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Nanogel as Transdermal Drug Delivery System Review Article

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ABSTRACT-Nanogels are nanoparticle counterparts of hydrogels which combine the properties of gels with those of colloids such as high surface- volume ratio, microheterogeneous structure and small sizes. Called as “gel nanoparticle” and “nanoscale hydrogels”,etc. Nanogels (NGs) are nanosized particles generated by physically or chemically cross-linked polymer networks that are well dissolved in a suitable solvent. Because of the bilayer composition and structure, they are considered more effective and less hazardous than conventional formulations. In the formulation of topical dosage forms, medication carriers that ensure adequate localization or penetration of the drug within or through the skin are employed to increase local and minimise systemic effects, or to ensure adequate percutaneous absorption. Topical formulation reduces GI irritation, prevents medication metabolism in the liver, and increases drug bioavailability. Topical treatments work by acting directly on the affected area. Nanogels' ability to control drug release has been extensively documented in the literature, and researchers are always working to improve drug release control from nanogels by developing novel polymers with unique sensitivity to a chemical or physical stimulus. In this review, we briefly discuss the definition of nanogels, properties, general characteristics, nanoparticle size, higher drug loading capacity, applications in therapeutic, mechanism of drug release from nanogels. It also points the high potential of nanogels in the list of candidates for transdermal drug delivery systems.

KEYWORDS:Nanogel, properties, general characteristics, nanoparticle size, transdermal drug delivery system.

I. INTRODUCTION

Despite its promise, transdermal pharmaceutical administration is a difficult technology to deploy for both local and systemic drug effects. Topical drug administration is a development in pharmaceutical technology that encourages formulation scientists to look into routes other than oral/parenteral for delivering drugs to the target site that are effective, efficient, and active. The skin, which is one of the most easily accessible organs on the human body for topical administration, is the primary route of topical medicine delivery. Topically applied drugs have a confined effect at the place of application due to the efficacy of the drug penetration into the layers of the skin or mucous membrane. These topical medication delivery methods are typically employed to treat local skin infections or in situations where other drug administration routes are ineffective. The topical approach entailed delivering the medicine to the body's surface area in a formulation that could be absorbed. The fundamental benefit of transdermal drug delivery is that it bypasses first-pass metabolism, avoiding the risks and issues associated with intravenous therapy, as well as conditions of absorption such as pH fluctuations, enzyme presence, and gastric emptying time. The skin covers the bulk of the human body and is one of the most easily accessible organs for topical pharmaceutical administration. Nanogels are miniature hydrogels with characteristics of both gels and colloids, including a high surface-to-volume ratio, microheterogeneous structure, and microscopic dimensions. Nanogels are stable, soft, and swollen in excellent solvents. It's made up of a few solid components entangled with polymers spread in a large volume of liquid, with the solids forming a three-dimensional network with nanoscale size, resulting in a large surface area and biconjugation of active targeting sites. Nanogel networks can contain and protect medicinal molecules hydrogel by physically and chemically cross-linking polymer at nanoscale scales. Nanogel is a type of material with a size range of 10-100 nm. The most major advantage of topical NSAIDs is the lack of substantial adverse effects associated with systemic NSAIDs, particularly in elderly people. Oral NSAID therapy has been linked to an increase in gastrointestinal (GI) and renal damage. Evidence suggests that topical formulations can attain therapeutic medication concentrations in localised tissues while lowering serum drug levels and avoiding systemic toxicity. Nanogels have been shown to be a viable



structure for systemic drug release, the design of multifunctional nanocarriers such as theranostics, and controlled drug release at the target location throughout the first decade of their development. These molecules can include diverse compounds due to the huge surface area and changeable size of nanogels.

The Advantages of Nanogel Drug Delivery

1. It protects against the biodegradation of medicines within the body.
2. Nanogel physical properties, such as size, can be easily changed and maintained depending on the desired delivery molecule.
3. Only a tiny amount of medication is needed, and the number of dosages is kept to a minimum.
4. Improves the medicinal molecule's bioavailability and reduces the medicine's toxicity
5. Drug-loaded nanogels can be injected into the body and applied topically without causing any negative side effects.
6. These can pass across the blood-brain barrier as well as physiological barriers such as the skin.

The Disadvantages of Nanogel

1. To thoroughly eliminate the solvents and surfactants at the conclusion of the process, costly procedures are required.
2. Surfactant traces can occasionally cause toxicity.
3. Scale up is not easy due to mean size and weight.

