Open Access

Recent Progress in Materials

LIDSEN Publishing Inc.

Review

Biohydrogels (BioHGs): Sources, Physicochemical Properties, Applications, Current Challenges - A Review

Nilesh Sankeshware [1], Ayesha Mulla [1], Shrikant Hulkane [1], Asmita Prabhune [2,*], Ibrahim M. Banat [3,*], Surekha K. Satpute [1,*]

1. Department of Microbiology, Savitribai Phule Pune University, Ganeshkhind, Pune - 411007, Maharashtra, India; E-Mails: nilesh2003official@gmail.com; mullaayesha713@gmail.com; hulkaneshri1795sr@gmail.com; drsurekhasatpute@gmail.com; satputesk@unipune.ac.in; ORCID: 0009-0009-1214-8479; 0009-0001-7340-3359; 0009-0001-2361-8888; 0000-0003-0065-4939
2. Green Pyramid Biotech Pvt. Ltd, Incubation Center, NCL Innovation Park, Dr Homi Bhabha Rd, Pashan, Pune - 411008, Maharashtra, India; E-Mail: asmita.prabhune@gmail.com; ORCID: 0000-0003-1839-2105
3. School of Biomedical Sciences, Faculty of Life and Health Sciences, University of Ulster, Coleraine, NI BT52 1SA, UK; E-Mail: im.banat@ulster.ac.uk; ORCID: 0000-0001-8964-2840

* **Correspondences:** Asmita Prabhune, Ibrahim M. Banat and Surekha K. Satpute; E-Mails: asmita.prabhune@gmail.com; im.banat@ulster.ac.uk; drsurekhasatpute@gmail.com; satputesk@unipune.ac.in; ORCID: 0000-0003-1839-2105; 0000-0001-8964-2840; 0000-0003-0065-4939

Academic Editor: Paschalis Alexandridis

Special Issue: Synthesis, Properties and Applications of Hydrogels

Recent Progress in Materials
2026, volume 8, issue 3
doi:10.21926/rpm.2603007

Received: April 26, 2026
Accepted: August 10, 2026
Published: August 25, 2026

Abstract

Since 1894, hydrogels (HGs) have advanced from simple water-swollen colloids to poly (2-hydroxyethyl methacrylate) (pHEMA)-based biomedical materials introduced in 1960. Further, the journey continued towards innovative, stimuli-responsive hybrid systems in 2025. Once limited to wound dressings and contact lenses, HGs have now formed a multi-billion-dollar

market. Biohydrogels (BioHGs) are biomaterials with remarkable physicochemical properties, enabling their widespread applications. However, several challenges also restrict their translational potential, including poor mechanical robustness, limited long-term stability, variability in natural polymer sources, and difficulties in large-scale production. Although numerous reviews have summarized BioHGs and their applications, a clear understanding of how biomaterial properties relate to HG functionality and performance remains underexplored. This review article collates esteemed, interesting, and up-to-date information on sources, properties, applications, and challenges of BioHGs. Superlative BioHGs can be produced by precisely optimizing formulation and processing parameters (polymer concentration, pH, temperature, and mechanical strength) to ensure desirable features. It was found that biomaterials spanning an extensive molecular-weight range have been utilized for HGs fabrication, enabling the tailoring of physicochemical and biological properties for specific applications. It is pertinent to note that synthetic HGs demonstrate the highest mechanical strength, natural HGs excel in swelling behaviour and porosity. In contrast, hybrid HGs achieve the most favourable overall performance by effectively balancing all anticipated properties. Briefly, further information on future research directions toward sustainable, high-performance biomaterials has been provided. We highlight recent advances focused on the development of hybrid and composite BioHGs, the incorporation of bioactive agents, and the engineering of multifunctional systems to address these limitations. The integration of novel components, such as biosurfactants (BSs), chitosan, protein-based polymers, and nanoparticles, into nanocomposites offers new opportunities for designing advanced HGs with enhanced performance.

Keywords
Biohydrogels; biosurfactants; crosslinking strategies; drug delivery; hybrid/composite hydrogels; structure-property relationship; tissue engineering

1. Introduction

'Biomaterials' have been acknowledged as a transformative class of resources that are designed to function in biological systems for promising applications. In the modern era, biomaterials appear to be one of the established approaches in the medical field, including drug delivery, tissue engineering, wound healing, etc. [1]. Among these, hydrogels (HGs) are hydrophilic polymers formed through several Interactions (Chemical: covalent and ionic; physical: hydrogen bonding and van der Waals forces). The cross-linking nature of HGs allows them to absorb and retain sizable quantities of water while maintaining their flexibility and shape. The flexibility means, in terms of the formulation, composition, manufacturing processes, or application-related aspects in biological systems. Consequently, the overall properties of HGs have encouraged researchers across diverse fields since the first report by Wichterle and Lim in the 1960s [2]. Likewise, recent articles by several research groups [3-7] show the importance of this research area. Elasticity, low adhesiveness, and softness are influenced by HGs' hydrophilic properties. The quantity of absorption is subject to (1) Polymer structure, (2) Crosslink density, (3) Solution composition, and (4) Technique employed for synthesis of HGs [1, 8]. Owing to their unique, largely reversible properties, HGs have found

applications across diverse areas and are primarily fabricated through physical or chemical cross-linking to form stable polymeric matrices. However, physically crosslinked biohydrogels (BioHGs), where biomaterials used possess reversible intermolecular interactions, thereby offer greater safety compared to the crosslinking network observed in chemical-based HGs [9, 10].

Hydrogels are basically classified as (1) Natural/biological (2) Synthetic, and/or (3) Hybrid materials that can be crosslinked through physical/chemical, or by both means. Synthetic polymers such as (i) Polyethylene glycol (PEG), (ii) Polyvinyl alcohol (PVA), (iii) Polyvinylpyrrolidone (PVP), and (iv) Polyacrylic acids (PAA) are particularly valued for their customised mechanical properties and smoothening in their functionalization [11-13]. Compared to natural or hybrid-based HGs, synthetic polymer-based HGs offer advantages chemical refining and in scaling up production, but they have limited bioactive nature and degradation-related challenges. The persistence of chemical-based HGs contributes to plastic pollution, reducing their suitability for biomedical applications that demand a biocompatible and sustainable solution or biomaterial-based HGs like BioHGs [11].

Conversely, HGs derived from natural polymers or BioHGs have gained considerable attention as an eco-friendly substitute, owing to their intrinsic biodegradability, biocompatibility, and abundance in nature [14]. BioHGs are fabricated from natural/biological polymers derived through biochemical reactions, isolation from natural sources, and photosynthesis. Different materials used for preparing BioHGs include collagen, chitosan, gelatin, cellulose, starch, hyaluronic acid etc. [1, 11]. Compared with natural tissues, the flexibility of BioHGs enables their use in the production of non-toxic byproducts. It thus makes them suitable for broader applications in medical sector. [1]. Additionally, plant-derived polymers are of great interest due to their thermostable nature [15].

The literature indicates that, since the 1960s, research has gradually shifted toward natural polymers. The crosslinked synthetic polymer-based HGs are in the limelight [2]. Contribution by Yannas et al. [16] documented the wound healing ability of collagen HGs, showcasing the potential of BioHGs in the biomedical field. Meanwhile, innovations in this field led to the balanced development of formulations for the medical sectors. The discoveries on the HGs in agriculture, biosensors, and environmental remediation are widespread [5]. Nevertheless, few challenges like batch-to-batch variations, poor solubility, non-biodegradability, weak mechanical strength, high crystallinity, residual monomers, toxic crosslinkers, and scalability have been persistently acknowledged in HGs production technology. These drawbacks can be resolved by combining both natural and synthetic HGs to produce hybrid HGs with superior properties [17].

This review broadly portrays information on BioHGs, with emphasis on their sources, including natural, synthetic, and hybrid polymers; structural and physicochemical characteristics; and crosslinking strategies. Further prominence is given to biosurfactants (BSs) and evolving biopolymers in adapting BioHGs preparations. Brief information on the multifunctional potential of BioHGs in the biomedical and biotechnological sector has been described. The materials influencing the properties and tunability of BioHGs are discussed. Moreover, current applications, key challenges are discussed, and future research directions are highlighted, focusing on the development of sustainable, high-performance biomaterials.

