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Review

Nanoscale Hydrogel System

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Abstract

Nanoscale hydrogel systems consist of cross-linked polymeric networks that have superb water-retention properties, are biocompatible, and can be loaded with drugs. Nanogels have the capacity to encapsulate small molecules, proteins, peptides, and nucleic acids, thereby protecting them from degradation and allowing for their slow or targeted release. Nanogels are showing enhanced therapeutic efficacy and decreased systemic toxicity in oncology, dermatology, vaccinology, and tissue engineering. Additionally, they can be used to improve the permeability and retention (EPR) effect, which facilitates preferential accumulation in disease sites, particularly in tumors and inflamed tissues. Although these benefits exist, challenges remain in large-scale synthesis, reproducibility, long-term stability, and regulatory approval. This review presents the basic concepts of nanogel design, classification, drug loading, and drug release processes, as well as their biomedical applications and limitations, and their potential as next-generation drug delivery systems.

Keywords: Nanogels, oncology, dermatology, vaccinology, and tissue engineering.

1. INTRODUCTION

Nanotechnology has had a significant impact on studies in biomedical research, particularly in the development of innovative methods for drug delivery. Nanogels are among them, and amidst the others, this type of gel has garnered growing interest because it combines the strengths of hydrogels and nanoscale vehicles. Nanogels are cross-linked polymeric networks that can swell in aqueous conditions, typically ranging in size from 20 to 200 nm. Nanogels find applications in sensing, diagnostics, and bioengineering; however, they are also utilized in the delivery of drugs. Hence, nanogels offer a substitute for delivering drugs that cannot be easily dissolved, which also lack solubility and stability. They can penetrate tissues more and into cells better due to their small size, and they can be encapsulated and deliver therapeutic agents due to the high-water content, high biocompatibility, and protection. This review will then explore the basic nature of nanogels, their various synthesis strategies, major characteristics, and their fast-growing applications, especially in the fields of targeted drug delivery, gene therapy, and medical imaging.

2.PROPERTIES OF NANOGELS

The biocompatibility and degradability of the Nanogel-based drug delivery system are highly biocompatible and biodegradable. Due to these characteristics, it is a highly promising field nowadays.

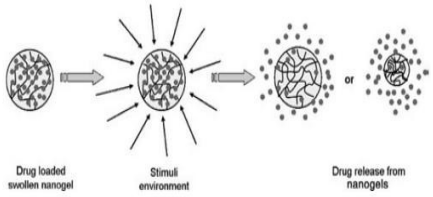

Figure 1.1 Properties Nano Gel

2.1. Swelling Behavior in Aqueous Environments:

The most advantageous characteristic of nanogels lies in their swift swelling and deswelling dynamics.

2.2. Enhanced Drug Encapsulation Capacity:

- The superior drug loading capabilities of nanogels are attributed to the functional moieties present within the polymeric framework. These functional moieties significantly influence drug incorporation and release characteristics, with certain groups possessing the ability to form conjugates with therapeutic agents or antibodies for targeted delivery purposes.
- Furthermore, the existence of functional moieties at the interface with pharmaceutical or protein molecules contributes to enhanced loading efficiency.

2.3 Dimensional Characteristics:

- Nanogels generally exhibit diameters ranging from 20–200 nm, making them sufficiently large to circumvent rapid renal clearance while remaining small enough to evade capture by the reticuloendothelial system.
- Enhanced penetration capabilities result from their exceptionally small dimensions. Notably, these systems can traverse the blood-brain barrier (BBB).

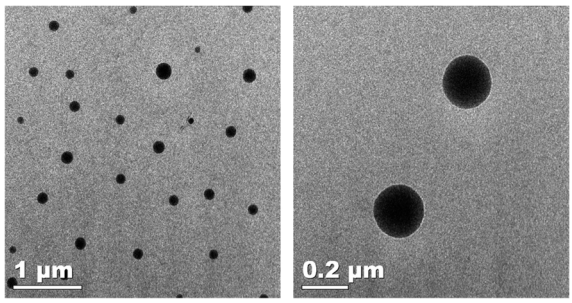

Figure 1.2 Dimensional characteristics

2.4 Solubility:

Nanogels possess the capability to dissolve lipophilic pharmaceuticals and contrast agents within their central structure or gel matrix networks.

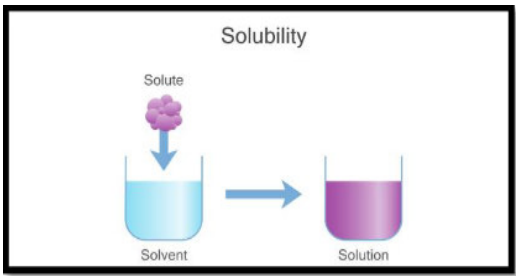

Figure 1.3 Solubility

2.5 Electromobility:
Nanogels can be synthesized without requiring external energy input or severe processing conditions like ultrasonication or mechanical homogenization, which represents a crucial advantage when incorporating biological macromolecules.

