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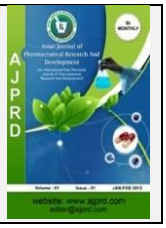

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Review Article

Nanogels as Advanced Topical Drug Delivery Systems: Innovations and Therapeutic Potential

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A B S T R A C T

Nanogels constitute a significant advancement in topical drug delivery systems, effectively addressing critical limitations inherent in conventional formulations such as poor solubility, limited bioavailability, and systemic toxicity. These nanoscale, three-dimensional polymeric networks exhibit distinctive properties including high water content, biocompatibility, and responsiveness to physiological stimuli such as pH, temperature, and enzymatic activity, thereby facilitating controlled and targeted drug release. Nanogels enhance dermal penetration via multiple pathways, improve drug stability, and mitigate local irritation, rendering them particularly suitable for managing dermatological conditions including acne, psoriasis, and atopic dermatitis. Fabrication techniques such as free radical polymerization, ionic gelation, chemical crosslinking, and self-assembly enable the customization of nanogel characteristics to meet specific therapeutic requirements. Despite challenges related to stability, scalability, and production costs, nanogels offer considerable advantages including sustained drug release, targeted delivery, reduced systemic toxicity, and enhanced bioavailability for both hydrophilic and hydrophobic agents. Current review emphasizes the development of smart, stimuli-responsive nanogels and personalized medicine applications, aiming to translate promising preclinical outcomes into clinical practice. Overall, nanogels represent a promising class of next-generation drug carriers, offering safer, more effective, and patient-centric topical therapies.

Keywords: Nanogels, Topical Drug Delivery, Stimuli-Responsive, Controlled Release

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INTRODUCTION:

Two primary challenges exist for drug delivery systems. First the solubility of drugs is an issue, with approximately 40% being classified as poorly-soluble, thus causing low absorption into the body and requiring high dosages, thereby increasing the risk of toxicity(1).Second, the majority of currently available drug delivery methods do not allow delivery to a specific area within the body; therefore, drugs delivered via these systems are distributed throughout the entire body,causing damage to normal cells (as in the case of chemotherapeutic-related toxicity). This has driven the development of more targeted systems such as liposomes or nanoparticles which provide better accuracy for drug delivery and increased therapeutic safety(2).

Nanotechnology encompasses the development, creation, and application of materials and devices on the nanoscale (1-100 nm),where unique physicochemical properties develop that differ from those of the bulk material.Nanotechnology has changed the way drugs are delivered by allowing for more accurate control over the amount of drug released from a particular delivery device(3).

Advanced drug delivery systems are an adequate answer to the shortfalls associated with traditional pharmacotherapy, for example, low aqueous solubility of drugs contributes directly to poor therapeutic outcomes due to both low bioavailability of poorly soluble agents,which require larger doses and higher risk of systemic toxicity, and the non-targeted delivery of drugs, whichsubjects healthy tissues to toxic effects, resulting in myelosuppression and nephrotoxicity. The development of advanced drug delivery systems, such as nanoparticles, liposomes, polymeric micelles, and antibody-drug conjugates, provides improved drug solubility, prolonged circulation time,and spatial delivery of the drug resulting in a greater therapeutic index and less off-target toxicity(4).

Among these, nanogels have gained significant attention as versatile and efficient carriers for drug delivery.

NANOGELS:

Nanogels are polymers designed at the nanoscale and 3D crosslinked to form a polymeric structure with a high-water content and stable shape(5). Due to their unique physical and chemical characteristics, such as high surface area, adjustable size, biocompatibility, and responsiveness to external factors, they hold potential for many types of biomedical applications(5). Various therapeutic agents that can be encapsulated within these systems include small molecules, proteins, and nucleic acids. Encapsulation serves to protect these agents from degradation and allows for the controlled and sustained release of the drug over time (5,6). Nanogels have shown significant potential for improving topical drug delivery systems, in part because they improve skin penetration, allow for drug action at the site of use, and reduce systemic side effects(7,8).Due to their soft and pliable nature, as well as their high-water content, nanogels enhance the interaction with the outer layer of the skin (the stratum corneum), increase hydration, and enhance drug permeation across the stratum corneum(7,8). This makes nanogel formulations an attractive option for the treatment of various dermatoses (e.g., psoriasis and acne), providing localized drugdelivery with minimal systemic side effects(7,8).