2. Sources of Hydrogels

In the preparation of BioHGs, natural (protein- and polysaccharide-based), synthetic, and hybrid polymers have been used extensively. These biomaterials permit the formation of single, double, or

multi-network structures, where their activity is greatly influenced by factors like the composition of the polymers, methods (chemical or physical) employed for crosslinking, electrical charge, and structural organization, i.e. crystalline, semi-crystalline, and amorphous [5, 9, 11, 12, 18]. Figure 1 outlines varied sources explored in BioHGs preparations. The polymeric nature of the materials utilized influences the physicochemical and functional characteristics of HGs. To overcome the drawbacks associated with natural HGs, hybrid HGs have been developed [8, 11, 12, 18]. Integrating the advantages of biological materials with the robustness of synthetic materials is a remarkable accomplishment. Table 1 summarizes the properties and applications of materials (PEG, PVA, PVP, and PAA), and selected hybrid systems, including Pectin/PVA/GO/APTES, PAA-WPI-F, SF/SL, PVP/PEG/MMT, and SCS/PAA employed for the preparation of HGs. These improvements have expanded the utility of HGs across a broader range of applications, representing an important advancement in biomaterials research [4, 5].

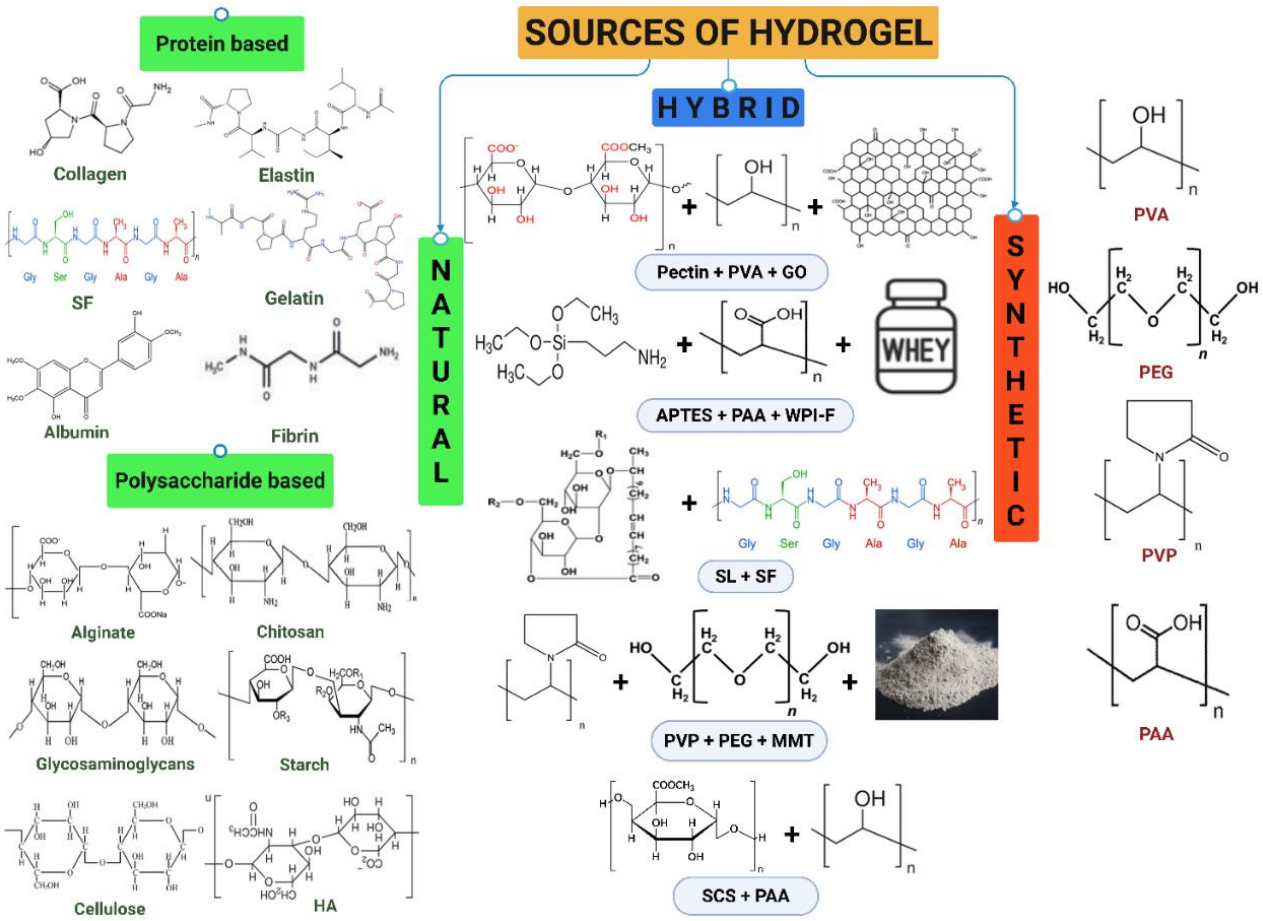

Figure 1 Overall representation of natural (protein and polysaccharide-based), synthetic, and hybrid polymers routinely employed for the preparation of Hydrogels. SF: Silk fibroin; HA: hyaluronic acid; Pectin + PVA + GO: Pectin + Polyvinyl alcohol + Graphene oxide; APTES + PAA + WPI-F: 3-aminopropyltriethyloxysilane + Polyacrylic acids + Whey protein isolate amyloid Fibril; PVP + PEG + MMT: Polyvinylpyrrolidone + Polyethylene glycol + Montmorillonite; SCS + PAA: Sodium carboxymethyl starch + Polyacrylic acids; PVA: Polyvinyl alcohol; PEG: Polyethylene glycol; PVP: Polyvinyl pyrrolidone; PAA: Polyacrylic acids; WPI-F: Whey protein isolate amyloid Fibril; SL: Sophorolipid; MMT: Montmorillonite.

Table 1 Properties and applications of natural, synthetic, and hybrid polymers employed for the preparation of Hydrogels.

Sources		MW (kDa)	Properties - Physical, chemical, biological	Application/s	References
NATURAL					
Protein	Collagen	300	Thermo-sensitivity, antioxidant properties, & mechanical stiffness	Tissue engineering, bone regeneration & wound dressing	[19-21]
	Elastin	60-70	Antioxidant activity	Wound healing	[22]
	Silk fibroin (SF)	100	Strong mechanical strength, biocompatibility, biodegradability with lower immune response	Tissue engineering, drug delivery, regeneration of tissues, & smart devices	[23, 24]
	Gelatin	90-100	Good stiffness, tensile strength, fracture resistance, biocompatibility, tissue mimicking	Uterine tissue repair	[25]
	Albumin	66.4-66.5	High biocompatibility, anti-inflammatory, & low mechanical properties	Wound dressing & tissue repair	[26]
	Fibrin	340	Stable stiffness, biocompatible, biodegradable, easy cell migration, microstructural organization	Wound healing, tissue engineering, periodontal tissue regeneration, and osteogenesis	[27, 28]
Polysaccharide	Alginate	10-600	Rapid ionic gelation, biocompatibility	Biomedical, algae cultivation	[29, 30]
	Chitosan	10-1000	Stable mechanical, biocompatibility antimicrobial properties	Food preservation & bone regeneration	[20, 31]
	Glycosaminoglycans	10-100	Biocompatible	Wound healing, skin tissue regeneration & maturation	[32]
	Starch	10^2-10^5	Biocompatibility, degradability, mechanical strength, & water retention capacity	Drug delivery, soil protection, tissue engineering, wastewater treatment & food packaging	[33, 34]

	Cellulose	50-1000	Biodegradable, mechanical properties, biocompatibility, conductivity, stretching ability	Food packaging, multifunctional sensors & wound healing	[35-37]
	Hyaluronic acid (HA)	100	Biomimicry, hydrophilicity, biocompatibility, & antibacterial properties	Bone tissue generation, cardiovascular applications & wound healing	[38, 39]
Synthetic					
Polyvinyl alcohol (PVA)		9-200	High biosafety, material accessibility, biocompatible, non-biodegradable, stabilizer	Biomedical applications, drug delivery & food packaging	[36, 40]
Polyethylene glycol (PEG)		2-40	Biocompatibility, highly aqueous soluble, non-corrosive	Biomedical dressing, thermal energy storage & smart textiles	[41, 42]
Polyvinylpyrrolidone (PVP)		2.5-1,300	Antioxidant, mechanical, biocompatible, antibacterial	Drug release and wound healing	[43]
Polyacrylic acids (PAA)		1-4,000	Biocompatibility, hygroscopic, self-healing, adhesion, & mechanical properties	Drug delivery, cartilage substitutes, wound dressings & ligament and tendon healing	[44]
Hybrid					
Pectin + PVA + GO + APTES		-	Biocompatible, mechanical strength, flexibility, structural stability, controlled swelling, crosslinker, antibacterial activity, drug release	Drug delivery, wound healing dressing	[45]
PAA - WPI-F		-	Mechanical, microstructure, swelling behaviour	Iontophoretic transdermal drug delivery systems	[46]
SF + SL		-	Self-assembling, pH-responsive	Biomedical applications	[47]
PVP/PEG/MMT		-	pH-responsive	Delivery of curcumin to cancer cells	[48]

SCS + PAA	-	Mechanical, adhesive, Electrical Conductivity, broad-spectrum antibacterial activity	Flexible wearable sensor materials	[49]

MW: Molecular weight; PVA: Polyvinyl alcohol; PEG: Polyethylene glycol; PVP: Polyvinyl pyrrolidone; APTES: Aminopropyltriethyloxysilane; PAA: Polyacrylic acids; SCS: Sodium carboxymethyl starch; SF: Silk fibroin; SL: Sophorolipid; WPI-F: Whey protein isolate amyloid fibril; GO: Graphene oxide; APTES: 3-aminopropyltriethyloxysilane; WPI-F: Whey protein isolate amyloid Fibril; SL: Sophorolipid; MMT: Montmorillonite.

