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ANTIBACTERIAL SILVER NANOPARTICLES-EMBEDDED HYDROGELS FOR PERIODONTAL DRUG DELIVERY: A FORMULATION NARRATIVE REVIEW

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ABSTRACT

Periodontal is a provide a substantial barrier to oral healthcare, effective drug delivery systems are required. Hydrogels containing silver nanoparticles have demonstrated promise as periodontal therapeutic options because of their unique properties. The purpose of this systemic review to assess for current stage of research on periodontal medication delivery using hydrogels embedded with silver nanoparticles. After a thorough search of pertinent databases, studies that satisfied the inclusion criteria were reviewed. Important discoveries on these hydrogels' synthesis, characterization, biocompatibility, antibacterial activity, and clinical uses are explored. In addition, the field's future goals and challenges are discussed to help researchers create the best possible treatment delivery plans for treating periodontal disease.

KEYWORDS: Chlorhexidine, hydrogels, periodontal drug delivery, silver nanoparticles.

INTRODUCTION

Periodontal is an umbrella term used to define long-term soft tissue inflammation or supporting tissues surrounding the teeth. Chronic gingival bleeding and periodontitis are the clinical signs of edema, the development of periodontal pockets, additionally, it is challenging to treat periodontitis effectively due to the variety and complexity of the pathogenic pathways. Creation of innovative smart hydrogels intended to treat periodontitis. In the near future, new researchers may outcome with smart hydrogels where open up a new possibility for the treatment of periodontitis[1, 2]

With a global prevalence of around 11%, periodontal it regarded is one of the most dangerous ongoing medical condition. Globally, between 800 million and 1.4 billion people are estimated to have severe periodontitis, treatments are also needed for the clinical treatment of periodontitis to prevent the rapid growth for pathogenic diseases and create an environment that reduces inflammation and improves periodontal tissue healing[3].

Different periodontal types I. Gingivitis is an inflammation, as was previously mentioned of the gums that can be treated with good oral care. Regular exams and proper oral hygiene can help reverse it. Typically, there is a clinical Attachment loss of 1-2 mm or less than 15% of surrounding bone is lost, when the depth of the probing is 4 mm or less. II Chronic periodontitis the signs of this kind of periodontal disease might include extreme bad breath, bleeding when brushing or flossing, and gum inflammation that lasts for a long time. Loss of ligaments, bone, and epithelium that cannot be reversed. III. Aggressive periodontitis Both localized, and widespread this early-onset persistent inflammatory periodontal disease often appear form the onset of puberty till the start of the third decade of life.

Same symptoms to chronic periodontals are present. Necrotizing IV. Necrotizing ulcerative gingivitis People with HIV, immune suppressants, and malnutrition are the main populations affected. Necrosis is the death of a live tissue or cell. It typically happens as a result of not getting enough food, which is necessary for people to stay healthy. V. Systemic chronic periodontitis Patients with systemic condition are prone to this kind of persistent oral disease. System diseases including the diabetes, heart disease, respiratory disorders, can be reason gum inflammation.[4]

Silver nanoparticles have effective antibacterial qualities due to their extraordinarily significant surface area that allows for best contact for microbes. Both in the bacterium and the cell membraning, the nanoparticles attach together. Silver nanoparticles have shown to be the most

successful due to the strong antibacterial the action against other aukaryotic microorganisms, viruses, and bacteria.

According to the current research, silver nanoparticles and metallic silver, both of which have low toxicity to human cells, great thermal stability, and low volatility, can be used in dentistry.[5]

Hydrogels drug delivery systems methods have development into the smart hydrogels in recent years. Treatment for periodontal with hydrogels mediated local drug delivery system has been suggested. Hydrogels are low-viscosity fluids that can be easily injected with a syringe in the inflammatory particular for periodontal embedded. They are made of biocompatible and biodegradable matrices in order to treatment periodontal disease. These hydrogels can react to physical, chemical, or biological signals in situ induced the reversible changes in the periodontal pocket from the solution phase to the solid state are made achievable by smart hydrogels with stimuli-response.[6]

