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A REVIEW ON HYDROGELS AS DRUG DELIVERY SYSTEM

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ABSTRACT
Hydrogels are three-dimensional, hydrophilic polymer networks widely recognized for their potential in drug delivery systems (DDS) due to their high water content, excellent biocompatibility, and adjustable physical properties. These materials can incorporate a broad spectrum of therapeutic agents, including small molecules, proteins, and nucleic acids, enabling tailored and sustained drug release profiles. This review provides an in-depth analysis of hydrogel classification based on origin (natural or synthetic), type of crosslinking (physical or chemical), and responsiveness to external stimuli such as pH, temperature, or enzymatic activity. Various drug release mechanisms – such as diffusion, swelling, and matrix degradation – are discussed in detail. The integration of hydrogels with nanotechnology, biosensors, and tissue engineering has expanded their potential in regenerative medicine and personalized treatment approaches. As research advances, hydrogel-based DDS are poised to play a vital role in next-generation therapeutic strategies. This review highlights their significance in shaping the future of precision medicine.
KEYWORDS: *Hydrogel, Drug delivery, Controlled release, Stimuli-responsive, Nanoparticles*

1. INTRODUCTION

Hydrogels are cross-linked polymer networks that swell in water but do not dissolve due to physical or chemical crosslinking. Their high water content and tissue-like elasticity make them ideal carriers for delivering therapeutic agents. First introduced in the 1960s for biomedical uses, they now serve diverse functions in modern pharmaceutics from oral to localized therapies. Hydrogels are hydrophilic polymer networks capable of absorbing and retaining substantial amounts of water or biological fluids, making them ideal candidates for drug delivery applications. Their versatility, stemming from chemical and physical crosslinking, enables customized delivery profiles based on therapeutic needs]. With increasing demand for targeted and sustained drug release systems, hydrogels provide a platform that is both biocompatible and responsive to physiological cues.(1)

In recent years, nanoparticles (NPs) have significantly advanced the field of drug delivery, offering great potential for the targeted and controlled release of therapeutic agents. Due to their small size, high surface area, and tenable physicochemical properties, nanoparticles can efficiently penetrate biological barriers, enhance drug solubility, and improve bioavailability, thereby reducing systemic toxicity and enhancing therapeutic efficacy. Among various nanoparticle platforms, hydrogel nanoparticles (HNPs) have emerged as promising carriers, particularly in cancer therapy, owing to their biocompatibility, hydrophilic nature, and high drug-loading capacity.(2)

The primary aim of this review is to provide a comprehensive overview of hydrogel nanoparticles as an innovative platform, with a particular focus on their application in cancer drug delivery. We will explore the mechanisms of drug loading and release, various targeting strategies to enhance tumor specificity, and recent advances in the design and engineering of hydrogel nanoparticles. Furthermore, we will address the current limitations and challenges in the clinical application of these nanocarriers, including scalability, reproducibility, and long-term efficacy. Finally, we will discuss emerging trends and future perspectives in the field, highlighting innovative approaches to overcome existing barriers and enhance the therapeutic potential of hydrogel-based nanoparticles, especially in cancer treatment.(3-5)

2. REVIEW OF LITERATURE

1. **Peppas et al. (2006)** reported that hydrogels are three-dimensional, hydrophilic polymer networks with high water content and biocompatibility, making them suitable for controlled drug delivery and biomedical applications.
2. **Asefnejad et al. (2024)** classified hydrogels based on polymer origin and stated that natural hydrogels offer biodegradability, while synthetic hydrogels provide better mechanical strength and controlled physicochemical properties.
3. **Peng et al. (2022)** demonstrated that hybrid hydrogels combining natural and synthetic polymers improve mechanical stability and biological performance, particularly in wound healing and skin regeneration.
4. **Chen et al. (2022)** and **Jiang et al. (2020)** described stimuli-responsive hydrogels that respond to pH, temperature, and enzymes, enabling targeted and site-specific drug release.
5. **Lu et al. (2018)** and **Parhi (2017)** explained hydrogel formation through physical and chemical crosslinking, noting that chemically crosslinked hydrogels exhibit enhanced stability and controlled degradation.

