

RESEARCH PAPER

Nanogel-Based Topical Delivery of NSAIDs: Design Strategies, Therapeutic Advances, and Future Perspectives

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Abstract

Background: The longevity of Class II restorations in primary molars depends largely on the restorative material used. Giomer and Alkasite (Cention N) are contemporary bioactive restorative materials with favorable mechanical and esthetic properties; however, comparative clinical evidence in primary teeth is limited.

Aim: To evaluate and compare the clinical effectiveness of Giomer and Alkasite (Cention N) as restorative materials in Class II cavities of primary molars.

Materials and Methods: This prospective randomized split-mouth longitudinal clinical study was conducted in 20 children aged 4–7 years. Thirty Class II cavities in primary molars were randomly allocated into two groups: Group I (Giomers, n=15) and Group II (Alkasite/Cention N, n=15). Restorations were evaluated at baseline, 3, 6, 9, and 12 months using Modified United States Public Health Service (USPHS) criteria for colour match, marginal adaptation, marginal discoloration, anatomic form, and secondary caries. Radiographic evaluation was performed to assess secondary caries. Data were analyzed using Cochran's Q test, Chi-square test, and Fisher's exact test, with $p \leq 0.05$ considered statistically significant.

Results: Both restorative materials demonstrated clinically acceptable performance throughout the 12-month follow-up. Giomer exhibited significantly better colour stability at 6 and 9 months ($p < 0.05$) and superior marginal adaptation at 12 months ($p = 0.0067$) compared with Alkasite. No statistically significant differences were observed between the groups for marginal discoloration, anatomic form, or secondary caries ($p > 0.05$). Radiographic evaluation revealed minimal secondary caries in both groups without significant intergroup differences.

Conclusion: Both Giomer and Alkasite (Cention N) were clinically acceptable restorative materials for Class II cavities in primary molars over 12 months. However, Giomer demonstrated superior colour stability and marginal adaptation, suggesting better overall long-term clinical performance.

Keywords: Giomer, Alkasite, Cention N, Primary molars, Class II restoration, Modified USPHS criteria, Pediatric dentistry.

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INTRODUCTION

Topical drug delivery has emerged as an important strategy in modern therapeutics, enabling localized treatment while minimizing systemic exposure and avoiding first-pass metabolism. This approach is particularly beneficial for dermatological conditions, improving bioavailability, reducing side effects, and enhancing patient compliance through convenient dosage forms such as gels and creams.

Among advanced delivery systems, nanostructured lipid carriers (NLCs) have improved topical formulations by enhancing drug solubility, stability, and skin penetration, along with providing controlled release. However,

nanogels have gained significant attention as a superior alternative due to their nanoscale size (20–200 nm), high surface area, and excellent swelling capacity, which allow efficient drug encapsulation and sustained release. Their three-dimensional polymeric network enables incorporation of both small molecules and macromolecules, while chemically crosslinked nanogels offer enhanced stability and better control over drug release.

Non-steroidal anti-inflammatory drugs (NSAIDs) are extensively used in the management of pain and inflammation; however, their prolonged oral administration is associated with significant adverse effects,

including gastrointestinal irritation, ulceration, and systemic toxicity. In addition, drugs such as diclofenac undergo extensive first-pass metabolism, limiting their systemic availability. These limitations have driven the development of

alternative delivery strategies, particularly topical systems. In this context, nanogel-based formulations have demonstrated considerable potential by enhancing skin permeation, enabling sustained drug release, and improving localized anti-inflammatory efficacy. Collectively, these features position nanogels as advanced and effective carriers for topical NSAID delivery.