Chlorhexidine has a broad spectrum antiseptic action and is defectiveness against both Gram positive and Gram negative bacteria. During the procedure of oral rinsing, chlorhexidine gluconate functions as an antibacterial; nevertheless, it is unclear what therapeutic importance this antimicrobial activity has. The study does not yet provide a novel finding, but the benefits of chlorhexidine are clearly shown.[7] Curcumin is a traditional medicine for various human diseases, curcumin displays wide variety of demonstrated, such as antibacterial, anti-inflammatory, antioxidant. This study designs, characterizes, and assesses the safety and effectiveness of a hydrogel loaded with curcumin solid lipid nanoparticles for sub gingival application in vitro against oral microorganisms. Long-term clinical research to assess the benefits of using curcumin-loaded nanoparticles in various ways and at different concentrations demonstrated that curcumin can cause bacterial membrane, which can reason both Gram positive and Gram negative bacteria to suffer irreversible harm. These bacteria are very harmful and contribute significantly to the emergence of tooth cavities, curcumin was demonstrated to possess antibacterial properties against the majority of common microorganisms linked to pulpitis, and curcumin treats rats with experimental periodontitis just as well as chlorhexidine. It has been shown to that periodontitis-related bone loss[8, 9].

Ginger family Zingiberaceae contains excellent antifungal, anti-inflammatory, and antioxidant properties widely used herb that can be used as a spice and to treat any number of diseases such as periodontal disease. The two main types of components found in ginger are volatile and non-volatile[10].

Various antiseptics drugs

Benzalkonium Chloride: Other research shows a connection between resistance to several antibiotics and tolerance to benzalkonium chloride. One of the causes of the benzalkonium chloride cross-resistance is the multi-drug effect the protein, in which was found in E. coli. Nalidixic acid or ceftriaxone resistance was limited. Some of the species, such Escherichia coli, are very relevant to infections linked to healthcare[11].

Chlorhexidine Di-gluconate: chlorhexidine gluconate frequently leads to antibiotic resistance, which has only been shown in strains of bacteria that are sensitive to biocide found in organic food. Low-level exposure to chlorhexidine gluconate may dramatically enhance the horizontal congjugation based on the mobile antibiotic resistance element transfer.

The overall outcome for low exposure to chlorhexidine was similar.[12]

Iodophors and iodine: Iodophors and iodine since it is less reactive than chlorine and has been used for 150 years, iodine has been recognized to be an efficient antiseptic since the 1800s. It is also rapidly bactericidal, fungicidal, veridical, and sporicidal. The way iodine works is that it can readily enter the bacterial cell wall and form clusters of unsaturated fatty acids and amino acids that disrupt cell membranes and protein production[13].

Hexachlorophene: Bacteriostatic strong against microorganism that are gram positive, but less effective fungus, mycobacteria, and gram negative bacteria, a biphenyl antiseptic agent, hexachlorophene is made up of three moieties including chlorine, which has bacteriostatic properties, and two phenolic groups. The final product formulation containing 3% hexachlorophene was mostly utilized as sanitizers, surgical scrubs[14].

Pathogenesis of Periodontal

A progressive inflammatory condition, periodontitis is linked to the build-up of tooth gum, host mediated dysprosium reason for the bacteria. The pathological process of it can go through many stages, like as gingivitis developing into periodontitis. Common sigs of periodontal include inflammation of the periodontal tissue, bleeding upon probing embedded, radiographic evidence of the alveolar bone resorption, moment of the supporting teeth, and pathologic migration.

A few systemic risk factors include immunodeficiency, depression, smoking.[15] Gum inflammation and redness, as well as swelling and structural alterations, as well as bleeding from the gum line, are clinical signs of periodontitis cardiovascular, the circulatory system, heart disease, diabetes, liver, respiratory, pregnancy, central nervous, and even cancerous systems of the body are all associated with these systemic disorders. People who have periodontal disease are spread in whole system in the body[16].