2.6 Colloidal Stability:
Nanogels or polymeric micellar nanogel formulations demonstrate enhanced stability compared to surfactant-based micelles and display reduced critical micelle concentrations, diminished dissociation kinetics, and extended drug retention periods.

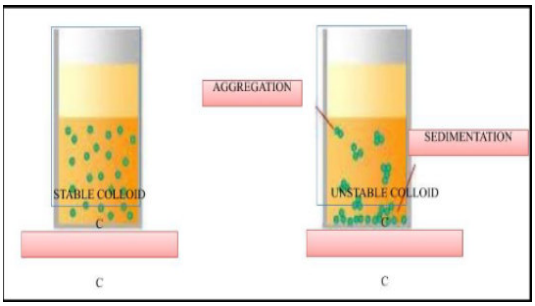

Figure 1.4 Colloidal Stability

2.7 Non-Immunologic Response:
Such pharmaceutical delivery mechanisms typically exhibit an absence of immunological reactions.

3. CLASSIFICATION OF NANOGEL

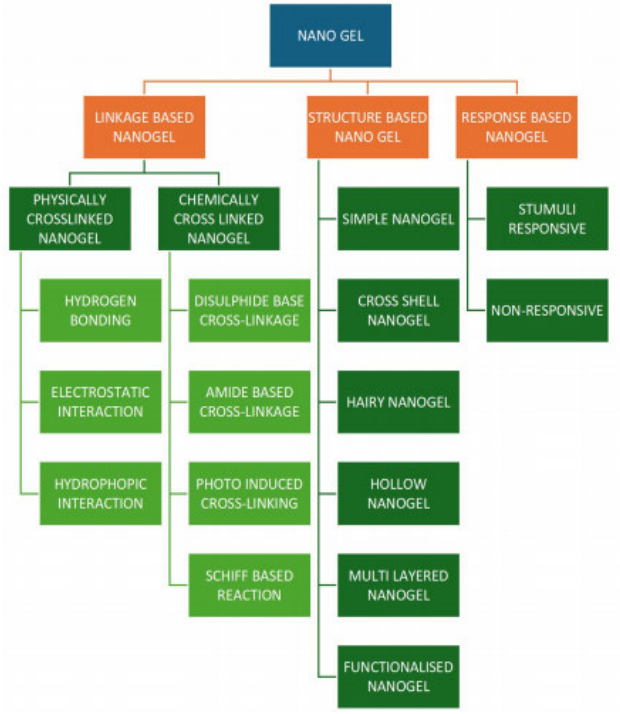

Figure 1.5 Classification of Nanogel

Nanogels may be classified according to their environmental responsiveness or the nature of interactions maintaining their polymeric network structure:

3.1 Non-Responsive Nanogels:
These systems demonstrate basic swelling characteristics upon contact with aqueous media. They uptake water and increase in volume, yet their structural modifications remain largely unaffected by external environmental factors.

3.2 Stimuli-Responsive Nanogels:
In contrast to non-responsive variants, these systems alter their swelling and deswelling characteristics when subjected to particular external stimuli. Environmental parameters, including temperature, pH, ionic strength, or magnetic fields, can control their volumetric changes and therapeutic agent release patterns, rendering them particularly valuable for controlled pharmaceutical delivery applications.

3.3 Classification According to Cross-Linking Mechanism:

Nanogels may additionally be classified based on the cross-linking type present within their polymer network. A significant subcategory includes:

3.3.1 Physically Cross-Linked Nanogels (Pseudo-Gels):

- ❖ Parameters including polymer concentration, gelation temperature, medium ionic strength, and the cross-linking agent utilized substantially influence their characteristics.
- ❖ Various relatively straightforward methodologies are employed for their preparation, encompassing amphiphilic block copolymer association, polymeric chain self-assembly, and electrostatic complexation between oppositely charged polymeric species.

3.3.2 Liposome Modified

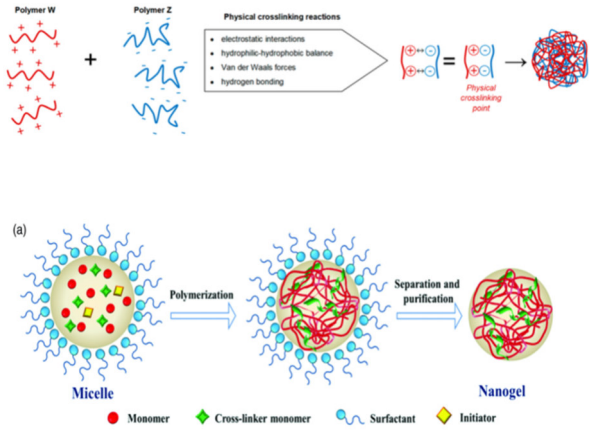

Figure1.6 Liposome Modified Nanogels

Nanogels:

- ❖ Liposome-modified nanogels represent an advanced category of **stimuli-responsive, physically cross-linked**
- ❖ **nanogels** designed for transdermal drug delivery applications. These systems combine the structural advantages of liposomes with the adaptability of nanogels, making them suitable for controlled and targeted delivery of therapeutic agents.

