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Potential of Nanogel for Dental Disorder: A Comprehensive Review

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ABSTRACT

Objective: *The aim of the present work was to develop and evaluate an oral nanogel for brushing containing clove oil and tannic acid with antimicrobial/antibacterial activity which will cure/protect from various periodontal diseases such as periodontitis, gingivitis and pyorrhea. The novelty of the work is combination of the components and its delivery via nanogel formulation technology.*

Method: *There are so many methods are used to prepare the nanogels. Some of them are*

- *Photolithographic techniques*
- *Fabrication of biopolymers*
- *Micro molding method*
- *Water-in-Oil (W/O) heterogeneous emulsion methods*
- *Inverse (mini) emulsion method*
- *Reverse micellar method*
- *Membrane emulsification*
- *Chemical cross linking*
- *Carbodiimide coupling*
- *Heterogeneous free radical polymerization*
- *Precipitation polymerization*
- *Dispersion polymerization*
- *Inverse (mini) emulsion polymerization*
- *Inverse microemulsion polymerization*
- *Heterogeneous controlled/living radical polymerization*
- *Reversible Addition Fragmentation Transfer (RAFT) process*

Outcomes and significance: *The novel nanogel form represents an effective and better carrier for the dental preparations. Nanogels based materials have high drug loading capacity, biocompatibility, and biodegradability which are the key points to design a drug delivery system effectively. It has a wide spectrum of antibacterial activity against a number of periodontal pathogens; hence it is selected for the treatment of periodontitis.*

Keywords: Clove oil, Tannic acid, Periodontal diseases, Nanogel, Synergistic effect, Gingivitis

INTRODUCTION

Gels are semisolid organic or inorganic colloids rich in liquid, consisting of hydrated threads or granules of the dispersed phase intimately associated with the dispersion medium. Periodontal disease is one of the most important concern for dentists and patients. It is recognized as a major public health problem throughout the world and is the most common cause of tooth loss in India. The periodontium is the specialized tissues that both surround and support the teeth, maintaining them in the maxillary and mandibular bones. A variety of triggering factors like bacterial causes, dyscrasias, avitaminosis etc., cause inflamed gums leading to gingivitis.

In the India 50% of adults have gingivitis affecting at least 3-4 teeth; two-thirds of the population has sub gingival calculus, and about a one-third have periodontitis. Periodontal treatment aims to cure inflamed tissue, reduce the number of pathogenic bacteria and eliminate the diseased pockets.

Mechanical therapy, chemotherapy and systemic administration of antibiotics are some of the clinical methods being utilized currently. Synergistic effects of clove oil along with tannic acid showed a higher level of inhibition on various type of micro-organisms and bacteria. Clove oil gives anti-inflammatory or anti-microbial action and tannic acid help to healing of gum inflammation or show anti-bacterial action against oral pathogens. Nanogels based materials gives strong inhibition at very low quantity.

This study was aimed to develop and evaluate dental nanogel containing clove oil and tannic acid as the chief constituent for the treatment of dental problems by novel approaches.

The term 'Nanogel' defined as the nanosized particles formed by physically and chemically crosslinked polymer networks that is swell in a good solvent. The term "Nanogel" was first introduced to define cross-linked bifunctional networks a polyion and a nonionic polymer for delivery of polynucleotides and Polyethylene Glycol (PEG). They are soluble in water and allow spontaneous loading of drugs in aqueous media [1].

Synergistic effects of clove oil along with tannic acid showed a higher level of inhibition on various type of micro-organisms and bacteria. The Chinese used cloves to get rid of bad breath over 2000 years ago. Clove oil gives anti-inflammatory or anti-microbial action and tannic acid help to healing of gum inflammation or show anti-bacterial action against oral pathogens. Nanogels based materials have high drug loading capacity, biocompatibility, and biodegradability which are the main features to design a drug delivery system effectively. Here, on the basis of synthetic procedure and mechanism of drug release from nanogel carrier are an intensive study of clinical trial in future. Different types of nanogels are used as a suitable carrier for drug delivery via oral, pulmonary, nasal, parenteral, intra-ocular and topical route [2-4].

Periodontitis also known as pyorrhea. Pyorrhea is a set of inflammatory diseases affecting the periodontium, i.e. the tissues that surround and support the teeth. Periodontitis is caused by micro-organisms that adhere to and grow on the tooth's surfaces, alongside an over-aggressive immune response against these micro-organisms. Periodontitis involves progressive loss of the alveolar bone around the teeth, and if left untreated, can cause to the loosing and subsequent loss of teeth [5-6].

