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Review Paper

A Review on Modern Treatment Approach-Nanogel Against Bacterial Conjuctivitis

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ABSTRACT

A common eye condition called bacterial conjunctivitis can be brought on by two prevalent pathogens: Staphylococcus aureus and Streptococcus pneumoniae. Conventional antibiotic treatments are becoming less effective as the prevalence of resistance among these bacterial types rises. This study investigates the etiology of bacterial conjunctivitis as well as the clinical manifestations and symptoms of affected individuals. Due to corneal epithelial impermeability and precorneal loss, current ocular medication administration techniques frequently have insufficient bioavailability. These drawbacks are extensively discussed. Nanogel technology holds promise as a solution to these problems, providing better drug delivery. Nanogels exploit their unique physiochemical properties to allow the controlled and extended release of therapeutic chemicals, therefore addressing challenges of rapid drug clearance and insufficient penetration into target tissues. This study describes a variety of methods for creating nanogels, including ionic gelation, emulsion solvent diffusion, nanoprecipitation, and emulsion evaporation, and highlights how they might improve the outcomes of therapy for eye conditions. This work demonstrates how nanogel systems is have the effective treatment of bacterial conjunctivitis by combining innovative formulation techniques, delivery methods, and knowledge of medication resistance.

INTRODUCTION

Non-traumatic inflammatory disease known as bacterial conjunctivitis affects the conjunctival mucosa and can lead to major issues. It is characterized by pain, inflammation, yellow-white mucopurulent discharge, and obscured vision. Studies show that bacterial infections were responsible for 50–70% of conjunctival occurrences [1].

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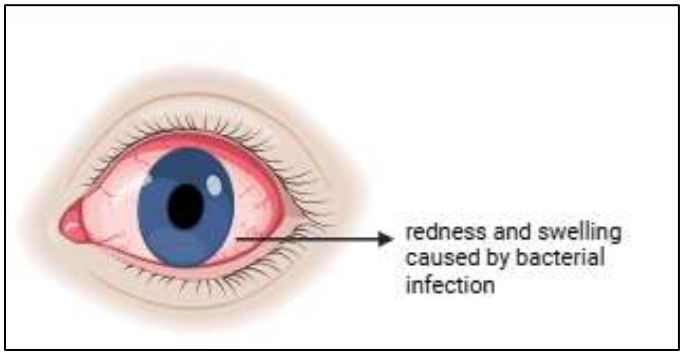

Figure no 1: Bacterial conjunctivitis

Newborns and people of all ages are susceptible to bacterial conjunctivitis. Streptococcus pneumoniae, Haemophilus influenzae, Neisseria gonorrhoeae, Staphylococcus aureus, Staphylococcus epidermidis, and others are the main contributing species [2, 3]. Some diseases, such primary meningococcal conjunctivitis caused by Neisseria meningitides serotype B strain, are particularly fatal. It results in meningococcal disease, which causes severe conjunctivitis, especially in children [4]. Newborn conjunctivitis cases have also been linked to other organisms, including Neisseria cinerea, Neisseria gonorrhoeae, the bacteria that causes gonococcal conjunctivitis, is frequently linked to STIs and can be found in neonates through delivery-related maternal transmission However, there is evidence that Gonococcal Conjunctivitis can be caused by different types of Neisseria gonorrhoeae are not associated with STIs [5,6,7,8]. Another common bacteria that is passed from an infected mother to the newborn after birth is chlamedia. In nature, Chlamydia trachomatis-induced neonatal conjunctivitis which results in acute infection occurs far more frequently. Pseudomonas are further bacteria that are frequently detected in neonatal conjunctivitis [9].

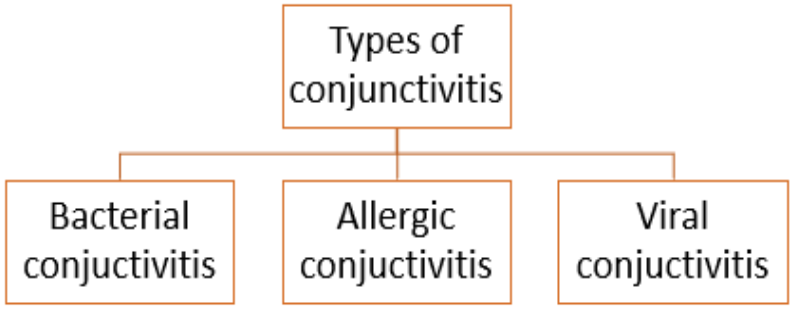

Chart no 1: Types of bacterial conjunctivitis

a) Bacterial conjunctivitis: The pathogenic bacteria that cause bacterial conjunctivitis include Staphylococcus aureus, S. pneumoniae, and Haemophilus influenzae. Bacteria can be disseminated by coming into touch with infected hands or personal objects, including towels [10, 11]. Bacterial conjunctivitis manifests as eyelid swelling, discomfort, ocular secretions (which may stick to the eyelids), and a feeling of a foreign body in the eye [12, 13].

b) Allergic conjunctivitis: Allergens environment, including dust, animal fur, etc., can cause allergic conjunctivitis. This kind of conjunctivitis can be caused by both seasonal and persistent allergies. The symptoms are eye

redness, acute itching, watery secretions, swelling of the eyelids, weeping, and burning feeling in the eye [14].

c) **Viral conjunctivitis**: Adenoviruses are the leading cause of viral conjunctivitis, however other viruses such herpes simplex, chickenpox zoster, and enteroviruses can also cause the condition. These viruses are easily spread by direct touch or respiratory droplets [15].

Table no 1: Clinical cause and physical examination findings for the different causes of conjunctivitis [16]

Types	Causes	Identification
Bacterial	Acute purulent discharge, either unilaterally or bilaterally, accompanied with adhesion and mattering	Substantial discharge, usually yellow or green
Viral	A sharp burning or scratchy sensation that frequently coexists with prodromal symptoms including fever, coughing, and rhinorrhea	Conjunctival follicular appearance and watery discharge
Allergic	Usually persistent and seasonal, bilateral eye itching is frequently accompanied by atopic symptoms.	Conjunctival follicular appearance, chemosis, and watery discharge

Pathophysiology of bacterial conjunctivitis [17,18].