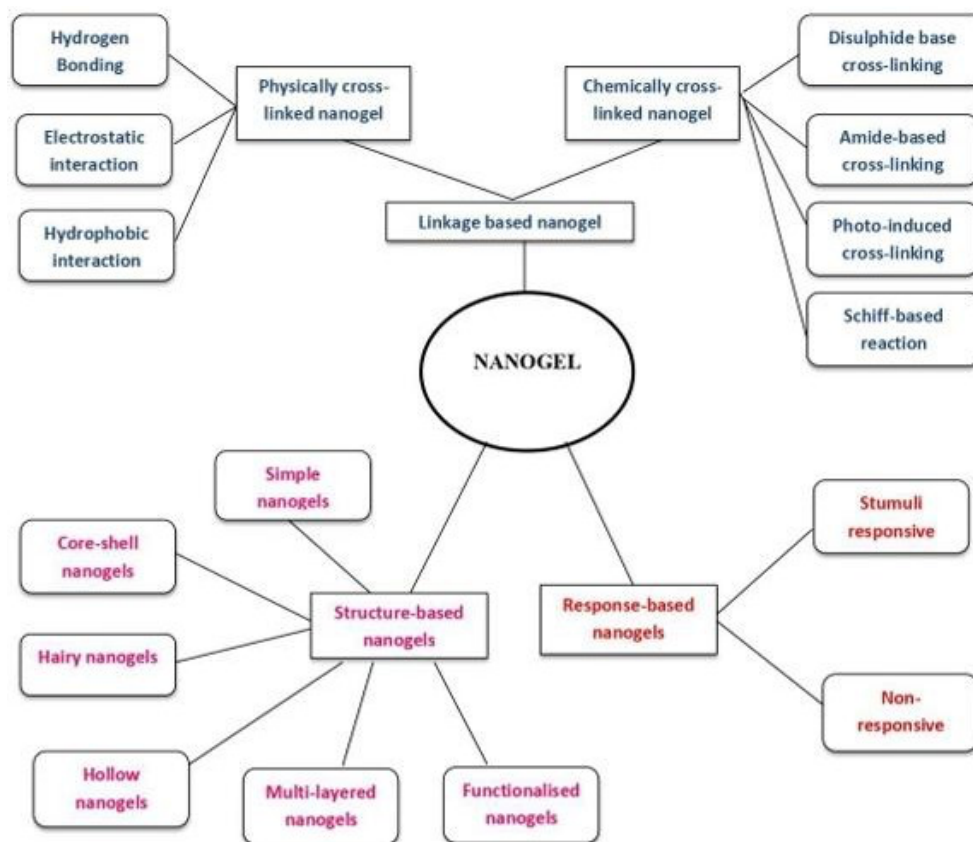
Advantages of Nanogels

- Nanogels (NGs) are advanced drug delivery systems that provide better control over drug loading and release compared to conventional nanoparticles.
- Their swelling property creates a large internal network, allowing higher drug loading capacity.
- NGs can encapsulate various therapeutic agents including small molecules, peptides, proteins, nucleic acids, and inorganic nanoparticles like gold or iron oxide.
- Multiple drugs can be loaded into a single nanogel system for combined therapeutic and diagnostic (theranostic) applications.
- Their soft and highly hydrated structure improves biocompatibility and interaction with biological systems.
- The nanoscale size and flexibility of NGs reduce immune system clearance and prolong circulation time.
- NG swelling is controlled by osmotic pressure and the elasticity of the polymer network.
- NGs can be designed to respond to stimuli such as pH, temperature, light, or enzymes for targeted drug release.
- Their large surface area allows attachment of targeting ligands to enhance cellular uptake. NGs are particularly effective for intracellular delivery of siRNA, peptides, oligonucleotides, and chemotherapeutic drugs.

Properties of Nanogels

- High water retention and swelling capacity: Nanogels exhibit strong hydration ability, enabling efficient drug encapsulation and controlled, sustained release through their crosslinked polymeric network.
- Softness and structural flexibility: Their deformable nature allows tunable mechanical properties, improving tissue penetration and interaction with biological membranes.
- Colloidal stability:
 - Nanogels maintain stability in biological fluids due to electrostatic repulsion and steric stabilization from hydrophilic polymers, preventing aggregation.
- Biocompatibility and biodegradability: Fabricated from polymers such as chitosan, alginate, and dextran, nanogels are non-toxic and degrade safely without accumulation in tissues.
- Nanoscale size and permeability: Typically ranging from 20–200 nm, nanogels enhance penetration across skin and biological barriers while reducing rapid clearance.
- Solubility enhancement: Their three-dimensional network improves solubility and stability of poorly water-soluble drugs, enhancing bioavailability.
- Stimuli-responsive behavior: Nanogels undergo swelling or deswelling in response to pH, temperature, or ionic changes, enabling controlled and targeted drug release.
- Mild fabrication conditions: Preparation under gentle conditions preserves the
 - structural integrity of sensitive biomolecules such as proteins and peptides.
- Non-immunogenic nature: Nanogels generally evade immune recognition, allowing prolonged circulation and improved therapeutic efficiency.