Nanogel can be termed as dispersion of hydrogel by physical and chemical cross-linking polymer at nanoscale size. "Nanogel" was first introduced to define cross-linked bifunctional networks a polyion and a nonionic polymer for delivery of polynucleotides and Polyethylene Glycol (PEG). They are soluble in water and allow spontaneous loading of drugs in aqueous media. Nanogel has ability to regulate size, composition depending upon the application. Nanogel can be used as additive in various applications such as paint, cosmetics, medical etc. Nanogel is employed to load drugs and followed by stimuli-sensitive, multi-responsive, magnetic and targeted drug delivery application and also in bioimaging. Comparison to other preparations nanogel shows a strong inhibition at very low quantity [7-8].

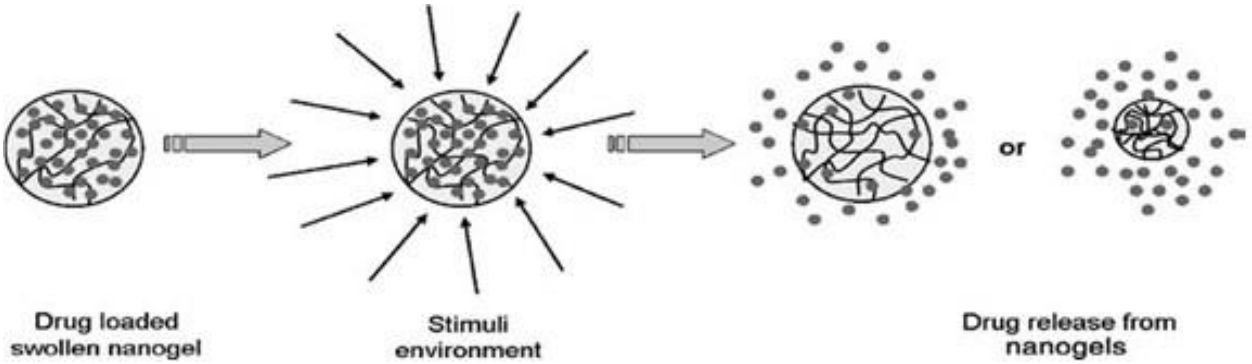


Figure 1. Drug release model from Nanogel

Merits: The merits of nanogel delivery over other transport systems are as follows [9-10]:

- Nanogel is biodegradable
- Nanogel is highly biocompatible
- Good permeation capabilities due to extreme small size
- Good transport characteristics
- Release of therapeutics are often regulated by cross-linking densities
- Non immunological responses
- Applied to both hydrophilic and hydrophobic drugs and charged solutes
- Invasion by reticuloendothelial system is prevented

Demerits

- Surfactant or monomer traces may remain and can impart adverse effects of toxicity
- Expensive technique to completely remove the solvents and surfactants at the end of preparation

Properties of Nanogel

- Biocompatibility and degradability: Nanogel based drug delivery system is highly biocompatible and biodegradable due to this characteristic, it's highly promising field now a days
- Swelling property in aqueous media: The most beneficial feature of nanogels is their rapid swelling/de-swelling characteristics
- Higher drug loading capacity: The properties of higher drug loading capacity of nanogels depend upon the functional group present within the polymeric unit. These functional groups have a tremendous effect on drug carrying and drug-releasing properties, and a few functional groups have the potential to conjugate with drugs/antibodies for targeting applications
- Particle size: Nanogels typically range in size of 20 nm-200 nm, India meter and hence are effective in avoiding the rapid renal exclusion but are small enough to avoid the uptake by the reticuloendothelial system. Good permeation capabilities due to extreme small size. More specifically, it can cross the Blood Brain Barrier (BBB)
- Solubility: Nanogels are ready to solubilize hydrophobic drugs and diagnostic agents in their core or networks of gel.
- Electromobility: Nanogels might be prepared without employing energy or harsh conditions like sonication or homogenization, which is critical for encapsulating biomacromolecules
- Colloidal stability: Nanogels or polymeric micellar nanogel systems have better stability over the surfactant micelles and exhibit lower critical micelle concentrations, slower rates of dissociation, and longer retention of loaded drugs
- Non-immunologic response: This type of drug delivery system usually doesn't produce any immunological responses.
- Others: Both type of drugs (hydrophilic and hydrophobic drugs and charged solutes) are often given through nanogel. Such properties of nanogel are significantly influenced by temperature, presence of hydrophilic/hydrophobic groups within the polymeric networks, the cross-linking density of the gels, surfactant concentration, and type of cross-links present in the polymer networks [11-14]

Classification of nanogel

Nanogels are more commonly classified into two major ways. The "First Classification" is based upon their responsive behavior, which may be either stimuli-responsive or nonresponsive [15-17].