3.3.3 Micellar nanogels:

- ❖ Micellar nanogels represent nanoscale transport systems formed via self-organization of amphiphilic graft copolymers or supramolecular associations between hydrophilic and hydrophobic polymer segments within aqueous environments. This dual-segment configuration produces a core-shell architecture, wherein hydrophobic portions constitute the central core while hydrophilic polymer chains extend peripherally, establishing a stabilizing outer layer (corona).
- ❖ Due to their biocompatibility, structural integrity, and adjustable drug release characteristics, micellar nanogels have attracted considerable interest as efficient platforms for controlled and targeted pharmaceutical delivery.

3.3.4 Hybrid Nanogel:

Hybrid nanogels represent sophisticated delivery systems consisting of nanogel components distributed throughout organic or inorganic matrices, merging the benefits of polymeric networks with hybrid nanomaterial frameworks. These designs capitalize on nanogel structural adaptability combined with matrix stability to achieve superior drug encapsulation and customized release characteristics.

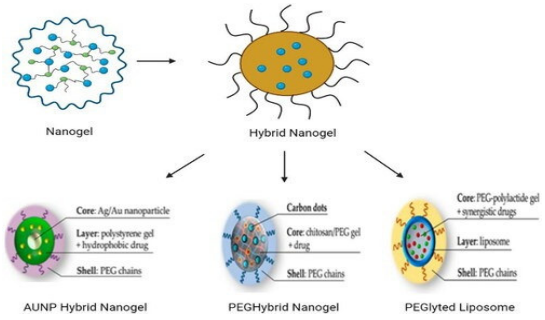

Figure 1.7 Hybrid Nanogel

3.3.5 Optimal Properties of Pharmaceutical Compounds for Nanogel Systems:

The pharmaceutical compound should possess low molecular weight characteristics. The therapeutic agent must demonstrate compatibility with the polymeric materials employed in nanogel fabrication.

3.4 Covalently Cross-Linked Nanogels:

Covalently cross-linked nanogels represent a specialized category of nanogel platforms that exhibit enhanced structural integrity and mechanical properties compared to physically cross-linked counterparts. In contrast to physically cross-linked systems that depend on weak intermolecular forces, including hydrogen bonds, hydrophobic associations, or electrostatic interactions, covalently cross-linked nanogels achieve stabilization through irreversible covalent linkages, offering enhanced robustness and precise drug release control.

Generally, water-soluble polymers or amphiphilic block copolymers serve as preferred foundation materials, as they enable aqueous swelling behavior while ensuring compatibility with various therapeutic compounds. A particularly noteworthy strategy encompasses the development of nanogels within the 20–200 nm dimensional range utilizing polymeric backbones containing pendant sulfhydryl functionalities, which participate in eco-friendly thiol-mediated cross-linking processes. This methodology guarantees biological compatibility while preserving nanogel structural coherence.

4. MECHANISM OF ACTION

4.1 Ph-Responsive Mechanism:

This mechanism involves drug liberation in response to environmental pH variations. Specifically, therapeutic agents are released within distinct physiological compartments characterized by varying pH levels. Optimal drug discharge occurs at specific pH conditions, ensuring targeted delivery to body regions with corresponding pH characteristics. This approach relies on polymers incorporating pH-sensitive functional groups that undergo ionization within the polymeric structure. The deprotonation process leads to enhanced osmotic pressure, matrix expansion, and increased porosity, subsequently facilitating the liberation of electrostatically associated compounds.

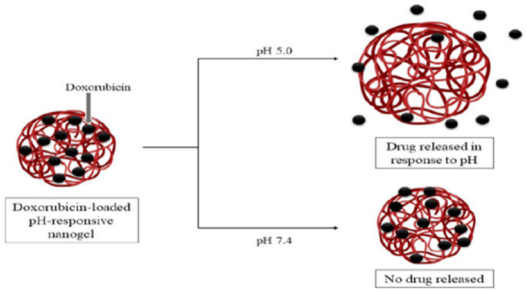

Figure 1.8 pH-responsive mechanism

4.2 Thermosensitive and Volume Transition Mechanism:

Specific nanogels demonstrate temperature-dependent behavior, particularly at a critical threshold termed the volume phase transition temperature (VPTT). At temperatures below the VPTT, the polymeric matrix maintains hydration and expansion, facilitating drug encapsulation and regulated release. However, when environmental temperature exceeds the VPTT, the nanogel experiences rapid contraction, resulting in drug expulsion. Initial thermoresponsive nanogels sometimes produced unwanted cellular damage due to sudden volumetric changes. To address this limitation, polymer composition adjustments have been implemented to optimize the lower critical solution temperature (LCST). A significant illustration involves poly(N-isopropylacrylamide)-chitosan magnetic nanogels, which demonstrate biocompatibility alongside magnetic field-directed drug delivery, rendering them especially valuable for hyperthermic oncological treatments.

