology [51]	Evaluate the effectiveness of 1.2 ATV gel, as an adjunct to SRP in the treatment of infrabony defects in chronic periodontitis in subjects with DM2	1.2% Atorvastatin	9 months	75 individuals 40–50 years old. 38 males and 37 females	60 Acceptable statin toleration SS greater mSBI and PD reduction, RAL gain, and IBD reduction in the statin group.	Local delivery of 1.2% ATV into periodontal pockets of type 2 DM patients stimulated a significant improvement in clinical and rx parameters as compared to placebo gel
Soni et al,2022 Indian Journal of Dental Research[52]	Patients with Chronic Periodontitis (CP) treated with 1.2% Atorvastatin (ATV) gel and 1.2% Rosuvastatin (RSV) gel as	1.2%	6 months	40 patients (20 in each group)	Both groups significantly improved Clinical Attachment Level (CAL) and Probing Depth (PD). The RSV group showed better results than the ATV group. Plaque Index (PI) and Gingival Index (GI) improved	Both ATV and RSV gels showed improvement in clinical parameters when combined with Scaling and Root planning

	local drug delivery				but were not statistically significant.	(SRP). RSV gel was more effective than ATV gel.

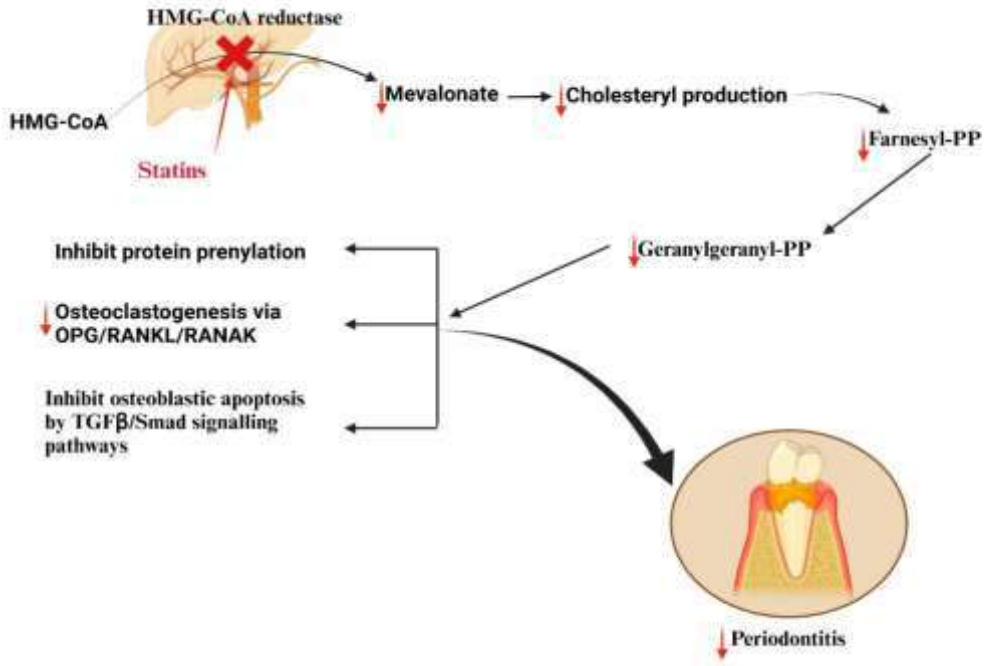

Figure 3: -Mechanism of statins in Periodontitis

This figure illustrates by reducing levels of farnesyl pyrophosphate (FPP) and geranylgeranyl pyrophosphate (GGPP), which is crucial for proper cell signalling and function. This inhibition can also impact osteoclastogenesis, the process responsible for forming cells that break down bone, potentially through the OPG/RANKL/RANK pathway. Furthermore, statins may inhibit osteoblastic apoptosis, the programmed death of bone-building cells. This image is generated by Biorender.com.

Need of Statins for In-Situ Gel to Management of Periodontitis:

Statins are commonly used to lower blood cholesterol levels in patients with hyperlipidaemia and atherosclerosis, thereby reducing the risk of cardiovascular diseases, can also be used for the management of periodontitis as stated earlier. However, most of the statins are less bioavailable perorally, due to systemic first pass metabolism. So local application of statins to treat periodontic disorders may be better way to treat so that systemic metabolism could be minimized. Local delivery thus may be effective in this Another important factor is the role of AMPK (AMP-activated protein kinase) in statins. AMPK activation is linked to reducing inflammation and improving the surface of the teeth; this means HMG-CoA inhibitors contribute to better outcomes for the management of periodontitis.[53] The advantage of in situ gel is the local delivery of HMG-CoA inhibitor by delivery of drugs directly to the affected area of the teeth by high concentration of its osteogenic effects by minimizing the side effects of the drugs. In situ gel allows the application of accurate amounts directly into the periodontal area, ensuring that the medication delivered applies to the affected area.[54] This target enhances the effectiveness of the in-situ gel by treating the affected area of the gums; the gel can easily be injected

through a syringe, thus making it eco-friendly for patients and the environment. This method is very easy to apply and enhances patient compliance.[55] The gelation temperature of in situ gel is around (34°C - 37°C), close to human body temperature, which allows the liquid to convert to a gel state upon contact with the internal environment of the oral cavity and minimizes discomfort in that affected area. The stability of in situ gel is at least 30 days from the day of application.[56] Therefore, the formulation is designed to release HMG-CoA reductase drugs over time, approximately 75%. However, the direct anti-inflammatory effects of statins on periodontal tissue had not been previously demonstrated to address this periodontal disease.[9] Thus, the HMG-CoA reductase enzyme emphasizes the importance of managing periodontics and improving the ongoing formulation's characterization and drug release rate to develop more effective treatment options for periodontitis. The statin group contributes more future research to target the affected area and reduce side effects compared to other traditional treatments.[57] This is very important for patient compliance and overall treatment success and needs further application to enhance clinical studies for the periodontal disease. The HMG-CoA reductase enzyme significantly contributes to periodontitis treatment by providing an in-situ solution to gel formulations with their components. Further research is needed to enhance its clinical application.[58]

CONCLUSION:

In conclusion, in situ gels incorporating statins represent a groundbreaking approach to periodontal therapy, offering a targeted, efficient, and patient-friendly alternative to traditional treatments. Their capability to deliver statins locally with minimal side effects, provide prolonged therapeutic action, and ensure ease of application makes them a promising solution for managing periodontitis. As research advances, incorporating in situ gels into routine periodontal treatment could revolutionize the field of periodontal drug delivery, significantly enhancing clinical outcomes and improving patient quality of life.

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CONFLICT OF INTERESTS:

The authors declare no conflict of interests.

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