- In the case of non-responsive microgels, they simply swell as a result of absorbing water
- Stimuli-responsive microgels swell or de-swell upon exposure to environmental changes such as temperature, pH, magnetic field, and ionic strength. Multi-responsive microgels are responsive to more than one environmental stimulus
- The "Second Classification" is based on the type of linkages present in the network chains of gel structure, polymeric gels (including nanogel) are subdivided into two main categories:
- Physical cross-linked gels: Physical gels or pseudo gels are formed by weaker linkages through either Vander Waal's forces; Hydrophobic, Electrostatic interactions or Hydrogen bonding. A few simple methods are available to obtain physical gels. These systems are sensitive and this sensitivity depends on polymer composition, temperature, ionic

strength of the medium, concentrations of the polymer and of the cross-linking agent. The association of amphiphilic block copolymers and complexation of oppositely charged polymeric chains leads to the formation of micro and nanogels in just a couple of minutes. Physical gels also can be formed by the aggregation and/or self-assembly of polymeric chains

- Chemically cross-linked gels: Chemical gels are comprised of permanent chemical linkages (covalent bonds) throughout the gel networks. The properties of cross-linked gel system depend upon the chemical linkages and functional groups present within the gel networks. Different nanogels are synthesized using different strategies for chemical linking of polymeric chains. Usually, hydrophilic polymers and hydrophilic-hydrophobic copolymers are obtained by the polymerization of vinyl monomers within the presence of multifunctional cross-linkers that are the launch cross-linking points within and between the polymeric chains. These crosslinking points allow modifying entire physicochemical properties of the gel systems. A few versatile cross-linking agents have been reported

Example: It has been demonstrated a facile approach for nanogel (20 nm-200 nm) preparation during which pendant thiol groups are incorporated into the polymeric chains and their subsequent intramolecular disulfide cross-linking is achieved through "environmentally friendly chemistry" (green chemistry).

Applications of nanogel

- Nanogel-based drug delivery formulations improve the effectiveness and safety of certain anti-cancer drugs, and many other drugs, due to their chemical composition, which have been confirmed from in vivo study in animal models. There is still some work to do before these products are ready for human trials [18-20].
- Cancer: Cancer treatment involves targeted delivery of drugs with expected low toxicities to surrounding tissues and high therapeutic efficacy
- In stopping bleeding: A nanogel composed of protein molecules in solution has been used to stop bleeding, even in severe gashes. The proteins self-assemble on the nanoscale into a biodegradable gel
- Autoimmune disease: The Nanogels are attractive because of their intrinsic abilities to enable greater systemic accumulations of their cargo and to bind more immune cells in vivo than free fluorescent tracer, which, we reason, permits high, localized concentrations of MPA. This new drug delivery system increases the longevity of the patient and delays, the onset of kidney damage, a common complication of lupus
- Ophthalmic: pH-sensitive PolyVinyl Pyrrolidone-Poly (Acrylic Acid) (PVP/PAAc) nanogels prepared by γ radiation induced polymerization of Acrylic Acid (AA) in an aqueous solution of PolyVinyl Pyrrolidone (PVP) as a template polymer were used to encapsulate pilocarpine in order to maintain an adequate concentration of the pilocarpine at the site of action for prolonged period of time
- Anti-inflammatory action: Poly (lactide-co-glycolic acid) and chitosan were used to prepare bi-layered nanoparticles and the surface was modified with Oleic acid. Hydroxy Propyl Methyl Cellulose (HPMC) and Carbopol with the specified viscosity were utilized to prepare the nanogels
- Neurodegenerative: Nanogel is a promising system for delivery of oligonucleotide to the brain. A novel system for oligonucleotides delivery to the brain based on nanoscale network of cross-linked poly (Ethylene Glycol) and polyethyleneimine ("nanogel") is used for the treatment of neuro-degenerative diseases. Nanogels bound or encapsulated with spontaneously negatively charged oligonucleotide results in formation toxicity compared to the free drug. This is a ongoing approach for clinical trial

Dental disorders

"Dental Disorders are caused or influenced by the same preventable risk factors as over 100 noncommunicable diseases". Oral diseases are closely associated to lifestyle. Dental health encompasses the likelihood of creating healthy choice in reference to diet, smoking, tobacco, oral hygiene, and utilization of dental health services. The rise in the use of sugar diet, bakery products, and carbonated drinks increase the prevalence of cavity. Lack of oral hygiene leads to accumulation of plaque and calculus, which is that the major etiology factors for gingivitis and periodontitis. The oral cavity can be a mirror image of other areas of the body and many systemic illnesses are manifested in the soft tissue of the oral mucosa of the mouth. When oral health is compromised, overall health is often affected. Traditional plants and natural phytochemicals can treat bacterial infections and are considered to be an honest alternative to synthetic chemicals [21-22].

