



# Hydrogels: Recent Advances

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## Abstract

Hydrogels represent a class of highly versatile, three-dimensional polymer networks renowned for their exceptional water absorption capacity, biocompatibility, and tunable physicochemical properties. This review comprehensively examines the diverse landscape of hydrogels, delineating the fundamental characteristics and applications of synthetic, natural, and advanced hybrid systems. It highlights the superior mechanical strength of synthetic hydrogels and the enhanced biocompatibility of their natural counterparts, while positioning hybrid hydrogels which synergistically combine both as multifunctional platforms with tailored properties for demanding biomedical applications. A significant focus is placed on antimicrobial hydrogels, detailing strategies for imparting antimicrobial functionality, including the incorporation of agents like peptides, antibiotics, and nanoparticles, to combat drug-resistant infections. Furthermore, the review underscores the profound significance of hydrogels in different fields. This work consolidates current advancements to illustrate the immense potential of hydrogels as innovative materials addressing complex challenges in healthcare, sustainability, and technology.

**Keywords:** Antibacterial Hydrogel; Biomedical Applications; Nanoparticles; Physicochemical Properties; Sustainability

## Introduction

Hydrogels are tri-polymer networks that absorb body fluids but are water-insoluble, created through physical and chemical crosslinking techniques, offering unique mechanical, swelling, and biological properties [1]. They are soft materials with high water content, biocompatibility, and diverse applications in biomedical fields like drug delivery, tissue engineering, wound healing, and sensor technologies [2]. Body fluids can be absorbed by three-dimensional polymer networks called hydrogels. They are employed in medicine for tissue engineering, wound dressings, and medication delivery. They can be cross-linked chemically or mechanically [3]. Hydrogels are networks of hydrophilic polymers that are cross-linked and swelled with water. They can absorb water, keep their structure, and transport molecules. They find use in drug delivery, nanotechnology, microfluidics, and biomaterials [4]. Three-dimensional networks of biopolymers with a high-water content are called hydrogels. Because of their controlled release, protection, and encapsulating qualities, they are used in food-grade delivery systems [5].

## Synthetic and Natural Hydrogels

Synthetic hydrogels are engineered materials designed and fabricated through specific processes. They often struggle to replicate the mechanoresponsive features of natural tissues, such as strain-stiffening and self-healing [6]. On the other hand, natural hydrogels, like those derived from polysaccharides, offer good biocompatibility but may lack mechanical strength and stability compared to synthetic hydrogels [7]. Blending natural and synthetic polymers can lead to superior properties in hydrogels, with natural polymers like lignocellulosic materials offering biocompatibility and flexibility, while synthetic polymers can mimic natural properties [8]. Natural hydrogels, derived from polymers like polysaccharides and proteins, are biocompatible and preferred over synthetic hydrogels. They offer potential as biomimetic alternatives for various applications in food and biomedical fields [9].

## Hybrid Hydrogels

Hybrid hydrogels are advanced materials that combine different types of polymers (synthetic and natural) or networks to create multifunctional systems with unique properties. Numerous fields, including tissue engineering, drug delivery, wound healing, and biomedical engineering,



WebLog Open Access Publications

Article ID : wjbtbe.2026.c2704  
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**Received Date:** 04 Mar 2026

**Accepted Date:** 25 Mar 2026

**Published Date:** 27 Mar 2026

### Citation:

Mahmood A, Mansoor HB, Hafeez G, Anwar MA, Jan SA. Hydrogels: Recent Advances. *WebLog J Biotechnol Biomed Eng.* wjbtbe.2026.c2704. <https://doi.org/10.5281/zenodo.19319953>

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can benefit from the use of these hydrogels. They can be composed of supramolecular networks, polymeric networks, nanomaterials, and responsive elements like electric and magnetic fields [10]. By leveraging compositional changes and dynamic cross-linking strategies, hybrid hydrogels can be tailored to exhibit specific mechanical properties suitable for diverse applications, from blood vessels to cartilage regeneration [11]. Additionally, hybrid hydrogels can possess features like enhanced antibacterial properties, tunable mechanical and adhesive properties, controlled drug release, and excellent biocompatibility, making them promising materials for various biomedical purposes.