2.1 Physicochemical Properties of Hydrogels

The physicochemical properties of HGs play a decisive role in employing the biomaterial for its intended purposes. Their networking ability, biocompatibility, conductivity, swelling behaviour, and functional adaptability permit their applications across diverse industrial sectors. For example, the PAM-S-CNT (polyacrylamide- carbon nanotube - sandwich-structured) composite-based HG poses superior mechanical strength (stress: 126.41 kPa), (strain: 367.9% at 500% - water-solid ratio), and considerable conductivity (34.02 S/m) at around 50% water-solid ratio, and rapid responsiveness (20 ms). Thus, multifunctional applications of carbon nanotube-HG composites are enabled by the dual-conductivity mechanism [50]. The administration of HGs in these applications is certainly guided by their physicochemical properties, such as mechanical modulus, swelling capacity, diffusion behaviour, and responsiveness to external stimuli. The hybrid HGs have been produced by combining polymers with complementary characteristics, thereby enhancing biocompatibility, mechanical strength, stability, and functional versatility [8, 11, 12, 18]. As stated by Wei et al. [51], the photo-crosslinked chitosan methacrylate (CSMA) HGs exhibit notable properties with a substitution degree of 49.61%, enabling efficient grafting of C=C bonds and a high crosslinking density. The optimized CSMA7 HGs achieved 97.96% ε-polylysine (ε-PL) loading efficiency, equilibrium swelling (407.65%), and retained 304.16% re-swelling capacity after 5 cycles. Sustained ε-PL release within 480 minutes provided long-term antibacterial activity, extending salmon shelf life from 3 to 19 days (@4°C), underscoring its ability in aquatic product preservation. Synthetic HGs show the highest mechanical strength, with Young's modulus reaching up to 1000 MPa and tensile strength up to 60 MPa, making them the best for load-bearing applications. However, they have low swelling (<100-3000% g/g) and often slow or non-degradable behaviour (up to 180 days). In contrast, natural HGs exhibit the highest swelling capacity (up to 3000% g/g) and excellent porosity (up to 95%), along with fast degradation (within 2-60 days) and moderate gelation times, but are mechanically weak (≤5 MPa). Hybrid HGs provide the best balance, combining moderate-to-high mechanical strength (up to 5 MPa) with controlled swelling (≤1200% g/g), tunable gelation (2-30 min), and extended degradation (up to 90 days). Overall, synthetic HGs are best for strength, natural HGs for swelling and porosity, and hybrid HGs offer the most optimized overall performance across all parameters [52, 53].

The physicochemical and biological properties of HGs can be improved using nanocomposite HGs, which have potential for bone tissue engineering applications. Research contribution by Yodpatum et al. [54] demonstrated the synthesis of thermosensitive chitosan-collagen HGs by using ZnONPs and AgNPs (0.01%). These chitosan-collagen HGs exhibited effective antibacterial activity, structural integrity, water absorption, and thermal stability, while having improved mechanical properties. The authors recommended their application in chitosan-collagen-based HGs preparations for grafting alveolar bone.

One of the imperative properties of HGs is their stimulus-responsive behaviour, which enables them to undergo reversible sol-gel or volume phase transitions when exposed to external physical or chemical cues. These stimuli may be physical (temperature, light, pressure, and electromagnetic fields) or chemical/biochemical (pH changes, ionic strength, and specific molecular interactions). The responsiveness of HGs is largely determined by the (1) Monomer composition, (2) Charge density, (3) Pendant chains, and (4) Crosslinking degree, with the magnitude of action is proportional to the applied stimulus [55]. Natural polymers like chitosan, cellulose, and gelatin, as

well as synthetic polymers such as poly-N-isopropylacrylamide, PEG, PAA, and PVA, are commonly employed to design such smart HGs [56]. Their adaptability has led to diverse applications (environmental remediation, drug delivery, and smart textiles), including positioning stimuli-responsive HGs as a pivotal class of advanced biomaterials [5]. For instance, thermo-responsive HG (poloxamer-based) has been designed for drug loading and delivery of a 'hydrophilic-nature Traditional Chinese Drug' to treat atopic dermatitis by applying it onto Shrewd fabrics [57]. Such innovations are encouraging and suggest many more such opportunities for the benefit of mankind.

Dubey et al. [47] prepared sophorolipids (SLs) and silk fibroin (SF) based HGs and examined the effect of pH on SL-SF interactions and gel development through (1) Rheology, (2) Fluorescence spectroscopy, (3) Small Angle Neutron Scattering - SANS, and (4) Nuclear Magnetic Resonance - NMR. SLs are a popular low-molecular-weight biosurfactant (BS) and, due to their amphiphilic nature, act as a self-assembling gelation molecule. SLs accelerate the polymer gelation process while improving its mechanical stability. Furthermore, the antimicrobial properties of SLs positively encourage their usage in HGs preparations and applications, particularly in the medical sector. Dubey et al. [47] reported that increasing pH from 6 to 8 reduces the assembly of SLs (two forms: acidic sophorolipids - ASL and lactonic sophorolipids - LSL), altering their hydrophobic association with SF, resulting in chain unfolding and rapid gelation. As the structural design and fabrication methods change, the functional performance also differs. Altogether, the incorporation of LSL meaningfully influenced the physicochemical properties of SF-based HGs by modifying their self-assembly behaviour, gelation kinetics, and structural organization. The adjacent link between preparation strategy, property profile, and application emphasizes the versatility of HGs in modern research.

2.2 Applications of Biohydrogels

Variations in properties directly shape their applications, enabling HGs to serve diverse roles in biomedical fields as well as non-medical areas, including food preservation, environmental remediation, and smart devices. Thus, this section focuses on the versatility of HGs across different areas, i.e., their applications, arising from the dynamic interplay between intrinsic properties and tailored design strategies.

2.2.1 Applications of Hydrogels in the Biomedical Sector

The BioHGs have been recognised as promising candidates for designing wound dressings due to their exceptional properties and capacity to mimic an optimal healing environment. Wound-healing applications: The BioHGs have sparked research interest in the biomedical sector due to their high water retention, porous structure [58], and ability to maintain a moist environment that accelerates healing and supports tissue regeneration. For instance, polyurethane-based HGs synthesized from renewable components exhibit excellent cell compatibility and promote cell proliferation. The controlled release of curcumin (a cross-linking agent, free radical scavenging) and *Panax notoginseng saponins* (PNS) enhances their therapeutic efficacy, making them a promising candidate for treating mechanically damaged skin prone to infection and bleeding [59]. Another contribution appeared from the research group of Ghahfarokhi et al. [60], recommending the role of HGs in tissue engineering and the wound healing process. Here, HGs serve as scaffolds that mimic the extracellular matrix, supporting cell attachment, growth, and differentiation [61, 62]. Excellent

cytocompatibility, facilitating cell viability and spreading, is demonstrated by Methacrylate quaternized chitosan/oxidized Kappa-carrageenan (MQC/OKC) based HGs. For soft tissue engineering applications specifically, MQC/OKC-M HGs exhibit tunable mechanical properties, controlled degradation, and adjustable swelling behaviour, making them highly suitable [60].

In addition to wound healing, HGs have also been widely explored for drug delivery, cancer therapy, and other biomedical applications. Their ability of HGs to respond to environmental stimuli enables targeted and sustained release of therapeutic agents. For example, bacterial ghosts (BGs) incorporated into HGs and loaded with the anticancer drug doxorubicin (DOX) exhibited pH-responsive drug release behaviour, attributed to the ionization of HGs under varying pH conditions [63]. It's noteworthy that biomedical applications of BioHGs represent the largest share among all HGs applications, owing to their unique properties. In the year 2020, Kim et al. [64] designed an injectable scaffold biocompatibility delivery system by engineering alginate with poly (ε-caprolactone-co-lactide)-b-poly (ethylene glycol)-b-poly (ε-caprolactoneco-lactide) and O-phosphorylethanolamine to promote expedited bone biomineralization. Overall, in gene therapy, they facilitate the safe and efficient delivery of genetic material. At the same time, in tissue engineering, they serve as scaffolds that mimic the extracellular matrix to support cell growth and regeneration.