Nanogel pores can be filled with tiny molecules or macromolecules, and nanogels are typically one to hundreds of nanometers in diameter. Some features of the nanogel can be regulated, such as swelling, degradation, and chemical functionality [7, 8]. Nanogels have been studied for generating various agents such as quantum dots, dyes, and other diagnostic agents over a longer period of time than for medication delivery [9, 10]. The importance of nanogels has grown as a result of the specialized delivery system expectations, the broad diversity of polymer systems available, and the simplicity with which physical-chemical properties can be changed. Nanogel has been proven to have promising clinical usefulness in recent investigations [11, 12]. Nanogels are exploited in the field of gene therapy since gene transfer within cellular organelles for gene silencing is now achievable [13]. The volume fraction of a nanogel can be varied by employing different solvent quality and branching to preserve a three-dimensional structure [14]. For the creation of multiresponsive nanogels, polymer–nanogel composites like interpenetrated networks (IPNs) and core–shell particles are especially useful, as they allow controlled release profiles of multiple active principles and for targeting therapy, respectively. Magnetic nanogels as magnetic resonance imaging contrast agents, gold hybrid nanogels as relevant bioimaging devices, silver containing nanogels well known for their antimicrobial properties and optical properties as potential biodiagnostic imaging, and superparamagnetic iron nanoparticles (SPION) as magneto-transducers (MTs) as potential biodiagnostic imaging. Some of the benefits of nanogels created from natural polymers include the following.

Routes of Administration

- Oral
- Pulmonary
- Nasal
- Parenteral
- Intra-ocular
- Topical

II. HIGHER DRUG LOADING CAPACITY.

In comparison to bulk hydrogels, nanogels are extremely valuable as drug delivery systems because they can incorporate and release a wide range of active compounds (cargo), including bioactive molecules (drugs, peptides, proteins, antigens, oligonucleotides, genes, carbohydrates, DNA) and inorganic molecules (quantum dots, silver and gold nanoparticles, magnetic nanoparticles). Furthermore, nanogels that can solubilize hydrophobic medicines can be loaded with both hydrophilic and hydrophobic pharmaceuticals. The type of functional groups contained in the polymeric chains, which have a significant impact on drug delivery and drug releasing capabilities, influence nanogels'

ability to include a large number of pharmaceuticals. Some functional groups can conjugate with therapeutic agents via physical interactions such as hydrogen bonding or van der Waals forces, which improve drug-carrying efficiency and have a high potential for targeting applications, whereas functional groups at the drug/protein molecules interface ensure a higher loading.

III. CONJUGATION OF COVALENT COMPOUNDS

Covalent conjugation in biological agents can be used to make nanogels. Acrylic groups are altered with enzymes and copolymerized with acrylamide in an inverted microemulsion or a dilute aqueous solution to form a nanosized hydrogel. Imprisonment in the physical sense Proteins were entrapped in cholesterol-modified pullulan nanogels and siRNA in HA nanogels by physical entrapment [14]. When hydrophobic molecules were added to nonpolar domains, a hydrophobic chain formed, which may be found in some nanogels. In cholesterol-modified pullulan, for example, prostaglandin E2 is readily soluble. N – hexyl carbamoyl – 5 – fluorocil (HCFU) noncovalently integrated in cross-linked nanogels of N – isopropylacrylamide (NIPAAm) and N – vinylpyrrolidone (VP) copolymers. Doxorubicin was also put into pluronic F127-based amphiphilic cross-linked nanogels. Because of the hydrophobic contact, drug molecules are loaded into nanogels to relatively modest degrees in the majority of cases (not more than 10 %).

IV. SELF-ASSEMBLY

Self-assembly occurs when independent groups of components are aggregated into structurally well-defined structures. It has advantages such as

1. Minimal thermodynamics, which results in structures that are stable and robust.
2. Adaptable and simple to use,
3. It is a cost-effective solution.

Many molecules self-assemble through diffusion, followed by specific connection of molecules via non-covalent interactions, hydrophobic associations, or electrostatic interactions. It has a weak and dominates the structural and conformational behaviour of the assembly because to the vast number of interactions involved [15]. Electrostatic attractions cause oppositely charged polysaccharides to rapidly associate [16]. Interactions with neutral polysaccharides result in weaker or non-existent interactions; nevertheless, chemical modification can cause assembly to be required. The polysaccharides, which are extremely water soluble, cause nanoparticle production through hydrophobic interactions. There are three ways to employ this type of amphiphilic polymer.

1. Grafted hydrophilic chains onto a hydrophobic backbone (grafted polymer).
2. grafted hydrophobic chains onto a hydrophilic backbone
3. Alternatively, alternate hydrophilic and hydrophobic portions (block polymers).

When amphiphilic polymers come into contact with water, they produce self-aggregated nanoparticles by forming intramolecular or intermolecular associations between the hydrophobic moieties, largely to reduce the interfacial free energy. The hydrophobic section aggregates in the internal core and the hydrophilic region to the polar or watery medium, which is an important physicochemical property. Critical micelle concentration or critical aggregates refers to the concentration at which polymeric chains assemble.