Classification of nanogel



Composition of Nanogel

Nanogel formulations are composed of a nanoscale carrier system in which the drug is incorporated within a polymeric network. The formulation typically includes polymers, co-polymers, cross- Table: Composition of Nanogel Formulation High drug loading capacity: Functional groups within the polymer matrix enable efficient drug incorporation via entrapment, electrostatic interaction, or covalent bonding. linking agents, and stabilizers, each contributing to the structural integrity, stability, and drug-delivery performance of the nanogel.

Sr. No.	Component	Description and Examples
1	Polymers	Polymers form the primary structural framework of nanogels. They may be of natural or synthetic origin. Natural polymers: collagen, fibrin, hyaluronic acid, chitosan, alginate, starch, etc. Synthetic polymers: polyethyleneimine (PEI), poly(lactic-co-glycolic acid) (PLGA), poly(N-isopropylacrylamide) (polyNIPAM), polyacrylates, polystyrene, poly(ε-caprolactone), Carbopol, hydroxypropyl methylcellulose (HPMC), etc.
2	Co-polymers	Co-polymers are used to modify physicochemical properties such as flexibility, hydrophilicity, and drug-loading capacity. Common examples include polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), polyethylene glycol (PEG), polyacrylic acid, poly(glycolic acid), polyethylene oxide (PEO), and polypropylene oxide (PPO).
3	Cross-linking agents	Cross-linkers are responsible for forming and stabilizing the three-dimensional polymer network of nanogels. Examples include poly(ethylene glycol) dimethylacrylate, sodium tripolyphosphate, and various acrylic acid derivatives.

4	Stabilizers	Stabilizers help maintain colloidal stability and prevent aggregation during storage and application. Commonly used stabilizers include Poloxamer F68, Pluronic F127, and polysorbates.
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Drug Loading Techniques in Nanogels

Effective drug loading into nanogels is crucial for maximizing therapeutic efficiency while minimizing carrier burden. Various strategies are employed to incorporate bioactive agents into nanogel systems:

1. Covalent Conjugation

In this approach, drugs or bioactive molecules are chemically linked to the nanogel network via covalent bonds. Conjugation can be achieved either during nanogel synthesis or through post-synthetic modification of preformed nanogels. This method ensures stable drug incorporation and controlled release but may require careful design to preserve drug activity.

2. Physical Entrapment

Physical entrapment involves encapsulating drug molecules within the porous structure of the nanogel matrix without chemical bonding. The efficiency of this method depends on the compatibility between the nanogel mesh size and the drug molecule. For example, cholesterol-modified pullulan nanogels can encapsulate proteins and hydrophobic drugs, while hyaluronic acid-based nanogels can form hydrophobic domains capable of entrapping sensitive biomolecules such as siRNA, thereby protecting them from degradation. Additionally, non-specific interactions between the drug and polymer network may enhance loading efficiency.

3. Self-Assembly

Self-assembly is a thermodynamically driven process in which amphiphilic polymers spontaneously organize into stable nanostructures through non-covalent interactions such as hydrogen bonding, van der Waals forces, electrostatic interactions, and hydrophobic effects. In aqueous environments, hydrophobic segments aggregate to form the core, while hydrophilic segments extend outward, stabilizing the structure. This process typically occurs above the critical micelle concentration (CMC), leading to the formation of nanogel structures capable of efficiently encapsulating drugs within their core.