Facts about oral health

- Oral conditions are the most common conditions of humankind
- Worldwide, between 60 and 90% of school children have dental caries
- Oral cancer is the world's 8th most common cancer and the 3rd most common cancer in Southeast Asia

- 50% of gum disease is caused by tobacco use
- 25% of all genetic birth defects are craniofacial malformations
- 30% of people worldwide aged 65-74 years have lost all their natural teeth
- The burden of dental disease is higher among poor and disadvantaged population groups
- Oral disease share risk factors with other non-communicable diseases
- Brushing teeth twice daily using fluoride toothpaste helps to prevent tooth decay and gum disease [23]

Effects of clove oil on oral health

Antimicrobial activity against oral pathogens: Clove oil has an inhibitory action against various organisms like *Streptococcus aureus*, *Listeria monocytogenes* and *Aspergillus*. Synergistic effects of clove oil along with other oils of cilantro, dill, coriander and eucalyptus showed a higher level of inhibition on Gram-negative bacteria, thus proving that the synergism aggravates the antimicrobial activity of clove oil. S. mutants are the main causative organism for dental caries. S. mutants is that the normal flora present in every individual's mouth. Compared to all other oil extracts, clove oil extract shows a strong inhibition at very low concentration [24]. Using Clove oil for tooth pain [25]:

- Place two to three drops of the oil in a clean, small container. Add one-fourth to half teaspoon of olive oil. This mixture will prevent any soft tissue irritation that's common when using clove oil on its own
- Soak a small piece of cotton within the oil mixture until it's saturated. Blot the cotton on a piece of tissue to remove the excess oil before placing the cotton in your mouth
- Using a clean pair of tweezers, hold the cotton on the painful area for 10 seconds, making sure you do not swallow any of this oil
- Once complete, rinse your mouth with saline solutions this step may be repeated 2-3 times daily. Clove oil should only be used as a temporary way to relieve pain from a toothache. The best pain remedy is to see a dentist

Clove oil to treat halitosis: Halitosis is widespread and is believed to affect one quarter of the population around the world and most people halitosis (bad breath) is mainly due to the pathogens present in the oral cavity, these pathogens will proteolyze the amino acid and release volatile sulfur. Clove oil is often short remedy for halitosis since it's anti-microbial, but can't be used long term because it lacks the pro-biotic activity. The Chinese used cloves to get rid of bad breath over 2000 years ago.

Effects of Tannic acid on oral health

- Dental caries: Caries is caused by bacterial acid production in tooth plaque, which may cause deep localized lesions if it remains too near the tooth for any length of your time. If left the bacteria then may penetrate the tooth further and progress into the soft pulp tissue. Untreated dental cavity can cause incapacitating pain, potential tooth loss and loss of dental function. The development and progression of dental cavity is due to a variety of factors, specifically bacteria in the dental plaque (particularly *Streptococcus* mutants) on susceptible tooth surfaces and therefore the availability of fermentable carbohydrate on of tooth decay. The commonly understood reason is that the chemical structure of a tannin allows it to bind to large numbers of bacteria and hence prevent caries. Another reason is that tannins in tea can inhibit salivary amylase thereby reducing the cariogenic potential starch-containing foods
- Dental plaque: Tannins, tannic acid, Sulfated compounds and benzyl isothiocyanate, are reported to have antimicrobial effects and help the healing of gum inflammation. A number of studies have also demonstrated that tannic acid inhibits the growth of S. mutants bacteria, a major factor in the build-up of dental plaque
- Periodontal: Periodontal disease results from inflammation of the gum (gingivitis) that gradually causes destruction of the bone supporting the teeth. Gingivitis usually results from infection from debris that has accumulated at crevices at the bottom of the teeth. It has been suggested that tannins also promote periodontal health by reducing inflammation, preventing bone resorption and limiting the expansion of certain bacteria related to periodontal diseases. Also, it was found that the tannin-fluoride preparation, which might have a caries-reductive, plaque inhibiting and astringent action, could reduce the incidence of gingival inflammation around abutment teeth
- Oral carcinoma: Tannins have been gaining immense interest in recent years due to its antioxidant properties. So, these polyphenols are expected to reduce the effects of various life style related diseases such as cancers etc. More than 500 varieties of hydrolysable tannins have been found useful as anti-viral, anti-tumor promoting and for inhibition of some enzymes. Ellagitannin (a newly derived tannin) was found to be more potent than other types of tannins
- Oral ulcers: Again, this anti-inflammatory and anti-ulcer effects are attributed to the antioxidant properties of tannins. Tannins are used in medicine primarily because of their astringent properties. These properties are due to the fact that tannins react with the tissue proteins with which they come into contact. In ulcers, this tannin-protein complex layer