Advantages of Nanogels Over Conventional Drug Delivery Systems

Nanogels offerseveral advantages over traditional drug delivery methods (e.g., creams, ointments, and solutions). They are more effective at encapsulating drugs than other formulationsand, therefore, protect drugs from breaking down through enzymatic activity or being released prematurely(6). Nanogels penetrate deeper into tissues and distribute more evenly at the site of action than traditional carriers (9). Nanogels can also respond to changes in temperature and pH and exhibit redox activity under these conditions. This enables more controlled drug delivery compared to traditional delivery systems(10). Because nanogels are biocompatible and have a high-water content, patients experience less local irritation and have greater compliance than with traditional topical formulations (11). Finally, by providing localized drug effects, nanogels reduce the amount of drug absorbed systemically and decrease the side effects associated with the drug delivery; which is a significant limitation of traditional delivery approaches (9, 11).

Types of Nanogels

Based on Polymer Type

Natural Polymerbased Nanogels

Nanogels made from natural polymers, consist of biocompatible polysaccharides and proteins(9). Chitosan nanogels have been studied most thoroughly as a cationic polymer with mucoadhesive properties, as well as having the capacity to create stable, cross-linked networks for binding both hydrophilic and hydrophobic drugs (12). Alginate nanogels, however, are anionic polymers that gel using divalent cations, such as calcium ions, and are incredibly biocompatible, as well as capable of gelling under mild conditions suitable for preserving sensitive biomolecules, such as proteins and nucleic acids (13,6). Both chitosan and alginate nanogels are biodegradable, are non-toxic, and are readily functionalized for targeted drug delivery, making them excellent candidates for the pharmaceutical and biomedical industries (9, 12, 13).

Synthetic Polymer-Based Nanogels

Nanogels are made of synthetic (versus naturally occurring) polymer-based materials. They are made with polymers that can be defined chemically, and thus can be produced with much greater reproducibility and tunability as compared to naturally occurring polymer materials(9). Nanogels have been produced using PEG polymers that have stealth properties owing to the reduction in opsonization, resulting in an increased duration of systemic circulation, thus increasing drug bioavailability (9). Additionally, nanogels based on polyacrylamide polymers provide excellent mechanical stability, tunable porosity, and large drug-loading capacities, which allows controlled and sustained release of drugs (6). Owing to the high degree of control over the density of crosslinking, size, and surface chemical properties of nanogel particles, these synthetic nanogel materials can provide great versatility as advanced therapeutic delivery systems (6).

Based on Responsiveness to Stimuli

pH-Sensitive Nanogels

Nanogels that are sensitive to pH were designed to be stable at regular body temperatures and to swell or break down when exposed to acids. This swelling or breakdown triggers the release of drugs from the nanogels at specific locations. The first study conducted on this technology used cancer therapy as a prime example because the acidic environment created around the tumor by the Warburg effect allowed drugs to be selectively released from the nanogels only inside the tumor and to left healthy cells unaffected (14). One way that this technology can also be leveraged through topical application,and topically applied pH-responsive nanogels can utilize the slightly acidic pH of the skin (pH between 4.5 and 5.5) to regulate the release of drugs from the nanogels, thus improving the localized treatment of skin inflammatory conditions such as psoriasis and eczema (11, 15,8).

Temperature-Sensitive Nanogels

Nanogels that exhibit temperature sensitivity have been extensively studied as stimulus-responsive systems for drug delivery. The leading material used for fabricating temperature-sensitive nanogels is poly(N-isopropylacrylamide) (PNIPAM), which has a lower critical solution temperature (LCST) of approximately 32 °C, close to the physiological temperature of the skin, making it an excellent candidate for topical and transdermal drug delivery applications (7). Below the LCST, the PNIPAM polymer chain exists in a swollen, hydrophilic state, providing a mechanism for retaining drugs within the network. Conversely, above the LCST, the polymer chain collapses to release the drug from the network in a controlled manner (7). This thermoresponsive behavior enables controlled drug release during localized inflammation or upon external heat

application, resulting in a precise and non-invasive therapeutic approach (8).