Methods of Nanogel Preparation

1. Emulsion Solvent Diffusion Technique

In this method, the drug is dissolved in an organic solvent to form the organic phase, while the polymer and gelling agent are prepared in an aqueous phase. The organic

phase is added dropwise into the aqueous phase under homogenization at 6000 rpm, resulting in the formation of an oil-in-water nanoemulsion. High-speed homogenization reduces droplet size to the nanoscale. Triethanolamine is subsequently added to induce gelation, and the system is further stirred at 8000 rpm for 1 hour. pH adjustment facilitates nanogel formation and enhances formulation stability.

2. Nanoprecipitation Technique

This technique involves the addition of an organic solution containing drug and polymer into an aqueous phase with a surfactant. Rapid solvent diffusion leads to polymer precipitation and nanoparticle formation. Following removal of the organic solvent, stable polymeric nanoparticles are obtained. These nanoparticles are then incorporated into a gel matrix using an appropriate gelling agent. Final pH adjustment ensures optimal consistency and stability of the nanogel system.

3. Solvent Evaporation Technique

In this approach, the drug-polymer solution is introduced into an aqueous phase under continuous stirring at 1000 rpm for approximately 2 hours. The resulting nanospheres are isolated by filtration and dried at 40°C for 24 hours. For nanogel preparation, the polymer is hydrated in water and subjected to high-speed agitation to form a uniform dispersion. The nanosphere suspension is then incorporated into the gel base along with permeation enhancers, followed by pH adjustment to obtain a stable nanogel formulation.

4. Reverse Micelle Method

In this method, the drug, polymer, and surfactant are dissolved in an organic solvent, followed by the addition of a crosslinking agent to initiate nanoparticle formation. The reaction is typically allowed to proceed overnight. After purification, the solvent is removed to obtain a dried nanoparticle mass. These nanoparticles are then dispersed into an aqueous gel system containing a gelling agent. Final pH adjustment ensures proper gel formation and stability.

5. Modified Diffusion Emulsification Method

In this technique, the drug is dissolved with a polymer in an organic solvent to form the organic phase. This phase is gradually introduced into an aqueous stabilizer solution under stirring (5000–10,000 rpm), forming an emulsion. Controlled addition using a syringe ensures uniform dispersion. The system is further homogenized at high speed (10,000–

25,000 rpm) to reduce droplet size, followed by sonication for 5–10 minutes to obtain nanoscale particles and improve formulation stability.

Mechanism of Drug Release from Nanogels

Drug incorporation into nanogels occurs through physical entrapment, covalent bonding, or self-assembly via non-covalent interactions, depending on drug properties and therapeutic needs. Drug release takes place through mechanisms such as diffusion, polymer degradation, ionic exchange, and stimuli-responsive swelling. The release behavior is mainly influenced by the mesh size of the polymer network and drug–polymer interactions. Larger mesh size promotes faster release, while stronger interactions provide sustained and controlled drug delivery.

Diffusion-Controlled Release In diffusion-controlled systems, drug molecules are physically entrapped within the nanogel matrix and released in a controlled manner via passive diffusion. The release kinetics are primarily governed by the mesh size of the crosslinked polymer network and the molecular size of the drug. Increased crosslinking density restricts diffusion, while drug–polymer interactions, such as hydrophobic and electrostatic forces, further modulate release behavior. This mechanism is extensively employed in nanogel-based topical formulations to achieve sustained therapeutic efficacy.

1. **Degradation-Mediated Release** In degradation-mediated systems, drug release occurs through the controlled breakdown of the nanogel network via hydrolytic or enzymatic processes. This degradation increases the mesh size, facilitating drug diffusion from the matrix. The release rate can be tuned by altering polymer composition and crosslinking density. Biodegradable polymers are commonly used to ensure safe degradation, enabling sustained release while minimizing carrier accumulation and enhancing biocompatibility.
2. **Ionic Displacement Mechanism** In ion-sensitive nanogels, drugs are bound to the polymer network through electrostatic interactions and released via ionic exchange with surrounding biological fluids. The release depends on the ionic strength and composition of the medium. Counterions or biomolecules can displace the drug, while intracellular agents may further destabilize the network. This mechanism supports stimulus-responsive and site-specific drug delivery.
3. **pH-Responsive Release** pH-responsive nanogels contain ionizable groups that undergo protonation or deprotonation in response to pH changes, leading to swelling or contraction of the network. Swelling increases mesh size and enhances drug diffusion, while

contraction restricts release. This property is useful for targeting sites like inflamed tissues with altered pH. Thus, pH-sensitive nanogels enable site-specific and controlled drug delivery with reduced systemic exposure.