## Composition

Hybrid hydrogels are composed of a combination of synthetic polymers and natural polysaccharides, such as Polyvinyl Alcohol (PVA) and Sodium Alginate (SA) in a 1:1 mass ratio [12]. In order to achieve a wide range of mechanical properties, these hydrogels can also be hybridized with an ionically cross-linked alginate network or incorporate acrylic monomers such as N-Acryloyl Glycinamide (NAGA) and Acrylic Acid (AAc) in single network hydrogels [11]. Additionally, supramolecular-polymeric hybrid hydrogels consist of co-assembled networks like DBS-COOH/Naproxen and polymeric networks like gelatin/quaternary ammonium group/phenylboronic acid groups-grafted chitosan, offering multi-functionality for wound healing applications [13]. Nature-inspired hybrid hydrogels can be formed by combining natural or synthetic polymers with a nonionic fibrous peptide hydrogelator, allowing for tunable gel strength and low cytotoxicity towards cells [14].

## Methods of Preparation

Hybrid hydrogels can be prepared using various methods. One approach involves combining a nonionic fibrous peptide hydrogelator with natural or synthetic polymers at low concentrations [15]. Another technique is to create co-networks, Interpenetrating Networks (IPNs), or semi-interpenetrating networks (semi-IPNs) by copolymerizing methacrylated gelatin with artificial polymers like alginate [16]. Furthermore, by fusing acrylic networks with an ionically cross-linked alginate network - a process that uses dynamic, non-covalent cross-linking for adjustable mechanical properties - hybrid hydrogels can be produced [11]. Hybrid hydrogels can also be created by copolymerizing diallyl dimethylammonium chloride and 2-hydroxyethyl methacrylate with alginate, bromothymol blue, and fume silica, enabling  $p^H$ -responsive properties suitable for sensor applications. Lastly, incorporating low molecular weight gelator peptides with polysaccharides like agarose results in bioactive and mechanically reinforced hybrid hydrogels for tissue engineering application [17].

## Properties

Hybrid hydrogels exhibit a variety of properties that make them promising materials for biomedical applications. These properties include tunable mechanical and adhesive properties, responsiveness to external stimuli like electric and magnetic fields, enhanced antibacterial properties, antioxidant capabilities, and the ability to scavenge reactive radicals. Additionally, hybrid hydrogels can demonstrate strong compressive capacity, low friction coefficients, and excellent lubricity, making them suitable for applications in cartilage repair and replacement [18]. Furthermore, Hybrid hydrogels' compositional flexibility enables dynamic, non-covalent cross-linking to be used to fine-tune mechanical properties, enabling specific targeting for various tissue engineering applications such as blood vessels and cartilage regeneration [11]. Overall, the multifunctionality and diverse properties of hybrid hydrogels position them as attractive platforms for tissue engineering, drug delivery, and wound healing applications.

## Applications

Hybrid hydrogels find diverse applications in various fields. They are utilized in tissue engineering and drug delivery, offering versatile platforms for bone, cartilage, neural, heart, and skin regeneration. Additionally, multifunctional hybrid hydrogels responsive to external stimuli are explored for biomedical applications, soft robotics, electronics, and energy science [11]. In wound healing, hybrid hydrogel dressings incorporating drug-loaded mesoporous silica and polymers have shown promise in diabetic wound treatment, accelerating healing with dual  $p^H$  and glucose responsiveness [19]. Moreover, hybrid hydrogels with tunable mechanical properties through compositional changes are crucial for tissue engineering, enabling specific targeting for different applications like blood vessels and cartilage. Furthermore, thermo-responsive drug-loaded hybrid hydrogels with natural phenolic compounds exhibit antibacterial efficacy and enhanced cell viability, making them potential materials for medical applications [20]. Detail of some of the new synthesized hydrogels and its applications is given in Table 1.