2.2.2 Applications of Hydrogels in Environmental Remediation and the Agriculture Sector

While biomedical applications represent the largest domain for BioHGs due to their varied and remarkable features, these materials have also expanded for environmental bioremediation purposes and agricultural fields. In wastewater remediation, HGs serve as efficient adsorbents for heavy metals, pollutants, and dyes. In the agriculture sector, HGs serve as powerful soil conditioners and water-retaining agents, gradually releasing water and nutrients to promote sustainable farming practices. As a powerful platform for environmental remediation, the combination of HGs with Biochar (BC-HG) unveils superior mechanical stability, enhanced swelling capacity, and strong pollutant affinity. Biochar is a carbon-rich material produced by heating organic materials such as agricultural waste, wood, and leaves under limited-oxygen conditions, i.e., the pyrolysis process [65]. For diverse environmental applications, these preparations integrate the varied properties of HGs, offering a sustainable, eco-friendly solution [66].

Hydrogel preparations are also helpful in the removal of toxic organic dyes. Research by Mondal et al. [67] demonstrated the usage of bovine serum albumin (BSA) in removing methylene Blue (MB), Coomassie Brilliant Blue (CBB), and Bismarck Brown Y (BBY) from wastewater. The HGs exhibited supreme adsorption capacities (509.92: BBY), (607.72: MB), and (305.56: CBB) mg g^{-1} at 298 K. Moreover, metals like Pb^{2+} and Cd^{2+} were removed by about 90% from wastewater. Collagen-Xanthan gum (XG) semi-IPN HGs enable the gradual release of plant-relevant compounds, achieving a protein concentration (≈19.5 mg/L, phosphorus ≈1.7 mg/L). Biological assays confirmed excellent biocompatibility, as tomato-derived cells adhered, migrated, and proliferated with enhanced metabolic activity. At the whole-plant level, HGs application supported normal growth for 60 days under low-input conditions, highlighting their multifunctional potential with required hydration, degradation, and nutrient-release properties [68].

Similarly, Rebelo et al. [69] demonstrated that cellulose-HGs exhibited strong resistance to pH and salinity, enhancing soil water retention by ~20% with only 1.0 wt% incorporation. The cellulose-

HGs delayed fertilizer release for over 1 week and biodegrade within 12 weeks approximately, offering an eco-friendly solution aligned with sustainable agricultural practices. BioHGs transcend their role as passive adsorbents by functioning as dynamic interfaces between pollutants and ecological systems. Their ability to conjugate biodegradability with selective adsorption and controlled nutrient release not only mitigates contamination but also actively restores environmental balance.

2.2.3 Other Industrial Sectors - Food, Electronics, etc.

The HGs have also carved a niche in diverse technological and industrial arenas, as well as in medicine and environmental and/or agricultural sustainability. The unique properties of HGs enabled applications in flexible electronics, sensors, food preservation, and smart packaging. This section highlights the emerging directions, underscoring how HGs are evolving into versatile platforms that bridge basic science, biology, materials science, and industries together. The incorporation of polymer-based HGs with sensing capabilities is a current trend that enables biomaterials to detect and respond to biological signals such as pH changes, biomarkers, or enzyme activity. By embedding sensors within HGs, continuous monitoring of disease progression, therapeutic efficacy, and drug release status is now possible. Smart polymer-sensor integration positions HGs as advanced platforms for real-time biomedical monitoring [12].

Recently, in 2026, Li et al. [70] developed a starch-based fluorescence HG by using CDs and Eu^{3+}. The fluorescent-HG sensor was used to selectively detect methyl parathion (MP). The starch-based HGs exhibited excellent mechanical performance, with elongation (up to 976%) and a 70% compression ratio. Their high adsorption energy (-65.3 kcal/mol) ensured strong selectivity for MP, while the fluorescent sensor achieved detection up to 0.4 μM, demonstrating superior sensitivity, stability, and reusability. This study introduces a visual, non-destructive approach for detecting specific pesticide residues, even at lower concentrations, guiding advanced applications of HG-based sensors [70]. Such studies are extremely useful when multi-colour fluorescent HG-sensors could be used to detect and differentiate several components.

A demonstration by Alasalvar et al. [71] anticipated that pectin-chitosan HG films enriched with extract (solvent) derived from *Hibiscus sabdariffa* exhibited strong antioxidant activity and were useful for enhancing oxidative stability in food packaging. Although the solvent increased water vapour permeability and reduced barrier performance; the films showed promising results for direct-contact use with perishable foods. The visible colour changes of the food enabled freshness monitoring, while pH responsiveness, antioxidant functionality, and mechanical flexibility supported smart packaging applications of HGs. In recent times, HGs, across their wide spectrum of applications, have revealed themselves not simply as materials but as adaptive approaches capable of sensing, protecting, nourishing, and communicating with their surroundings. This unique duality, i.e., functioning both as guardians of sustainability and enablers of advanced technologies, marks HGs as limit-breaking innovations poised to redefine the future of material science. Figure 2 illustrates overall applications of BioHGs in different industrial sectors.

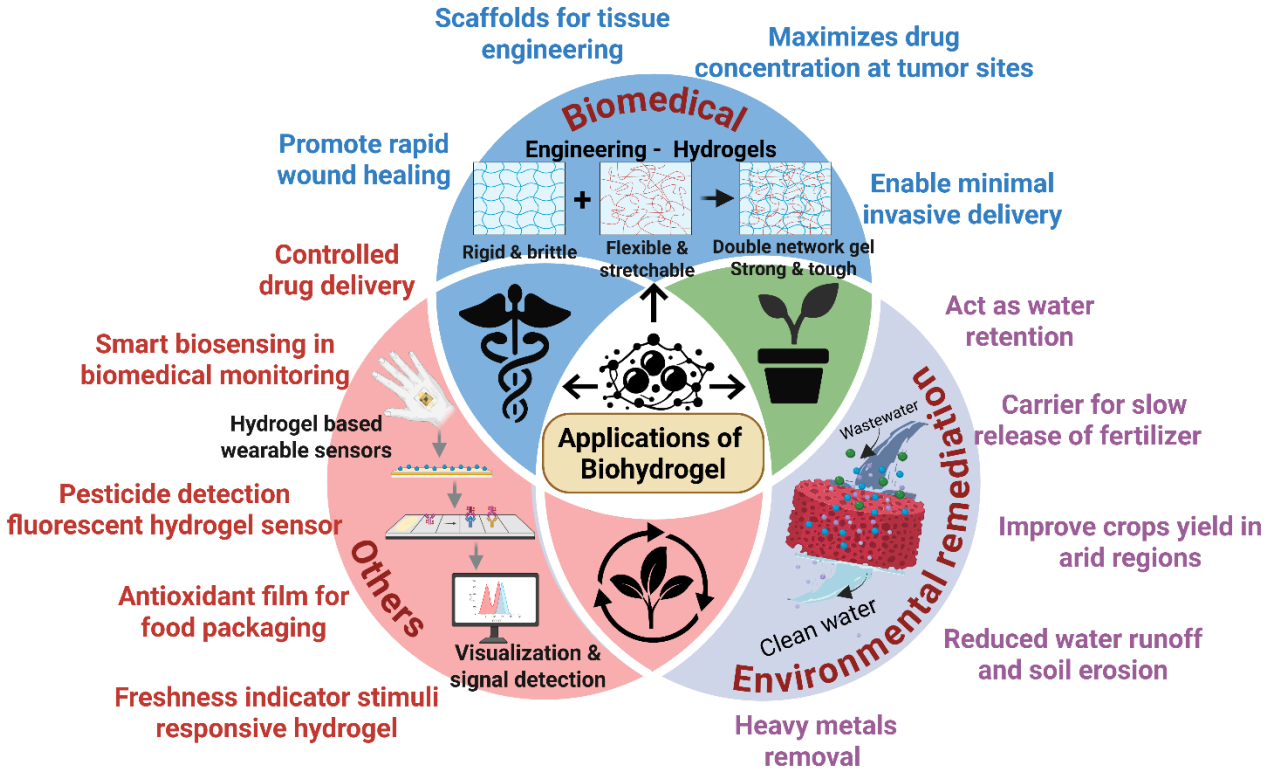

Figure 2 Applications of biohydrogels in different industrial sectors.