4. **Stimuli-Responsive (Photo/External) Release** Stimuli-responsive nanogels are engineered to release drugs in response to external triggers such as light, temperature, or magnetic fields. In photo-responsive systems, light exposure induces structural changes in the polymer network, resulting in controlled drug release. Some systems also generate reactive species that enhance cellular uptake. These approaches provide precise spatial and temporal control, making them promising for advanced targeted drug delivery.

Nanogel-Based Topical Delivery of NSAIDs

Topical delivery of non-steroidal anti-inflammatory drugs (NSAIDs) is widely preferred due to its ability to provide localized therapeutic effects while minimizing systemic exposure and gastrointestinal adverse effects associated with oral administration. However, poor aqueous solubility, limited skin permeability, and variable bioavailability restrict the clinical performance of many NSAIDs. Nanogel-based formulations have emerged as advanced carriers to address these limitations. Their nanoscale size and three-dimensional crosslinked polymeric network enhance drug solubilization, improve dermal penetration, and enable controlled release. Additionally, nanogels can encapsulate both hydrophilic and lipophilic NSAIDs, resulting in improved drug loading, prolonged skin retention, and enhanced therapeutic efficacy.

1. Diclofenac Sodium Nanogels

Diclofenac sodium is one of the most widely used NSAIDs for the topical treatment of osteoarthritis, rheumatoid arthritis, and localized musculoskeletal pain. Conventional formulations often exhibit limited skin penetration and short residence time, reducing therapeutic effectiveness. Nanogel-based systems overcome these limitations by enhancing solubility, permeability, and sustained drug release. Diclofenac nanogels are commonly prepared using emulsification–diffusion, nanoprecipitation, or polymeric crosslinking techniques with polymers such as carbopol, chitosan, and polycarbophil. These systems exhibit nanoscale particle size, high entrapment efficiency, and controlled release profiles. Enhanced hydration of the stratum corneum and increased surface contact promote deeper dermal penetration. Studies have demonstrated improved drug diffusion, higher skin retention, and prolonged anti-inflammatory activity compared to conventional gels, with reduced systemic exposure.

2. Ibuprofen Nanogels

Ibuprofen, a widely used propionic acid

derivative, is limited by poor aqueous solubility and gastrointestinal side effects upon oral administration. Nanogel formulations have been developed to improve its topical delivery and therapeutic performance. These systems are typically prepared using biodegradable polymers such as chitosan, carbopol, or thermoresponsive polymers. The nanoscale structure enhances drug solubilization and ensures uniform distribution within the gel matrix. Improved permeation across the stratum corneum and prolonged skin residence contribute to sustained drug release. Advanced formulations incorporating pH- or temperature-sensitive polymers enable site-specific drug release at inflamed tissues, thereby enhancing therapeutic efficacy while minimizing systemic absorption.

3. Ketoprofen Nanogels

Ketoprofen exhibits potent anti-inflammatory and analgesic activity but is associated with variable skin permeation and photosensitivity reactions in conventional formulations. Nanogel-based systems have been investigated to improve stability and controlled drug delivery. These formulations are typically developed using nanoemulsion-based gels or crosslinked polymeric networks capable of efficiently encapsulating lipophilic drugs. Nanogels provide uniform drug distribution and enhanced dermal permeation due to their small particle size. Sustained release from the polymeric matrix maintains therapeutic drug levels over extended periods, potentially reducing dosing frequency. Additionally, nanogel incorporation may improve photostability and reduce adverse skin reactions.