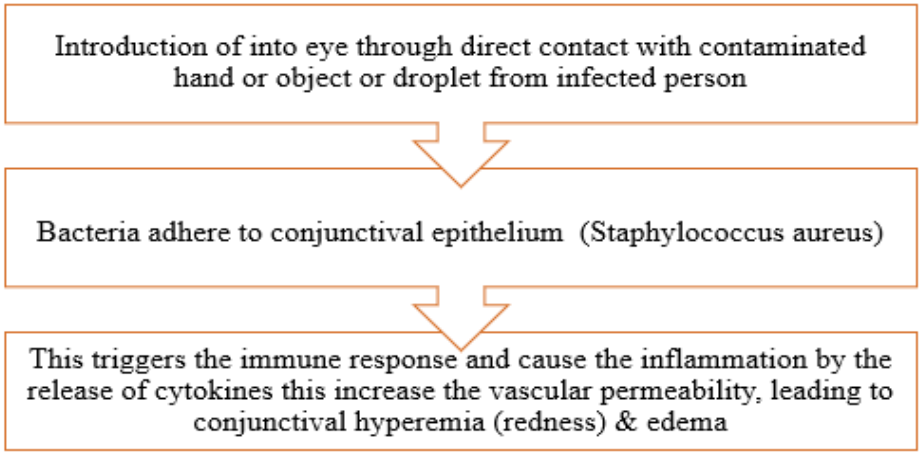

Chart no 2: Pathophysiology of bacterial conjunctivitis

Agents Used to Treat Bacterial Conjunctivitis & Their Bacterial Resistance

1. Aminoglycosides & Polymyxin B

Aminoglycosides such as tobramycin, gentamicin were the first topical medicines to treat bacterial conjunctivitis. Gentamicin and tobramycin are bactericidal, especially against gram-negative bacteria and Staphylococci, but less so against Streptococci [19]. Polymyxin B-based combinations (e.g., polymyxin B/trimethoprim, polymyxin B/bacitracin, and polymyxin B/bacitracin/neomycin) are beneficial for mild instances of bacterial conjunctivitis but are not always bactericidal several studies have demonstrated resistance to aminoglycosides and polymyxin B. In a 10-year surveillance study of bacterial conjunctivitis (1994–2003) done in South Florida, 5.4% of S. aureus isolates were resistant to gentamicin [20, 21, 22].

2. Fluoroquinolones

Fluoroquinolones are broad-spectrum bactericidal anti-infectives that are effective against both gram-positive and gram-negative microorganisms responsible for bacterial conjunctivitis. In sensitive species, fluoroquinolones block DNA gyrase and topoisomerase IV, inhibiting DNA replication. The newer fluoroquinolones (e.g., moxifloxacin, gatifloxacin, and besifloxacin) appear to have greater activity against common gram-positive pathogens associated with bacterial conjunctivitis, including some strains of Staphylococci and Streptococci resistant to other antibiotics, due in part to structural modification leading to more balanced binding of DNA gyrase and topoisomerase IV [23,24]. Resistance to fluoroquinolone antibiotics can be caused by either a single or several mutations. A single-step mutation imparts so-called "low-level" resistance and may not lead to clinical treatment failure as long as the concentration in the eye stays over the MIC90 for the isolated pathogen. Multistep mutants, often known as "high-level" resistance, occur when bacterial isolates acquire two or more mutations, frequently leading to clinical treatment failures. Multiple-step mutations are thought to arise from repeated treatment with less than bactericidal dosages [25, 26].

3. Macrolides

The macrolide drugs erythromycin and azithromycin are bacteriostatic antibacterial agents. Erythromycin ophthalmic ointment has been marketed since 1982, however it is now widely advised exclusively for the prevention of newborn conjunctivitis since action against S. aureus has decreased. Azithromycin is less potent against gram-positive bacteria than erythromycin, but more effective against gram-negative bacteria, including H. influenza [27]. Monitoring susceptibility trends among respiratory isolates such as S. pneumoniae has shown that resistance to macrolide antibiotics has increased. Among all respiratory isolates of S. pneumoniae collected in the United States between October 2005 and April 2006 (respiratory infection season), 34% were resistant to azithromycin, and 80.6% of those resistant to penicillin were also resistant to azithromycin [28, 29, 30, 31].

Challenges in ophthalmic drug delivery systems

One of the problems in ocular drug delivery systems is designing a therapeutic system that can deliver a medicine at the target region at the optimal concentration while retaining good therapeutic efficacy. Most ocular dosage forms have limited bioavailability because of precorneal loss, which includes lacrimation, solution drainage, tear dynamics, tear dilution, conjunctival absorption, nonproductive absorption, and the brief residence duration in the cul-de-sac, and tear turnover. Additional difficulties include the corneal epithelial membrane's relative impermeability, which makes it difficult to transport medications to the anterior section after topical administration. Transferring medications to the anterior region after topical treatment is difficult due to ocular issues, including the corneal epithelial barrier's notable impermeability. Due to a number of physiological and anatomical barriers, only 1% or less of the medication's implanted dose reaches the intraocular tissues, which reduces drug absorption.