2.3 Challenges Associated with the Use of Hydrogel-Based Systems for Application Purposes

2.3.1 Mechanical Strength

Hydrogels made from natural polymers is associated with certain limitations, including inferior mechanical properties due to their origin. Therefore, limiting their use in load-bearing biomedical applications demands rigorous structural integrity testing. These challenges are serious in tissue engineering of cartilage, bone, and also in wound-healing scaffolds, where stability of the materials under physiological conditions is critical [11]. Native cartilage exhibits compressive moduli of ≈0.5-1 MPa, where properties (softness and brittleness) of natural polymer HGs result in premature failure to compensate under physiological conditions [72]. To overcome the said challenges, approaches such as crosslinking, composite formation, and nanomaterial amalgamation improve their mechanical properties for sustainable applications. On the contrary, classical HGs (monomer usage, cross-linkers) affect toughness, stiffness, and tensile strength. Current research is directed toward innovative strategies for producing HGs with improved mechanical properties [73] through a double-network (DN). Achieving higher energies and tensile strengths (>1-3 MPa) is essential [74] to use for the desired applications. Furthermore, nano-composite HGs impregnated with graphene oxide, nano-clay, or cellulose nanofibers establish greater strength and improved flexibility compared to conventional HGs.

Nano-composite HGs exhibit improved elasticity due to strong polymer-filler bonding [75, 76]. Gong et al. [74] synthesized a new material category of HGs in the form of a “double network”, which was derived from several cross-linking processes between two polymer networks. In conclusion, nanocomposite HGs, impregnated with nanomaterials, possess higher strength and

improved flexibility than traditional HGs. These advancements highlight the transition toward mechanically robust applications of specific nanocomposite-based HG systems.

2.3.2 Biocompatibility and Biodegradability

These properties of HGs are advantageous for biologically related applications. However, significant batch-wise variation can be expected in performance and composition of HGs. The molecular weights of varied biomaterials used for rearing HGs are also a major concern. Additionally, impurities in the raw substrates could be a major hurdle [77]. Overall, the factors described here significantly affect the consistency in key characteristics of BioHGs. These HGs derived from natural biomaterials (chitosan, starch, alginate, pectin, etc.) may represent the extracellular matrix and provide simulation and supporting interactions within cell populations without affecting immunological pathways [11]. Generally, the following aspects influence the overall performance of HGs for intended applications. Along with the quality of the raw material, their usage, and the exploitation of advanced analytical techniques, and refined extraction processes, these factors ensure consistent performance of HGs [61]. However, despite their ever-growing usage, HGs face several interlinked challenges related to their intrinsic properties, sources, and applications, which ultimately limit their full potential for proposed applications. For example, controlled drug delivery is another critical limitation, as variations in physiological conditions (enzymatic activity, temperature, and acid/alkali conditions) in the body's environment can lead to unpredictable release profiles, reducing therapeutic efficacy. Refining extraction processes, standardizing raw material quality, and using advanced characterization techniques are essential to mitigate these challenges and ensure reliable HGs performance. An overall summary highlighting source-based limitations of HGs and related impact on physicochemical properties and biomedical applications is presented in Table 2.

Table 2 Source-dependent limitations of hydrogels: Impact on physicochemical properties and biomedical applications.

Hydrogel Source	**Property Variation (Source-dependent)**	**Proposed Limitation**	**Impact on Applications**	**References**
Natural polymers	Variability in molecular weight, purity, & composition	Poor reproducibility, Batch inconsistency	Unpredictable gel strength, swelling, & drug release	[62, 78]
Natural HGs	Non-uniform ionic/ enzyme crosslinking Enzyme-mediated degradation	Too fast biodegradation Poor scalability	Loss of the scaffold before tissue regeneration completes Difficult large-scale production	[52, 62, 79, 80]
Natural HGs (animal-derived)	Presence of endotoxins, proteins	High immunogenicity risk	Limits clinical translation and regulatory approval	[62, 81]
Chitosan	pH-sensitive solubility, low mechanical strength	Weak structural integrity	Limited use in load-bearing tissue engineering	[82, 83]
Hyaluronic acid (HA)	Rapid enzymatic degradation (2-14 days)	Poor stability	Short residence time in vivo	[84, 85]
Silk fibroin	Source-dependent molecular weight	Batch variability	Inconsistent mechanical properties	[52, 62]
Protein-based hydrogels (SPI, gluten)	Allergenic, pH sensitivity	Poor mechanical strength, Immune response	Limited biomedical use	[4, 86]
Synthetic HGs	Chemically defined structure Lack of degradability (e.g., PEG, PVA)	Low bioactivity Accumulation in the body	Poor cell adhesion unless modified; limited long-term implantation	[11, 52, 87]
PEG HGs	Polydispersity, molecular weight variation Balance between degradation and stability	PEG-HGs Polydispersity, molecular weight variation Batch inconsistency in degradation & stiffness Difficult tuning	Unpredictable drug release & mechanical behaviour Failure in orthopaedic/ neurosurgical implants	[88-91]

PVA HGs	Non-biodegradable nature	Long-term accumulation	Limited in vivo applications	[88, 89, 92]
Poloxamer HGs	Temperature-dependent gelation High concentration toxicity	Weak mechanical strength Cytotoxicity risk	Poor long-term cell viability Limits injectable applications	[89, 93]
PLA/PLGA HGs	LA/GA ratio variation Swelling degradation coupling	Unpredictable degradation & swelling, coupling Complex kinetics	Difficult drug release control Unreliable drug delivery systems	[58, 94, 95]
Hybrid-HGs	Mixing natural + synthetic or degradable products	Complex processing Potential toxicity	High cost & scalability issues Biocompatibility concerns	[86, 88, 96]

HGs: Hydrogels; PEG HGs: Polyethylene glycol hydrogels; PVA HGs: Polyvinyl alcohol hydrogel; PLA/PLGA HGs: Polylactic acid/Poly-lactic-co-glycolic acid hydrogels; LA/GA: Lactic-co-glycolic acid.

2.3.3 Production Cost and Scalability

The production cost of BioHGs is primarily determined by the quality of biomaterials (crude or pure), the type and nature of crosslinking agents, and the purification processes used during their manufacture. The use of highly purified materials increases the overall monetary burden. Added expenses may arise from functionalization strategies designed to expand superlative durability, chemical modifications/complex fabrication, bioactivity, mechanical strength, or other performance characteristics. Furthermore, contributions to the financial burden can arise from the implementation of sterilization protocols, specialized equipment, and stringent control procedures. Costs associated with storage, transportation, and a limited shelf life also need to be considered. Rigorous regulatory compliance and quality control amendments also require significant financial resources. Despite enormous application potential, the large-scale production of BioHGs encounters several challenges at scalable production [78]. Also, inherent limitations with in batch-to-batch variability associated with natural biopolymers and the availability of consistent/reliable sources of biomaterial used can adversely affect product performance and uniformity. Moreover, the extraction, purification, and processing of natural polymers are often labour-intensive and time-consuming. These issues result in significant barriers to industrial-scale manufacturing and clinical translation. Achieving process standardization, reproducibility, and quality consistency across large production batches remains a critical challenge. These constraints make commercial-scale BioHGs production less competitive than the manufacture of more readily processed synthetic alternatives. Therefore, the development of cost-effective extraction methods, scalable processing technologies, and standardized modification strategies is essential to facilitate widespread industrial adoption of BioHGs.

3. Conclusions & Future Prospects

This review has endeavoured to integrate the current framework of BioHGs, covering their sources, physicochemical properties, and multifunctional applications across diverse sectors. The structural diversity and adaptability of BioHGs for diverse industrial sectors are unquestionably incredible. The extracellular matrix architecture of BioHGs allows controlled release profiles, making them highly suitable for tissue engineering, drug delivery, wound healing, bio-sensing, agriculture, etc. Biomedical uses remain dominant due to biocompatibility and therapeutic precision, yet ecological and agronomic roles emphasize sustainability. Critically, the balance between natural and synthetic BioHGs dictates degradability, mechanical strength, and scalability, while challenges of reproducibility, cost efficiency, and regulatory hurdles remain unresolved. Despite significant advances, major gaps persist, including limited mechanical robustness, batch-to-batch inconsistencies in natural polymers, unpredictable drug-release profiles, and challenges with scalability and standardization. To address these limitations, future research should focus on developing reproducible synthesis protocols, advanced hybrid nano-enabled systems, and precisely tunable multi-stimuli responsive HGs. Additionally, integrating green synthesis approaches, computational modelling, and clear regulatory pathways will be crucial to translate these materials into reliable, viable, application-specific next-generation biomaterials. At the microstructural level, HGs engineered with nanoreinforcements and microscale patterning offer customization of transport properties, targeted adsorption capabilities, and superior mechanical robustness. Integration with imaging technologies, microfluidics, membrane systems, and real-time sensor

platforms could lead to adaptive, intelligent therapies and water-treatment solutions. Overall, HGs demonstrate exceptional promise for enabling next-generation applications that address emerging societal and technological challenges. Emphasis is placed on advanced strategies, improved standardized processing methods, and more cost-effective production techniques to enable the development of HGs to ensure consistent and reliable performance and controlled functionality in real-world applications. Since their first description in 1894, hydrogels (HGs) have undergone significant development. They have progressed from early colloidal systems in 1960 to biomedical materials and ultimately to sophisticated smart, stimuli-responsive hybrid systems by 2025. Ultimately, BioHGs and smart biopolymer gels are poised not only as versatile materials but as transformative platforms driving innovation at the interface of human health, sustainability, and advanced technology.

