

# Recent Advances In Natural Polymer-Based Hydrogels And Their Applications: A Comprehensive Review

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## Abstract:

Wound healing remains a critical area of medical and pharmaceutical research, necessitating the development of innovative and effective therapeutic materials. Among these, hydrogels have gained significant attention due to their unique physicochemical properties, including high water content, biocompatibility, and the ability to deliver therapeutic agents in a controlled manner. This review provides a comprehensive overview of recent advancements in the design and application of natural polymer-based hydrogels for wound healing. Emphasis is placed on various biopolymers such as chitosan, alginate, gelatin, and hyaluronic acid, exploring their mechanisms of action, crosslinking strategies, and roles in different phases of the wound healing process. The review also discusses the incorporation of bioactive agents and nanoparticles to enhance antimicrobial activity, tissue regeneration, and angiogenesis. Finally, current challenges and future prospects for translating these biomaterials into clinical practice are examined, highlighting the potential of natural hydrogels as next-generation wound dressings.

**Keywords:** Hydrogels, Nano particles, Tissue regeneration, Biopolymers.

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## I. Introduction:

Hydrogels are a class of three-dimensional (3D) polymeric networks capable of absorbing and retaining significant amounts of water or biological fluids without dissolving, owing to their hydrophilic functional groups. Since their discovery by Wichterle and Lím in 1960 for use in contact lenses, hydrogels have gained immense attention in diverse fields such as biomedicine, pharmaceuticals, tissue engineering, wound healing, agriculture, and biosensing. Their exceptional ability to mimic the natural extracellular matrix (ECM), biocompatibility, and tunable physicochemical properties make them ideal for various biological and therapeutic applications.<sup>(1,2)</sup>

Structurally, hydrogels consist of crosslinked polymer chains—either natural, synthetic, or a hybrid of both—which enable the material to swell in aqueous environments while maintaining structural integrity. The crosslinking can be either physical (e.g., hydrogen bonding, ionic interactions) or chemical (e.g., covalent bonding via polymerization), influencing the hydrogel's mechanical strength, porosity, and responsiveness to environmental stimuli.<sup>(1,3)</sup>

Hydrogels can be classified based on various parameters:

- ✓ **Source:** Natural (e.g., alginate, gelatin, chitosan) vs. Synthetic (e.g., polyvinyl alcohol, polyethylene glycol)
- ✓ **Nature of crosslinking:** Physical vs. Chemical
- ✓ **Responsiveness:** Conventional vs. Smart hydrogels (e.g., pH-sensitive, thermoresponsive, photoresponsive)
- ✓ **Degradability:** Biodegradable vs. Non-biodegradable<sup>(4)</sup>

One of the key advantages of hydrogels is their high-water content, which provides a moist environment essential for cellular functions and wound healing. Additionally, they can be engineered to be injectable, self-healing, or stimuli-responsive, expanding their utility in minimally invasive therapies, targeted drug delivery, and regenerative medicine.<sup>(4)</sup>

In the pharmaceutical and biomedical realm, hydrogels have emerged as promising carriers for controlled drug release, tissue scaffolds, biosensors, and wound dressings. Particularly in wound healing, hydrogels serve multiple roles: maintaining hydration, absorbing exudate, providing a protective barrier, and even delivering therapeutic agents such as phytoconstituents, growth factors, or antimicrobials to enhance tissue repair and regeneration.<sup>(5)</sup>

This review aims to provide a comprehensive overview of hydrogels, focusing on their types, properties, methods of preparation, and biomedical applications—with a particular emphasis on emerging trends and their potential in phytoconstituent-based wound healing.<sup>(6)</sup>