•The following categories describe the difficulties with ocular medication delivery systems:

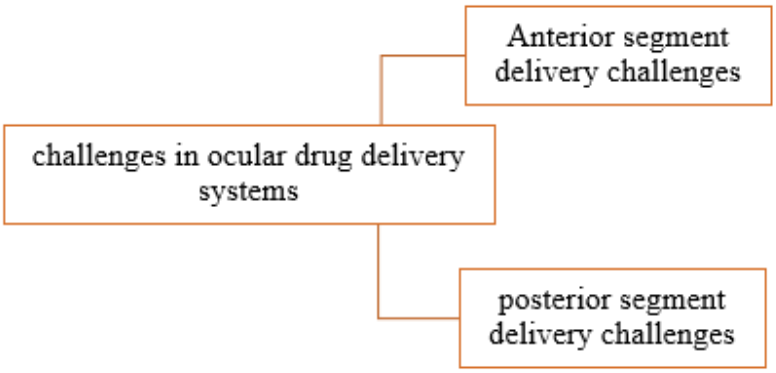

Chart no 3: Ocular drug delivery challenges

a) Anterior segment delivery challenges

Because the drug molecule must first face the tear film and conjunctiva, which are first in the pathway and slow the penetration of the active moiety in the eye, before it can reach the anatomical barrier of the cornea, topical formulations are usually preferred over systemic formulations in the ocular delivery system. In the majority of ocular formulations, precorneal loss factors result in low drug bioavailability.

b) Posterior segment delivery challenges

BRB protects the back of the eye from topical medications. In the posterior region of ocular tissue, some variables limit the diffusion of medications, which also lowers ocular bioavailability. When given intravenously, the BRB controls the posterior location of drug distribution by restricting the systemically supplied drug's ability to reach the retina [32, 33]. High doses of vitreal medications are required to address conditions affecting the back of the eye. Because BRB is more permeable to lipophilic compounds, these medications can be administered to the posterior region of the eye. Side effects may arise from high medication concentrations and frequent dosing [34].

Limitations of conventional delivery systems employed for ocular therapeutics

Eye drops

Eye drops are the most widely utilized, suitable, secure, and instantaneously effective type of ophthalmic treatment. It is the main treatment option for the majority of ocular conditions, especially those that impact the back of the eye. The fact that liquid medicine makes it easy to reach every part of the eye may be the reason for its extensive use. In essence, 1–5% of the amount administered intraocularly penetrates the eye and reaches the intended site in a concentration that works. Usually, the remaining 90% is wasted for a number of reasons [35].

Eye Ointment

A different kind of carrier system designed for topical application is ophthalmic ointments. Ocular ointment is composed of a mixture of solid and semisolid hydrocarbons (paraffin), where the melting point is at the normal ocular temperature of 34 °C. The basis for choosing hydrocarbons is biocompatibility. Ointments help to improve ocular bioavailability and sustain drug release. Because of their stickiness, which can produce momentary obscured vision and signal inappropriate dosing or ocular pain, removing ointments can be challenging [36].

Intravitreal Injection

In order to treat eye disorders, an intravitreal injection involves injecting or surgically implanting a medication into the vitreous, a region of the eye. Drug delivery systems of this kind were developed to ensure that medication is consistently supplied to the posterior or intermediate regions of the eye. Significant risks are connected to the painful and intrusive procedure [37].

Intraocular Implants

In order to deliver medications to posterior ocular tissues, implants are frequently placed intravitreally. This involves making a little incision at the pars plana, which is located anterior to the retina and posterior to the lens. Because of the associated advantages, such as longer drug release, fewer side effects, local drug release to sick ocular tissues at therapeutic levels, and the ability to pass through the blood retinal barrier, these devices are gaining popularity despite the invasive nature of implantation [38, 39, 40].

Emulsions

A system having a continuous phase and a dispersed phase is produced by an emulsion, which is a combination of two or more immiscible liquids. The bioavailability and solubility of pharmaceuticals are enhanced by this kind of ocular drug delivery method. It is a simple way to increase the length of stay and the extent of medication release while reducing the challenges associated with treating eye conditions. The two primary forms of emulsion therapy are water-in-oil and oil-in-water [41, 42, 43].

Nanotechnology in ocular drug delivery

In medicine, nanotechnology has been applied for many different reasons. By developing effective drug delivery systems (DDSs) that encourage increased bioavailability and drug penetration across different ocular barriers, it may be used for a variety of purposes, including better ocular medication delivery. This enhances medication delivery to the eye and shows the variety of applications for various nanosystems that hinder drug clearance by the eye's defense mechanisms [44].

Nanoparticles

Nanoparticles are colloidal carriers with sizes between 10 and 1000 nm. Drug-filled nanoparticles might be nanospheres or nanocapsules. In nanospheres, the drug is evenly dispersed throughout the polymeric matrix, whereas in nanocapsules, it is contained inside the polymeric shell. Over the past few decades, there has been interest in using nanoparticles to deliver medications into the eyes. Several researchers have attempted to develop drug-loaded nanoparticles that can enter the anterior and posterior ocular tissues [45, 46].

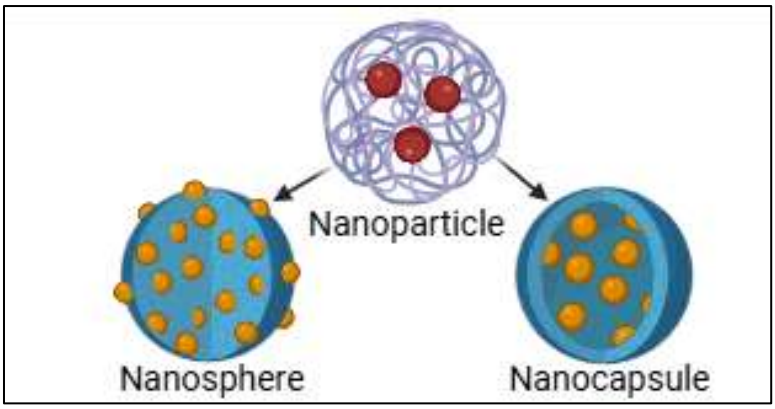

Figure no 2: Nanoparticle

Nano suspensions

Nano suspensions are colloidal dispersions of submicron drug fragments stabilized by one or more polymers or surfactants. It is now a practical way to give drugs that are hydrophobic. Among the advantages it provides for ocular administration are sterilization, ease of formulation of eye drops, reduced pain, extended precorneal residency time, and enhanced ocular bioavailability of drugs that are insoluble in tear fluid [47].