Abbreviations/Acronyms

APTES	Aminopropyltriethyloxysilane
BBY	Bismark brown Y
BC-HG	Biochar-hydrogel
BGs	Bacterial ghosts
BioHGs	Biohydrogels
BSA - HGs	Bovine serum albumin-hydrogels
CBB	Coomassie brilliant blue
CSMA	Chitosan methacrylate
DES	Deep eutectic solvent
DN	Double-network
EC	Electrical conductivity
GO	Graphene oxide
HA	Hyaluronic acid
HGs	Hydrogels
MB	Methylene blue
MMT	Montmorillonite
MQC/OKC	Methacrylate quaternized chitosan/oxidized kappa-carrageenan
MQC/OKC-M HG	Medium-oxidized hydrogel
MW	Molecular weight
NMR	Nuclear magnetic resonance
PAA	Polyacrylic acids
PAM-S-CNT	Polyacrylamide-S-carbon nanotube
PEG	Polyethylene glycol
PLA/PLGA HGs	Polylactic acid/Poly-lactic-co-glycolic acid hydrogels
PNS	Panax notoginseng saponins
LA/GA	Lactic-co-glycolic acid
PVA	Polyvinyl alcohol
PVP	Polyvinyl pyrrolidone
SANS	Angle neutron scattering
SCS	Sodium carboxymethyl starch

SF	Silk fibroin
SL	Sophorolipid
WPI-F	Whey protein isolate amyloid fibril
XG	Xanthan gum
ε-PL	ε-polylysine

Acknowledgments

The authors are grateful to Savitribai Phule Pune University, Pune, Maharashtra, India, for providing financial support to complete the proposed research.

Author Contributions

Nilesh Sankeshware, Ayesha Mulla, and Shrikant Hulkane were involved in writing the original draft, data curation, and visualization, including the creation of images. Asmita Prabhune, Ibrahim M. Banat, and Surekha K. Satpute were involved in conceptualization, supervision, validation, and writing—review and editing. All authors carefully reviewed and approved the final version of the manuscript.

Funding

Mr. Shrikant Hulkane, thanks to the University Grants Commission (UGC), Government of India, for Junior Research Fellowship (JRF) (Student ID - 211610152301). Dr. Surekha K. Satpute expresses gratitude towards the Department of Science & Technology-Fund for Improvement of S & T Infrastructure (DST-FIST 2021/LS-1/851), Government of India, Anusandhan National Research Foundation (ANRF), New Delhi (File No ANRF/PAIR/2025/000015/PAIR-B), and Rashtriya Uchchatar Shiksha Abhiyan (Ref: RUSA-CBS-TH-3.2) for financial support.

Competing Interests

The authors declare that they have no conflict of interest.

AI-Assisted Technologies Statement

The authors declare they have not used AI tool to generate, analyze, or interpret the scientific content. However, AI tool was partly used to improve the language and grammar of the article.

Images were created using a licensed copy of 'BioRender software' (Professional Science Figure creator, BioRender, Toronto, Ontario, Canada) purchased by the Department of Microbiology, Savitribai Phule Pune University, Pune, Maharashtra, India.

References

1. Catoira MC, Fusaro L, Di Francesco D, Ramella M, Boccafoschi F. Overview of natural hydrogels for regenerative medicine applications. J Mater Sci Mater Med. 2019; 30: 115.
2. Wichterle O, Lim D. Hydrophilic gels for biological use. Nature. 1960; 185: 117-118.

3. Kasai RD, Radhika D, Archana S, Shanavaz H, Koutavarapu R, Lee DY, et al. A review on hydrogels classification and recent developments in biomedical applications. Int J Polym Mater Polym Biomater. 2023; 72: 1059-1069.
4. Zhao L, Zhou Y, Zhang J, Liang H, Chen X, Tan H. Natural polymer-based hydrogels: From polymer to biomedical applications. Pharmaceutics. 2023; 15: 2514.
5. Karoyo AH, Wilson LD. A review on the design and hydration properties of natural polymer-based hydrogels. Materials. 2021; 14: 1095.
6. Klein M, Poverenov E. Natural biopolymer-based hydrogels for use in food and agriculture. J Sci Food Agric. 2020; 100: 2337-2347.
7. Ullah F, Othman MB, Javed F, Ahmad Z, Akil HM. Classification, processing and application of hydrogels: A review. Mater Sci Eng C. 2015; 57: 414-433.
8. Jacob S, Nair AB, Shah J, Sreeharsha N, Gupta S, Shinu P. Emerging role of hydrogels in drug delivery systems, tissue engineering and wound management. Pharmaceutics. 2021; 13: 357.
9. Augustine R, Alhussain H, Zahid AA, Raza Ur Rehman S, Ahmed R, Hasan A. Crosslinking strategies to develop hydrogels for biomedical applications. In: Nano hydrogels: Physico-chemical properties and recent advances in structural designing. Singapore: Springer; 2021. pp. 21-57.
10. Hu W, Wang Z, Xiao Y, Zhang S, Wang J. Advances in crosslinking strategies of biomedical hydrogels. Biomater Sci. 2019; 7: 843-855.
11. Nanda D, Behera D, Pattnaik SS, Behera AK. Advances in natural polymer-based hydrogels: Synthesis, applications, and future directions in biomedical and environmental fields. Discov Polym. 2025; 2: 6.
12. Yadav P, Singh S, Jaiswal S, Kumar R. Synthetic and natural polymer hydrogels: A review of 3D spheroids and drug delivery. Int J Biol Macromol. 2024; 280: 136126.
13. Madduma-Bandarage US, Madihally SV. Synthetic hydrogels: Synthesis, novel trends, and applications. J Appl Polym Sci. 2021; 138: 50376.
14. Ali A, Ahmed S. Recent advances in edible polymer based hydrogels as a sustainable alternative to conventional polymers. J Agric Food Chem. 2018; 66: 6940-6967.
15. Pirsa S, Khodaei SM, Karimi Sani I, Ghasemi Y, Jawhar ZH, Eghbaljoo H. Hydrogels and biohydrogels: Investigation of origin of production, production methods, and application. Polym Bull. 2023; 80: 10593-10632.
16. Yannas IV, Tzeranis DS, Harley BA, So PT. Biologically active collagen-based scaffolds: Advances in processing and characterization. Philos Trans A Math Phys Eng Sci. 2010; 368: 2123-2139.
17. Kumar A, Pandey S, Kumar K, Krishnamoorthi S, Tungala K. Hydrogels: Classification, cross-linking methods, characteristics, and current trends in biomedical applications. Polym Bull. 2026; 83: 49.
18. Chamkouri H. A review of hydrogels, their properties and applications in medicine. Am J Biomed Sci Res. 2021; 11: 485-493.
19. Kandhan SJ, Gayathri C, Jayakumar GC, Balaraman M. Development of collagen based hydrogel from tannery raw trimming waste for biomedical 3D printing applications. Clean Chem Eng. 2026; 14: 100222.
20. Ningrum EO, Perwitasari TS, Fahreza NA, Abidin SZ, Gotoh T, Triastuti WE, et al. Sustainable marine waste-derived hydroxyapatite/collagen/chitosan hydrogels as bioactive composite materials for bone-related applications. Biochem Eng J. 2026; 230: 110134.