V. SIZE OF NANOPARTICLES.

For nanogel use in a specific biological application, particle size is critical. Nanoparticles with smaller diameters, such as those ranging from 10 to 100 nm, are more favourable and suited for bypassing biological barriers via tissue diffusion, extravasation, improved blood circulation time, and evasion of hepatic filtration (Alexis et al. 2008). In most cases, an increase in extravasation rate (excellent permeation capabilities) across tissues is necessary, particularly in tumour therapy, and they can also cross the blood-brain barrier (BBB). Other properties include: – controlled swelling in aqueous media – electromobility – excellent colloidal stability, while natural polymer-based polymers have good biocompatibility and degradability. Nanogels, on the other hand, have similar problems, such as the cost of cleaning the finished product of leftover solvent, surfactants, and unreacted monomers at the end of the synthesis process; these residues might induce toxicity (Rossetti et al. 2002; Xu et al. 2007).

Properties

As previously stated, natural polymer-containing NGs have increased bioavailability, a large surface area for multivalent bioconjugation, high drug loading capacity, targeted and very effective drug delivery, and hydrophilicity,

biocompatibility, and biodegradability. Aside from these benefits, stimuli responsive nanogels provide more effective disease therapies due to their efficient ability to operate as intelligent drug delivery systems that can perceive and adapt to pathophysiological situations (Soni et al. 2015). The fast swelling and de-swelling of nanogels causes changes in their size and characteristics, which has various benefits in drug delivery. Crosslinker concentration, polymer type, ionic strength, temperature, polyelectrolyte charge (related to osmotic pressure), biological characteristics, and other factors all influence the swelling of nanogels in water. Swelling is also influenced by hydrogen bonding interactions between polymeric chains and solutes (Kabanov and Vinogradov 2008). Because of the reliance on the diffusion mechanism, the swelling is time dependent. While the swelling happens over days at the macroscale, the nanogel response occurs in minutes. In the 25–45 °C temperature range, temperature-responsive swelling k-carrageenan nanogels undergo a gel-to-sol transition, which entails the breaking apart of physical connections in the gel (fig.1).

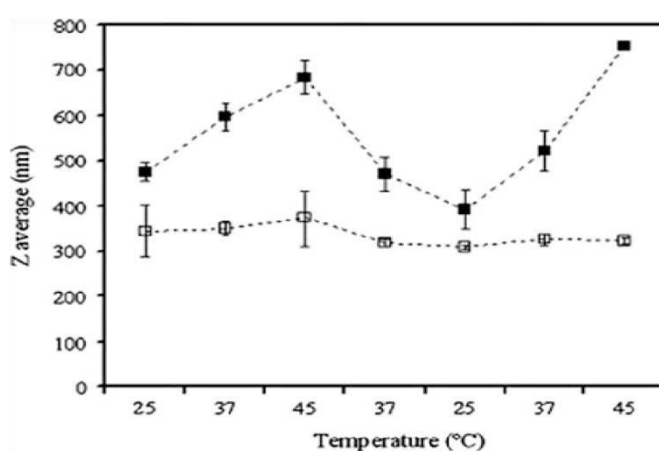


Figure 1: Hydrodynamic diameter ($Z_{average}$) of 1 wt% (open squares) and 4 wt% (full squares) carrageenan nanoparticles in PBS determined by DLS during alternate increasing and reducing temperature cycles. The dashed lines are only for visual aid. (Elsevier granted permission for Daniel-da-Silva et al. 2011)

The zeta potential of the nanospheres at physiological pH was shown to be invariant with k-carrageenan content because the polysaccharide k-carrageenan is a polyelectrolyte. The association/dissociation rate constants and equilibrium constants of the multipoint protein recognition process are influenced by the flexibility (as measured by Young's modulus) and polymer density of nanogel particles, which increased with decreasing crosslinking degree for swollen phase NGs, but were unaffected by crosslinking degree for collapsed phase NGs (Nakamoto et al. 2014; Manirujjaman et al. 2013). The electromobility of some nanogels is linked to their zeta potential. The zeta potential refers to the electric potential at the double layer's boundary. Nanoparticles with zeta potentials larger than +25 mV or less than -25 mV have good colloidal stability, while lower values cause aggregation. The size (200–1000 nm) and zeta potential (+20 and +60 mV) of the NPs formed by ionic gelation of chitosan with charged amino groups and diblock copolymer in the presence of a polyanion as sodium tripolyphosphate were regulated by changing the composition. Proteins such as bovine serum albumin, tetanus toxoid and diphtheria toxoid, insulin, and oligonucleotide interacted well with the NPs produced (Soppimath et al. 2001). Some NGs' cyclodextrin-coated NPs significantly reduced surface negativity, preventing mononuclear phagocytic system absorption. Particles having a particle size of 150 nm and a negative charge aggregate more efficiently in malignancies (He et al. 2010).