## Characterization

Characterization of hybrid hydrogels involves a multidisciplinary approach encompassing physicochemical, mechanical, and biological analyses. Physicochemical methods, such as rheology measurements and electron microscope scanning, are utilized to study viscoelastic, swelling, and transport properties of hybrid hydrogels. Tensile testing, compression testing, and rheological measurements are used to thoroughly analyze mechanical qualities, showcasing the tunability of these hydrogels [21]. Additionally, morphological conformation, swelling behavior, mechanical properties, and biodegradation are key aspects studied in hybrid hydrogels for tissue engineering applications.

**Table 1:** List of some of the new synthesized hydrogels and its applications.

Sr. No.	Hydrogel Type	Activity/Impact	Citation
1	Collagen/gelatin-based hydrogels	Shows antibacterial activities against <i>Staphylococcus aureus</i> and <i>Escherichia coli</i> . In addition, it shows anti-inflammatory, anti-cancer, and cytotoxicity properties.	[45]
2	Polymerizable ionic liquid Hydrogel	Shows antibacterial activities against <i>Staphylococcus aureus</i> and <i>Escherichia coli</i> . Also shows Anti-inflammatory properties.	[46]
3	Multifunctional hydrogel coloaded with Chitosan-Curcumin and Silver Nanoparticles	Shows antibacterial activities against <i>Staphylococcus aureus</i> and <i>Escherichia coli</i> .	[47]
4	Conventional hydrogel and a nanoparticle-based hydrogel containing <i>Satureja khuzestanica</i> essential oil	Shows antibacterial activities against <i>Staphylococcus aureus</i> and <i>Pseudomonas aeruginosa</i> .	[48]
5	Fluoropolymers and silver nanoclusters-based hydrogels	Shows antibacterial activities.	[49]

Biological characterization includes assessing biocompatibility, biodegradability, and osteo-conductivity, crucial for applications like bone regeneration [22]. Overall, the comprehensive characterization of hybrid hydrogels is vital for understanding their potential in various fields, from tissue engineering to 3D printing applications [14].

## Antimicrobial Hydrogels

Human health has been at risk worldwide from bacterial infectious illnesses and bacterially contaminated diseases. Medicinal plants play key role in controlling and treatment of bacterial and other diseases [23-28]. In addition, the antibacterial biomaterials are developed as potential antibiotic alternatives due to the growing resistance of microorganisms resulting from misuse or overuse of antibiotics. Antibacterial hydrogels are gaining popularity because of their easy manufacturing techniques and adaptability to different topologies through covalent bonds or noncovalent physical interactions in their chemical cross-linkers. Numerous novel applications can be derived from these characteristics, which include excellent conductivity, high toughness and stretch ability, injectability, self-healing, tissue adhesiveness and quick hemostasis, easy loading and controlled drug release, and exceptional biocompatibility and antioxidation [29].

## Strategies to Achieve Antimicrobial Properties in Hydrogels

Hydrogels are biocompatible, resembling natural tissues, and can be engineered to possess specific physical and chemical properties. Incorporating antimicrobial agents into hydrogels imparts additional functionality, enabling them to combat microbial infections. The antimicrobial properties of hydrogels can be achieved through several strategies [9]. One common approach involves the incorporation of antimicrobial agents, such as antibiotics, antimicrobial peptides, or metal nanoparticles, into the hydrogel matrix. These agents can inhibit the growth of bacteria or fungi, preventing infections. Another strategy involves the use of smart hydrogels that respond to specific stimuli, such as  $p^H$ , temperature, or enzymes produced by pathogens. These hydrogels can release antimicrobial agents in response to the presence of pathogens, providing a targeted and controlled delivery mechanism [30].