**Advantages:**

1. **Biocompatibility:** Hydrogels are made from water-loving (hydrophilic) materials that are gentle on living tissues. This makes them perfect for use in medical applications, such as wound dressings, contact lenses, and even implants.
2. **High Water Content:** Hydrogels can hold a huge amount of water, making them super useful for applications like wound healing, where keeping the wound moist is essential.
3. **Soft and Flexible:** Hydrogels are soft, flexible, and can be easily molded into different shapes. This makes them ideal for use in medical devices, like catheters, and even in cosmetic applications, like skin care products.<sup>(6,7)</sup>
4. **Tunable Properties:** Hydrogels can be designed to have specific properties, like strength, stiffness, or degradation rate. This makes them super versatile and useful for a wide range of applications.
5. **Sustained Release:** Hydrogels can be used to release drugs or other molecules slowly over time. This makes them useful for applications like drug delivery, wound healing, and even agriculture.
6. **Cell Support:** Hydrogels can provide a supportive environment for cells to grow and thrive. This makes them useful for applications like tissue engineering, regenerative medicine, and even 3D cell culture.
7. **Self-Healing:** Some hydrogels have the ability to self-heal, which means they can repair themselves after being damaged. This makes them super useful for applications like wound healing and tissue engineering.<sup>(7)</sup>
8. **Thermoresponsive:** Some hydrogels are thermoresponsive, meaning they can change their properties in response to changes in temperature. This makes them useful for applications like drug delivery, wound healing, and even smart textiles.
9. **Electroresponsive:** Some hydrogels are electroresponsive, meaning they can change their properties in response to electrical stimuli. This makes them useful for applications like drug delivery, wound healing, and even bioelectronics.
10. **Environmentally Friendly:** Hydrogels can be made from biodegradable and renewable materials, making them a more environmentally friendly option compared to traditional materials.<sup>(8)</sup>

**Disadvantages:**

1. **Mechanical Weakness:** Hydrogels are often mechanically weak, which means they can be easily damaged or broken. This can limit their use in applications where mechanical strength is important.
2. **Limited Durability:** Hydrogels can degrade over time, especially when exposed to water, heat, or light. This can limit their use in long-term applications.
3. **Swelling and Shrinking:** Hydrogels can swell or shrink in response to changes in their environment, which can affect their performance and stability.
4. **Limited Optical Clarity:** Some hydrogels can be cloudy or opaque, which can limit their use in applications where optical clarity is important.
5. **Toxicity Concerns:** Some hydrogels can be toxic or cause allergic reactions, especially if they are made from synthetic materials.
6. **High Cost:** Hydrogels can be expensive to produce, especially if they are made from high-quality or specialized materials.
7. **Limited Cell Adhesion:** Some hydrogels can have limited cell adhesion properties, which can make it difficult for cells to attach and grow on their surface.
8. **Difficulty in Sterilization:** Hydrogels can be difficult to sterilize, especially if they are sensitive to heat, radiation, or chemicals.
9. **Limited Shelf Life:** Hydrogels can have a limited shelf life, especially if they are sensitive to moisture, heat, or light.
10. **Complex Manufacturing Process:** Hydrogels can be complex to manufacture, especially if they require specialized equipment or techniques.
11. **Limited Control over Degradation:** Hydrogels can degrade in unpredictable ways, which can make it difficult to control their performance and stability.
12. **Scalability Issues:** Hydrogels can be difficult to scale up for large-scale applications, especially if they require specialized equipment or techniques.
13. **Limited Compatibility with Other Materials:** Hydrogels can have limited compatibility with other materials, which can make it difficult to integrate them into complex systems.
14. **Difficulty in Characterizing Properties:** Hydrogels can be difficult to characterize, especially if they have complex or dynamic properties.
15. **Regulatory Challenges:** Hydrogels can face regulatory challenges, especially if they are used in medical or food applications.<sup>(9,10)</sup>

## **Classification of Hydrogels**

### **Based on Origin**

1. **Natural hydrogels:** e.g., alginate, chitosan, gelatin, hyaluronic acid
2. **Synthetic hydrogels:** e.g., poly(ethylene glycol), poly(vinyl alcohol), poly(acrylic acid)
3. **Hybrid hydrogels:** combination of natural and synthetic polymers<sup>(11,12)</sup>

### **Based on Crosslinking**

1. **Physical hydrogels:** formed through non-covalent interactions
2. **Chemical hydrogels:** formed via covalent bonds

### **Based on Stimuli-Responsiveness**

1. pH-sensitive
2. Temperature-sensitive
3. Enzyme-responsive

### **Based on Structure**

1. Amorphous
2. Semi-crystalline

## **Properties of Hydrogels**

Hydrogels possess unique characteristics that make them suitable for biomedical use:

- ✓ **Swelling Behavior:** Absorbs water without dissolving, affecting drug release.
- ✓ **Biocompatibility:** Non-toxic and non-immunogenic.
- ✓ **Mechanical Properties:** Tunable elasticity and strength.
- ✓ **Degradability:** Biodegradable via hydrolysis or enzymatic actions.
- ✓ **Drug Release Behavior:** Controlled and sustained release capabilities.<sup>(13)</sup>

## **Methods of Hydrogel Preparation**

Hydrogels can be synthesized using **physical or chemical crosslinking** methods, each resulting in different structural and functional characteristics. The method chosen depends on the desired application, required mechanical strength, biocompatibility, and degradation profile.