VI. STABILITY OF COLLOIDAL PARTICLES

Nanogels exhibit stronger colloidal stability, lower critical micelle concentrations, slower rates of dissociation, and longer drug retention than surfactant micelles.

VII. THE RESPONSE IS NON-IMMUNOLOGIC

There was no immune reaction to nanogel-based drug delivery methods.

VIII. MORPHOLOGY.

The morphology of nanogels is determined by their content and manner of manufacture. TQ-loaded myristic acid-chitosan (MA-chitosan) nanogels made using the self-assembly approach (Dehghania et al. 2015) had round forms and smooth surfaces, with particle sizes ranging from 150 to 200 nm.

Microspheres with dimensions ranging from 60.2 to 79.2 mm were produced using a multi-(amino acid) copolymer (MAC) based on α -aminocaproic acid, γ -aminobutyric acid, L-alanine, L-lysine, L-glutamate, and hydroxyproline, as well as MAC microspheres encapsulating bovine serum albumin (BSA) prepared using a double-e (Chen and colleagues, 2014). As the surfactant ratio of Tween 80 to Span 80 fell, the size of microspheres shrank (Fig. 1)

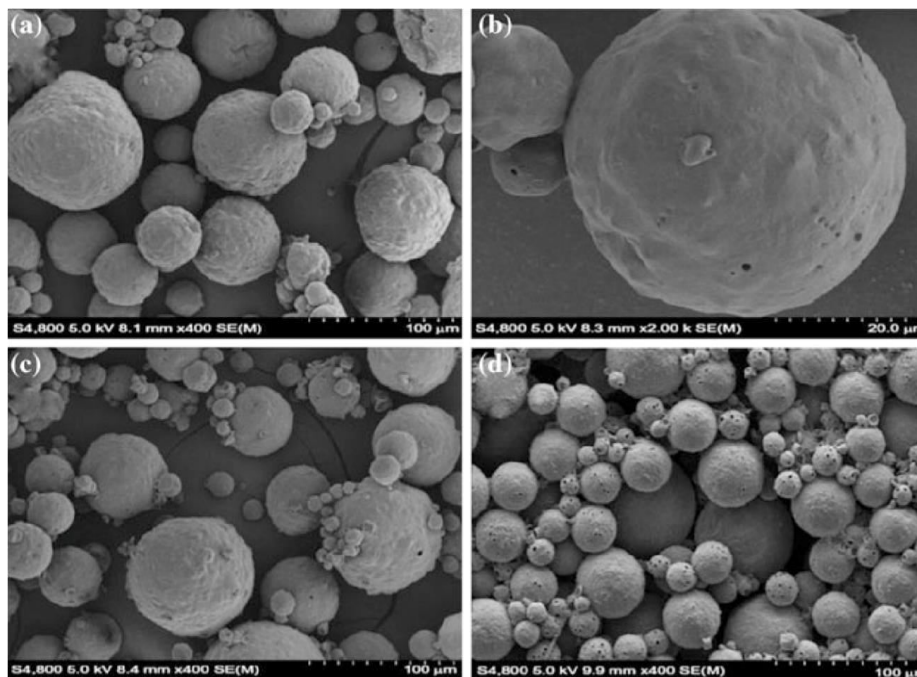


Fig.1 SEM pictures of the morphology of BSA-loaded microspheres made with varying surfactant ratios of Tween 80 to Span 80 of 3:2 (a and b), 7:3 (c), and 4:1 (d) (reproduced with permission from Dove Medical Press for Chen et al. 2014).