protects the oral mucosa by promoting greater resistance to chemical and mechanical injury or irritation. Moreover, in several experimental models of ulcer, tannins are shown to present antioxidant activity, promote tissue repair etc. The presence of tannins explains the anti-ulcer effects of the many natural products [26-29]

METHOD OF PREPARATION

Water-in-Oil (W/O) heterogeneous emulsion methods

W/O emulsion methods involve generally two steps: Emulsification of aqueous droplets of water-soluble biopolymers in continuous oil phase with an Aid of oil-soluble surfactants and cross linking of biopolymers with water-soluble cross linkers.

Reverse micellar method

Similar to the inverse (mini) emulsion method, the reverse micellar method also involves a W/O dispersion; however, a relatively large amount of oil-soluble surfactants is used to form a thermodynamically stable micellar solution consisting of aqueous droplets dispersed in the continuous oil phase. The resulting micellar droplets have a submicron size ranged from tens to hundreds of nanometers in diameter. Tumor targeted CS-based nanogels were prepared in inverse microemulsion of hexane containing Aerosol OT as a stabilizer in the presence of doxorubicin (Dox)-modified Dex. Aqueous glutaraldehyde was used to crosslink CS. The resulting Dox-encapsulating CS-based nanogels have a diameter of around 100 nm.

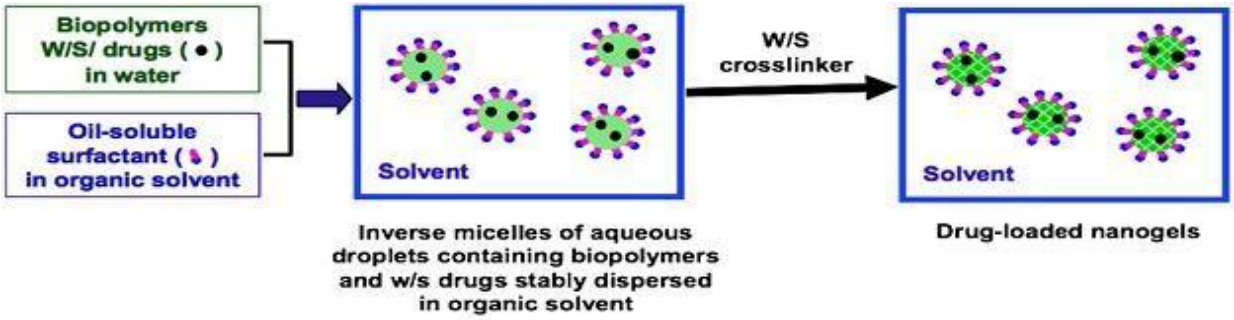
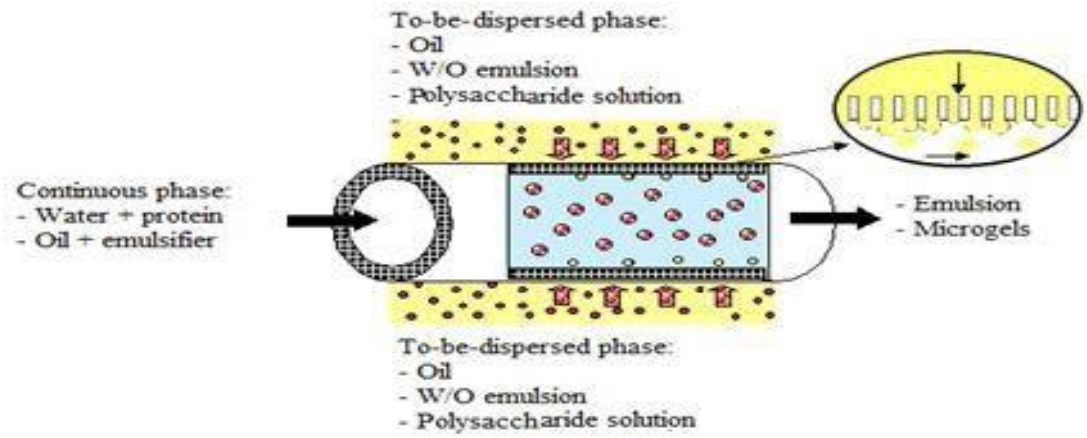