4. Indomethacin Nanogels

Indomethacin is a potent NSAID commonly used in inflammatory conditions but is associated with significant gastrointestinal toxicity when administered orally. Nanogel formulations offer a promising alternative for localized delivery. These systems are typically prepared using emulsification–diffusion or nanoprecipitation techniques with biodegradable polymers. Nanosizing improves drug dispersion within the aqueous

gel matrix and enhances permeation through the stratum corneum. The crosslinked nanogel network enables sustained drug release and prolonged dermal retention. Studies have reported improved in vitro diffusion and enhanced anti-inflammatory activity compared to conventional formulations, along with reduced systemic exposure.

5. Piroxicam and Naproxen Nanogels

Piroxicam and naproxen are long-acting NSAIDs used in chronic inflammatory disorders such as osteoarthritis and rheumatoid arthritis. Their prolonged oral use is associated with gastrointestinal irritation and systemic side effects, making them suitable candidates for topical nanogel delivery. Piroxicam nanogels are formulated using crosslinked hydrophilic polymers that enhance drug solubility, uniform dispersion, and sustained release. Similarly, naproxen nanogels are developed using biodegradable polymeric systems combined with homogenization or sonication techniques to achieve nanoscale particles. These formulations demonstrate improved entrapment efficiency, enhanced dermal permeation, and prolonged drug retention. Controlled release behavior reduces dosing frequency and maintains consistent drug levels at the target site, improving therapeutic outcomes.

Collectively, these findings demonstrate the significant potential of nanogel-based systems for topical NSAID delivery. However, despite promising outcomes, comparative evaluation across different formulations remains limited. Variations in polymer composition, preparation techniques, and particle size significantly influence drug release kinetics and dermal permeation. While diclofenac and ketoprofen nanogels often exhibit superior permeation due to their lipophilicity, drugs such as ibuprofen and naproxen may require further formulation optimization to achieve comparable efficacy. Additionally, long-term stability and scalability remain critical challenges that must be addressed for successful clinical translation.

NSAID	Limitation (Oral/Conventional)	Nanogel Advantage	Outcome
Diclofenac	First-pass metabolism, GI irritation	Enhanced permeation, sustained release	Improved skin retention
Ibuprofen	Poor solubility, GI side effects	Improved solubilization, controlled release	Better bioavailability

Ketoprofen	Photosensitivity, variable permeation	Stabilization, sustained release	Reduced side effects
Indomethacin	High GI toxicity	Localized delivery	Reduced systemic exposure
Naproxen	Slow onset, GI irritation	Enhanced dermal delivery	Prolonged action
Piroxicam	Long half-life, toxicity	Controlled release	Reduced dosing frequency

Applications of Nanogels

Nanogel-based drug delivery systems have gained significant attention due to their unique properties, such as high water content, biocompatibility, structural flexibility, and controlled drug release. These features enhance drug solubility, stability, and therapeutic efficacy while minimizing toxicity to healthy tissues. Additionally, *in vivo* studies have demonstrated that nanogels are more effective than conventional formulations in achieving targeted and localized drug delivery.

1. **Transdermal Drug Delivery** Nanogels have shown considerable potential in transdermal applications by improving dermal penetration and sustaining drug release. For instance, nanosized aceclofenac dispersions prepared via the emulsion-solvent diffusion method and incorporated into Carbopol 940 gel exhibited favorable stability, optimal porosity, and prolonged drug release. Such systems enhance therapeutic efficiency and patient compliance compared to conventional topical formulations.
2. **Antifungal Applications** Nanogels are widely explored as carriers for antifungal agents due to their ability to provide controlled and sustained drug release. Fluconazole-loaded chitin nanogels have demonstrated prolonged antifungal activity, ensuring continuous drug availability. Similarly, vitamin E-based nanoemulsion nanogels containing amphotericin B have shown significantly enhanced skin deposition, improving treatment outcomes in dermal fungal infections.
3. **Vaginal Drug Delivery** Nanogel formulations incorporating antibacterial and antiretroviral agents have been investigated for the treatment of vaginal infections and prevention of HIV transmission. Tenofovir-loaded gelatin nanoparticles integrated into bioadhesive nanogels have demonstrated effective localized delivery with prolonged retention. However, certain limitations, such as restricted use during menstruation and pregnancy, remain.
4. **Antidiabetic Applications** Glucose-responsive injectable nanogel systems have been developed for insulin delivery. These systems consist of oppositely charged nanoparticles that form stable nano-networks upon administration. In

vivo studies have reported sustained glucose reduction and improved glycemic control compared to conventional insulin therapy.