IX. DRUG RELEASE MECHANISM FOR NANOGELS

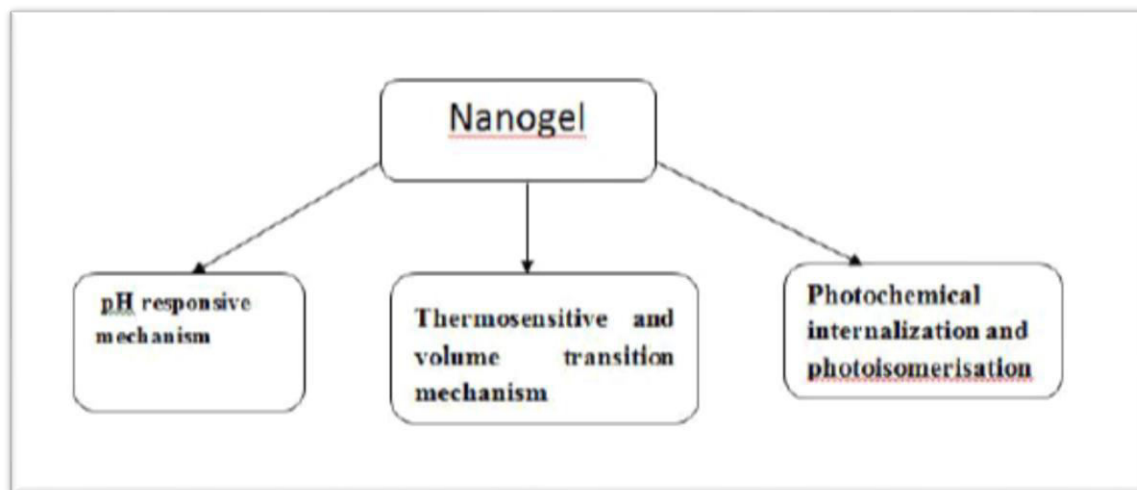


Figure No.2 Drug release mechanism of Nanogel

Drug delivery systems are often designed to carry drugs and distribute them in a regulated manner to the problematic location in order to increase drug concentration. To achieve the optimal therapeutic effect, the characteristics affecting medicine release should be considered during the design stages. These parameters are connected to I drug-material interactions, which are determined by numerous characteristics such as the drug's and carrier's hydrophilicity/hydrophobicity, and ii) the carrier's biodegradability processes and clearance time (Felice et al., 2014). Controlling the pace of drug release profile and biodegradation, as well as systemic circulation stability, is a difficult task. In addition, many drug delivery systems exhibit a burst release event, which is characterised by an initial significant bolus release of drug following the administration of the drug delivery system or its insertion in the release medium (Felice et al., 2014; Huang and Brazel, 2001). As a result, hydrophilic and hydrophobic medicines are lost from circulation shortly after administration. Within the nanogel, a limited amount of medication remains intact and is able to reach the target spot (Soni and Yadav, 2016). A combination of polymer or modified polymers should be utilised to inhibit the release of the medication from the nanogel, preferably in a regulated manner, in order to control the drug's release. Siepmann et al. (Siepmann and Siepmann, 2008) provided a thorough analysis of the many processes influencing drug release. The aqueous phase at the nanogel's surface, aqueous penetration, drug dissolution, change of excipient transition phase, excipient degradation, change in microenvironment, or simple diffusion can all cause drug release from nanogels. Chemical or physical triggers alter their swelling behaviour or cause breakdown of the polymeric network and structure, affecting the drug release profile. Temperature, pressure, electrical, and magnetic fields are the most common physical triggers, whereas pH, ionic change, enzymes, and chemical agents are the most common chemical triggers (Luckanagul et al., 2018; Ullah et al., 2015; Zhu et al., 2019). Simple diffusion, chemical, and physical triggers are the three basic release mechanisms that have been reported: Fick's law (Fick, 1995) governs drug release by diffusion. The polymer chain acts as a physical impediment to solute release by lowering the average free volume available to the solute. As a result, the density of polymer chains can be used to regulate medication release via diffusion (Amsden, 1998). ii) Physical triggers, such as temperature, irradiation, and others, can promote swelling or breakdown of the polymeric network, influencing drug transport. The increase in matrix area exposed to the dissolution liquid caused by the triggering phenomena controls the release kinetics (Bettini et al., 1994). iii) The drug's chemical release mechanism is based on polymer chain breakdown, which causes hydrolysis of the gel network, resulting in surface erosion and drug diffusion (Lin and Metters, 2006).

X. pH RESPONSIVE MECHANISM

Mechanism that reacts to the presence of pH Reactive oxygen species scavenge the on & off catalytic activity by platinum nanoparticles containing nanogel and for the reason of protonation of crosslinked poly (2 – (N, N – diethylamino) methacrylate) core and PEG in the acidic skin pH due to protonation of crosslinked poly (2 – (N, N – diethylamino) methacrylate) core and PEG [11]. When the pH is low, the polymers methacrylic acid – ethyl acrylate are

insoluble 3D structures. Acidic groups ionise due to polymeric chain repulsions when the pH is elevated, resulting in a particular release profile of procaine hydrochloride [14]. The swelling impact of PH sensitive polyacrylic acid chains in the medication temozolidine regulates the release kinetics [24]. The release of doxorubicin was considerably increased due to the pH sensitivity of glycol chitosan nanoparticles and the grafting of diethylaminopropyl groups [25]. The pH of human tissues changes, as does the pH of dysregulated cellular microenvironments, such as inflammation or cancer. As a result, pH-triggered release systems hold a lot of promise for achieving precise drug release at the diseased site. Crosslinked polyelectrolytes containing weak acidic or basic groups, or a combination of both, make up pH-sensitive nanogels (Zha et al., 2011). The degree of ionisation of the polyelectrolyte chain fluctuates as the pH of the environment changes. Deprotonation generates an increase in osmotic pressure, swelling, and porosity in the polymer, which causes electrostatically bonded molecules to be released (Tan et al., 2010).