Figure 2. Illustration of the reverse micellar method for the preparation of nanogels

Membrane emulsification

In the membrane emulsification technique, the to-be dispersed phase is passed through the membrane (glass or ceramic), which possesses uniform pore size. Under certain conditions the emulsion droplets or microgels with specific morphology are formed on the surface of the membrane and afterwards, with a continuous phase that is flowing across the membrane, these fabricated emulsion droplets or microgels are recovered [30]. These fabricated emulsion droplets can be in different emulsion formation such as Water-in-Oil (W/O), Oil-in-Water (O/W), Oil-in-Water-in-Oil (O/W/O), and Water-in-Oil-in-Water (W/O/W). The size of the formed droplet is controlled by the membrane pore size, velocity of the continuous phase, and pressure of the trans-



membrane.

Figure 3. Schematic diagram of the membrane emulsification technique

Precipitation polymerization

Precipitation polymerization involves the formation of homogeneous mixture at its initial stage and the occurrence of initiation

and polymerization in the homogeneous solution. As the formed polymers are not swellable but soluble in the medium, the use of crosslinker is necessary to crosslink polymer chains for the isolation of particles. As a consequence, the resulting crosslinked particles often have an irregular shape with high polydispersity. Synthesized narrow size distribution poly (methacrylic acid-g-ethylene glycol) (P (MAA-g-EG)) nanospheres through precipitation polymerization for the oral delivery of proteins. They obtained better control over particle size and particle size distribution by controlling monomer concentration in water. They also revealed that increasing the cross-linker concentration during polymerization decreased the equilibrium swelling of the nanospheres [31].

Dispersion polymerization

In the process, most ingredients including monomers, polymeric stabilizers, and initiators are soluble in an organic solvent as a continuous phase. At the onset, polymerization occurs in a homogeneous reaction mixture; however, the formed polymers become insoluble in the continuous medium, ultimately leading to the formation of stable dispersion of polymeric particles with an aid of colloidal stabilizers Hydrophilic monodisperse micron-sized particles of PHEMA were also prepared by dispersion polymerization in the presence of PEO-b-poly (1,1,2,2-tetrahydroperfluorodecyl acrylate) deblock copolymer as a stabilizer in supercritical carbon dioxide, and meth acryloyl terminated PMMA in a 55/45 (wt./wt.) mixture of 2-butanol/toluene. Drugs and magnetic nanoparticles were either physically incorporated or chemically attached to microgels. The resulting microgels were effective as drug delivery carriers and for DNA applications [32].

Inverse (mini) emulsion polymerization

Inverse (mini) emulsion polymerization is a W/O polymerization process that contains aqueous droplets (including water-soluble monomers) stably dispersed with the aid of oil soluble surfactants in a continuous organic medium. Stable dispersions are formed by mechanical stirring for inverse emulsion process and by sonification for inverse mini emulsion polymerization. Upon addition of radical initiators, polymerization occurs within the aqueous droplets producing colloidal particles.

Reversible Addition Fragmentation Transfer (RAFT) process

Reversible Addition Fragmentation Transfer (RAFT) process adopted a single step of synthesis for PEGylated poly (N, N'-dimethyl amino methyl methacrylate) nanogel utilizing an amphiphilic macro RAFT agent trichion carbonate with hydrophobic dodecyl chain supporting polymerization rather than two-step process which produced 500 nm-800 nm size. However single step process presented advantage of reduced radii of nanogel (10 nm) apt for gene delivery [33].

- Dodecanethan oil and tetra butyl ammonium bromide mixed and N2 passed at 10˚C temperature
- Then Carbon di-sulfide and acetone added drop wise
- After then, Chloroform and sodium hydroxide added
- 30 minutes later yellow ppt obtained
- Ppt dissolve in Isopropanol and crystallized in hexane, RAFT agent obtained
- PEG reacted with RAFT in dichloroethane
- Polymerization in polymer with aqueous dispersion with RAFT agent to obtain nanogel

The nanogel of clove oil and tannic acid were prepared by membrane emulsification method. The antibacterial activity of the clove oil was higher than tannic acid against all tested oral bacteria. Furthermore, the MIC and MBC were reduced to one half-one sixteenth as a result of the combination of clove oil with tannic acid. The synergistic interaction was verified by time kill studies using the clove oil or eugenol with tannic acid. 30 min of treatment with MIC of the clove oil or eugenol with tannic acid resulted in an increase in the rate of killing in units of CFU/mL to a greater degree than was observed with alone. The results suggest that the clove oil and eugenol could be employed as a natural antibacterial agent against cariogenic and period onto pathogenic bacteria.