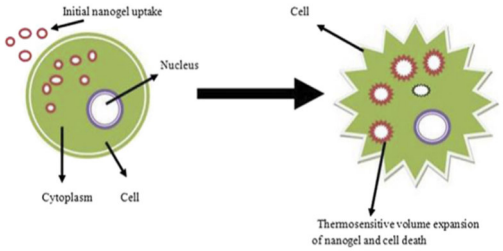

Figure 1.9 Thermosensitive and Volume Transition Mechanism

4.3 Photochemical Internalization and Photoisomerization:

Light-responsive nanogels utilize illumination-triggered structural modifications to control therapeutic agent release. Photoisomerization takes place when compounds containing double bonds (such as azobenzene derivatives) experience conformational transitions from trans to cis configurations following light exposure. Upon illumination of photosensitizer-containing nanogels, reactive oxygen species (ROS), including singlet oxygen, are produced, which oxidize intracellular compartments and promote therapeutic agent diffusion into the cytoplasm.

A representative case involves azodextran nanogels containing aspirin, wherein light-triggered cis-trans isomerization of azobenzene moieties improves drug release effectiveness. In particular, the conversion to the E-configuration of the azo group yields an enhanced release pattern relative to the Z-configuration, illustrating the efficacy of photocontrolled drug delivery systems.

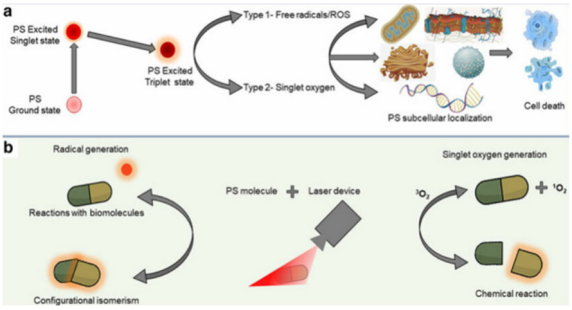

Figure 1.10 Photochemical Internalization and Photoisomerization

5. Formulation of Nanogels

Nanogel formulation encompasses the selection of appropriate polymers, crosslinking agents, and therapeutic compounds, subsequently followed by preparation through designated methodologies. The formulation approach governs nanogel dimensions, stability characteristics, and drug release profiles.

5.1 Polymers Used in Nanogels:

5.1.1 Natural Polymers:

Chitosan, alginate, gelatin, and hyaluronic acid represent common natural polymers. These materials offer biocompatibility and biodegradability advantages. Chitosan nanogels serve as an example for insulin delivery applications.

5.1.2 Synthetic Polymers:

Polyethylene glycol (PEG), polyvinyl alcohol (PVA), polyacrylic acid (PAA), and poly(N-isopropylacrylamide) constitute synthetic polymer options. These materials provide enhanced stability, controlled characteristics, and reproducible properties.

5.1.3 Crosslinking Agents:

Crosslinking establishes stable network architectures through chemical crosslinkers such as glutaraldehyde and carbodiimide, or through physical interactions including hydrogen bonding, ionic interactions, and hydrophobic forces.

5.1.4 Drug Incorporation:

Therapeutic agents may be entrapped within gel networks or adsorbed onto surfaces. Both hydrophilic and hydrophobic compounds can be incorporated, with insulin representing hydrophilic drugs and ketoconazole exemplifying hydrophobic agents.

5.1.5 Additives / Excipients:

Stabilizers prevent aggregation, surfactants regulate particle dimensions, and buffers maintain pH stability within formulations.

5.1.6 Steps in Formulation:

The process involves polymer and crosslinker selection, polymer dissolution in aqueous media, drug addition to polymer solutions, crosslinking reactions (chemical or physical), purification for unreacted material removal, and drying or lyophilization to obtain nanogel powder.

6. NANOGEL SYNTHESIS TECHNIQUES

6.1 Emulsion Solvent Diffusion Approach:

In this technique, the pharmaceutical compound's aqueous solution undergoes solubilization within an organic phase. The polymer and gelling components are dissolved in water to establish the drug-containing phase, which is subsequently introduced dropwise into the aqueous phase that has undergone homogenization at 6000 rpm for 30 minutes. Through homogenizer processing, the emulsion is transformed into nanodroplets, resulting in the formation of an oil-in-water emulsion.

Nanogel formation is achieved by incorporating triethanolamine into the oil-in-water emulsion system, followed by continuous agitation at 8000 rpm for one hour.