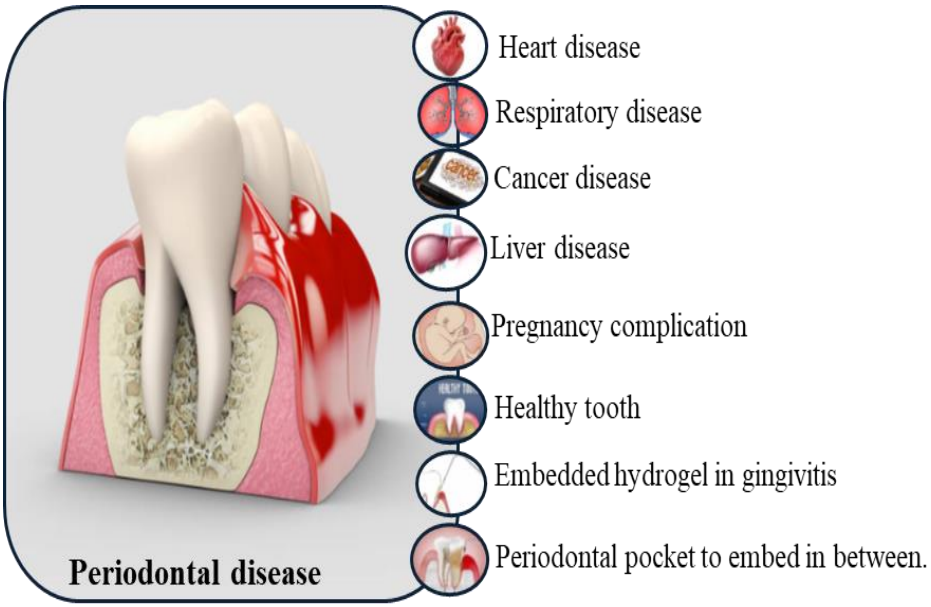

Figure.1: Periodontal disease (Pathogenic). Author designed this figure. (Accessed on 20 February 2024).

A hydrogel is an excipients network that is cross linked and swells when it comes in contact with water. It is produced when one or more monomers react simply.it can also be thought of the polymeric substsnace that, al thougt expending and retaining a sizabled, will not soluble in water, on because of their extraordinary promise in a variety of applications. Recent, hydrogels are two of water filling the void left by macromolecules and a three polymer chain network in three dimensions. These arrangements are also able to include varying amounts of water in an equilibrium that it depending on the characteristion of the polymer (or polymers) utilization; usually in the swelled form, in a hydrogel, the mass the mass fraction of polymer is significantly smaller than the percentage of water. Actually, to achieve appreciable levels of swelling, synthetics polymers that are soluble in water in their not cross lined state are typically used.

Hydrogel products and classification

1. Categorization based on polymeric constituency:
(a) Homo-polymeric Hydrogel: Made from a single monomer species, this hydrogel possesses a photopolymerization-derived cross-linked skeletal structure.
(b) Copolymeric Hydrogel: Consisting of two or more distinct monomers, preferably hydrophilic at least one, grouped either randomly or in block configurations.
(c) Interpenetrating Polymeric Network (IPN): A special kind of hydrogel composed of two separate, artificially or naturally occurring cross-linked polymeric networks. One cross-linked and one non-cross-linked polymer make up semi-IPN.
2. Configuration-Based Classification:
Hydrogels with no discernible crystalline structure are classified as

2. (a) Vagus (non crystalline).
(b) Semi crystalline: The hydrogel's mixture of crystalline and amorphous areas.
(c) Crystal Clear: Hydrogels displaying complete crystalline organization.
3. Grouping According to Type of the Cross linking:

3. (a) Hydrogels that are chemically a cross linked

Methods of preparation of hydrogels with various techniques

Bulk polymerization:

Hydrogel compositions, a thing amount of cross linking agent is added always, the radiation, and UV light. The kind of monomers and solvents being employed determination. There are several different ways to manufacturing the polymer hydrogels, such as film and membranes, rod, particle size, and an emulsions. The simplest method, bulk polymers, uses simply monomers and monomer soluble an initiator. During polymerization, the viscosity of the process increases dramatically with conversion, producing heat. By controlling the response, these issues can be avoided. The homogenous hydrogel created by bulk polymerization of monomers the result in a clear, and extremely durable polymers matrix. The glassy matrix swell to become soft and flexible when submerged in water.[45]

Polymerization by irradiation

As a result of the macro radicals recombining on numerous chains to form covalent bonds, a cross linked structure is created. like polymers that are cross linked using the radiation approach are poly (acrylic acid), and poly (vinyl alcohol), the biggest benefit of radiation performance for chemical commencement as opposed to generation of hydrogels that are generally pure and free of catalysts. To make hydrogels of unsaturated molecules, initiators such ionizing high energy radiation, including gamma rays and electron beams, have been used. Radiation applied to an aqueous polymer solution causes radicals to form on the polymer chains. Example: Applying radiation to make acrylamide hydrogel Experiments on the effects of duration, pH, c-ray dose, and solution concentration have been performed out.