## Common Antimicrobial Hydrogel

By mixing lignin with poly (ethylene glycol) and poly (methyl vinyl ether-co-maleic acid) through an esterification reaction, lignin-based hydrogels with antibacterial characteristics were created. In comparison to Poly Vinyl Chloride (PVC), which is frequently used in medical materials, the hydrogels demonstrated substantial antibacterial action against *Staphylococcus aureus* and *Proteus mirabilis*, with up to a 5.0-fold reduction in adhesion [31]. The hydrogels demonstrated their promise as drug-eluting coverings for medicinal materials by maintaining the release of a model hydrophobic drug (curcumin) for up to 4 days [31]. To improve efficiency, the cross-linking of the hydrogels with the help of a microwave was investigated. In comparison to traditional approaches, the process produced hydrogels with higher cross-linking degrees and reduced swelling, suggesting enhanced antibacterial capabilities [32]. The ability of lignin-based hydrogels to prevent pathogen adhesion, even after rinsing, highlights their durability and potential for clinical applications in preventing infections in medical device coatings [33].

## Effectiveness of Peptide Hydrogels Against Microbial Targets

Peptide hydrogels are effective against microbial targets due to their ability to interact selectively with microbial cells while sparing mammalian cells, which is crucial for antimicrobial applications. The effectiveness stems from the chemical and structural components within the peptides, allowing for specific interactions with microbial membranes, such as initial electrostatic interactions with anionic bacterial membranes, leading to microbicidal activity [34]. Peptide hydrogels can be tailored to target specific microbial strains, like Gram-positive or Gram-negative bacteria, including drug-resistant strains like MRSA, showcasing their versatility and potential in combating various infections. The integration of peptide hydrogels with existing medical approaches, such as combining them with standard antimicrobials or medical device coatings, further enhances their effectiveness in preventing and alleviating infections, making them a promising tool in the fight against microbial contamination [34].

## Significance of Hydrogels

In Pharmaceuticals: Hydrogels' special qualities and adaptability have drawn a lot of interest in pharmaceutical applications. They are used in oral, ophthalmic, topical, transdermal, subcutaneous, orthotropic, rectal, and intraperitoneal drug delivery systems [35]. Hydrogels offer benefits such as biocompatibility, biodegradability, and controlled release profiles, making them ideal for delivering both hydrophilic and hydrophobic molecules [36]. Hydrogels show promise in formulating topical hormone drugs due to their potential as carriers for enhanced skin absorption, addressing limitations like low stability and bioavailability of hormones [37].

In Agriculture: Because they increase the efficiency with which water and nutrients are used in agriculture, hydrogels are extremely important, particularly in arid and semi-arid countries where water shortage is a major issue [38, 39]. These intelligent hydrogels can respond to various stimuli and release nutrients in a controlled manner, promoting seedling growth, seed germination, and overall crop yield [40]. They act as reservoirs of water, sustaining optimal moisture levels during water stress and reabsorbing water in moist conditions [41].

In Environment: Hydrogels find diverse applications in environmental sensing and remediation. Optical hydrogels (OHs) offer fast pollutant detection [42], while g-C<sub>3</sub>N<sub>4</sub>-based hydrogels show promise in removing bisphenol A from water through adsorption and photodegradation [43]. Organohydrogels, with unique properties like anti-freezing abilities and shape memory, are being explored for flexible sensors and biomedicine applications [44]. Hydrogels are appropriate for a range of environmental applications, including tissue regeneration, medication delivery, and wound dressings because of their poroelasticity and non-linear elasticity [30].

## Conclusion

In conclusion, hydrogels are immensely versatile materials whose evolution into advanced hybrid and antimicrobial systems has solidified their critical role across diverse fields. Their tunable properties allow for customized applications in biomedicine, from tissue engineering and controlled drug delivery to combating infections. Furthermore, their significance extends to enhancing agricultural sustainability and enabling environmental remediation.

Continuous innovation in hydrogel technology promises to deliver even more effective solutions to global challenges in health, agriculture, and environmental conservation.

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