6. **Peppas et al. (2000)** reported that diffusion is the primary mechanism of drug release from hydrogels, while **Wei et al. (2019)** showed that swelling-controlled release is important in injectable hydrogel systems.
7. **Chen et al. (2018)** highlighted that biodegradable hydrogels enable degradation-controlled drug release, which is advantageous for sustained and localized therapy.
8. **Kianfar et al. (2025)** reviewed hydrogel nanoparticles and emphasized their potential in drug delivery, especially in cancer therapy, due to improved drug loading and targeting efficiency.
9. **Coutinho et al. (2020)** and **Sabra et al. (2019)** reported that nanoparticle-based hydrogel systems enhance drug stability, bioavailability, and site-specific delivery.
10. **Ritik et al. (2025)** summarized the broad biomedical applications of hydrogels, while **Alkayyali et al. (2012)** identified limitations such as poor mechanical strength, burst release, and scale-up challenges.

3. AIM AND OBJECTIVES

AIM

The aim of this project is to review and evaluate hydrogels and hydrogel-based nanoparticles as advanced drug delivery systems, with emphasis on their classification, mechanisms of drug release, biomedical applications, limitations, and future potential in targeted and controlled drug delivery.

OBJECTIVES

- To understand the fundamental structure and physicochemical properties of hydrogels relevant to drug delivery applications.
- To classify hydrogels based on polymer source (natural, synthetic, hybrid) and network structure.
- To study different hydrogel formation techniques, including physical and chemical crosslinking methods.
- To analyze the role of crosslinking density and polymer composition in determining hydrogel swelling behavior and mechanical strength.
- To evaluate various drug loading strategies used in hydrogel-based systems.
- To review the mechanisms of drug release from hydrogels, including diffusion-controlled, swelling-controlled, degradation-controlled, and stimuli-responsive release.
- To examine stimuli-responsive hydrogels and their response to pH, temperature, enzymes, and other biological triggers.
- To study the development and significance of hydrogel nanoparticles and nanocomposite hydrogels in improving targeting efficiency and drug bioavailability.
- To assess the application of hydrogels in cancer drug delivery, with emphasis on localized and targeted therapy.
- To review the use of hydrogels in wound healing, ophthalmic drug delivery, injectable systems, and tissue engineering.
- To analyze the biocompatibility, biodegradability, and safety aspects of hydrogel-based drug delivery systems.
- To identify the limitations and challenges associated with hydrogel-based formulations, including mechanical weakness, burst release, and sterilization issues.
- To discuss strategies to overcome current limitations, such as hybrid systems and nanocomposite approaches.
- To explore emerging trends such as smart hydrogels, 4D hydrogels, and hydrogel systems for gene and vaccine delivery.
- To highlight the future prospects and clinical potential of hydrogel-based drug delivery systems in precision medicine

4. NEED OF THE WORK

Conventional drug delivery systems often have problems like poor drug absorption, frequent dosing, side effects, and low patient compliance. To overcome these issues, advanced drug delivery systems are needed that can release drugs in a controlled, targeted, and sustained manner.

Hydrogels are promising because they are biocompatible, absorb water, and can carry different types of drugs such as small molecules, proteins, and nucleic acids. They can also be designed to release drugs in response to specific stimuli like pH, temperature, or enzymes, which is useful for targeted therapies, especially in cancer.

However, hydrogels also have challenges like weak mechanical strength, burst drug release, and difficulty in sterilization. Therefore, studying and reviewing hydrogels and hydrogel nanoparticles is important to understand their advantages, limitations, and potential applications in drug delivery.

This project helps to analyze current research, identify challenges, and explore future trends in hydrogel-based drug delivery systems for better and safer treatment options.