Solution polymerization/cross-linking

The extractable and soluble polymer, the cross linking agent, the initiator, and additional impurities. Phase separation development and the heterogeneous hydrogel is produced when the water content during polymerization exceed the water content corresponding to the maximum swelling. Common liquids for the solution polymerization of hydrogels are ethanol, water, benzyl alcohol, and mixtures of the two. The synthesis solvents can be dissolved from the hydrogels by inflating particles in water once the gel has formed. When the amount of water during polymerization exceeds the water content proportionate to the maximum swelling, heterogeneous hydrogel is formed and phase separation takes place. Most of the solvents for the solution polymerization of hydrogels include ethanol, water, and benzyl alcohol, in addition to mixture of the two. Example: Building up and optimizing the process.

Inverse suspension polymerization

Dispersion of polymerization is a useful for technique when it minimizes the need for grinding by producing goods in the form of powder. Because to the selection of the water in oil (W/O) method above the more frequently utilized oil-in-water (O/W) technique, the polymerization process is known as inverse suspension. This method distribute to initiator, monomers consistently throughout the hydrocarbon phase. The type of dispersants, rotor design, agitation speed, and viscosity of the monomer solution are the key variables that affective the size and shape of the resin particles.
Several extensive investigations have already been produced on hetero phase polymerizations.

The dispersion needs to be continually mixed and must use a low hydrophilic lipophilic balance (HLB) suspending chemical due to its thermodynamic instability. Example: Using a suspension polymerization method, develop hydrogels beads and streamline the process. Inverse-suspension is an innovation for producing hydrogels with quick absorption kinetics and strong swelling capacity. An initiator soluble in water shows that parameters controlling the polymerization process were tuned to obtain a narrow size distribution, and clarity, and decrease the amount of non-bead material. The kind and quality of the initial substance, the amount of salt present, the temperature at which the polymerization occurs, the kind and quantity of the suspending agent, the speed and direction to stirring, and the ratio of the two phases are continuous phase.

Grafting to a support

Grafting method have been an employees to synthesize hydrogel on a ranged of polymeric substrates. Hydrogels created by using bulk polymerization often have a fragile structure from the start. Hydrogels can be surface coated onto stronger supports and grafted to enhance their mechanical qualities. This method creates a chain of monomers that are covalently bound to the support by first polymerizing monomers directly onto a stronger support surface by the formation of free radicals on that surface. Grafting methods have been employed to synthesize hydrogel on a range of polymeric substrates. Example. Comprehensively examined the starch-g-acrylonitrile hydrogel's synthesis. The primary steps in this technique include combining water and starch, grafting with acrylonitrile, separating and drying, then precipitating within methanol, washing in water-free ethanol, and drying under vacuum for three hours by 60 °C. Free radicals with the symbol [OH} have been generated by a redox system (Fe2+/H2O2). A 10:1, 30°C grafting temperature, 90 minutes for grafting and saponification, 9 ml sodium hydroxide, 95°C signification the temperature, 20 ml/g of grafted starch used for precipitation and washing, water, 60°C drying temperature, and 3 hours for drying are all included. As a result, the hydrogel preparation took almost 5 hours in total.[45, 46]

Description of silver nanoparticles based on hydrogels:

1. X ray diffraction:

The presence of silver nanoparticles could be ascertained using X ray diffraction, analysis using a Bruker D8 Advance operated at 40 kV and 40 mA after the PVP/Alg/CS was subjected to gamma irradiation process.[25]