Nanofibers

Nanofibers are one-dimensional (1D) nanomaterials that have gained popularity for a variety of commercial and scientific applications. In comparison to other commonly used base materials, nanofibers have superior mechanical properties (such as stiffness and tensile power) and a diameter that is a thousand times smaller than human hair. Materials that can be used to make nanofibers include metals, metal oxides, carbon-based composite nanomaterials, and natural and synthetic polymers [48].

Nano liposomes

Lipid bilayers comprising amphiphilic molecules, mostly manufactured or natural phospholipids that are smaller than a millimeter in diameter are used by nano liposomes to capture aqueous phases. Additionally, nano liposomes decrease the formulation's rate of clearance, medication toxicity, and enzyme breakdown in ocular tissues [49].

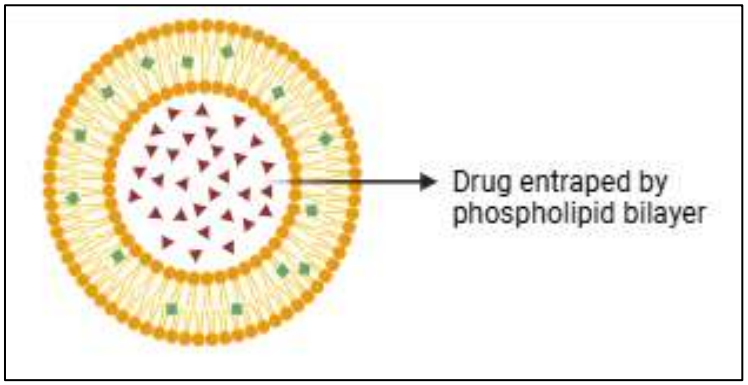

Figure no 3: Nano liposomes

Nano micelles

The molecule's hydrophilic half faces the polar solvent, while its hydrophobic half faces the opposite direction. Amphiphilic monomers with both hydrophilic (polar) and hydrophobic (non-polar) groups make up nano micelles [50].

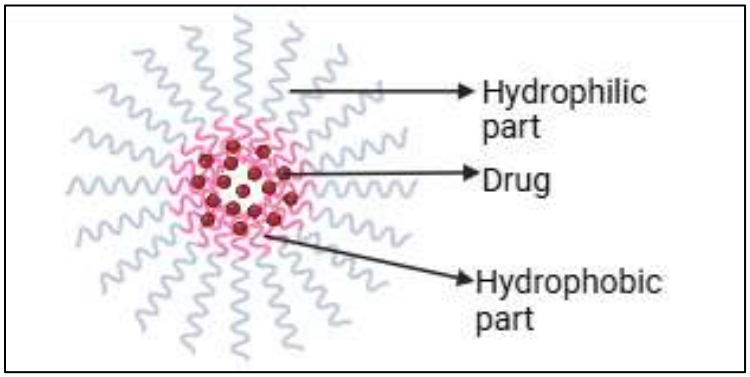

Figure no 4: Nano micelles

Drug loaded contact lenses

Contact lenses are tiny artificial lenses used to correct vision that are comprised of twisted plastic plates. Numerous advantages, such as bioavailability, enhanced and better patient compliance, and a reduction in overdose and unwanted side effects—especially in chronic illnesses like glaucoma—further promote the safe and comfortable use of contact lenses. Numerous contact lenses are used to provide pharmaceutical drugs, including ciprofloxacin, cyclosporine, dexamethasone, and timolol [51].

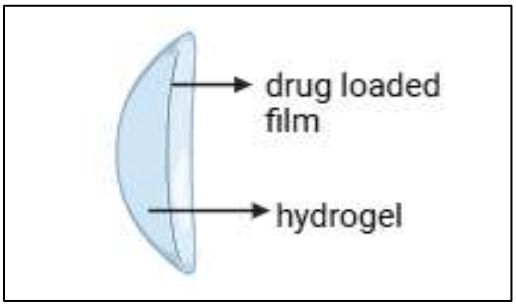

Figure no 5: Drug loaded contact lens

Microneedles

Microneedles (MNs) have advanced quickly as a medication delivery device within the last ten years. These gadgets' small needles have the capacity to puncture tissue and produce microscopic passageways that allow drug molecules to enter. Solid MNs coated with pilocarpine (500–700 μm) demonstrated fast drug breakdown in scleral tissue within 30 seconds after insertion [52, 53]. The mechanical strength of the MNs was demonstrated in vitro, and there were no side effects, which are commonly linked to systemic delivery or intraocular injections [54].

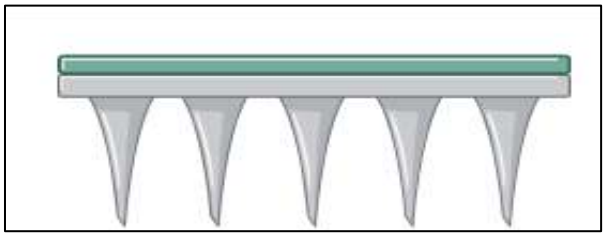

Figure no 6: Microneedle

Nanogels as delivery systems

The administration of medicinal drugs remains difficult despite developments, which is why developing new technologies like "Nano particulate drug delivery systems" is essential. The nanoscale area, around 1–1000 nm, is home to nanoparticle systems [55]. In nanogel delivery methods, the polymer is intercrossed chemically or mechanically to create three-dimensional hydrogel particles with a sub-micron particle size [56, 57]. Because of their numerous benefits over previous drug delivery techniques, including their variable size, ease of fabrication, swelling, biocompatibility, hydrophilicity, and sensitivity to a variety of stimuli (temperature, pH, light, biological agent, etc.), nanogels are known as next-generation drug delivery systems [58].

Characteristics of nanogels

- The nanogels have a higher surface area to volume aspect ratio and improve the solubility of hydrophobic medications due to their

nanometric dimensions and the existence of hydrophobic pockets created by crosslinks. Spherical nanogels are often made using a bottom-up method, but a top-down method is required to get a range of forms [59].