5. Plan of Work

1. **Literature Survey**
   - Study previous research on hydrogels and hydrogel nanoparticles.
   - Understand types, formation methods, and drug release mechanisms.
2. **Classification Study**
   - Review natural, synthetic, hybrid, stimuli-responsive, injectable, and nanocomposite hydrogels.
3. **Mechanisms of Drug Release**
   - Analyze diffusion, swelling, degradation, and stimuli-responsive release from hydrogels.
4. **Biomedical Applications**
   - Review applications in cancer therapy, wound healing, ophthalmic delivery, and tissue engineering.
5. **Advantages and Limitations**
   - Study the benefits and challenges of hydrogel-based drug delivery systems.
6. **Recent Advances**
   - Explore hydrogel nanoparticles, smart hydrogels, multi-responsive hydrogels, and gene/vaccine delivery platforms.

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7. **Future Perspectives**
   - Review ongoing research trends, clinical potential, and strategies to overcome existing challenges.
8. **Compilation and Report Writing**
   - Compile findings, prepare figures, and finalize the project report.

6. CLASSIFICATION OF HYDROGELS

Hydrogels come in a variety of types, each with its own unique properties and applications in drug delivery. These include the following biomaterials:

1. Natural Hydrogels

These hydrogels are made from naturally-derived polymers such as collagen, alginate, chitosan, and hyaluronic acid that offer excellent biocompatibility and biodegradability and can mimic the extracellular matrix and promote cellular interactions.

2. Synthetic hydrogels/ Based on polymer type.

These hydrogels are synthesized from polymers like polyethylene glycol (PEG), polyvinyl alcohol (PVA), and polyacrylic acid that provide tailored mechanical and degradation properties and allow for precise control over network structure and crosslinking. Based on polymer type, hydrogels are distributed into two categories: synthetic and natural hydrogels. Hydrogels formulated using natural or synthetic polymers. Natural polymers like chitosan, proteins as gelatin, lysozyme, collagen, fibrin and fibrin, or polysaccharides as alginate and hyaluronic acid. However synthetic hydrogels are formulated through polymerization of monomers chemically. They have a wide-ranging of chemical and mechanical properties. Synthetic polymers include poly vinyl alcohol, polyacrylamide, poly ethylene glycol and poly N-isopropyl acrylamide. These polymers should be biodegradable and biocompatible.[6-8]

3. Hybrid hydrogels.

These hydrogels combine natural and synthetic polymers to leverage the advantages of both classes and create advanced biomaterials with improved mechanical strength, degradation profiles, and biological functionality.

4. Stimuli-responsive hydrogels.

Moreover, Hydrogels may be classified into conventional or stimuli responsive hydrogels. Conventional hydrogels may not be affected by any change in the temperature, pH or electric field of the environment surrounding them because they are chains of cross linked polymer which absorb water and swollen and reversibly release water solutions when placed in an aqueous media.[9]

On the other hand, the stimuli responsive hydrogels also called smart hydrogels are sensitive to various stimuli as physical, chemical or biological and have the advantage of controlling drug release from hydrogel system in response to external or internal selected triggers.[10]

These hydrogels undergo reversible volume changes in response to environmental cues such as pH, temperature, light, or specific molecules to enable triggered drug release based on physiological conditions.

5. Injectable hydrogels.

These hydrogels can be administered in a minimally-invasive liquid form and they undergo in situ gelation to facilitate localized and targeted delivery of therapeutics.

6. Nanocomposite hydrogels.

These hydrogels incorporate nanoparticles, nanosheets, or nanofibers into the hydrogel network to enhance mechanical properties, drug loading, and controlled release capabilities, allowing researchers to design tailored DDS that can address specific physiological barriers, disease targets, and therapeutic needs, making hydrogels a versatile and promising platform for advanced pharmaceutical applications.[6]