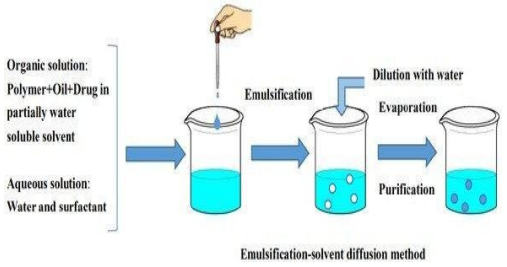

Figure 1.11 Emulsion Solvent Diffusion Method

6.2 Nano Precipitation Technique:

Upon interaction between the organic phase comprising drug and polymer with the surfactant-containing aqueous phase, polymer precipitation occurs. Following the elimination of surplus solvent, polymeric nanoparticles remain. Subsequently, after particle hydration, gelling agents and requisite quantities of nanoparticle suspension are incorporated. pH adjustment is achieved through triethanolamine utilization.

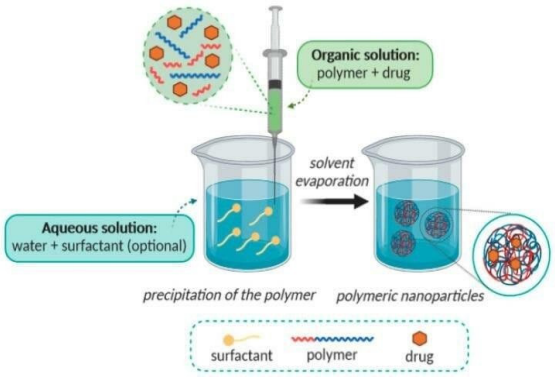

Figure 1.12 Nano Precipitation Technique

6.3 Evaporation of Solvent Method:

Throughout a two-hour treatment period, the pharmaceutical-polymer blend is introduced into the specified region of the aqueous medium. This procedure occurs under constant agitation at 1000 rpm using a magnetic stirring device.46 The resulting nanosponges undergo subsequent filtration, then desiccation in a heated air chamber set at 40°C for a 24-hour duration. The desiccated nanosponges are then meticulously placed into storage containers. For optimal uniform distribution, it is advisable to submerge the polymer in aqueous solution for two hours prior to gel formation initiation. Following this, the polymer requires mechanical mixing at 6000 rpm rotational velocity. pH adjustment is accomplished through the application of a pH-modifying substance. The aqueous mixture is then integrated with the optimized nanosponge dispersion and penetration-enhancing agents.

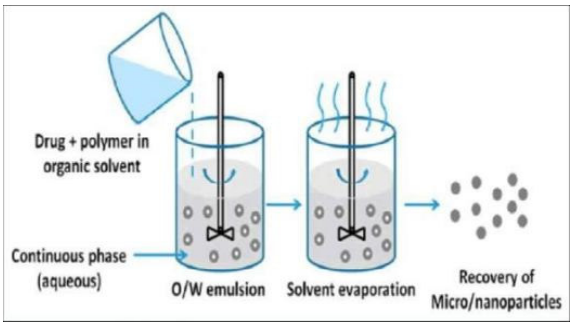

Figure 1.13 Evaporation of Solvent Method

6.4 Reverse Micellar Method:

A polymer, a medication, and a surfactant are dissolved in an organic solvent. After adding the cross-linking agent, it must be incorporated over an extended period of time during the night. After the nanoparticles have been purified, the solvent is evaporated, creating a desiccated bulk. It was created by dissolving the gelling component in water. When nanoparticles and an aqueous phase containing a gelling agent are combined, a nanogel is formed. The application of a neutralizing substance modifies the pH (19).

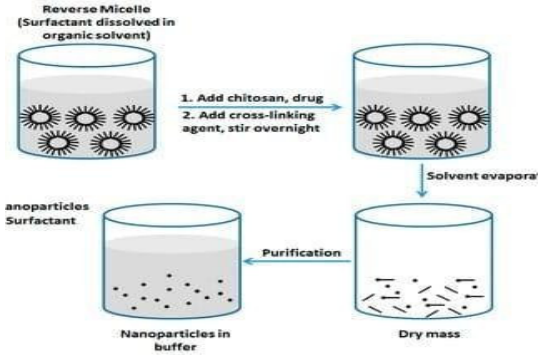

Figure 1.14 Reverse Micellar Method

6.5 Modified Diffusion Emulsification Method:

A polymer-solvent mixture is combined with the pharmaceutical compound according to a precisely determined proportion. The organic phase forms through continuous mixing of the drug-polymer combination within the aqueous phase while maintaining rotational speeds between 5000 and 10,000 rpm. The organic phase is introduced into the aqueous stabilizer solution via a needle-equipped syringe at a controlled rate of 0.5 mL per minute. Following six minutes of agitation at rotational velocities of (10000–25000) rpm, the resulting suspension undergoes sonication treatment for a duration of five to ten minutes.