Enzyme-Responsive Nanogels

Nanogels that respond to enzymes offer the possibility of creating systems that release therapeutic agents in a highly selective manner, due to their ability to release their contents only when exposed to specific types of enzymes known as triggers, which are overexpressed in pathological tissues (16). One example of an enzymetrigger is matrix metalloproteinases (MMPs), which have been shown to be elevated in tumor microenvironments and inflamed tissues(16). Nanogels can extend their therapeutic effects to diseased tissues and limit systemic exposure by including nanogel matrix substrates/cleavable crosslinks designed to be cleaved by specific MMPs as triggers (16,9).

Method of Preparation of Nanogels for Topical Drug Delivery

Nanogels are hydrophilic polymers with a three-dimensional nanoscale network, exhibiting hydrogel and nanoparticle characteristics (17). The method of nanogel preparation is extremely important in determining the size of the particle, degree of crosslinking, extent of gel swelling, drug retention, and skin penetration ability of nanogel(11, 18). Several fabrication methods exist for producing nanogels for topical applications. The method used to produce them depends on the type of polymer used, the type of drug being used, and the desired release properties being of the formulation(17, 19).

Free Radical Polymerization

Free radical polymerization of synthetic monomers is the most common method used to synthesize nanogels with precise control over the synthesis process (19). This method involves treating water-soluble monomers like N-isopropylacrylamide (NIPAM) and acrylic acid (AA), simultaneouly with a bifunctional crosslinking agent, most frequently N,N′-methylenebisacrylamide (MBA), using a free radical initiator, such as ammonium persulfate (APS)(19, 20). Polymerization and crosslinking of the polymers occur in the same aqueous phase, resulting in the direct production of a three-dimensional gel network at the nanometer scale (19). Other variations of free radical polymerization include surfactant-free emulsion polymerization (SFEP) and mini-emulsion polymerization (MEP). Methods like precipitation polymerization are being explored and developed, with varying degrees of control over the number of nanogel particles and their respective size distributions(19). For topical drug delivery, free radical polymerization has also been used to create pH-responsive nanogels (such as gelatin-g-poly(acrylic acid) nanogels cross-linked with the aid of APS and MBA), which enables the controlled release of drugs through the stratum corneum of the skin when exposed to pH changes that occurring on the skin (20). Nanogels made by this process typically have a particle size between 50 and 300 nm, and the particle size can be modified by changing the ratio of the monomer to the crosslinker, initiator concentration, and polymerization temperature (19, 20).

Physical crosslinking (Ionic Gelation)

Physical crosslinking, especially via ionic gelation, is the most frequently used technique for preparing nanogels from natural sources like chitosan, alginate, and gellan gum. Owingtoits ease, low temperatures, and elimination of potentially hazardous chemicals, this method is favored for topical applications (17, 21). Ionic gelation takes place when a positively charged polymer (like chitosan) is mixed with a negatively charged agent (like sodium tripolyphosphate), and they interact with one another to create an electrostatic bond(21). No organic solvents, heat, or initiators are required to form these gels, making them ideal for encapsulating compounds that are sensitive to heat (17, 21). Furthermore, chitosan-based ionically cross-linked nanogels are mucoadhesive and enhance penetration. As such, when drugs are applied transdermally using chitosan, the drug remains on the skin surface for longer duration, allowing for increased diffusion through the stratum corneum(22, 18). The size of nanoparticles produced via the ionic gelation method typically ranges from 100 to 600 nm, depending on the ratios of the polymer to the cross-linker, the molecular weight of the polymer, and the manner in which the materials are mixed (17). Particles prepared using ionic gelation generally produce nanogels with over 95% encapsulation efficiency and provide sustained drug release for at least 24h. These performance metrics demonstrate the high suitability of these formulations for topical application(23).