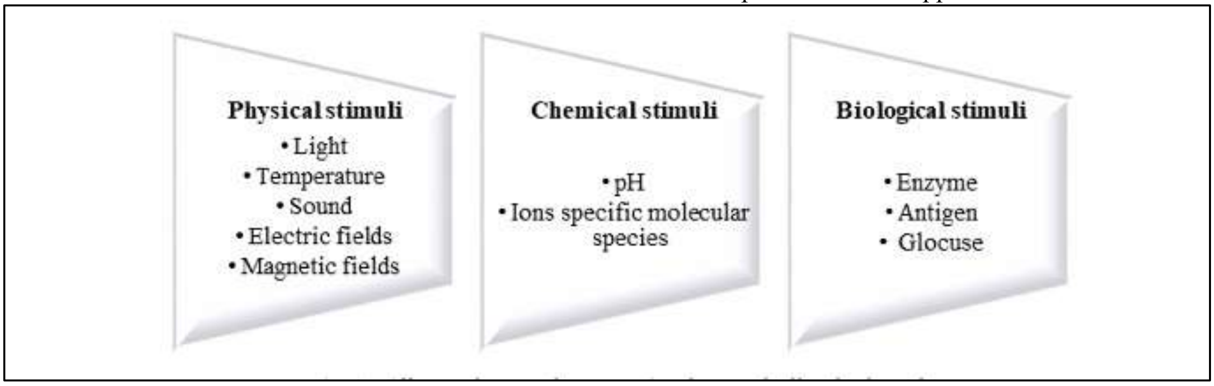

Fig. 1: Different factors that can stimulate and affect hydrogels

7. MECHANISM OF HYDROGEL FORMATION

Hydrogels are networks of polymers having hydrophilic nature. Generally, hydrogels are formed using hydrophilic monomers. However, hydrophobic monomers are sometimes used in preparation of hydrogel. Either natural or synthetic polymers could be used in preparation of hydrogels. The synthetic polymers have hydrophobic properties and chemically stronger compared to natural polymers. Because of their mechanical strength the degradation rate of synthetic polymers is slow, but this mechanical strength enhances their stability as well. A balance between these two opposed properties should be achieved to prepare an optimum hydrogel design. Moreover, Natural polymers could be used in the preparation of hydrogels provided that these polymers have appropriate functional groups. Hydrogels can be formulated by choosing the monomer or polymer type and the kind of hydrogel formation techniques. Hydrogels are designed by two methods either chemical crosslinking or physical crosslinking.[11-12]

Physical Hydrogels

Physical hydrogels are an important class of hydrogel materials that are formed through physical crosslinking mechanisms, in contrast to chemical hydrogels which rely on covalent bond formation. The network structure of physical hydrogels is held together by reversible, non-covalent interactions such as hydrogen bonding, hydrophobic effects, ionic interactions, and physical entanglement. This reversible crosslinking allows physical hydrogels to exhibit thermo reversible behaviour, where the material can transition between a solid-like gel state and a liquid-like sol state in response to changes in temperature. The reversible nature of the crosslinks in physical hydrogels provides several key advantages. First, the ability to undergo sol-gel transitions enables facile processing and injectability, as the hydrogel can be liquefied by heating or shearing and then reform the gel network upon cooling or cessation of the applied force. This makes physical hydrogels well-suited for minimally invasive biomedical applications such as in situ gelling for tissue engineering scaffolds or drug delivery depots. Additionally, the reversible crosslinks allow physical hydrogels to be dynamically remodelled and adapted to their environment, more closely mimicking the responsiveness of natural extracellular matrices. The specific crosslinking mechanisms used to construct physical hydrogels, such as hydrogen bonding, ionic interactions, or hydrophobic associations, can be tailored to impart desired properties. Hydrogels crosslinked through ionic interactions may be sensitive to changes in pH or ionic strength, enabling triggered swelling or degradation. Hydrophobically-associated physical hydrogels can exhibit thermoreversible gelation driven by the temperature-dependent hydrophobic effect. The versatility of physical crosslinking strategies allows for the rational design of hydrogel materials with customized mechanical, responsive, and degradation characteristics to meet the requirements of diverse biomedical applications. [13-14]