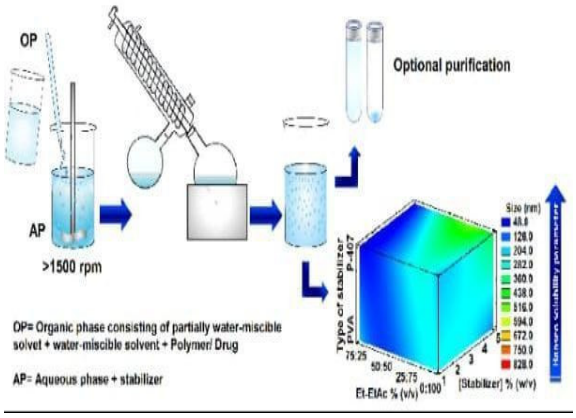

Figure 1.15 Modified Diffusion Emulsification Method

7. ASSESSMENT

These assessments validate the nanogel's appropriateness for pharmaceutical delivery applications, guaranteeing compliance with standards for therapeutic effectiveness, safety profiles, and stability characteristics required for its designated medicinal use.

7.1 Physical Assessment:

a) Physical Characteristics :

Examination of the nanogel's visual properties, pigmentation, and transparency to verify adherence to specified standards and absence of observable particulates or textural irregularities.

b) Yield Percentage

Determination of the nanogel synthesis process efficiency through quantitative analysis.

c) pH Measurement:

Assessment of the nanogel's acidity level to ensure proximity to dermal physiological pH values (approximately 5.5) for irritation prevention.

d) Uniformity:

Visual examination of the nanogel to verify consistent pharmaceutical distribution throughout the gel matrix.

e) Spreadability Analysis:

Quantification of the surface area covered during gel application to skin, indicating application convenience.

7.2 Physicochemical Assessment :

a) Scanning Electron Microscopy (SEM):

Generation of comprehensive structural and morphological imagery of the nanogel, validating nanoparticle presence and organization within the gel framework.

b) Dynamic Light Scattering (DLS):

Methodology employed for determining particle dimensions and size distribution of suspended nanogels through light scattering variation measurements.

c) Stability Investigation:

Evaluation of nanogel's structural and chemical integrity across time under diverse storage environments (including temperature and humidity variations) for shelf-life determination

d) Rheological Analysis:

Investigating the flow characteristics and deformation behavior of the nanogel is essential for understanding its consistency, texture, and performance during both production and application processes.

7.3 Biological Assessment of Nanogel:

Biological assessment encompasses laboratory and animal studies to evaluate safety and therapeutic effectiveness, incorporating cytotoxicity examinations, biocompatibility analyses (including hemolysis testing), therapeutic efficacy demonstrations (such as anti-inflammatory or wound healing properties), and pharmacokinetic/distribution studies to monitor nanogel behavior in biological systems.

A. Laboratory Evaluation:

These represent controlled laboratory investigations utilizing cellular or biological components to examine fundamental characteristics:

a) Laboratory Cytotoxicity Testing:
Determination of nanogel cellular toxicity. Superior biocompatibility (exceeding 70% cell survival) demonstrates nanogel safety for cellular applications.

b) Cellular Internalization:
Evaluation of cellular nanogel absorption efficiency is critical for targeted pharmaceutical delivery to specific cellular or tissue destinations.

c) Laboratory Immunocompatibility:
For immune-related applications, assessing the appropriate interactions of nanogels with immune components, including antigen-presenting cells (APCs).

B. Animal Model Evaluation:
These investigations utilize living animal models to assess the nanogel's overall performance and safety within complex biological environments:

i) Therapeutic Effectiveness:
Demonstration of intended biological effects, including anti-inflammatory responses (quantified through paw edema reduction), antimicrobial activity, or wound healing capacity (measured via wound contraction assessment).

8. APPLICATION

8.1 Local Anesthetics (La):
Local anesthetics represent a pharmaceutical category that provides analgesia and pain relief. The integration of local anesthetics within drug delivery platforms such as nanogels enhances their localized therapeutic administration. Bupivacaine serves as the predominant agent employed in nanogel formulations for local anesthesia, attributed to its efficacy and compatibility with nanocrystal incorporation within the nanogel matrix.

8.2 Cancer Treatment:
Nanogels have demonstrated exceptional potential as drug delivery systems capable of addressing limitations associated with traditional anti-cancer therapeutic approaches while enhancing treatment efficacy. Anticancer agents, including doxorubicin, epirubicin, paclitaxel, and gemcitabine, are encapsulated within nanogel systems to enhance their aqueous solubility, structural stability, and selective delivery to malignant cells (29).

8.3 Autoimmune Disease:
Therapeutic management of autoimmune conditions relies on the drug delivery system's capacity to specifically target and neutralize immune cells responsible for autoimmune responses. Pharmaceutical agents frequently utilized in nanogel systems for autoimmune disorders encompass mycophenolic acid (MPA) for systemic lupus erythematosus, methotrexate (MTX) for rheumatoid arthritis and related conditions, and anti-inflammatory compounds such as curcumin.