CONCLUSION

The early successes in antibiotic therapy yielded life-saving outcomes and is an example of possibly the most notable global scientific advance in modern medicine. The effectiveness of antibiotics used against a numerous of infectious microorganisms has been severely dissatisfied by the evolution of microbial resistance, arising as early as a decade following the discovery of penicillin. This worsening, ongoing trend has resulted in bacterial infections that are now completely resistant to all of the present-day conventional medicines previously capable of eradicating the infection. Consequently, the use of synergistic treatment regimens incorporating plant extracts or purified compounds derived from plants has become an emerging area of great interest in the medical and scientific community. Not surprisingly, many such plants are those traditionally used by indigenous communities to treat infectious diseases. The evidence is accumulating that the use of plant extracts enhances the antibacterial activity of conventional antibiotics, serving to repurpose these compounds rather than replacing them.

There are numerous other advantages associated with the use of synergistic therapies. The plant-derived component would

require a facile screening process to ensure that it is non-toxic, thus reducing the cost of development and testing while enhancing its speed to the market.

While it remains imperative that research continues in the area of the development of new synthetic drugs and new scaffolds, the use of extracts derived from a myriad of traditionally used plant species as synergistic potentiators of medicines that had been previously effective signals a coming of age in the treatment of highly resistant infectious diseases that threaten the global community. By regaining the susceptibility of such pathogens to rigorously tested antibiotics, the fight against pervasive, transmissible, and deadly bacteria may finally shift in favor of the clinical treatment of such illnesses.

Periodontal disease is one of the most important concern for dentists and patients. It is recognized as a major public health problem throughout the world and is the most common cause of tooth loss in India. The periodontium is that the specialized tissues that both surround and support the teeth, maintaining them within the maxillary and mandibular bones. A variety of triggering factors like bacterial causes, dyscrasias, avitaminosis etc., cause inflamed gums leading to gingivitis. In the India 50% of adults have gingivitis affecting a minimum of 3-4 teeth; two-thirds of the population has sub gingival calculus, and a few one-third have periodontitis. Periodontal treatment aims to cure inflamed tissue, reduce the number of pathogenic bacteria and eliminate the diseased pockets. This study was concluded to develop dental nanogel containing clove oil and tannic acid as the chief constituent for the treatment of dental problems by novel approaches.

REFERENCES

[1] Sultana, F., et al., An Overview of Nanogel Drug Delivery System. *Journal of Applied Pharmaceutical Science*, **2013**. 3(8): p. 95-105.

[2] Labhasetwar, V., Diandra, L., Leslie, P., Biomedical applications of nanotechnology. *Nanogels: Chemistry to drug delivery*, **2007**. 1(1): p. 131-172.

[3] Aliyar, HA., et al., Synthesis of polyacrylamide nanogels by intramolecular disulfide cross-linking. *Journal of bioactive and compatible polymers*, **2005**. 20(2): p. 169-181.

[4] Gonçalves, C., et al., Self-assembled dextrin nanogel as curcumin delivery system. *Journal of Biomaterials and Nanobiotechnology*, **2012**. 3(1): p. 178-184.

[5] Look, M., et al., Nanogel-based delivery of mycophenolic acid ameliorates systemic lupus erythematosus in mice. *The Journal of clinical investigation*, **2013**. 123(4): p. 1741-1749.

[6] Abd El-Rehim, HA., et al., Developing the potential ophthalmic applications of pilocarpine entrapped into polyvinylpyrrolidone–poly (acrylic acid) nanogel dispersions prepared by γ radiation. *Biomacromolecules*, **2013**. 14(3): p. 688-698.

[7] Nivetha, R., et al., Effects of natural products on oral health: A review. *Asian Journal of Pharmaceutical and Clinical Research*, **2014**. 7(5): p. 279-282.

[8] Chandrasekaran, S., Role of Tannins in Oral Health Care. *International Journal of Pharmaceutical Science and Health Care*, **2014**. 3(4): P. 39-43.

[9] Takesh, T., et al., Effects of a Novel Whitening Formulation on Dental Enamel. Dentistry. *Dentistry*, **2017**. 7(4): p. 1-9.

[10] Al-Samadani, KH., The effect of preventive agents (Mouthwashes/Gels) on the color stability of dental resin-based composite materials. *Dentistry Journal*, **2017**. 5(2): p. 18.

[11] Singh, GR., et al., Herbal formulations: The next level in oral care. *International Journal of Green Pharmacy*, **2016**. 10 (3): p. 114.