Chemical Hydrogels

Chemically crosslinked hydrogels are formed by creating covalent bonds between polymer chains, often through reactions between amine and carboxylic acid groups. In this approach, the carboxylic acid groups are first activated, typically using a coupling agent, to become more reactive toward nucleophilic attack by amine groups. Upon mixing the amine- and carboxylic acid-functionalized polymers, an amide bond forms, resulting in a stable, covalently crosslinked hydrogel network. The covalent nature of the crosslinks in chemical hydrogels provides enhanced mechanical strength and stability compared to physical hydrogels. Importantly, the crosslinking chemistry can be designed to be responsive to various environmental triggers, including pH, temperature, or light. Hydrogels crosslinked through acid-amine reactions can be made pH-sensitive, where the gelation is promoted at physiologically relevant pH values but can be disrupted in more acidic or basic environments. Temperature-responsive chemical hydrogels utilize thermally-sensitive crosslinking moieties that promote gelation at body temperature but remain soluble at lower temperatures, enabling minimally invasive delivery and in situ solidification. Photo-crosslink able chemical hydrogels leverage light-activated reactions to allow spatiotemporal control over the gelation process, which is particularly useful for applications like 3D bioprinting or photopatterning. The ability to engineer chemical hydrogels with stimuli responsive behavior unlocks a wide range of opportunities for biomedical therapies.[15]

8. MECHANISMS OF DRUG RELEASE

Drug release from hydrogels occurs via diffusion, swelling, degradation, or external stimuli such as temperature and pH. These mechanisms can be tailored through polymer composition and network structure to achieve controlled and sustained release. Enzyme-sensitive hydrogels degrade in response to specific biological environments, enhancing targeted delivery.

Diffusion-Controlled Release

The most common drug release mechanism from hydrogels is diffusion, where drug molecules move from the polymer matrix into the surrounding biological fluids following a concentration gradient. In this case, the hydrogel acts as a reservoir, and the rate of release depends on factors like mesh size of the polymer network, drug molecular size, and drug-polymer interactions. Hydrogels with larger mesh sizes allow faster diffusion, while tighter crosslinking slows release.[16]

Swelling-Controlled Release

Hydrogels absorb water and swell when placed in aqueous environments. This swelling enlarges the network mesh, facilitating drug diffusion out of the matrix. For some hydrogels, drug release is initially limited by water uptake and swelling kinetics. The swelling can be modulated by polymer composition and crosslink density, influencing the release rate. Swelling-controlled release is especially relevant in stimuli-responsive hydrogels that change volume in response to environmental triggers.[17]

Degradation-Controlled Release

In biodegradable hydrogels, drug release occurs through polymer chain cleavage and matrix erosion. As the hydrogel degrades via hydrolysis, enzymatic action, or other mechanisms, the entrapped drug is released in a controlled fashion. This mechanism is particularly advantageous for long-term delivery, as drug release kinetics can be tailored by controlling degradation rates through polymer chemistry.[18]

Stimuli-Responsive Release

Stimuli-responsive hydrogels undergo physicochemical changes in response to specific environmental cues, leading to triggered drug release. For example: pH-sensitive hydrogels swell or shrink depending on local pH, releasing drugs preferentially in acidic tumour sites or the gastrointestinal tract. Thermo-responsive hydrogels can undergo sol–gel transitions at body temperature, releasing drugs in a temperature-dependent manner. Enzyme-responsive hydrogels degrade selectively in the presence of specific enzymes overexpressed in disease states, enabling site-specific drug release. Such smart hydrogels allow on-demand, localized delivery, minimizing systemic side effects.[19]

Combined Mechanisms
Often, hydrogel-based DDS utilize a combination of the above mechanisms. For example, a hydrogel might swell to allow diffusion while simultaneously degrading to release drugs encapsulated within its matrix. The synergistic effects enable finely tuned drug release kinetics for various therapeutic requirements. Understanding and manipulating these mechanisms through polymer selection, crosslinking, and hydrogel design is key to developing efficient, patient-specific drug delivery platforms.[20]