Chemical Crosslinking

Theuse of chemical cross-linking agents, leads to the formation of permanent covalent bonds between polymer chains, resulting in chemically crosslinked nanogels that exhibit superior mechanical stability, structural integrity, and resistance to physiological conditions compared with physically crosslinked systems (17, 21). Common chemical cross-linking strategies include the use of bifunctional agents likeglutaraldehyde, genipin, and EDC-NHS (carbodiimide-based) reagents, which react with the functional groups of natural polymers (chitosan, gelatin, albumin, and hyaluronic acid) to form stable amide, imine, or ester linkages (21). The extent of chemical crosslinking directly affects the mesh size of the gel network, hence controlling the rate of drug diffusion through the nanogel matrix and the swelling characteristics upon exposure to skin secretions and interstitial fluid (21, 18). Increased crosslink density results in stiffer nanoparticleswith viscoelastic properties, lower swelling capacity, and decreased drug release rates, whereas decreased crosslink density results in more compliant nanogels with greater swelling capacity and drug diffusion rates, which can be intentionally adjusted for either localized dermal retention or transdermal permeation (18). Chemically crosslinked nanogels are especially advantageous for topical applications, where sensitive macromolecules (e.g., proteins, peptides, and nucleic acids) can be delivered as a robust covalent network that protects the cargo from degradation by enzymes in the dermal environment (17, 21). The typical size of chemically crosslinked nanogels is approximately 100 to 500 nm (19, 21).

Self-Assembly Method

The self-assembly approach for producing nanogels is becoming increasingly popular as it uses the inherent physical and chemical characteristics of amphiphilic or modified polymers to create nanoscale gel-like structures without the use of crosslinkers or other harsh processing conditions (19, 11). In this method, amphiphilic block copolymers, hydrophobically modified polysaccharides, and supramolecular polymer constructs are dissolved in an aqueous medium and are driven by hydrophobic interactions, hydrogen bonding, or host-guest molecular recognition to self-organize into three-dimensional nanogels (19). Self-assembled host-guest supramolecular nanogels have been shown to serve as penetration enhancers for the topical delivery of drugs as evident from the significantly greater rate of dermal drug permeation from cyclodextrin (CD)-based supramolecular nanogels compared to traditional formulations(24, 25). The self-assembly process is very sensitive to the parameters of the solution, such as the concentration, temperature, pH, and ionic strength of the medium, and these parameters can be utilized to develop "smart" nanogels that will release their drug in a controlled manner based on the microenvironment of the skin(19, 18). Nanogels that are created via self-assembly typically consist of particles that are 20 to 200 nm in diameter, making them the smallest of all variants and therefore very amenable to traversing follicular pathways for topical delivery (18, 22).

Nanogels in Topical Drug Delivery

When counted together, the integumentary system is the largest organ in the body. The skin has many roles but primarily protects us from outside sources through both immune and physical barriers(26). It is composed of three major layers: the epidermis, dermis, and hypodermis (26, 27).The epidermis forms the outermost layer of skin, primarily consisting of keratinocytes and is separated further by four main layers (stratum basale, stratum spinosum, stratum granulosum, stratum corneum (SC)) (26). The SC ranges from approximately 10 to 20 µm in thickness and consists of compacted keratinized dead cells surrounded by a multilayer lipid lamella matrix of ceramides, cholesterol, and fatty acids to create the largest rate-limiting barrier to the transcutaneous delivery of pharmacologic agents (26). Underneath the epidermis liesdermis (approximately 2-3 mm thick) contains collagen and elastic fibers, blood vessels, lymphatics, hair follicles as well as sebaceous glands and acts to provide overall support for the epidermis (27). The hypodermis is the deepest layer of the skin and primarily consists of adipose tissue that acts as a thermal barrier and metabolic storage site (26). To be delivered through the skin (topically), drug molecules that are to be applied topically must pass through the epidermis-dermis-hypodermis layer sequentially via either a transcellular, intercellular lipid or appendageal follicular route, with the SC layer being the primary barrier to drug administration in nearly all instances (27). The vast majority of traditional topical formulations have proven ineffective at sufficiently overcoming the SC barrier leading to the necessity for advanced drug delivery options such as nanotechnologies and/or nanocarrier systems such as nanogels (28).