- Another feature of a non-ionic nanogel is its swelling, which may be explained by two opposing free-energy forces: the network's elasticity, which prevents swelling, and the swelling brought on by the polymer's interaction with the solvent. Ionization of groups also causes swelling in the ionic gel, which is different from the two forces mentioned before [60].
- Swelling behavior may be controlled by structural features such as the degree of crosslinking, the chemistry of the polymer matrix, the charge concentration in polyelectrolyte gels, and environmental influences [61].

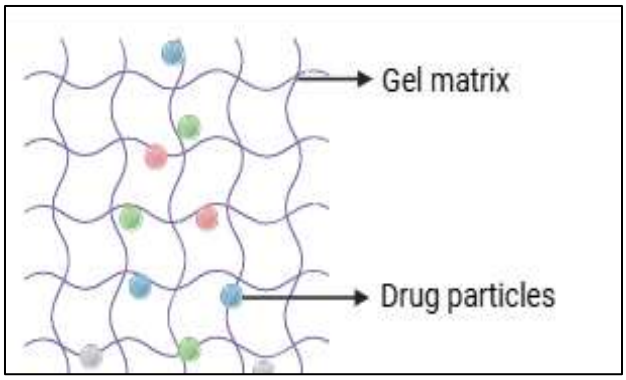

Figure no 7: Nanogel

Classification of Nanogels [62]

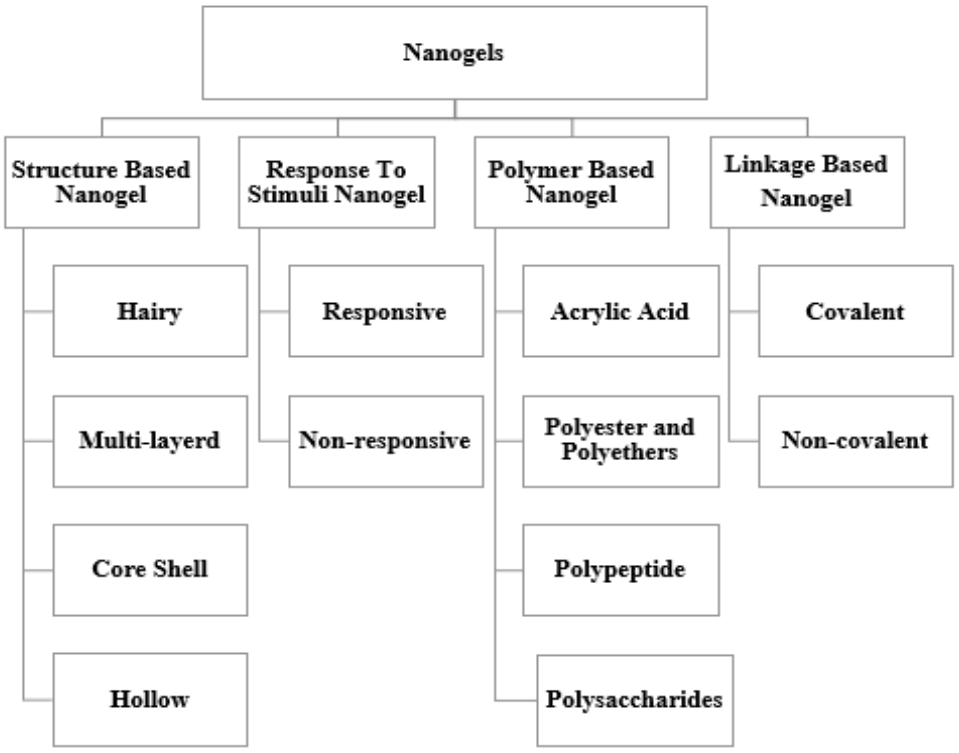

Chart no 4: Types of nanogel

Mechanisms governing drug release

Depending on the characteristics of the polymer used to create them, nanogels can release either tiny molecules or biomolecules. The mesh size of the matrix is crucial for maintaining the release, which can occur through stimuli-mediated release or simple diffusion from the matrix system. Here are some examples of basic release mechanisms:

a) Swelling

b) Erosion of the nanogel matrix

c) Changes in the surrounding environment's pH

d) Displacement-based release by ambient counter ions

e) Triggered release by external energy sources like magnetic fields, light, etc.

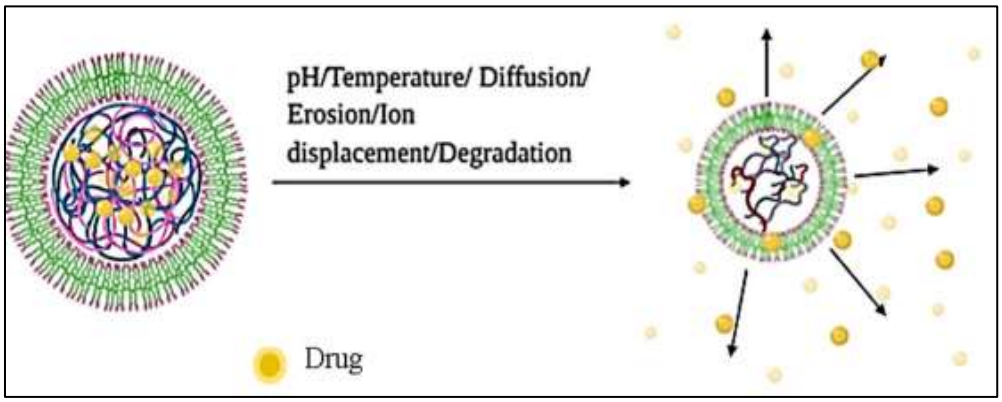

Figure no 8: Mechanism of drug release from nanogel

The type of polymer, texture, consistency, swellability, matrix integrity, and viscosity all affect the kinetics of drug release. Providing a controlled release of the drug was the main objective of these devices. Thus, obtaining zero order kinetics is their main objective. These systems are expected to have controlled release characteristics due to the kinetic and thermodynamic stability of nanogels. Nanogels release medicines more slowly than micelles because they are more stable in biological liquids. Micelles release drugs faster. Since these systems are hydrophilic, a lower degree of crosslinking aids in faster drug release. The majority of formulations containing nanogels employ multiple crosslinking cycles to fine-tune the drug release, and the drug release from the nanogels is evaluated using basic kinetic models, including the zero-order kinetic model, Higuchi model, Korsmeyer-Peppas model, etc., [63].