Dynamic light scattering

Using an Agilent Technologies Carry 8454 UV-Vis spectrophotometer, UV-Vis absorbance data were collected. Zetasizer Nano ZS-90 (Malvern Instrument) was used for dynamic light scattering (DLS) experiments. The Hitachi H-7500 device was used to perform transmission electron microscopy (TEM) obtained using a JEOL.[25,25]

UV-visible spectra

UV Vis (UV-visible spectrophotometer) UV visible spectra were used to track the bio-reduction of Ag ions, and a UV-Vis spectrophotometer (Optizen POP; Mecasys) was used to record the results from 300 to 800 nm.[26]

FTIR spectrophotometer

The production of Ag-NPs, the incorporation of silver salt, and the hydrogel formation in hydrogel networks are all identified using an FTIR spectrophotometer. The hydrogel, Ag salts-loaded hydrogel, and Ag-NPs-embedded hydrogel samples were all thoroughly dried 60 degree record their FTIR spectra. Using the KBR disk approach, these samples were read on a Bruker IFS 66V FTIR spectrometer between 600 and 4000 cm^1.[28]

Table: 1 Investigated hydrogel drug delivery for the treatment of periodontal disease

Drugs	Polymers	Functions	Ref: No
Chlorhexidine	Poly(acrylic acid) lactic co-glycolic acid)	The additional chlorhexidine gluconate led to a higher reduction in periodontal embedded depth, as evidenced by recent results of multicenter clinical trials.	(29,30)
Resveratrol	1, 2-distearoyl-snglycerol-3-phosphoethanolamine-n-(polyethylene glycol) 2000.	It has been determined that local administration of Nano medicine provides therapeutic effects by allowing medications to directly reach the targeted tissue.	(30)
tetracycline	Poly-hydroxyl-butyric acid (PHBA) and poly-lactase co-glycolic acid (PLGA).	The mechanism to maintain therapeutic levels over an extended length of time, instead, they are made to administer drugs locally in the periodontal pocket.	(33)
Triclosan, Doxycycline and metronidazole	poly("-caprolactone) (PCL) hydroxyethyl cellulose (HEC) poly (vinylpyrrolidone) (PVP)	Potential uses for large and effective antibacterial activity in the therapeutic treatment of periodontal disease MNZ delivery in periodontitis for up to 24 hours.	(34)
Quaternary Ammonium Salts	Poly(ethylene glycol)(PEG)cross-linked polymers, oily (2-methyloxazoline)	They are having receive a lot of attention lately due of their increased sustainability, improved efficacy, lower toxicity, and higher selectivity.	(35)

Pyridine and imidazole. pyridinium	N-alkylated poly(N-vinyl imidazole)	Nowadays, people take for granted that they live free from major illnesses caused by germs like bacteria.	(36)
Benzocaine, tetra Caine, and lidocaine.	Chitosan, polyvinyl alcohol (PVA) fibers, hex methylene 1, 6-di(amino carboxy-sulfonate, polyvinyl pyrrolidone (PVP)	Similar to chitosan, it is mostly insoluble in liquids but soluble in weak hydrochloric and nitric acids.	(37)
Vancomycin	Poly(glycerol subacute) (PGS	Non-toxic and no immunogenic, biodegradable, and biomimetic.	(38)
Metronidazole	Collagen (Metro gene) have been developed	The gel formulation containing chlorhexidine exhibits a statistically significant decrease in, although only two experiments demonstrated a statistically significant increase.	(39)
Chlorhexidine (CHX) and Octenidine (OCT).	Collagen, Chitosan, poly-lactid (PLA), poly-glycoside (PGA), poly-caprolactone (PCL)	glutathione (GSH),tri polyphosphate, or a,b-glycerophosphate crosslinking are examples of eptidomimetic derivatives.	(40)
Chlorhexidine, gentamicin, rifampicin.	polyimide, gold, poly (methylmethacrylate), polytetrafluoroethylene, and polyurethane	antibiotics, which have a preventative effect on the growth of certain bacteria	(41)
Vancomycin	(monomethyl poly (ethylene glycol)-*b*-poly (ε-caprolactone) (3-oxapentane-1,5-diylbis (ethylene phosphate)	Recently there has been a focus on creating angels in watery environments.	(42)
Neosporin (bacitracin, neomycin, polymyxin)	Poly (ethylene oxide).	The complicated antibacterial activities of plasma polymerized POx coatings are attributed to cross-linking and chemical activity.	(42)
Chlorhexidine, doxycycline	Poly (ethyleneglycol) block-poly(L-lactide)	The addition of CHE nanoparticles to GIC not only enhances its antibacterial properties, but also marginally strengthens its micros hear bond.	(42)

