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Biodegradable Polymer Based Nanogels: Platform for Drug Delivery System

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Abstract: ***Hydrogel with three - dimensional (3D) tunable porous structure are known as nanogels having particle size range of 1 to 100 nm and used as drug delivery carrier. Nanogels can be used to encapsulate small drug molecules, oligonucleotides, and proteins. They are made of a variety of natural or synthetic polymers. Because of its 3D structure, which allows for the encapsulation of hydrophobic or hydrophilic pharmaceuticals in their internal network, nanogels are able to retain their highly hydrated nature and shrinking - swelling capabilities, potentially safeguarding these drugs from deterioration during storage. Additionally, by altering their surface, nanogels can be made to be more targeted and multifunctional, and their circulation time can be extended. Currently, drug delivery systems based on nanogel have gained popularity and made a big effect due to their pharmacological uses. In this review article, we summarize an overview of the development of different bioploymeric nanogels and their use in drug delivery systems***

Keywords: Nanogels, Drug Delivery, Topical, Polymers, Nanogel structure

1. Introduction

The term "nanogel" refers to the nanoparticles that swell in a suitable solvent and are created by chemically and physically cross - linked polymer networks. When polynucleotide delivery via cross - linked bifunctional networks of a polyion and a nonionic polymer. Diffusion can cause the drugs to come out of the nanogel. This releasing mechanism is easy to use and has been used effectively [1]. The development of nanogel that may release biological agents in response to environmental cues at the intended site of action is gaining more attention. Due to excellent biocompatibility, high drug loading capacity, high biodegradability (and consequently minimal cytotoxicity), good penetration capabilities, and tissue mimicking qualities, nanogels are a promising method of delivering a wide range of medications to various organs within the body. They are perfect for incorporating large drug molecules like proteins, peptides, oligonucleotides, and other macromolecules due to their excellent water retention [2]. Chemically or physically cross - linked polymers with hydrophilic or amphiphilic macromolecular chains give rise to the three - dimensional structure of nanogels, which can swell by retaining a large amount of water without dissolving and keeping the structure intact [3].

Advantages of Nanogel

- Highly biocompatible, eliciting immune reactions because of its high water content and ability to function like genuine tissue
- Nontoxic due to the carrier's biodegradability
- Quickly break free from the reticulo - endothelial system's entrapment.
- Tuning can be used to adjust drug delivery crosslinking densities. Because of nano - size, biological membranes provide better penetration.
- Due to the drug's small volume, it can easily permeate tissues through either transcellular or paracellular pathways, reaching even the smallest capillary vessels.
- Hydrophilic and hydrophobic drugs can be used in the nanogel drug delivery
- Extended drug release from the nanogel with polymeric network [4]

Disadvantages of Nanogel

- Expensive method to completely remove surfactants and solvents in the nanogels
- Scaling up process is difficult due to average weight and size of the drug molecule [5].

Nanogel Based Drug Delivery System

Diclofenac sodium Nanogels

Using the emulsion solvent diffusion approach, a nanogel with smaller particles was created to increase the anti - inflammatory drug of Diclofenac sodium's bioavailability. This investigation revealed that diclofenac sodium nanogels were prepared using various polymers (Eudragit S - 100 and HPMC) and a permeation enhancer (propylene glycol, alcohol), and the outcomes demonstrated superior flux enhancement when compared to nanogels prepared with methyl cellulose and HPMC. According to the study's findings, diclofenac sodium - Eudragit S - 100 nanogels with propylene glycol acting as a permeation enhancer and carbopol 940 acting as a gelling agent demonstrated superior flux augmentation [6].

Ciclopirox olamine nanogels for Dermatitis

Using a homogenization process, ciclopirox olamine nanogels were combined with carbopol 940 as a gelling agent to produce a smooth antifungal nanogel (F1 - F6). Fourier transform infrared analysis of antifungal nanogels (F1–F6) revealed no interactions between the drug and excipients. The F6 formulation was determined to be the best one, exhibiting a high in - vitro drug release of 83.42% after 8 hours. The particle size and zeta - potential values obtained were 230 nm and - 27 mV, respectively. According to in - vitro drug release kinetic models, F6 exhibited first - order kinetics. An in - vivo investigation using mice revealed that the optimal formulation, F6, had a superior therapeutic effect for dermatitis. According to the study's findings, formulation F6 demonstrated superior in - vitro drug release and increased antifungal efficacy [7].