XI. THERMOSENSITIVE & VOLUME TRANSITION MECHANISM

When temperatures are kept above the lower critical solution temperature (LST), thermosensitive polymers such as poly (N – isopropyl acrylamide) cause early shrinkage in gel volume and indomethacin drug efflux [17]. The polymer (N – isopropyl acrylamide – co – acrylamide) with 5 – fluorouracil is helpful in rats because of the low temperature and release at body temperature [18]. The pluronic superficial modification of polyethylene mine nanogels has been successfully used as a gene delivery method due to its thermoresponsive features in terms of size [19]. Physical breakdown of the cellular network expands thermally triggered volume of poly alkylene oxides nanogels up to 1 m in nanogel size [20].

The lower critical solution temperature could be changed by changing the polymer ratio in nanogels such as poly (N – isopropyl acrylamide) and chitosan, and used in hyperthermic cancer treatments [21].

XII. PHOTOCHEMICAL INTERNALIZATION & PHOTO ISOMERIZATION

Excitation of photosensitizer-loaded nanogels produces singlet oxygen and reactive oxygen, which causes oxidation of cellular compartment walls such as endosomal barrier walls, allowing therapeutics to enter the cytoplasm more easily, which would otherwise be hampered by intracellular compartment [22]. Utilizing photoregulation in the azobenzene the Cis – trans isomerization, it was discovered that when an azo dextran loaded nanogel with aspirin as a model drug was exposed to 365 nm radiation, the E – configuration of the azo group resulted in a better drug release profile than the Z – configuration [23].

XIII. MECHANISM OF DIFFUSION

Doxorubicin is a stable hydrogel nanoparticle based on puronic block copolymer that follows diffusional release. Various nanomedicines, such as polymeric micelles that have already reached the clinical stage, use this mechanism and straightforward technique.

XIV. APPLICATION OF NANOGELS

1. Therapeutic and Biomedical Applications of Natural-Based Nanogels.

Natural polymers are known to have certain specific advantages and exceptional characteristics over synthetic polymers, such as good biocompatibility, non-toxicity, degradability, non-antigenicity, high nutritional value, and extraordinary drug binding capacity, as well as the possibility of less opsonization by the reticuloendothelial system (RES) and good stability during storage and in vivo conditions (E). Nanogels, on the other hand, have hydrophilicity, flexibility, versatility, high water absorption, and biocompatibility, as well as a tiny size, and can target active chemicals to the chosen biophase actively or passively. Biodegradability, cellular absorption, and drug release are all affected by nanoparticle size. When nanogels are disseminated in water, they maintain a highly stable structure. A strong

interaction between drug and polymer can reduce nanogel hydrophilicity and cause the structure to collapse, entrapping drug molecules irreversibly and increasing the hydrophilicity of the nanogel matrix (Kabanov and Alakhov 2002; Vinogradov et al. 2002), and surfactant or monomers present in nanogels can cause adverse effects in formulations (Kabanov and Alakhov 2002; Vinogradov et al. 2002). (Kabanov and Alakhov 2002; Vinogradov et al. 2002). Garg and Goyal (2014, Garg and Goyal). Drug loading efficiency and drug release regulation are both low in some nanogels (Wang and von Recum 2011).

2. Ophthalmic Nanogel

Stopping Bleeding by Nanogel

Even in serious gashes, a protein molecule in solution that has been employed to produce a nanogel has been used to stop bleeding. The proteins have a mechanism for self-assembling into a biodegradable gel on the nanoscale [28].

3. Nanogel as NSAIDS

To make the nanogels, NSAIDS Carbopol and Hydroxypropylmethylcellulose (HPMC) with the desired viscosity were utilised. To make bilayered nanoparticles, the same polymer chitosan and poly – (Lactide – co – glycolic acid) were employed, and the surface was changed using oleic acid. As an example, two anti-inflammatory medicines, spantide II and ketoprofen, were synthesised in nanogel and administered topically to treat allergic contact dermatitis and psoriatic plaque. The findings suggest that nanogel improves the absorption of these two medications into deeper skin layers via percutaneous absorption for the treatment of diverse skin inflammatory conditions [29].

4. Autoimmune Diseases and Nanogels

With mycophenolic acid, oligomers of lactic acid – poly (ethylene glycol) that were ended with an acrylate end group, and Irgacure 2959 photo initiator, cyclodextrin quickly solubilized the loading liposomes. The PEG oligomers are photopolymerized after being subjected to UV light. Due to their innate capacities to bind to immune cells in vivo and allows high localised concentrations of mycophenolic acid, nanogels have a stronger systemic accumulation than free fluorescent tracer. This mode of drug delivery will increase patient compliance while also delaying the onset of renal impairment, which is a common lupus complication [30].