8.4 Bone Regeneration:
Effective bone regeneration requires biodegradable cellular scaffolds capable of controlled and localized release of lithium and additional therapeutic agents. Lithium has been demonstrated to enhance osteogenesis (18)

8.5 Diabetics:
Given the increasing global prevalence of diabetes mellitus, innovative therapeutic strategies are being explored for disease management. Pharmaceutical compounds, including metformin, gliclazide, curcumin, and ferulic acid, are incorporated into nanoformulations to enhance therapeutic efficacy and address diabetic complications, such as wound healing, through diverse delivery mechanisms.

8.6 Ophthalmology:
Dexamethasone-loaded ophthalmic formulations were developed through solvent evaporation or emulsification techniques utilizing 2-hydroxypropyl-γ-cyclodextrin (HP γ CD) medium containing γ-CD nanogel for prolonged drug release.

9. Advantages Of Nanogels
Nanogels have garnered considerable interest in pharmaceutical research due to their numerous advantages over traditional drug delivery approaches. The porous polymeric structure enables nanogels to accommodate substantial quantities of therapeutic compounds. These systems facilitate controlled and prolonged release profiles, whereby medications are discharged gradually over extended periods, thereby decreasing dosing frequency requirements. Many nanogels demonstrate excellent biocompatibility and safety profiles,

particularly those constructed from natural polymers such as chitosan, alginate, and gelatin, which exhibit non-toxic and biodegradable characteristics. The amphiphilic properties of nanogels enable encapsulation of both hydrophilic and hydrophobic therapeutic agents with varying solubility profiles. Their nanoscale dimensions (20–200 nm) facilitate efficient tissue penetration and traversal of biological barriers, including the blood-brain barrier. Intelligent nanogels possess responsiveness to environmental stimuli such as pH, temperature, or enzymatic conditions, enabling site-specific drug release. The Enhanced Permeability and Retention (EPR) effect contributes to their therapeutic potential. Nanogels offer versatile functionalization capabilities, as their surfaces can be readily modified with targeting moieties, including antibodies and peptides, enabling active targeting of specific cellular receptors. The stimuli-responsive characteristics allow nanogels to be engineered for response to particular triggers such as pH, temperature, redox environments, or enzymatic activity, making them optimal candidates for intelligent drug delivery applications.

10. LIMITATION

- Despite the numerous benefits of nanogels, several constraints and challenges must be addressed during their development and therapeutic application(49).
- Production economics remain problematic due to the utilization of costly polymeric materials, crosslinking agents, and sophisticated manufacturing technologies. Drug encapsulation capacity exhibits limitations for specific molecular entities, particularly large or hydrophobic compounds that demonstrate poor incorporation efficiency within nanogel matrices(42).
- Crosslinking agent safety poses potential risks, as chemical crosslinkers such as glutaraldehyde may retain harmful residues requiring comprehensive purification protocols and rigorous safety assessments(32). Regulatory compliance creates additional hurdles since nanogel-based delivery systems represent emerging therapeutic technologies subject to stringent regulatory oversight, necessitating extensive toxicological and pharmacological investigations for clinical authorization(31).
- Biological environment instability affects nanogel performance when exposed to physiological conditions, including pH variations, enzymatic activity, and ionic strength fluctuations, potentially causing uncontrolled degradation or premature drug liberation. Manufacturing consistency challenges emerge during large-scale production where maintaining uniform characteristics such as particle dimensions, drug loading capacity, and surface properties proves technically demanding and economically burdensome.
- Material biocompatibility concerns exist regarding certain synthetic polymers employed in nanogel construction that may exhibit cytotoxic or immunogenic responses. Synthesis complexity requires intricate multi-stage procedures that are both time-intensive and financially demanding. Controlled release optimization remains technically challenging when attempting to achieve precise, prolonged, or environmentally-responsive drug liberation in various nanogel configurations.

11. COMMERCIAL NANOGEL FORMULATIONS

11.1 Nanogel-Based Influenza Vaccination (Japan):

Manufacturer: Daiichi Sankyo, Japan; Composition: Live attenuated influenza vaccine incorporated in nanogel matrix; Administration: Intranasal spray delivery; Application: Seasonal influenza prophylaxis; Distinctive characteristics: Eliminates needle requirement and promotes robust mucosal and systemic immune responses(37).

11.2 Nanogel Solar Protection Products (India):

Manufacturer: Ethicare Remedies (extensively distributed across India); Active ingredients: Zinc oxide nanoparticles, Titanium dioxide nanoparticles; Product type: Aqueous nanogel sunscreen formulations with SPF 30/40/50; Application: Comprehensive UVA and UVB radiation protection(38); Distinctive characteristics: Non-adherent texture with

transparent application and superior stability relative to conventional cream formulations(42).