EVALUATION

The review investigates these hydrogels' potential as a viable substitute for traditional medication delivery methods like curcumin, ginger in the treatment of oral disease. The review finds pertinent research and evaluates their quality using thorough literature searches and meticulous data extraction. Results point to the possibility of using hydrogels containing chlorhexidine silver nanoparticles for efficient periodontal medication delivery, Results point to the possibility of using hydrogels coated with chlorhexidine silver nanoparticles for efficient periodontal drug delivery, with advantages including better treatment results and prolonged release of active components. To completely understand their effectiveness, safety profile, and clinical value, more research is necessary. The review emphasizes how critical it is to continue researching this topic in order to improve periodontal disease treatment plans. It looks at possible modes of action, security issues, and prospective paths for further research. In order to maximize their clinical relevance, the section emphasizes the significance that these innovative drug delivery methods play in individualized periodontal care as well as the necessity of interdisciplinary teamwork. It talks about improvements in characterisation procedures, formulation strategies, and medicinal efficacy. It may be necessary to conduct sensitivity analyses and subgroup analysis to investigate differences in study results.

CONCLUSION

The conclusion highlights the evolutionary history of hydrogels coated with chlorhexidine silver nanoparticles in periodontal medication delivery and summarizes the major findings from the comprehensive review. In order to fully realize the promise of these novel formulations for enhancing periodontal health outcomes, it emphasizes the significance of continuing research efforts. Comprehensive exploration of relevant databases, studies meeting the inclusion requirements were examined. Significant findings are investigated regarding the biocompatibility, antibacterial activity, production, characterisation, and clinical applications of these hydrogels. To aid in the development of the most effective treatment delivery to treatment of periodontics disease, the field's future objectives and difficulties are also covered. Our review demonstrates the potential for hydrogels embedded into chlorhexidine silver nanoparticles to solve the problems with traditional periodontal medication delivery techniques. Due to the addition of silver nanoparticles, these hydrogels have improved antibacterial qualities, targeted delivery to periodontal tissues, and prolonged release of therapeutic chemicals. Although the results point to a significant potential for enhancing periodontal therapy outcomes through the use of hydrogels embedded with chlorhexidine silver nanoparticles, a number of areas warranting additional investigation and advancement have been highlighted. These include conducting clinical trials to determine efficacy in real-world situations, assessing long-term safety and biocompatibility profiles, and improving formulation characteristics for improved drug release kinetics. Chlorhexidine works are against both Gram positive and Gram negative bacteria and has effective antiseptic effect. This systematic study highlights the importance of continuous innovation in periodontal medication delivery systems and embedded with chlorhexidine silver nanoparticles to revolutionize the treatment of periodontal illnesses. Toward individualized and successful treatment techniques for boosting patient outcomes and increasing periodontal health by deepening our understanding of these innovative formulations.

REFERENCE

1. Wang Y, Li J, Tang M, Peng C, Wang G, Wang J et al Smart stimuli-responsive hydrogels for drug delivery in periodontitis treatment. Biomed Pharmacother. 2023,162:114688.
2. Mensah A, Rodgers AM, Larrinaga E, McMullan L, Tambuwala M, Callan JF, et al Treatment of Periodontal Infections, the Possible Role of Hydrogels as Antibiotic Drug-Delivery Systems. Antibiotics. 2023; 12(6):1073.
3. Wang Y, Li J, Tang M, Peng C, Wang G, Wang J, et al Smart stimuli-responsive hydrogels for drug delivery in