5. Nanogel in Cancer

Nanogel is utilised in cancer to deliver particular targeted drugs with low toxicity and high therapeutic efficacy.

XV. DRUG DELIVERY SYSTEMS

Pills, ointments, eye drops, and intravenous solutions are the most common types of medication administration. New medication delivery methods have been developed in a variety of ways. Chemically modified medicines, drug entrapment in polymeric materials, and drug entrapment in microscopic pores that are injected subsequently into the bloodstream are examples of these systems (Sali 2016).

Nanohydrogels have shown to have strong therapeutic activity at the target site, with long-lasting effects on the target area over days or even weeks (Thampanchira et al. 2016).

Nanogels provide an internal three-dimensional environment for the loading of (bio) molecular drugs, and when compared to conventional hydrogels and other nanoparticles, they are expected to have a higher drug loading capacity and perform one or more of the following functions: drug protection by minimising drug degradation and inactivation during administration; site recognition by increasing the fraction of drug delivered in the pathological area; and actuation by drug release activation through an enzymatic reaction. Due to the importance of size distribution in drug delivery, evenly sized nanoparticles must be prepared (Pujana et al. 2013). Injectable, oral, topical, implantable, inhalable, and transdermal drug delivery are among the applications for which nanoscale drug delivery systems can be created by combining diverse biological and synthetic modules.

According to Sivaram et al. (2015), some nanogels interact with proteins more strongly by forming complexes than liposomes or amphiphilic peptide carriers. These complexes have the ability to absorb proteins from within cells. Shimoda et al. (2011) developed a nanogel based on ethylenediamine and cholesteryl group-bearing pullulan for intracellular protein delivery. A two-step procedure was used to make a hybrid nanogel made of cadmium chloride quantum dots, super paramagnetic Fe₃O₄, and chitosan loaded with the anti-diabetic medication insulin (Shen et al. 2012). Thioglycolic acid-capped cadmium chloride quantum dots were produced using a hydrothermal method, and

subsequently Fe₃O₄ nanoparticles were added to ensure superparamagnetic properties. A hybrid nanogel was created by crosslinking with chitosan. At pH 7.4, insulin loading hybrid nanogels had the best insulin release profile.

Lim et al. (2010) used a novel injectable bone morphogenic protein-loaded alginate nanohydrogel to help human bone marrow stromal cells proliferate and differentiate into osteoblasts.

Hyaluronic acid nanogels can improve hydrophobic drug water solubility, control drug release at the target location in response to external stimuli, improve biocompatibility and bioavailability, and reduce non-specific adverse effects (Zhang et al. 2014).

In the disciplines of medicine and pharmacy, loading metallic nanoparticles in polymeric materials has a wide range of uses (Jovanovic et al. 2011; Juby ET al.2012). Because of its excellent antibacterial and anticancer action (Petchthanasombat et al. 2012) and inexpensive cost of manufacture, zinc oxide (ZnO) has become a preferred nanosized metal oxide. ZnO is non-toxic in the micron size range, but when lowered to nanoscale dimensions, it may create a new type of toxicity. In polymeric nanogels, the introduction of nanosized metal-oxide nanoparticles allows for a slow and sustained release rather than a burst release. A covalently crosslinked sodium alginate/gum acacia nanogel filled with ZnO nanoparticles capable of sustained release behaviour was described (Chopra et al. 2015).

Non-specific drug accumulation and its side effects are one of the most difficult aspects of cancer chemotherapy. Nanotechnology aids in the development of medication delivery agents capable of eliminating cancer cells while causing minimal damage to healthy normal cells, as well as eradicating cancer cells before they can multiply into a tumour (Uthaman et al. 2014).

D'Arrigo et al. (2014) investigated gellan-based nanohydrogels for the treatment of cancer cells by combining an anticancer medication (paclitaxel, PCT) with the steroid prednisolone for combination therapy. Prednisolone was chemically linked to the polymer for this purpose, and the anticancer medication was put into the network using the solvent casting approach. PCT may have been loaded within the hydrophobic domains created by the interaction with prednisolone, according to one theory.

XVI. CONCLUSION

The convergence of nanoscience and biomedical applications has resulted in significant advances in nanomedicine, particularly in biomedical research and clinical procedures, such as drug delivery systems. A detailed overview of published studies on nanogels, transdermal drug delivery systems, Drug Release Mechanism for Nanogels, and numerous nanogel applications is provided in this report. Overall, the data gathered from the literature and presented in this review demonstrated an increasing interest in nanogels and their potential to address issues in the treatment of severe diseases. The mechanism of the blood-brain barrier and cytosolic destination over endosomal or nuclear destinations will need to be studied in the future for precise and targeted drug delivery.