5. **Anticancer and Tumor Therapy** Nanogels have been extensively investigated in cancer therapy due to their ability to enhance drug bioavailability and tumor accumulation via the enhanced permeability and retention effect. The crosslinked polymeric network protects encapsulated drugs from premature degradation while reducing systemic toxicity. Clinically relevant formulations, such as Genexol-PM, further demonstrate the therapeutic potential of nanogel-based systems. Additionally, nanogels address limitations of conventional chemotherapeutics, including poor solubility and non-specific toxicity, by enabling controlled and targeted drug delivery to tumor tissues.
6. **Diagnostics and Imaging** Nanogels have also been explored for diagnostic applications owing to their structural adaptability and biocompatibility. Gadolinium-loaded nanogels, synthesized through polymer crosslinking and surface modification, have shown enhanced circulation time and improved imaging contrast, supporting their role in advanced diagnostic imaging.
7. **Neurodegenerative Diseases** Nanogels offer promising potential for the delivery of oligonucleotides across the blood-brain barrier in the treatment of neurodegenerative disorders. Encapsulation of negatively charged biomolecules within nanogels results in stable nanoscale complexes with improved transport efficiency, particularly when functionalized with targeting ligands.
8. **Anti-Inflammatory Applications** Nanogel formulations incorporating anti-inflammatory agents, such as 3-acetyl-11-keto- β -boswellic acid (AKBA), have demonstrated enhanced therapeutic efficacy. Incorporation into Carbopol-based nanogels improves drug retention and enables controlled release, resulting in superior anti-inflammatory activity compared to conventional formulations.

Challenges and Future Directions

Nanogel (NG)-based drug delivery systems face challenges in achieving site-specific delivery

and safe elimination after therapy. Due to their high molecular weight (above the renal filtration limit ~40 kDa), intact nanogels are not easily excreted, making it essential to design biodegradable systems that break down into smaller, excretable fragments. Therefore, understanding degradation pathways, long-term accumulation, and safety of metabolites is crucial for clinical use.

Residual synthesis components such as unreacted monomers, initiators, surfactants, and metal catalysts may affect biocompatibility and cause toxicity, and their complete removal remains difficult. In addition, batch-to-batch variability is a concern, although advanced techniques like microfluidics and 3D printing can improve formulation consistency.

While stimuli-responsive linkages (e.g., acetals, hydrazones, disulfides) are widely used, further development of degradable polymers and crosslinking methods is needed for better control over degradation and drug release. Future research should focus on safer synthesis approaches, preferably aqueous, surfactant-free, and metal-free, along with the development of biodegradable and bioinspired materials to enhance the safety and clinical potential of nanogel systems.

A Perspective on Recent Research Trends

Nanogels have gained significant interest due to their biocompatibility, structural stability, and ease of functionalization. Their crosslinked network allows sustained and controlled drug release, making them suitable for advanced therapeutic applications. Recent advancements include nanogel–exosome hybrid systems for efficient intracellular delivery, where exosomal miRNA can serve both diagnostic and therapeutic roles, and magnetic nanogels that improve targeted delivery and tumor localization.

Thermoresponsive nanogels have shown promise in vascular embolization as imaging-guided agents, enabling better precision and reducing the risk of recanalization. In gene editing, nanogels can deliver CRISPR/Cas9 components while protecting them from degradation, improving cellular uptake, and reducing off-target effects, offering a safer alternative to viral vectors.

Additionally, nanogels are emerging in regenerative medicine, particularly in wound healing and tissue engineering, where self-assembling nanogels support cell growth and tissue formation. Overall, these advancements highlight the expanding role of nanogels in drug delivery, gene therapy, embolization, and tissue engineering, with future focus on multifunctional and biodegradable systems for clinical applications.

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