11.3 Diclofenac Nanogel Preparations:
Manufacturers: Multiple Indian pharmaceutical entities (including Cipla, Ranbaxy); Active component: Diclofenac diethylamine (1–2%) within nanogel matrix; Application: Topical anti-inflammatory and pain management; Therapeutic indications: Osteoarthritis, rheumatoid arthritis, muscular discomfort; Distinctive characteristics: Improved penetration through deeper dermal layers resulting in accelerated therapeutic response(39).

11.4 Minoxidil Nanogel Systems:
Manufacturers: Available through Mintop, Tugain brands (India); Active ingredient: Minoxidil incorporated in nanogel carrier; Application: Alopecia management (androgenetic alopecia in both genders); Distinctive characteristics: Superior scalp penetration with diminished irritation compared to alcohol-based formulations(40).

11.5 Antifungal Nanogel Products:
Representative compounds: Ketoconazole, Clotrimazole, Itraconazole nanogel formulations; Manufacturers: Sun Pharma, Glenmark, Ajanta Pharma; Application: Topical mycotic infections including dermatophytosis and candidiasis; Distinctive characteristics: Amplified antifungal efficacy through controlled drug release mechanisms(42,43).

11.6 Cosmeceutical Nanogel Applications:
Representative compounds: Hyaluronic acid (moisturizing), Vitamin C (antioxidant properties), Retinol (anti-aging effects); Manufacturers: L'Oréal, Neutrogena, Olay; Applications: Anti-aging treatments, UV protection, dermal rejuvenation.

12. PROSPECTIVE DEVELOPMENTS IN NANOGEL TECHNOLOGY

A) Regenerative Medicine & Wound Healing:

- Tissue engineering applications utilize nanogels as biomimetic structures that replicate extracellular matrix properties, facilitating controlled administration of growth factors and genetic material. These systems demonstrate significant promise for bone regeneration through injectable delivery mechanisms within scaffolding structures and may enhance compatibility with implanted devices.
- Wound management and hemostatic applications employ nanogel composites, including chitin-derived formulations containing hemostatic minerals, which have shown superior bleeding control capabilities and accelerated healing processes compared to existing therapeutic options.

B) Intelligent Drug Delivery & Targeting:

- Stimuli-responsive systems incorporate nanogels that respond to environmental triggers such as temperature variations, pH fluctuations, redox states, or ultrasonic stimulation, facilitating precise, localized therapeutic release.
- Surface modification strategies involve incorporating targeting moieties (antibodies, peptides) or nanoparticles (gold, magnetic) to enhance selectivity, while PEGylation techniques improve circulatory persistence and immune system evasion.

C) Diagnostics & Theragnostic Applications:

- Multimodal imaging capabilities enable nanogels to encapsulate contrast agents for MRI, CT, optical, or fluorescent imaging within unified platforms, enhancing targeting precision and contrast enhancement.
- Real-time monitoring systems through integration with sensing elements or reporter molecules could facilitate simultaneous therapeutic tracking and diagnostic assessment.

F) Prospective Developments of Nanogels in Biomedical Applications:
Nanogels demonstrate considerable potential within biomedical domains through their adjustable characteristics and multifunctional capabilities.

a) Synthesis Methodology Advancements:

- Microfluidic techniques facilitate precise regulation of nanoscale droplet

generation, yielding monodisperse nanogels with customized characteristics.

- Three-dimensional printing technology integrates nanogel synthesis with additive manufacturing processes to generate complex architectures for tissue engineering and regenerative medicine applications.

13. CONCLUSION:

Nanogels have gained significant attention in recent years as a novel and highly efficient drug delivery system because of their unique characteristics, such as small particle size, high surface area, excellent biocompatibility, and tunable physicochemical properties. Their ability to encapsulate a wide range of therapeutic agents, including proteins, peptides, nucleic acids, and small molecules, makes them a versatile platform for addressing the limitations of conventional dosage forms. Moreover, their stimuli-responsive nature allows for targeted and controlled release at the desired site of action, which not only enhances drug bioavailability but also minimizes systemic toxicity and side effects. Various studies have demonstrated their effectiveness in the treatment of cancer, infectious diseases, inflammatory disorders, diabetes, cardiovascular diseases, and neurodegenerative conditions, showing promising results in both in vitro and in vivo models. In addition, nanogels provide opportunities for crossing biological barriers such as the blood–brain barrier, thereby expanding their potential in treating challenging diseases.

However, despite these remarkable advantages, there are still challenges that need to be overcome, including large-scale and cost-effective production, long-term stability, reproducibility of formulations, and strict regulatory requirements for clinical approval. Addressing these issues through continuous research and technological advancements will be crucial for their successful translation from laboratory research to clinical practice. Overall, nanogels hold immense potential as next-generation drug delivery systems, and with ongoing progress in nanoscience and pharmaceutical technology, they are expected to revolutionize modern therapeutics and contribute significantly to the development of safe, effective, and patient-friendly treatment strategies.

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