periodontitis treatment. Biomedicine & Pharmacotherapy. 2023; 162:114688.
4. Dubey P, Mittal N. Periodontal diseases a brief review. Int. J.et al Oral Health Dent. 2020; 6:177-87.
5. Rai M, Yadav A, Gade A et al Silver nanoparticles as a new generation of antimicrobials. Biotechnology advances. 2009 ;27(1):76-83.
6. Wang Y, Li J, Tang M, Peng C, Wang G, Wang J, et al Smart stimuli-responsive hydrogels for drug delivery in periodontitis treatment. Biomedicine & Pharmacotherapy. 2023; 162:114688.
7. Fiorillo L. Chlorhexidine gel use in the oral district: A systematic review et al Gels. 2019 ;5(2):31.
8. Gupta S, Kaur A, Singh J, Sharma G, Ahmed B, Oberoi P et al Periodontitis Therapy Using Curcumin Solid Lipid Nanoparticle Hydrogel System: Pre-Clinical Design to Clinical Assessment.
9. Livada R, Shiloah J, Tipton DA, Dabbous MK et al The Potential Role of Curcumin in Periodontal Therapy: A Review of the Literature. Journal of the International Academy of Periodontology. 2017 ;19(3):70-9.
10. Kamal GM, Nazi N, Sabir A, Saqib M, Zhang X, Jiang B et al Yield and Chemical Composition of Ginger Essential Oils as Affected by Inter-Varietal Variation and Drying Treatments of Rhizome. Separations. 2023; 10(3):186.
11. Kampf G. Biocidal agents used for disinfection can enhance antibiotic resistance in gram-negative species et al Antibiotics. 2018; 7(4):110.
12. Nur Izyan, Wan Azelee, et al. "Antimicrobial disinfectants and sanitizers: an effective tool for breaking the circle of pandemic disease." (2020): 348-367.
13. Chen H, Zhang Y, Yu T, Song G, Xu T, Xin T et al Nano-Based Drug Delivery Systems for Periodontal Tissue Regeneration. Pharmaceutics. 2022 ;14(10):2250.
14. Bhuyan R, Bhuyan SK, Mohanty JN, Das S, Juliana N, Abu IF et al. Periodontitis and its inflammatory changes linked to various systemic diseases: a review of its underlying mechanisms. Biomedicines. 2022; 10(10):2659.
15. Hemmingsen LM, Giordani B, Pettersen AK, Vitali B, Basnet P, Škalko-Basnet et al Liposomes-in-chitosan hydrogel boosts potential of chlorhexidine in biofilm eradication in vitro. Carbohydrate Polymers. 2021; 262:117939.
16. Wong PY, Soo S, Wong ES, Praveen P, Clode P, Baker MV, et al A Novel Antimicrobial Hydrogel for the Management of Periodontal Diseases. international dental journal. 2023 ;73(3):354-61.
17. Khoshmaram K, Yazdian F, Pazhouhnia Z, Lotfibakhshaiesh N et al Preparation and characterization of 3D bioprinted gelatin methacrylate hydrogel incorporated with curcumin loaded chitosan nanoparticles for in vivo wound healing application. Biomaterials Advances. 2024; 156:213677.
18. Novientri G, Abbas GH, Budianto E et al Nanocomposite hydrogel-based biopolymer modified with silver nanoparticles as an antibacterial material for wound treatment. Journal of Applied Pharmaceutical Science. 2019; 9(11):001-9.
19. Kapralos V, Camilleri J, Koutroulis A, Valen H, Ørstavik D, Sunde PT et al Endodontic sealers after exposure to chlorhexidine digluconate: An assessment of physicochemical properties. Dental Materials. 2023.
20. Mohan YM, Lee K, Premkumar T, Geckeler KE. Hydrogel networks as nanoreactors et al A novel approach to silver nanoparticles for antibacterial applications. Polymer. 2007 ;48(1):158-64.
21. Varaprasad K, Mohan YM, Ravindra S, Reddy NN, Vimala K, Monika K, et al Hydrogel–silver nanoparticle composites: A new generation of antimicrobials. Journal of Applied Polymer Science. 2010; 115(2):1199-207.
22. Zakia M, Koo JM, Kim D, Ji K, Huh P, Yoon J, et al Development of silver nanoparticle-based hydrogel composites for antimicrobial activity. Green Chemistry Letters and Reviews. 2020 ;13(1):34-40.
23. Khampieng T, Wongkittithavorn S, Chaiarwut S, Ekabutr P, Pavasant P, Supaphol P Et al. Silver nanoparticles-based hydrogel: Characterization of material parameters for pressure ulcer dressing applications. Journal of Drug Delivery Science and Technology. 2018; 44:91-100.
24. Zakia M, Koo JM, Kim D, Ji K, Huh P, Yoon J, et al. Development of silver nanoparticle-based hydrogel composites for antimicrobial activity. Green Chemistry Letters and Reviews. 2020 ;13(1):34-40.
25. Singh H, Du J, Singh P, Yi TH et al. Extracellular synthesis of silver nanoparticles by Pseudomonas sp. THG-LS1. 4 and their antimicrobial application. Journal of pharmaceutical analysis. 2018 ;8(4):258-64.
26. Varaprasad K, Mohan YM, Ravindra S, Reddy NN, Vimala K, Monika K Et al. Hydrogel–silver nanoparticle composites: A new generation of antimicrobials. Journal of Applied Polymer Science. 2010; 115(2):1199-207.
27. Ttrjyrku
28. Aminu NA, Toh SM et al. Applicability of nanoparticles-hydrogel composite in treating periodontal diseases and beyond. Asian J Pharm Clin Res. 2017; 10(2):65-70.
29. Shi J, Zhang Y, Zhang X, Chen R, Wei J, Hou J, et al. Remodeling immune microenvironment in periodontitis using resveratrol liposomes as an antibiotic-free therapeutic strategy. Journal of Nanobiotechnology. 2021; 19:1-3.
30. Dusane J, Mogal V, Borse P, Thakare P, Kshirsagar S et al. Recent trends in treatment of periodontitis. Pharm. Biol. Eval. 2016; 3:19-31.
31. Baranov N, Popa M, Atanase LI, Ichim DL et al. Polysaccharide-based drug delivery systems for the treatment of periodontitis. Molecules. 2021; 26(9):2735.
32. Jagtiani E, Pulakkat S, Patravale V. Antimicrobial Polymers Containing Ammonia Derivatives et al. The Bombay Technologist. 2022.