Beta - Sitosterol Nanogels

To increase the hydrophobic drug's bioavailability, various formulations of beta sitosterol nanogel (F1–F4) were made using the dispersion approach, which involved dispersing carbopol 934 in water with smaller particle sizes. This study used Fourier transform infrared (FTIR) analysis and showed that nanogels (F1–F4) did not exhibit any drug - excipient interaction. The pH values of the F1, F2, F3, and F4 formulations range from 6.40 to 6.84. The F2 formulation demonstrated superior viscosity, extrudability, spreadability, drug content, and in vitro drug release. According to the study's findings, beta sitosterol nanogel demonstrated effective drug release and enhanced drug bioavailability [8].

Etoricoxib Nanogels

To improve the therapeutic impact and reduce the side effects of oral administration, various formulations of etoricoxib nanogel (F1 - F4) were made utilising the emulsion - solvent diffusion process with polymers such as polyvinyl alcohol and ethyl cellulose in varying ratios. According to this investigation, the F4 nanogel with a high polyvinyl alcohol and ethyl cellulose content demonstrated a greater drug release in 6 hours, at 103.8±0.76%. The F4 nanogel's polydispersity index was determined to be 0.481 and its particle size to be 211.2 nm. Using the carrageenan - induced paw oedema method, an in - vivo anti - inflammatory test was conducted. The results indicated that whilst traditional gel showed 77.2% suppression of paw oedema, etoricoxib nanogel showed 81.8% inhibition. This study found that etoricoxib nanogel was an efficient oedema inhibitor [9].

Clotrimazole nanogels

By adopting the solvent diffusion process (high speed homogenisation) with carbopol 940 and locust bean gum as polymers and triethanolamine as a gelling agent, clotrimazole nanogel (several formulations: F1 - F10) was created. According to this study, FTIR analyses showed that the medication and polymer are compatible when being prepared. It was discovered that the F9 - nanogel average particle size ranges were 410 nm to 530 nm. The homogenous and easily extrudable F9 nanogel was demonstrated by the extrudability investigation. The drug content of the F9 nanogel ranged from 82.16 to 90.15 percent. Moreover, Pappas's dissolution kinetics with controlled release mechanism are followed in in vitro diffusion tests of produced nano gel. According to this investigation, F9 nanogel was chosen as an optimal formulation with good morphological characteristics, drug content efficiency and controlled drug release [10].

Flubiprofen nanogels

The formulation of a nanoemulsion - based gel (nanogel) for the transdermal distribution of flurbiprofen involved testing a number of excipients, including ethanol (co - surfactant), tween 80 (surfactant), and oleic acid (oil). By utilising aqueous phase titration to create pseudo - ternary phase diagrams, the region of the nanoemulsions was found. The formulation was chosen as an optimal formulation and transformed into nanogel using chitosan as a gelling agent. It comprises 3.09 percent weight/weight of the oil phase, 60.54 percent weight/weight of Smix, and 36.36% weight/weight of distilled water. The produced nanogel had stronger anti - inflammatory properties. According to the study's findings, flurbiprofen's transdermal distribution could be enhanced by the created nanogel [11].

Nanogels with montelukast sodium niosomes

As non - ionic surfactant and cholesterol self - assemble when hydrated with aqueous medium, they create niosomes, which are vesicular carriers in the drug delivery system that encapsulate both polar and non - polar medicines. The lipid was thin - film hydrated using a rotary vacuum evaporator and a non - ionic surfactant to create montelukast sodium niosomes. Utilising carbopol 934 to create a nanogel, the produced montelukast sodium niosomes were added. According to this investigation, the created nanogel drug and polymer are compatible. The average niosome vesicle size was found to be 496.2 nm, and the polydispersity index (PI) was determined to be 0.680. The prepared nanogel formulation was confirmed to be stable based on the zeta potential analysis. According to the study's findings, niosomal gel is the most effective vesicular carrier for the topical administration of montelukast sodium [12].

Chitosan - based nanogels of myricetin

A chitosan - based oral administration nanogel comprising an inclusion complex of myricetin and HP - β - CD was developed, and the results of both in vitro testing and in vivo assessments were correlated. The HP - β - CD inclusion complex was added in the proper amount to myricetin - loaded nanogels that had been produced. This study found that myricetin - loaded nanogels with particle sizes ranging from 100 to 300 nm and an in vitro drug release study demonstrating a fickian mechanism increased myricetin's oral bioavailability through chitosan nanogel containing an inclusion complex of myricetin and HP - β - CD [13].