9. APPLICATIONS AND LIMITATIONS

❖ **Applications**

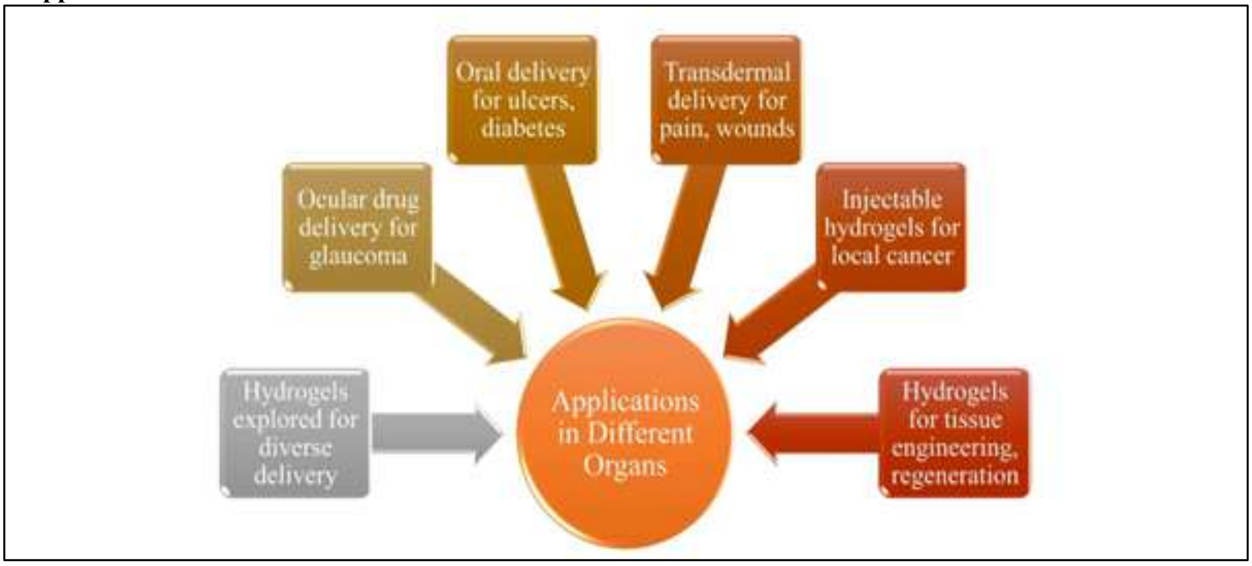

Fig. 2: Schematic illustration of the versatile application of hydrogels in targeted drug delivery to different organs and tissues.

Hydrogels possess unique properties such as high water content, tunable mechanical strength, and excellent biocompatibility that make them highly suitable for a wide range of biomedical applications.

Wound Healing
Hydrogels create a moist environment that supports cell migration and proliferation, accelerating healing while providing protection against infection. Incorporating antimicrobial agents or growth factors further enhances efficacy. Injectable and self healing hydrogels enable minimally invasive application.

Cancer Therapy
Hydrogels serve as localized depots for chemotherapeutics, reducing systemic toxicity and enhancing treatment. Stimuli responsive hydrogels release drugs in response to tumor microenvironment triggers like acidic pH or enzymes. Nanoparticle-loaded hydrogels further improve targeting.

Ophthalmic
Drug Delivery Due to their softness and transparency, hydrogels provide prolonged drug residence on the ocular surface. Thermoresponsive and mucoadhesive hydrogels allow controlled delivery in glaucoma and dry eye treatments.

Injectable Hydrogels
for Minimally Invasive Delivery Injectable hydrogels that gel in situ facilitate localized delivery with minimal discomfort, encapsulating various therapeutics including cells and proteins. They support sustained release and tissue regeneration.

Tissue Engineering and Regenerative Medicine
Hydrogels mimic extracellular matrix properties and serve as scaffolds for cell growth, supporting tissue repair in cartilage, bone, skin, and cardiac tissues]. Their tunable mechanical and degradation properties aid in customized regenerative therapies.