21. Escobar C, Figueroa T, González L, Ruíz I, Aguayo CR, Toledo JR, et al. Poly(vinyl alcohol) (PVA)/Graphene Oxide (GO)/Vitamin A Palmitate (VAP) hydrogels for wound care: Integrating mechanical robustness, photoprotection, and enhanced bioactivity. ACS Appl Polym Mater. 2026; 8: 901-918.
22. Moon SH, Kim SC, Kim NG, Heo SY, Heo SJ, Park WS, et al. Polyvinyl alcohol/pectin hydrogels incorporating marine elastin hydrolysates for enhanced wound healing and extracellular matrix remodeling. Int J Biol Macromol. 2026; 350: 151011.
23. Peng L, Zhou P, Liao F, Liu G, Bao S, Yang X, et al. Silk fibroin hydrogels: Gelation mechanisms, fabrication techniques, and biomedical applications. Int J Biol Macromol. 2025; 322: 146699.
24. Hirlekar S, Ray D, Aswal VK, Prabhune A, Nisal A, Ravindranathan S. Silk fibroin-sodium dodecyl sulfate gelation: Molecular, structural, and rheological insights. Langmuir. 2019; 35: 14870-14878.
25. Kolluru SS, Hamdaoui A, Rudewick HF, Zambuto SG, Oyen ML. Electrospun gelatin fiber-gelatin methacryloyl hydrogel composites for reproductive applications. J Mech Behav Biomed Mater. 2025; 174: 107258.
26. Firdaus M, Tahara AR, Cahyani SD, Wanty SS, Mulia EM, Putri RO, et al. Green synthesis of bioactive phloroglucinol derivatives and polyvinyl alcohol/carboxymethyl cellulose-based hydrogel modified with albumin-diacylphloroglucinol for potential wound healing. Next Mater. 2026; 11: 101713.
27. Ceylan M, Laine ML, Zandieh Doulabi B, Korfage HJAM, Dijkstra RJB, de Vries TJ, et al. Human gingival fibroblast-mediated remodeling of three-dimensional fibrin hydrogels. Matrix Biol Plus. 2026; 29: 100191.
28. Chiou G, Stagg S, Gonzales G, Danford L, Arredondo I, Bizios R, et al. Matrix influence of collagen: Fibrin interpenetrating hydrogels on microvascular networks and osteogenesis. Biomater Adv. 2025; 179: 214518.
29. Teshima R, Mukai M, Otsuka H. Current gelation technologies for alginate hydrogels and novel CO_2-induced gelation: Applications in biomaterials. Next Mater. 2026; 11: 101693.
30. Hategekimana F, Elçin AE, Elçin YM. Green synthesis of caffeine-catalyzed citric acid-PPG/PEG crosslinked alginate hydrogel scaffolds for prospective biomedical applications. Int J Biol Macromol. 2026; 360: 151850.
31. Huang Z, Tian S, Yang Y, Zhang J, Lan C, Li Y, et al. Crosslinking strategies and functionalization modification approaches for chitosan-based hydrogels in food preservation applications: A review. Food Hydrocoll. 2026; 175: 112475.
32. Soriano-Ruiz JL, Gálvez-Martín P, López-Ruiz E, Suñer-Carbó J, Calpena-Campmany AC, Marchal JA, et al. Design and evaluation of mesenchymal stem cells seeded chitosan/glycosaminoglycans quaternary hydrogel scaffolds for wound healing applications. Int J Pharm. 2019; 570: 118632.
33. Wang H, Yang L, Yang Y, Zhang D, Hao G. Multifunctional natural starch-based hydrogels: Critical characteristics, formation mechanisms, various applications, future perspectives. Carbohydr Polym. 2025; 357: 123458.
34. Lei J, Chen K, Qiu H. Preparation of pH-responsive starch/sodium alginate hybrid hydrogels for smart monitoring applications. Sustain Mater Technol. 2025; 45: e01551.

35. Chen JY, Lu BC, Zhang B, Chen XX, Yao XH, Zhang DY, et al. Hierarchically structured cellulose hydrogel with high stretchability, conductivity, and stability for flexible sensing applications. Int J Biol Macromol. 2026; 347: 150747.
36. Lu ZZ, Chen J, Jin J, Ge XR, Yao XH, Zhao WG, et al. Preparation of multifunctional hydrogel composed of polyvinyl alcohol/chitosan/cellulose nanofiber/anthocyanin and its application in intelligent food packaging systems. Food Res Int. 2026; 235: 119173.
37. Liang X, Ma F, Chen Y, Liu X, Yu C, Cheng G, et al. Development of polyvinyl alcohol-bacterial cellulose-chitosan oligosaccharide composite hydrogels for potential wound healing applications. Int J Biol Macromol. 2025; 338: 149668.
38. Farshbaf Shakib R, Haghbin Nazarpak M, Solouk A, Bahrami S. Biomimetic multi-layer scaffolds with aligned polyurethane nanofibers and tailored hyaluronic acid/gelatin hydrogels for sustained methylprednisolone release in potential cardiovascular applications. RSC Adv. 2026; 16: 231-245.
39. Andam S, Borhani F. 3D-printed hyaluronic acid-based hydrogel in wound healing applications: A review of environmentally friendly approaches. Eur Polym J. 2025; 236: 114140.
40. Premkumar H, Kumar V. Degradation kinetics of biodegradable chitosan, polyvinyl alcohol, and zinc oxide hydrogel for the amoxicillin drug delivery application. Next Mater. 2026; 10: 101458.
41. Yang J, Zhang J, Wu Y, Liang J, Huang Q, Liu C, et al. Investigation into the structural design of polyethylene glycol-based hydrogels and their application in human thermal management. Mater Today Chem. 2026; 52: 103426.
42. Asmat R, Farooq A, Islam A, Ara C, Shafiq N, Imtiaz F, et al. Graphene oxide-reinforced chitosan/polyethylene glycol/poly (acrylic acid) ternary blend hydrogels: A promising material for biomedical applications. Environ Technol Innov. 2025; 40: 104430.
43. Islam MM, Mondal MI. Biocompatible methyl cellulose/polyvinyl pyrrolidone biocomposite hydrogels for sustained release of quercetin drug. Int J Biol Macromol. 2025; 322: 146795.
44. Yang R, Xia C, Mei C, Li J. Integration of biopolymers in polyacrylic acid hydrogels: Innovations and applications in bioresources and bioproducts. J Bioresour Bioprod. 2025; 10: 145-169.
45. Manzoor H, Arshad N, Qureshi MA, Qadar S. Novel pH-responsive pectin-based hybrid smart hydrogels for in vitro drug release and in vivo wound healing applications. RSC Adv. 2026; 16: 5515-5534.
46. Chang CY, Hsu TL, Lai YR, Wu JW, Wang SS, How SC, et al. The application of poly (acrylic Acid)-whey protein isolate amyloid fibril-derived hybrid hydrogels in drug delivery. J Drug Deliv Sci Technol. 2025; 113: 107299.
47. Dubey P, Kumar S, Ravindranathan S, Vasudevan S, Aswal VK, Rajamohanan PR, et al. pH dependent sophorolipid assemblies and their influence on gelation of silk fibroin protein. Mater Chem Phys. 2018; 203: 9-16.
48. Pourmadadi M, Gerami SE, Ajalli N, Yazdian F, Rahdar A, Fathi-karkan S, et al. Novel pH-responsive hybrid hydrogels for controlled delivery of curcumin: Overcoming conventional constraints and enhancing cytotoxicity in MCF-7 cells. Hybrid Adv. 2024; 6: 100210.
49. Qiao C, Fu L, Lv X, Wang S, Ling Y, Xu C, et al. Hybrid cross-linked sodium carboxymethyl starch/polyacrylamide flexible sensing hydrogels with adhesion, antimicrobial properties and multiple responses. Int J Biol Macromol. 2023; 249: 126020.

50. Wang Y, Yang X, Li Y, Liu K, Xiang X. Sandwich-structured carbon nanotube-hydrogel composites with dual-conductivity mechanism for flexible multifunctional applications. Colloids Surf A Physicochem Eng Asp. 2026; 742: 140387.
51. Wei Q, Li Y, Bi J, Cong S, Zhang G, Hou H, et al. Photo-crosslinking chitosan-based antibacterial hydrogel pad: Long-term releasing of ε-polylysine and application in salmon preservation. J Future Foods. 2025. doi: 10.1016/j.jfutfo.2025.09.029.
52. Segneanu AE, Bejenaru LE, Bejenaru C, Blendea A, Mogoşanu GD, Biţă A, et al. Advancements in hydrogels: A comprehensive review of natural and synthetic innovations for biomedical applications. Polymers. 2025; 17: 2026.
53. Priya AS, Premanand R, Ragupathi I, Bhaviripudi VR, Aepuru R, Kannan K, et al. Comprehensive review of hydrogel synthesis, characterization, and emerging applications. J Compos Sci. 2024; 8: 457.
54. Yodpatum K, Nganbanditchai S, Piriyasathit P, Jenjob R, Yang SG, Toommee S, et al. Thermosensitive chitosan/collagen hydrogel with antibacterial zinc oxide and silver nanoparticles from aqueous fingerroot (*Boesenbergia rotunda* (L.) Mansf.) extract for alveolar bone applications. Carbohydr Polym Technol Appl. 2025; 12: 101029.
55. Bahram M, Mohseni N, Moghtader M. An introduction to hydrogels and some recent applications. In: Emerging concepts in analysis and applications of hydrogels. London, UK: IntechOpen; 2016. pp. 9-38.
56. Chatterjee S, Chi-leung HUI P. Review of stimuli-responsive polymers in drug delivery and textile application. Molecules. 2019; 24: 2547.
57. Wang W, Wat E, Hui PC, Chan B, Ng FS, Kan CW, et al. Dual-functional transdermal drug delivery system with controllable drug loading based on thermosensitive poloxamer hydrogel for atopic dermatitis treatment. Sci Rep. 2016; 6: 24112.
58. Lu P, Ruan D, Huang M, Tian M, Zhu K, Gan Z, et al. Harnessing the potential of hydrogels for advanced therapeutic applications: Current achievements and future directions. Signal Transduct Target Ther. 2024; 9: 166.
59. Wang J, Kang Y, Qiu H, Liu Z, Dong X, Wang C, et al. An antimicrobial and anti-inflammatory bio-based polyurethane hydrogel coating promotes mechanical wound healing via incorporation natural components. Prog Org Coat. 2026; 216: 110167.
60. Ghahfarokhi MR, Kharaziha M, Karimzadeh F. Engineering dual-crosslinked oxidized carrageenan-chitosan semi-IPN hydrogels with adjustable mechanical and biological performances for soft tissue applications. Carbohydr Polym Technol Appl. 2026; 14: 101054.
61. Mahmood A, Patel D, Hickson B, DesRochers J, Hu X. Recent progress in biopolymer-based hydrogel materials for biomedical applications. Int J Mol Sci. 2022; 23: 1415.
62. Xu F, Dawson C, Lamb M, Mueller E, Stefanek E, Akbari M, et al. Hydrogels for tissue engineering: Addressing key design needs toward clinical translation. Front Bioeng Biotechnol. 2022; 10: 849831.
63. Mehmood A, Masood S, Khan TF, Asghar D, Mujeeb A. Bacterial ghosts embedded in natural hydrogels as drug delivery vehicles for cancer treatment. RSC Adv. 2026; 16: 10400-10417.
64. Kim SH, Thambi T, Phan VG, Lee DS. Modularly engineered alginate bioconjugate hydrogel as biocompatible injectable scaffold for in situ biomineralization. Carbohydr Polym. 2020; 233: 115832.