Advantages of Nanogels in Topical Drug Delivery

Better Skin Penetration

The small size of nanogels (20-200 nm) enables them to penetrate into skin cells through intercellular, transcellular, and follicular pathways, leading to a greater ability to deposit medication deeper within the viable epidermis and dermis than what is typically achieved using traditional forms of medication (29). If the entire stratum corneum is not penetrated by nanogels, they accumulate in hair follicles and skin "grooves" (the furrows around hair follicles) to create concentrated areas where medication is deposited, eventually spreading into deeper areas of the skin (30). In addition, the surface charge of nanogels also affects their ability to penetrate the skin, with cationic nanogels binding to the negative charge on the surface of the skin, enhancing adhesion, retention and, permeation ofdrug at the site of application (29, 30).

Reduced Skin Irritation

Biocompatible, hydrophilic polymers—like chitosan, hyaluronic acid, and PEG—make up most of the composition of nanogels and are typically tolerated by skin tissues tissues, eliminating the needforchemical penetration enhancers or organic solvents that can cause skin irritation in traditional formulation (28, 30). Because they are made up of more than 90% water, nanogels provide a closely mimic the physiological water content of biological tissues;therefore, dryness and mechanical irritation upon application areminimal (28). Drug release from the crosslinked matrix results in no sudden spike in drug concentration on the skin surface, which will help to reduce the risk of local toxicity being caused by an elevated dose (28). A randomized, double blind, placebo controlled clinical trial conducted with 207 subjects who suffered from acne vulgaris confirmed that patients who received nanohydrogels experienced statistically fewer local adverse events compared to those who received traditional gels (13.3% vs 24.7%, p=0.04) (28).

Sustained Drug Release

A cross-linked polymeric structure of nanogels serves as a physical barrier to diffusion and will allow for controlled release of drug by means of a swell-diffuse mechanism once in contact with moisture present in the skin (28, 30). The degree of cross-linking, polymer composition and spatial network can be tailored to the specific therapeutic needs of the condition; therefore, the application will be either localized (epidermal retention) or prolonged (transdermal) (28). In addition, the use of stimuli-responsive nanogels enhances the ability to stimulate the release of the drug based on local changes in pH, temperature and/or proteolytic activity at the site of disease pathology, thus maximizing therapeutic effectiveness while minimizing systemic exposure (28, 29).

Targeted Drug Delivery

Nanogel drug delivery systems provide major advantages over traditional formulations. Their primary advantage is their ability to deliver compounds precisely to the site of drug action. Biological membranes can interact better with the nanogel due to their small particle size and surface

modification potential, which enhances localization of the drug at the target tissue and minimizes unintended effects on other off-target sites(31, 32, 33, 19).

Reduced Toxicity

Another key advantage is reduced toxicity. By enabling controlled and localized drug release, nanogels decrease systemic drug exposure, thereby reducing adverse effects commonly associated with conventional dosage forms (31, 33, 19).This is particularly beneficial in the treatment of chronic conditions and dermatological disorders where prolonged therapy is required.

Improved Bioavailability

Nanogels also contribute to improved bioavailability, especially for poorly water-soluble drugs. Their highwater content and ability to encapsulate both hydrophilic and hydrophobic drugs enhance drug solubilization and stability (28, 32, 31). Additionally, their controlled release properties help maintain therapeutic drug concentrations over an extended period, improving overall treatment efficacy (31, 28).

Applications

Dermatology

Acne Vulgaris

Acne vulgaris is a chronic inflammatory skin disease that affects approximately 85% of adolescents,and it can negatively affect a person's social and mental health. Traditional topical medications for acne vulgaris have poor tolerability, and often have side effects such as skin irritation, which can inhibit patients from following therapies (34). Nanotechnology-based nanogel formulations have provided a means of overcoming the limitations associated with these traditional medication forms by controlling the release of active ingredients, enhancing the transdermal permeation of active compounds, and mitigating localized skin irritation on application (34). Created using mixed micelles (a 50:50 combination of curcumin and fusidic acid) incorporated into a nanogel formulation, the specific formulation showed a uniform, spherical morphology with nanometer size, a negative surface charge, biphasic in vitro release over 48 hours, and a permeation coefficient that was two-fold higher than that of the plain nanogel, as well as an equivalent level of colloidal stability(35).