Aceclofenac Nanogels for Topical Application

The high - pressure homogenisation method was used to create the aceclofenac nanoemulsion. Aceclofenac nanogel was prepared by adding carbopol 940 as a gelling agent. This study showed that the optimised nanoemulsion's composition included transcutol HP with PEG 400 and ethanol as a cosurfactant, labrafil combined with triacetin as an oil, and tween 80 and cremophor EL together as a surfactant. With an optimal spreadability of 141.1 ± 3.65 nm and an optimised aceclofenac nanogel droplet size, our work suggests that a high - pressure homogenisation technique may be a good fit for achieving an optimised aceclofenac nanogel [14].

***Tailam* based Nanogels**

In traditional Siddha treatment, the Mattan tailam mixture has been widely utilised to heal ulcerous lesions. Rats were used to study in vivo wound healing after mattan tailam nanogel was created via the high - energy milling technique. According to this investigation, Mattan tailam nanogel exhibited an average particle size of 20–30 nm. Rats treated with matten tailam nanogel demonstrated a notable decrease in the area of the wound.10% Mattan tailam nanogel therapy increased the proportion of wound contraction on the sixteenth day. The 10% Mattan tailam nanogel group showed higher concentrations of hydroxyproline and a faster rate of epithelialisation. The results of this study indicate that the tensile strength, collagen synthesis, and wound contraction are greatly enhanced by the polyherbal Mattan tailam nanogel formulation [15].

Curcumin loaded alginate aldehyde–gelatin nanogels

A naturally occurring polyphenol called curcumin has anti - cancer and anti - chemopreventive properties. Curcumin was encapsulated in alginate aldehyde–gelatin (Alg Ald - Gel) nanogel utilising the inverse mini - emulsion technique to increase its bioavailability and therapeutic efficacy. According to this study, the hydrodynamic diameter of the curcumin - loaded nanogels was 431 ± 8 nm, and their zeta potential was − 36 ± 4 mV. The nanogels that were produced demonstrated an encapsulation effectiveness of 72.2 ± 2%. Curcumin was released from nanogels under controlled conditions over a 48 - hour period, according to in vitro drug release tests. The uptake of nanogels in MCF - 7 cells was validated by in vitro cellular uptake of the curcumin - loaded nanogels using confocal laser scanning microscopy (CLSM). According to the findings of this investigation, curcumin - loaded nanogel may be appropriate for targeted drug delivery system against breast cancer [16].

Fluconazole nanogels

Seborrhoeic dermatitis was designed to be treated with fluconazole nanogel. Fluconazole nanoparticles were synthesised by a streamlined evaporation technique, and subsequently integrated into nanogel through the utilisation of Eudragit RS and HPMC. The optimal particle size was found in the range of 119.0 nm to 149.5 nm in this study's produced nanoparticles made using Eudragit RS and Tween 80, with a cumulative percent drug release of 95% up to 18 hours. The optimised HPMC concentration in the nanogel formulation, with a particle size of 149.50±0.5 and a maximum drug release of 92.13±0.32%, was verified. Eudragit nanogel was shown to have good flow index, spreadability, and viscosity coupled with controlled drug release, making it an optimised nanogel according to the study's findings. This study found that topical medication distribution may be achieved with fluconazole nanogel [17].

Polyherbal anti - acne nanogels

The most prevalent skin condition that can result from a bacterial infection is acne. Every person may have pigmentation, acne, sunburn marks, and pimples at some point in their lives. The emulsion solvent diffusion method was used to formulate the polyherbal anti - acne nanogel, which contains extracts of orange, moong dal, coconut sheath scale, honey, and tea tree oil in an aqueous - based carbopol gel system. The obtained formulations did not significantly alter in colour, pH, spreadability, or viscosity over a 30 - day period following the stability investigation. The prepared nanogels had good rheological features, such as pH, homogeneity, and spreadability, good antibacterial activity against *Staphylococcus aureus* in the produced polyherbal nanogel. According to the study's findings, polyherbal nanogel is more effective to treat skin infection [18].

Conclusion

Nanogels can be used as a carrier system to accommodate drug molecules. The nanogels is madp up of natural or synthetic biopolymers with good swelling and softness properties. With this knowledge, it was observed that nanogels that are compatible with small drug molecules, and proteins, peptides, nucleic acids. Nanogels have been studied extensively for topical drug delivery system with *in vitro* model and reported for anti - bacterial, anti - fungal and other skin infections, but, we have to focus nanogel based drug delivery system on pre - clinical studies mainly *in vivo* study to understanding of their mechanism of action, pharmacokinetic and stability profiles of the nanogels.

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