METHODS OF NANOGEL PREPARATION

a) Emulsion Solvent Diffusion Method

The aqueous solution dissolves the drug in an organic layer, and the drug phase is introduced dropwise to the aqueous phase after it has been homogenized with a polymer and gelling agent for 30 minutes at 6000 rpm. When an emulsion is homogenized into a nano droplet using a homogenizer, an oil/water emulsion is created. Tri-ethanolamine is then added to the oil-in-water emulsion and constantly swirled for an hour at 8000 rpm in order to make nano gel [64].

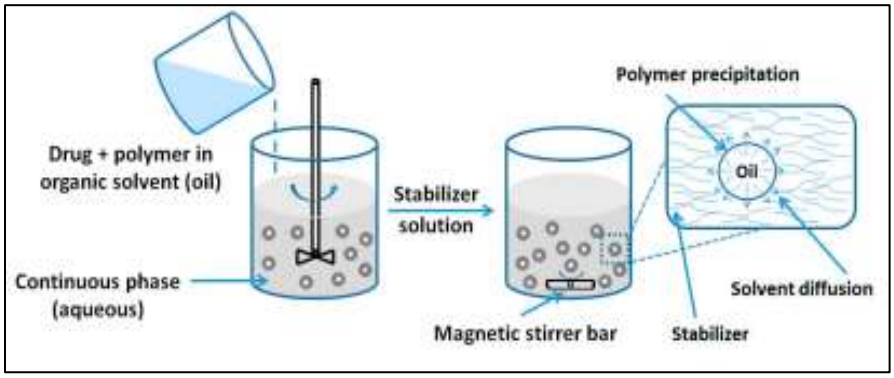

Figure no 9: Emulsion diffusion method

b) Nano Precipitated Method

The technique of nanoprecipitation, often referred to as solvent displacement or interfacial deposition, creates nanoparticles in a colloidal suspension by gradually adding the oil phase to the aqueous phase while stirring it slowly. It is a quick and easy method because it just needs one step and is immediate. Important manufacturing parameters that have a significant impact on the nanoprecipitation technique include the oil phase/aqueous phase ratio, the aqueous phase agitation rate, and the organic phase injection rate [65,66].

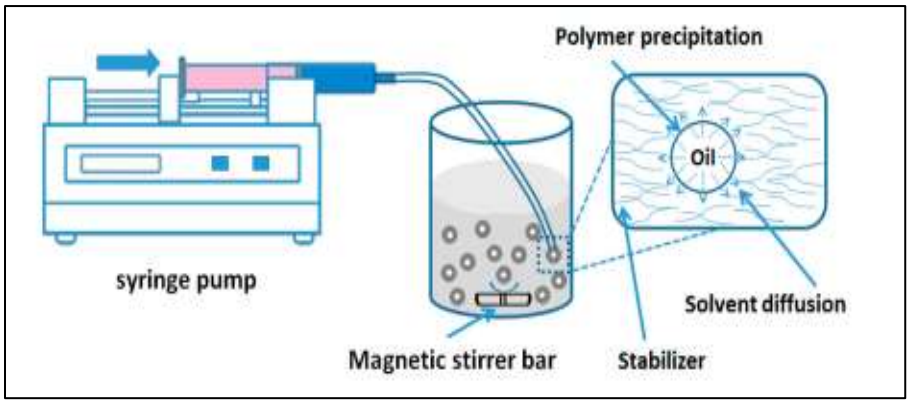

Figure no 10: Nano precipitation method

c) Emulsion Evaporation method

Emulsion evaporation has been utilized for a long time to produce polymeric NPs from as-prepared polymers. The process is based on the emulsification of polymer organic solution into a water phase, followed by organic solvent evaporation. First, the polymer is dissolved in an appropriate solvent (such as methylene chloride, chloroform, or ethyl acetate). To provide the emulsion stability, a surfactant is dissolved in the continuous phase (aqueous phase) after the organic phase has been added. High shear force is used during emulsification in order to minimize the size of the emulsion droplet. The ultimate particle size will be mostly determined by this technique. Following emulsification, the system uses vacuum to evaporate the organic solvent, resulting in the precipitation of polymers and the creation of nanoparticles [67].

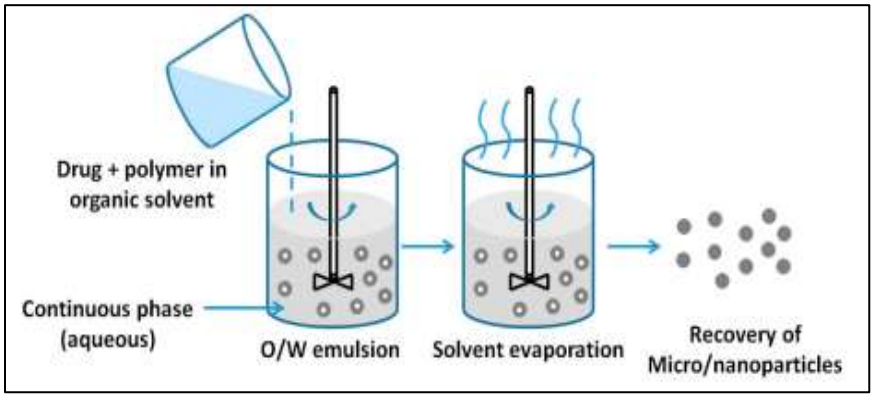

Figure no 11: Emulsion evaporation method

d) Reverse Micellar Method

An organic solvent dissolves a polymer, drug, and surfactant. The cross-linking agent needs to be added and then mixed in over the course of several hours at night. Following the purification of the nanoparticles, the solvent is removed, resulting in a dried bulk. The gelling ingredient was dissolved in water to make it. Nanogels are created by mixing nanoparticles with an aqueous phase that contains a gelling agent [68].