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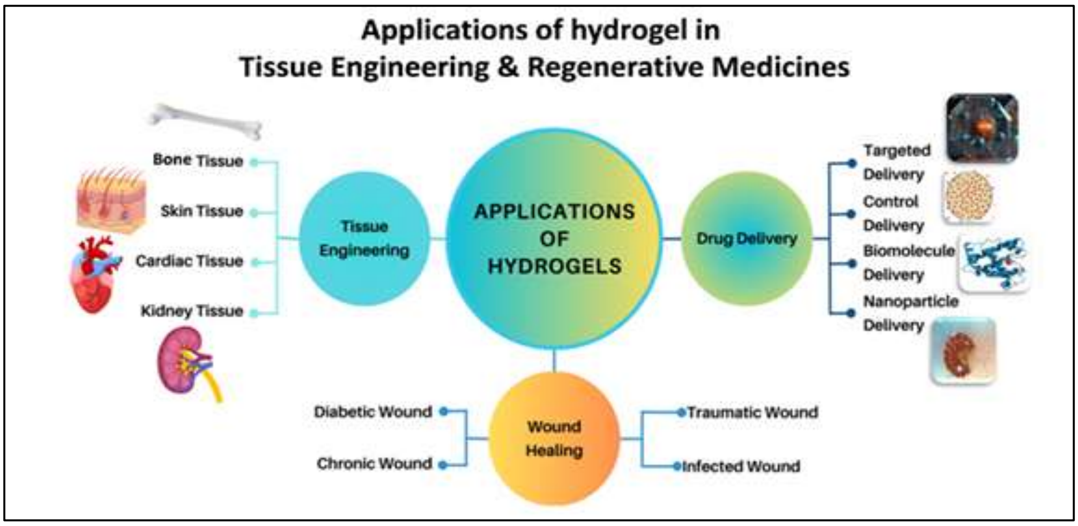

Fig. 3. Different biomedical applications of hydrogels in tissue engineering and regenerative medicines.

Controlled and Sustained Therapeutic Release
Hydrogels protect encapsulated drugs from degradation and enable sustained release of small molecules, proteins, peptides, and nucleic acids. Smart hydrogels respond to physiological stimuli for targeted delivery.

Emerging Biomedical Applications
Integration with biosensors allows feedback-controlled drug release. Hydrogels are crucial in 3D bioprinting and organ-on chip platforms for personalized medicine and drug screening. Vaccine and gene delivery applications are also emerging.[21]

❖ Limitations of Hydrogels

1. Poor Mechanical Strength
Most hydrogels possess low tensile strength and elasticity, especially those with high water content. This limits their use in:

- Load-bearing tissues
- Long-term implantable drug delivery systems

High swelling often compromises structural integrity, leading to fracture or deformation under stress.

2. Uncontrolled or Burst Drug Release
Many hydrogel systems exhibit initial burst release, particularly when drugs are physically entrapped. This can:

- Cause drug toxicity
- Reduce therapeutic efficiency
- Shorten duration of action

Precise control over release kinetics remains challenging.

3. Limited Drug Loading Capacity
Hydrogels are more suitable for hydrophilic drugs. Loading hydrophobic drugs is difficult due to:

- Poor solubility in aqueous matrices
- Weak interaction with hydrophilic polymer networks

This restricts their application for many small-molecule drugs.

4. Stability and Storage Issues
Hydrogels may suffer from:

- Microbial contamination due to high water content
- Structural instability during long-term storage
- Dehydration or syneresis

Maintaining sterility and shelf life is a major challenge.

5. Difficult Sterilization
Common sterilization techniques (autoclaving, gamma irradiation, chemical sterilants) can:

- Alter crosslinking density
- Degrade polymers
- Change swelling and release properties

This complicates regulatory approval and clinical use.

6. Poor Control Over Degradation Rate
Biodegradable hydrogels may degrade:

- Too quickly, leading to premature drug release
- Too slowly, causing accumulation or inflammation

Achieving a predictable degradation profile under physiological conditions remains difficult.