Psoriasis

Due to their properties of enhancing skin penetration, providing controlled drug release, minimizing systemic side effects, enhancing skin hydration, and aiding in restoring skin barrier function, nanogels are of special consideration in relation to psoriasis(36). An investigational study on nanogels loaded with methotrexate (MTX) against an imiquimod-induced model of psoriasis found that the MTX nanogel demonstrated superior therapeutic efficacy compared to the conventional free-drug gel when subjected to topical application, as evidenced by a more gradual release of MTX over time and more efficient elimination of psoriatic lesions; furthermore, a chitosan-based niosomal methotrexate gel yielded better clinical response with no adverse effects compared to marketed gels (22). In addition, bilayered, surface-modified PLGA/chitosan nanoparticles were incorporated into HPMC/Carbopol nanogels to co-deliver spantide II and ketoprofen to treat imiquimod-treated skin(37). Results from histological analysis of drug-treated versus plain drug gel showed statistically significant reductions in epidermal thickness, an attenuation of rete ridge elongation, and a normalization of keratinocyte differentiation with use of bilayered surfaces nanoparticles ($p < 0.001$) (37).

Atopic Dermatitis

Atopic dermatitis (AD) is an inflammatory skin condition characterized by a defective epidermal barrier, which is caused by an altered skin lipid composition. The skin of AD patients displays a reduction in ceramide 1 content in the stratum corneum as compared with healthy individuals. This decrease in ceramide 1 level disrupts the organization of the lamellar phase of the stratum corneum and leads to a compromised barrier; at the same time the levels of cholesterol are elevated in AD patients(17). Several other skin diseases exhibit a disruption of the lipid barrier due to alterations in ceramide concentrations and increased transepidermal water loss.Although glucocorticoidsare commonly prescribed, they exhibit an unsatisfactory safety profile and limited therapeutic efficacy,the use of encapsulated glucocorticoids in nanodelivery systems improves biocompatibility, bioavailability, topical administration and the overall risk-benefit ratio of glucocorticoids(38). Long-term use of topical glucocorticoids can lead to systemic side effects (including HPA suppression and Cushing's Syndrome) as well as local side effects (including epidermal atrophy and glucocorticoid-induced acne); nanocarrier-based glucocorticoid formulations in combination therapy have been heavily studied to improve the suitability of glucocorticoid therapy for these conditions (39).

Antifungal

Most topical cutaneous mycosestreatments consist of traditional antifungal cream and gel formulations that suffer from a multitude of negative effects associated with their usage. In contrast, miconazole nanogels, which were formulated from gelatin and chitosan, exhibited an approximate maximum drug release of 78%, as confirmed through XRD crystalline morphology characterization and ICH stability compliance; therefore, miconazole-based nanogels represent a highly beneficial method of delivery for the treatment of dermatophytosis(40). Similarly, luliconazole was entrapped within poly(acrylic acid)/sodium carboxymethylcellulose-based nanogels through free radical polymerization, creating particles approximately 259 nm in size and possessing a low polydispersity index of 0.2 (41). Lastly, poly(glycidol) nanogels modified with phosphoric acids were found to adhere to the hyphae of Aspergillus fumigatus and to internalize luliconazole more effectively than unmodified carbomers in protein-rich environments when evaluated against non-functionalized nanogels (42).

Antibacterial

Nanogels have tunable structures that allows targeted and controlled release of drugs which is a major benefit against antimicrobial resistance (which the World Health Organization views as one of the greatest threats to global health) because they can be functionalized with ligands to allow for site-specific delivery of drugs to biofilm-protected and intracellular infection sites (43). The nano-sized dimensions of nanogels also allows them to penetrate into biofilms due to their greater penetration abilitythan mupirocin and silver sulfadiazine against biofilms; they can penetrate directly into the bacterial cells without any toxic damage to host tissues (44). Additionally, common biopolymers used in nanogels, including silk fibroin, alginate, chitosan, collagen, and hyaluronic acid, have intrinsic antibacterial and anti-inflammatory activity.