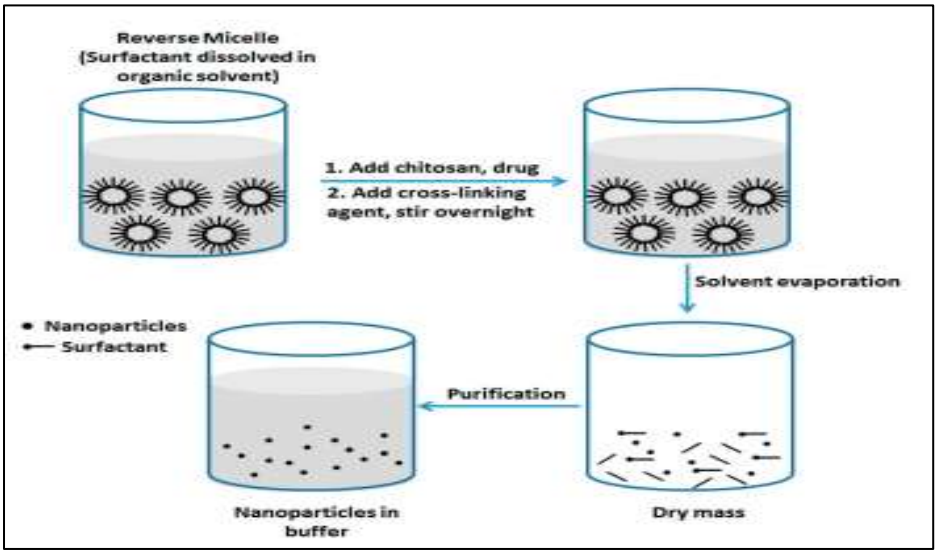

Figure no 12: Reverse micellar method

e) Ionic Gelation Method

The creation of complexation between the positively charged amine group of chitosan and negatively charged polyanion, such tripolyphosphate (TPP), is the basis for the ionic crosslinking technology's formulation of chitosan nanoparticles. The procedure is straightforward and gentle, and no organic solvent is needed for the whole preparation process, which may be carried out under aqueous conditions. Chitosan nanoparticles have been extensively investigated for use in medicinal applications because of their special quality. Anionic solution of TPP was produced by dissolving it in distilled water, while a cationic solution of chitosan was first produced by dissolving it in diluted acetic acid. The TPP solution was then gradually added to the chitosan cationic solution. When NPs were mechanically stirred at room temperature, the NPs is formed and they were collected by centrifugation and subjected to gel form to get nanogel [69, 70].

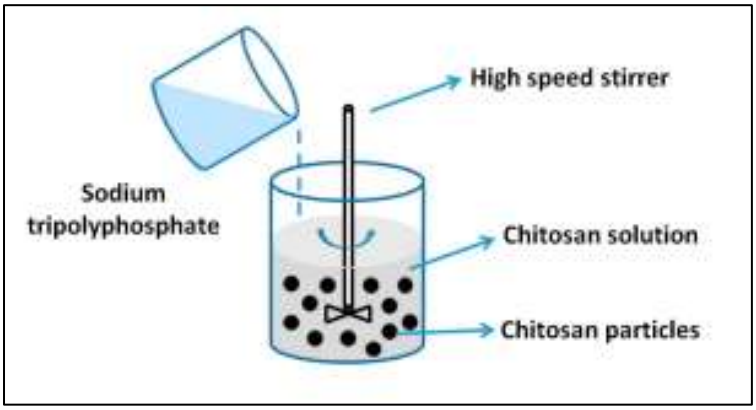

Figure no 13: Ionic gelation method

Characterization of nanogels [71]

It is a crucial for understanding their properties, behavior and suitability for specific applications on nanomaterials in biomedical fields. To analyze conductive nanogels on graphene and nano crystalline beads various techniques are employed to analyze physical, chemical and mechanical properties.

1. Size and Morphology Analysis

a) Dynamic Light Scattering (DLS): Measures the hydrodynamic size and distribution of nanogels in solution, principle involve in this is analyzing the scattering of laser light by particles in suspension to determine their size based on Brownian motion.
b) Transmission Electron Microscopy (TEM): Provides high-resolution photography of nanogels to evaluate their morphology and size, Electrons are transmitted through a thin sample and produce contrast based on density and thickness of nanogel structures.
c) Scanning Electron Microscopy (SEM): The information comprises a detailed morphological profile of the surface area. Scans a sample with focusing beam of electrons producing images based on secondary electron emission.

2. Surface Charge Analysis

a) Zeta Potential Analysis: Measures the surface charge of nanogels which is indicative of their stability in suspension. By applying an electric field, the movement of dispersed particles can be quantified and used to calculate the zeta potential.

3. Thermal Properties

a) Thermogravimetric Analysis (TGA): Determines thermal stability and composition by measuring weight changes with temperature, the sample is heated and weight loss is recorded indicating decomposition or loss of volatile components.
b) Differential Scanning Calorimetry (DSC): Evaluates thermal transitions such as melting, crystallization and glass transition temperatures, Compares the heat flow into a sample and reference under controlled temperature conditions.

4. Drug Loading and Release Studies

a) Encapsulation Efficiency: Evaluates how much drug can be loaded into the nanogel critical for drug delivery applications. Can be measured by using UV-is spectroscopy or HPLC by comparing the concentration of the drug before and after loading.
b) *In Vitro* Release Profiles: Studies how drugs are released from nanogels over time,

indicating their drug delivery abilities. Typically conducted using diffusion studies on dialysis membranes through which samples are periodically taken and analyzed.