[12] Kandekar, S., Bhujbal, N., Deshpande, Y., Novel Formulation for Enhanced Efficacy of LavangTaila(Clove oil) for Anti-Inflammatory Activity. *International Journal of Ayurveda and Pharma Research*, **2016**. 4(2): p. 24-27.

[13] Yadav, R., et al., Formulation and Characterization of Antimicrobial Oral Gel from Some Herbal Extracts for Treatment of Periodontal Diseases. *International Journal of Pharmacy and Pharmaceutical Research*, **2016**. 5(2): p. 191-201.

[14] Voleti, VK., et al., Formulation and development of dental gel containing clove oil for the treatment of human periodontal diseases. *Journal of Comprehensive Pharmacy*, **2016**. 3(1): p. 1-7.

[15] Sahiner, N., Sengel, SB., Tannic acid decorated poly (methacrylic acid) micro and nanoparticles with controllable tannic acid release and antioxidant properties. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, **2016**. 508(1): p. 30-38.

[16] Aarthi, G., et al., Characterization of Nanogel for Transdermal Drug Delivery System. *International Journal of ChemTech Research*, **2014**. 7(2): p. 786-789.

[17] Hoshino, Y., et al., Preparation of nanogel-immobilized porous gel beads for affinity separation of proteins: fusion of nano and micro gel materials. *Polymer Journal*, **2015**. 47(2): p. 220-225.

[18] Ramesh, C.N., et al., Formulation of Lipid Coated Nanogel Containing Curcuma Longford Antiseptic Activity. *International Journal of Biological and Pharmaceutical Research*, **2014**. 5(4): p. 350-353.

[19] Phatak, AA., Chaudhari, PD., Development and evaluation of nanogel as a carrier for transdermal delivery of aceclofenac. *Asian Journal of Pharmacy and Technology*, **2012**. 2(4): p. 125-132.

[20] Gonçalves, C., et al., Self-Assembled Dextrin Nanogel as Curcumin Delivery System. *Journal of Biomaterials and Nanobiotechnology*, **2012**. 3(1): p. 178-184.

[21] Chacko, RT., et al., Polymer nanogels: A versatile nanoscopic drug delivery platform. *Advanced drug delivery reviews*, **2012**. 64(9): p. 836-851.

[22] Milind, P., Deepa, K., Clove: A champion spice. *International Journal of Research in Ayurveda and Pharmacy*, **2011**. 2(1): p. 47-54.

[23] Murphy, EA., et al., Targeted nanogels: A versatile platform for drug delivery to tumors. *Molecular cancer therapeutics*, **2011**. 10(6): p. 972-982.

[24] Patel, HA., Patel, JK., Nanogel as a controlled drug delivery system. *International Journal of Pharmaceutical Sciences Review and Research*, **2010**. 4(2): p. 37-41.

[25] Nivetha, R., et al., Effects of natural products on oral health: A review. *Asian Journal of Pharmaceutical and Clinical Research*, **2014.** 7(5): p. 279-282.

[26] Kim, S., et al., Minimalism in fabrication of self-organized nanogels holding both anti-cancer drug and targeting moiety. *Colloids and Surfaces B: Biointerfaces*, **2008**. 63(1): p. 55-63.

[27] Dorwal, D., Nanogels as novel and versatile pharmaceuticals. *International Journal of Pharmacy and Pharmaceutical Sciences*, **2012**. 4(3): p. 67-74.

[28] Gaur, U.,Biodistribution of fluoresceinated dextran using novel nanoparticles evading reticulo-endothelial system. *International Journal of Pharmaceutics*, **2000**. 202(2): p. 1-10.

[29] Nakashima, T., Shimizu, M., Kukizaki, M., Particle control of emulsion by membrane emulsification and its applications. *Advanced drug delivery reviews*, **2000**. 45(1): p. 47-56.

[30] Robinson, DN., Peppas, NA., Preparation and characterization of pH-responsive poly (methacrylic acid-g-ethylene glycol) nanospheres. *Macromolecules*, **2002**. 35(9): p. 3668-3674.

[31] Oh, JK., et al., The development of microgels/nanogels for drug delivery applications. *Progress in Polymer Science*, **2008**. 33(4): p. 448-477.

[32] Dhadwal, D., Nanogels as novel and versatile pharmaceuticals. *Progress in Polymer Science*, **2012**. 3(8):57-84.

[33] Yan, L., Tao, W., One-step synthesis of pegylated cationic nanogels of poly (N, N′-dimethylaminoethyl methacrylate) in aqueous solution via self-stabilizing micelles using an amphiphilic macroRAFT agent. *Polymer*, **2010**. 51(10): p. 2161-2167.