Anti-Inflammatory Drugs

COX enzyme inhibition is the basis for anti-inflammatory actions of NSAIDs. For optimal effect when applying topically, an NSAID must penetrateinto inflamed regions at the required concentration; for systemic absorption, an drugs lipophilicity, molecular weight, partial charge, and aqueous solubility all contribute to its ability to penetrate into the body (45). A skin-invasive nanogel system using a PLGA/chitosan bilayered nanosphere and co-delivering ketoprofen (an NSAID) and spantide II (a mast cell stabilizer) in HPMC/Carbopol solution generated measurable results that significantly exceeded the topical use of each individual drug ($p < 0.001$) according to H&E and immunohistochemical analyses (17, 37). A sodium diclofenacnanogel created from emulsion/solvent diffusion and incorporated into Carbopol 940 showed optimal skin permeability, stability, and delayed release; nanogel delivery systems further enhance NSAID delivery rates, safety, and reduce the occurrence of systemic adverse events (41).

Limitations

Nanogel systems have many benefits, but several limitations impede their use in a broad range of applications. One of the major limitations is related to stability because nanogels can aggregate together structurally, or leak drugs too soon after being manufactured and stored. Thus, obtaining physicochemical stability over time is a continued concern(22, 46, 17).Scaling up nanogel production poses a significant challenge. The initial stage of production can be done relatively well in a laboratory; however, when trying to reproduce the same results from laboratory-scale processes on an industrial scale, problems may arise with reproducibility and consistency from one batch to another.Furthermore, the cost of production is relatively high compared to conventional drug delivery systems due to the use of specialized polymers and advanced fabrication techniques(17, 18, 33).

Future Perspectives

Drug delivery systems utilizing nanogels have significant promise for future drug development. Smart nanogels are engineered to respond to various physiological stimuli (i.e. pH, temperature, or enzymes), facilitating a new era of targeted drug delivery with increased precision of therapeutic effect(28, 32, 47). A second area that shows great promise is personalized medicine. Drug delivery systems could be personalized based on the patient's characteristics (including their genetics), how they may respond to drug therapy and the specific disease/condition being treated. This results in greater success in treating each patient(28, 22, 31). Ultimately, one of the main goals is to achieve a successful clinical translation. Already, many of the polymeric nanogels have demonstrated effectiveness in the preclinical studies, but more research needs to be done to determine if these products are safe, effective, and can be granted regulatory approval for clinical applications(31, 33).

CONCLUTION

Nanogel Delivery Systems (DDS) are poised to revolutionize modern medicine with their unique engineering characteristics, including nanoscale diameter, high drug loading capacity, exceptional biocompatibility, and controlled release profile. They can encapsulate both hydrophilic and hydrophobic drugs, provide improved stability of drugs, and deliver drugs specifically to the site of action.

Nanogels have also been shown to greatly increase the amount of drug absorbed through the skin, provide extended retention of drugs at a local site, and reduce the overall side effects of the treatment, thereby improving the efficacy of therapy, for various types of skin conditions. In addition, the development of "smart" and "stimuli-responsive" nanogels has extended the application of DDS to the areas of personalized medicine and targeted therapy.

Nanogels, as a component of modern medicine, represent an important advancement toward the creation of safer, more effective, and patient-friendly systems for administering drug therapies. The broad range of applications offered by nanogels (i.e., dermatology, oncology, gene therapy, and vaccine delivery) makes them valuable tools for multiple therapeutic uses. Despite challenges in the areas of stability, large-scale manufacturing, and clinical utilization, researchers and technologists continue to work on methods to resolve these challenges; therefore, it is anticipated that future commercialization will support their continued use in drug therapy and personalized medicine.

In conclusion, the manufacture and application of nanogel-based systems have great potential as next-generation drug carriers and will provide subsequent benefits in areas such as pharmaceutical formulation and targeted therapeutics.

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