5. Stability Studies

Testing long-term and accelerated stability, this study aims to determine how nanogels maintain their properties over tie under various storage conditions. Samples are subjected to different temperatures humidity levels and light exposure followed by regular assessment through previously mentioned characterization techniques.

Applications of Nanogels.

As previously stated, NGs have attracted a lot of interest in biological applications because of their distinct structural and functional characteristics. Their ability to encapsulate medications, proteins, and other biomolecules and their biocompatibility enable targeted and controlled release, which lowers adverse effects and improves therapeutic effectiveness. As was previously indicated, the potential for stimuli-responsive NGs enables the delivery of medications in a particular way. Various forms of surface functionalization can also control the cellular absorption and bio-distribution behavior of NGs; polarity and surface charge influence the NGs' hydrophilicity and blood-circulation duration. Additionally, it should be emphasized that the range of synthesis techniques described above are not limited to certain applications; rather, they may be modified to create NGs for various uses. Significant progress has been made in the design, optimization, functionalization, and use of NGs in recent years. Thus, the primary focus of this section will be on freshly released biomedical applications.

a) Nanogels as Drug Delivery system

Nanogel-based drug delivery systems are very efficient in precisely delivering drugs to their target sites, significantly reducing toxicity to surrounding healthy cells. This remarkable potential has led to extensive research into their application for the treatment of diseases with high morbidity and mortality rates, with the aim of improving traditional therapies and patients' quality of life. Many NGs have a high encapsulation efficiency and drug-loading capacity and can be suitable for transporting both hydrophilic and hydrophobic drugs, including small molecules such as chemotherapeutic agents and inhibitors, as well as macromolecules such as proteins, DNA, or RNA [72].

b) Nanogels as ophthalmology application

Poor medication bioavailability, which can be caused by tear turnover or the rapid drainage of conventional eye drops from the nasolacrimal system, is one of the issues that plague current treatment approaches for ocular illnesses. The corneal epithelium and the blood-retinal barrier are examples of penetration barriers that keep medications from getting to the deep ocular tissue [73,74]. Another major obstacle facing the area is the short residence time of conventional eye therapies, which necessitates regular administration of eye medicines to maintain enough levels for desired outcomes. Patients may become burdened by these circumstances, which might result in non-compliance and the failure to achieve the best possible treatment outcomes. Furthermore, because targeted distribution is frequently not attained, ophthalmic formulations, like many other therapies, may produce less than ideal results. Since nanogels efficiently entrap, protect, and enhance the residency of medications on the ocular surface while encouraging effective penetration in multiple eye compartments, they are being investigated intensively for eye illnesses [75].

c) Nanogels application for wound healing

Nanogels' special qualities have made them a viable nanomaterial for wound healing applications. Because of their high-water content and adjustable chemical and physical characteristics, they are ideal for use in wound healing applications. One of the biggest obstacles to wound healing is treating potential infections, which frequently involve bacteria that are resistant to antibiotics. In chronic wounds, inadequate tissue perfusion can also result in poor healing. Appropriate tensile strength, which shows the tissue's mechanical stability and integrity, is a crucial wound healing criterion. The more tissue healing, the less likely the tissue is to sustain more damage or to undergo wound dehiscence. Silver nanogels that were created showed improved beneficial effects, which yielded significantly higher tensile strength compared to the market drug Silverex. This result was achieved by applying silver nanogel at a significantly lower concentration than Silverex. Owing to their colloidal stability, nanogels provide an excellent platform for classical topical treatment for wound healing [76].

d) Nanogels application as anti-viral

Applications Healthcare professionals throughout the world have faced the difficulty of managing infectious diseases over the years. In order to safeguard and advance human health against the worldwide threat posed by pandemics, constant efforts have been conducted. The most dangerous and worldwide burden is the pandemic brought on by viral diseases. Above all, the current COVID-19 epidemic has prompted academics throughout the world to step up their efforts to study viral infections. Severe constraints include inadequate lymph node targeting and antigen-presenting cells inability to absorb SARS-CoV-2 spike protein (S-RBD), which hinders efficient immune responses, are addressed by nanogels. In order to target lymph nodes, dendritic cells, and macrophage accumulations more effectively, a reversible nanogel (S-RBD-NG) was created using S-RBD protein, which can function as a pro-antigen [77].

CONCLUSION

The advent of nanogels as a drug delivery system represents a pivotal advancement in the treatment of ocular diseases, particularly bacterial conjunctivitis. The challenges posed by traditional ocular delivery methods, such as poor bioavailability, rapid drug clearance, and limited penetration of therapeutic agents into ocular tissues, underscore the necessity for innovative solutions. Nanogels, characterized by their unique properties such as biocompatibility, tunable size, and controlled release capabilities, demonstrate significant potential in overcoming these barriers. By effectively encapsulating drugs and enhancing their residence time on the ocular surface, nanogels can significantly improve therapeutic efficacy and patient compliance.

Future Prospects

The future of nanogel technology in ocular drug delivery appears promising and multifaceted. Ongoing research is expected to focus on optimizing nanogel formulations to further enhance drug delivery efficiency and bioavailability, specifically targeting ocular tissues for improved therapeutic outcomes while minimizing side effects. The development of personalized medicine approaches utilizing nanogel systems tailored to individual patient needs represents an exciting opportunity to enhance treatment efficacy. In addition, exploring combination therapies that integrate nanogels with other drug delivery systems could yield synergistic effects in managing complex ocular conditions. Furthermore, as our understanding of nanogel

safety and effectiveness increases, streamlined regulatory pathways for these next-generation drug delivery systems may emerge, facilitating their translation from laboratory research to clinical practice. Finally, integrating digital health technologies with nanogel delivery systems could pave the way for personalized monitoring and management of ocular therapies, ultimately enhancing patient outcomes across various medical domains.

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