33. Yadav AN, Singh J, Singh C, Yadav N, editors. Current trends in microbial biotechnology for sustainable agriculture et al. Singapore: Springer; 2021.
34. Alsalhi A. Applications of selected polysaccharides and proteins in dentistry: A review. International Journal of Biological Macromolecules. 2024: 129215.
35. Torgbo S, Sukyai P. Biodegradation and thermal stability of bacterial cellulose as biomaterial: The relevance in biomedical applications. Polymer Degradation and Stability. 2020; 179:109232.
36. Soysa NS, Waidyarathne H, Ranaweera M, Alles CN. Clinical efficacy of local application of sustained-release metronidazole in periodontal therapy. Dentistry Review. 2021; 1(1):100006.
37. Maraldi M, Lisi M, Moretti G, Sponchioni M, Moscatelli D. Health care-associated infections: Controlled delivery of cationic antiseptics from polymeric excipients. International Journal of Pharmaceutics. 2021; 607: 120956.
38. Maraldi M, Lisi M, Moretti G, Sponchioni M, Moscatelli D. Health care-associated infections: Controlled delivery of cationic antiseptics from polymeric excipients. International Journal of Pharmaceutics. 2021; 607:120956.
39. Keskin D, Zu G, Forson AM, Tromp L, Sjollema J, van Rijn P. Nanogels: A novel approach in antimicrobial delivery systems and antimicrobial coatings. Bioactive materials. 2021; 6(10):3634-57.
40. Akdoğan E, Şirin HT. Plasma surface modification strategies for the preparation of antibacterial biomaterials: A review of the recent literature. Materials Science and Engineering: C. 2021; 131:112474.
41. Makvandi P, Gu JT, Zare EN, Ashtari B, Moeini A, Tay FR, Niu LN. Polymeric and inorganic nanoscopical antimicrobial fillers in dentistry. Acta biomaterialia. 2020; 101:69-101.
42. Sahu N, Gupta D, Nautiyal U. Hydrogel: preparation, characterization and applications. Asian Pacific Journal of Nursing and Health Sciences. 2020; 3(1):1-1.