65. Mulla A, Chakraborty R, Rai G, Kandwall B, Das T, Hulkane S, et al. Black gold-biochar: Transforming agro-based biomasses into sustainable environmental solutions. AIMS Bioeng. 2026; 13: 62-95.
66. Uddin MN, Badsha MA, Samwini AM, Solomon N, Yang Y, Uddin J, et al. Biochar-hydrogel composites as multifunctional materials for environmental remediation and circular resource recovery. J Hazard Mater Adv. 2026; 22: 101169.
67. Mondal A, Haque M, Aggarwal A, Kalita M, Roy AS. Protein-based hydrogel for environmental remediation: Removal of hazardous metal ions and toxic organic dyes from wastewater. J Mol Liq. 2025; 423: 127174.
68. Ortiz-Hernández GD, Claudio-Rizo JA, González-Morales S, León-Campos MI, Robledo-Olivo A, Cano-Salazar LF, et al. Sustainable collagen-xanthan gum hydrogel scaffolds with super-swelling behavior and biostimulatory activity for agricultural applications. Int J Biol Macromol. 2026; 356: 151551.
69. Rebelo RC, Fonseca AC, Coelho JF, Serra AC. A sustainable synthesis of cellulose hydrogels for agriculture with repurpose of solvent as fertilizer. Carbohydr Polym. 2025; 368: 124156.
70. Li X, Bo Y, Ye Q, Kang X, Lu L, Cui B, et al. A ratiometric fluorescence sensor based on starch/polyacrylamide/deep eutectic solvent hydrogel for visual and nondestructive detection of methyl parathion on foods. Food Chem. 2026; 511: 148790.
71. Alasalvar H, Karabulut G, Goksen G. Natural deep eutectic solvent-based pectin-chitosan composite hydrogel films: A novel pH-responsive color indicator for food packaging systems. Curr Res Food Sci. 2025; 11: 101241.
72. Bao W, Li M, Yang Y, Wan Y, Wang X, Bi N, et al. Advancements and frontiers in the high performance of natural hydrogels for cartilage tissue engineering. Front Chem. 2020; 8: 53.
73. Calvert P. Hydrogels for soft machines. Adv Mater. 2009; 21: 743-756.
74. Gong JP, Katsuyama Y, Kurokawa T, Osada Y. Double-network hydrogels with extremely high mechanical strength. Adv Mater. 2003; 15: 1155-1158.
75. Das P, Mai VC, Duan H. Flexible bioinspired ternary nanocomposites based on carboxymethyl cellulose/nanoclay/graphene oxide. ACS Appl Polym Mater. 2019; 1: 1505-1513.
76. Liu R, Liang S, Tang XZ, Yan D, Li X, Yu ZZ. Tough and highly stretchable graphene oxide/polyacrylamide nanocomposite hydrogels. J Mater Chem. 2012; 22: 14160-14167.
77. Kim HH, Song DW, Kim MJ, Ryu SJ, Um IC, Ki CS, et al. Effect of silk fibroin molecular weight on physical property of silk hydrogel. Polymer. 2016; 90: 26-33.
78. Palmese LL, Thapa RK, Sullivan MO, Kiick KL. Hybrid hydrogels for biomedical applications. Curr Opin Chem Eng. 2019; 24: 143-157.
79. Acciaretti F, Vesentini S, Cipolla L. Fabrication strategies towards hydrogels for biomedical application: Chemical and mechanical insights. Chem Asian J. 2022; 17: e202200797.
80. Catoira MC, González-Payo J, Fusaro L, Ramella M, Boccafoschi F. Natural hydrogels R&D process: Technical and regulatory aspects for industrial implementation. J Mater Sci Mater Med. 2020; 31: 64.
81. Thang NH, Chien TB, Cuong DX. Polymer-based hydrogels applied in drug delivery: An overview. Gels. 2023; 9: 523.
82. Sepe F, Valentino A, Marcolongo L, Petillo O, Calarco A, Margarucci S, et al. Polysaccharide hydrogels as delivery platforms for natural bioactive molecules: From tissue regeneration to infection control. Gels. 2025; 11: 198.

83. Elangwe CN, Morozkina SN, Olekhnovich RO, Polyakova VO, Krasichkov A, Yablonskiy PK, et al. Pullulan-based hydrogels in wound healing and skin tissue engineering applications: A review. Int J Mol Sci. 2023; 24: 4962.
84. Carton F, Rizzi M, Canciani E, Sieve G, Di Francesco D, Casarella S, et al. Use of hydrogels in regenerative medicine: Focus on mechanical properties. Int J Mol Sci. 2024; 25: 11426.
85. Suhar RA, Doulames VM, Liu Y, Hefferon ME, Figueroa III O, Buabbas H, et al. Hyaluronan and elastin-like protein (HELP) gels significantly improve microsphere retention in the myocardium. Biomater Sci. 2022; 10: 2590-2608.
86. Rana MM, De la Hoz Siegler H. Evolution of hybrid hydrogels: Next-generation biomaterials for drug delivery and tissue engineering. Gels. 2024; 10: 216.
87. Mndlovu H, Kumar P, du Toit LC, Choonara YE. A review of *biomaterial* degradation assessment approaches employed in the biomedical field. NPJ Mater Degrad. 2024; 8: 66.
88. Clegg JR, Adebowale K, Zhao Z, Mitragotri S. Hydrogels in the clinic: An update. Bioeng Transl Med. 2024; 9: e10680.
89. Liang X, Zhong HJ, Ding H, Yu B, Ma X, Liu X, et al. Polyvinyl alcohol (PVA)-based hydrogels: Recent progress in fabrication, properties, and multifunctional applications. Polymers. 2024; 16: 2755.
90. Isaac AH, Recalde Phillips SY, Ruben E, Estes M, Rajavel V, Baig T, et al. Impact of PEG sensitization on the efficacy of PEG hydrogel-mediated tissue engineering. Nat Commun. 2024; 15: 3283.
91. Gandin A, Torresan V, Panciera T, Brusatin G. A scalable method to fabricate 2D hydrogel substrates for mechanobiology studies with independent tuning of adhesiveness and stiffness. Methods Protoc. 2024; 7: 75.
92. Rahman Khan MM, Rumon MM. Synthesis of PVA-based hydrogels for biomedical applications: Recent trends and advances. Gels. 2025; 11: 88.
93. Tuszynska M, Skopinska-Wisniewska J, Bartniak M, Bajek A. Conceptualization and preliminary characterization of poloxamer-based hydrogels for biomedical applications. Bioconjug Chem. 2025; 36: 1169-1179.
94. Li L, Wang Y. Advancements in injectable hydrogels for controlled insulin delivery: A comprehensive review of the design, properties and therapeutic applications for diabetes and its complications. Polymers. 2025; 17: 780.
95. Ho TC, Chang CC, Chan HP, Chung TW, Shu CW, Chuang KP, et al. Hydrogels: Properties and applications in biomedicine. Molecules. 2022; 27: 2902.
96. Choudhary A, Sharma A, Singh A, Han SS, Sood A. Strategy and advancement in hybrid hydrogel and their applications: Recent progress and trends. Adv Eng Mater. 2024; 26: 2400944.