7. Reproducibility and Scale-Up Challenges
Laboratory-scale hydrogel synthesis often:

- Lacks batch-to-batch consistency
- Faces difficulties during large-scale manufacturing
- Requires strict control of reaction conditions

This affects commercialization and clinical translation.[22]

10. FUTURE PERSPECTIVES AND EMERGING TRENDS

Hydrogels continue to evolve as versatile platforms for advanced drug delivery, and several emerging trends highlight their potential in next-generation therapeutics:

1. **Stimuli-Responsive and Multi-Responsive Hydrogels**

Future hydrogel systems are being designed to respond simultaneously to multiple physiological stimuli such as pH, temperature, enzymes, redox potential, or light. These multi-responsive hydrogels enable precise spatiotemporal control of drug release, allowing site-specific and on-demand therapeutic delivery.

2. **4D and Smart Hydrogels**

4D hydrogels incorporate the dimension of time by undergoing dynamic structural or functional changes after implantation. This allows for programmable drug release, tissue remodeling, or self-healing properties, making them suitable for regenerative medicine and adaptive therapies.

3. **Nanocomposite and Hybrid Hydrogels**

Integration of nanoparticles, carbon-based materials, or bioactive molecules into hydrogel matrices can improve mechanical strength, drug-loading capacity, and targeted delivery efficiency. Hybrid systems combining natural and synthetic polymers continue to offer optimized biodegradability and stability for clinical applications.

4. **Gene and Vaccine Delivery Platforms**

Hydrogels are increasingly being explored for nucleic acid-based therapies, including mRNA, siRNA, and DNA vaccines. Their protective network allows controlled release while minimizing degradation, enhancing efficacy in cancer immunotherapy, infectious diseases, and gene therapy.

5. **Integration with Microfluidics and 3D Bioprinting**

Hydrogel-based systems are now being combined with microfluidic devices and 3D bioprinting technologies for organ-on-chip models, high-throughput drug screening, and tissue engineering. This approach enables personalized medicine and patient-specific therapeutic development.

6. **Clinical Translation and Regulatory Considerations**

Future research is focusing on scalable, reproducible, and sterilizable hydrogel formulations that meet regulatory standards. Addressing challenges such as burst release, long-term stability, and mechanical limitations will be essential to accelerate their adoption in clinical practice.

11. CONCLUSION

Hydrogels have emerged as highly versatile and promising platforms for drug delivery systems due to their unique three-dimensional polymeric networks, high water content, biocompatibility, and tunable physicochemical properties. Their ability to encapsulate a wide range of therapeutic agents—including small molecules, proteins, peptides, and nucleic acids—combined with controllable release mechanisms such as diffusion, swelling, degradation, and stimuli-responsive behavior, underscores their significant potential in advanced pharmaceutical applications.

This review has highlighted the diverse classification of hydrogels based on polymer origin, crosslinking strategies, and responsiveness to environmental stimuli, emphasizing how these factors govern hydrogel formation, stability, and drug release kinetics. The incorporation of nanotechnology, particularly hydrogel nanoparticles and nanocomposite hydrogels, has further expanded their functional capabilities by improving targeting efficiency, drug loading capacity, and therapeutic precision, especially in cancer therapy. Additionally, the integration of hydrogels with tissue engineering, biosensors, and regenerative medicine platforms has opened new avenues for personalized and localized treatment strategies.

Despite these advantages, several challenges—such as limited mechanical strength, burst drug release, difficulties in sterilization, scalability, and precise control over degradation rates—continue to hinder widespread clinical translation. Addressing these limitations through advanced crosslinking methods, hybrid and composite hydrogel systems, and standardized manufacturing approaches will be crucial for their successful commercialization.

Overall, continued interdisciplinary research integrating polymer chemistry, nanotechnology, biomedical engineering, and clinical sciences is essential to fully exploit the therapeutic potential of hydrogel-based drug delivery systems. With ongoing innovations and improved understanding of their mechanisms, hydrogels are expected to play a pivotal role in the development of next-generation precision medicine and targeted therapeutic strategies.

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