Nanotechnology is being used in medicine to produce better therapies and diagnostic methods for many ailments. This field's research moves at a breakneck pace, nearly on a daily basis. Because of their potential to efficiently encapsulate medicines and environmental stimuli controlled release, the multifunctional hybrid nanogel synthesis is focused on drug delivery systems.

REFERENCES

1. Karat H, Murthy RS. Nanotechnology in brain targeting. *Int J Pharm Sci Nanotechnol.* 2008; 1(1):10-24.
2. Vinogradov SV. Nanogels in the race for drug delivery. *Nanomedicine.* 2010 Feb 11; 5(2):165-8.
3. Jain N, Jain R, Thakur N, Gupta BP, Jain DK, Banveer J, Jain S. Nanotechnology: a safe and effective drug delivery system. *Asian J. Pharm. Clin. Res.* 2010; 3(3).
4. Raemdonck K, Demeester J, De Smedt S. Advanced nanogel engineering for drug delivery. *Soft Matter.* 2009; 5(4):707-15.
5. Kabanov AV, Vinogradov SV. Nanogels as pharmaceutical carriers: finite networks of infinite capabilities. *Angewandte Chemie International Edition.* 2009 Jul 13; 48(30):5418-29.
6. Dorwal D. Nanogels as novel and versatile pharmaceuticals. *Int J Pharm Sci.* 2012; 4(3):67-74.
7. Lee H, Mok H, Lee S, Oh YK, Park TG. Targetspecific intracellular delivery of siRNA using degradable hyaluronic acid nanogels. *Journal of Controlled Release.* 2007 Jun 1; 119(2):245-52.
8. Hayashi H, Iijima M, Kataoka K, Nagasaki Y. pHsensitive nanogel possessing reactive PEG tethere chains on the surface. *Macromolecules.* 2004 Jul 13; 37(14):5389-96.



9. Hasegawa U, Shin-chirp MN, Kaul SC, Hirano T, Akiyoshi K. Nanogel-quantum dot hybrid nanoparticles for live cell imaging. *Biochemical and biophysical research communications*, 2005; 331(4): 917-21.
10. Sun H, Yu J, Gong P, Xu D, Zhang C, Yao S. Novel core-shell magnetic nanogels synthesized in an emulsion-free aqueous system under UV irradiation for targeted radiopharmaceutical applications. *Journal of magnetism and magnetic materials*, 2005; 294(3): 273-80.
11. Oishi M, Miyagawa N, Sakura T, Nagasaki Y. pHresponsive PEGylated nanogel containing platinum nanoparticles: Application to on-off regulation of catalytic activity for reactive oxygen species. *Reactive and Functional Polymers*, 2007; 67(7): 662-8.
12. Kageyama S, Kitano S, Hirayama M, Nagata Y, Imai H, Shiraishi T, Akiyoshi K, and Scott AM, Murphy R, Hoffman EW, Old LJ. Humoral immune responses in patients vaccinated with 1- 146 HER2 protein complexed with cholesteryl pullulan nanogel. *Cancer science*. 2008 Mar 1; 99(3):601-7.
13. Raemdonck K, Demeester J, De Smedt S. Advanced nanogel engineering for drug delivery. *Soft Matter*. 2009; 5(4):707-15.
14. Mourey TH, Leon JW, Bennett JR, Bryan TG, Slater LA, Balke ST. Characterizing property distributions of polymeric nanogels by sizeexclusion chromatography. *Journal of Chromatography A*, 2007; 1146(1): 51-60.
15. Zhang S. Emerging biological materials through molecular self-assembly. *Biotechnology advances*, 2002; 20(5): 321-39.
16. Rinaudo M. Non-Covalent Interactions in Polysaccharide Systems. *Macromolecular bioscience*, 2006; 6(8): 590-610.
17. Shin Y, Chang JH, Liu J, Williford R, Shin Y-K, Exarhos GJ. Hybrid nanogels for sustainable positive thermosensitive drug release. *Journal of controlled release*, 2001; 73(1): 1-6.
18. Wang Q, Xu H, Yang X, Yang Y. Drug release behavior from in situ gelatinized thermosensitive nanogel aqueous dispersions. *International journal of pharmaceutics*, 2008; 361(1): 189-93.
19. Im Lee J, Yoo HS. Pluronic decorated-nanogels with temperature-responsive volume transitions, cytotoxicities, and transfection efficiencies. *European Journal of Pharmaceutics and Biopharmaceutics*, 2008; 70(2): 506-13.
20. Lee Y, Park SY, Kim C, Park TG. Thermally triggered intracellular explosion of volume transition nanogels for necrotic cell death. *Journal of Controlled Release*, 2009; 135(1): 89-95.



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