### **Physical Crosslinking Methods**

Physical hydrogels are formed through **non-covalent interactions**, which are generally reversible and occur under mild conditions. These methods avoid the use of chemical crosslinkers, making them more biocompatible.<sup>(14)</sup>

#### **Ionic Interactions**

- ✓ Occur between oppositely charged polymers or between a polymer and multivalent ions.
- ✓ **Example:** Alginate forms a gel when crosslinked with calcium ions ( $\text{Ca}^{2+}$ ).
- ✓ **Advantages:** Mild, biocompatible, and easily reversible.
- ✓ **Disadvantages:** Poor mechanical strength and potential instability.<sup>(15)</sup>

#### **Hydrogen Bonding**

- ✓ Polymers with functional groups like hydroxyl, amide, or carboxyl can form hydrogen bonds.
- ✓ **Example:** Poly(vinyl alcohol) (PVA) forms physically crosslinked hydrogels through freeze-thaw cycling that promotes hydrogen bonding and crystallization.
- ✓ **Applications:** Wound dressings, drug delivery systems.<sup>(16)</sup>

#### **Crystallization**

- ✓ Repeated freezing and thawing can lead to crystalline regions that physically crosslink polymers (e.g., PVA hydrogels).
- ✓ **Advantages:** No toxic reagents required.
- ✓ **Disadvantages:** Lower stability under physiological conditions.<sup>(17)</sup>

### **Chemical Crosslinking Methods**

Chemical hydrogels involve **covalent bonds** between polymer chains, resulting in more stable and often non-reversible networks.

### **Free Radical Polymerization**

- ✓ Involves initiation (via heat, light, or chemical initiators), propagation, and termination steps.
- ✓ **Monomers:** Acrylic acid, acrylamide, or methacrylate derivatives.
- ✓ **Crosslinkers:** N,N'-methylenebisacrylamide (MBA), glutaraldehyde.
- ✓ **Applications:** Controlled drug release, biosensors.
- ✓ **Drawbacks:** Residual monomers may be toxic.<sup>(18)</sup>

### **Schiff Base Reaction**

- ✓ Condensation between amine and aldehyde groups to form imine bonds (C=N).
- ✓ **Polymers involved:** Chitosan (amine) and oxidized dextran (aldehyde).
- ✓ **Advantages:** Injectable and in situ gelling systems.
- ✓ **Applications:** Tissue engineering, wound healing.<sup>(19)</sup>

### **Michael Addition**

- Nucleophilic addition of enolate to an electron-deficient alkene (e.g., acrylates).
- Occurs under physiological pH and is widely used in bioconjugation.
- **Advantages:** Mild reaction conditions, good control over gelation time.

### **Graft Polymerization**

- Involves grafting of vinyl monomers onto natural or synthetic polymer backbones.
- **Initiators:** Free radicals (thermal, chemical, or photoinitiated).
- **Example:** Grafting acrylic acid onto gelatin or chitosan.
- **Advantages:** Improves mechanical strength and adds new functionalities.
- **Applications:** Smart hydrogels, responsive systems.<sup>(20)</sup>

### **Radiation Polymerization**

- Uses high-energy radiation (e.g.,  $\gamma$ -rays, electron beams) to initiate crosslinking.
- **No need for chemical initiators;** highly pure hydrogels can be produced.
- **Advantages:** Sterile process, suitable for biomedical devices.
- **Disadvantages:** Requires specialized equipment.

### **Click Chemistry**

- ✓ A set of biocompatible reactions known for high yield, specificity, and mild conditions.
- ✓ **Examples:**
  - Azide-alkyne cycloaddition
  - Thiol-ene reactions
- ✓ **Advantages:** Fast, efficient, and produces minimal by-products.
- ✓ **Applications:** Smart and injectable hydrogels, 3D printing.<sup>(21)</sup>

### **Characterization Techniques of Hydrogels**

Characterizing hydrogels is essential to ensure their suitability for specific biomedical applications. Proper analysis provides insights into their chemical composition, physical structure, mechanical behavior, and biological performance. Below are detailed descriptions of key techniques used:

#### **Swelling Studies**

Swelling behavior reflects the hydrophilic nature and network structure of hydrogels. The equilibrium swelling ratio (ESR) is typically calculated by immersing dried hydrogels in water or buffer and recording weight gain over time. A higher swelling ratio generally correlates with lower crosslinking density and greater porosity, which can enhance drug diffusion but may compromise mechanical stability. Swelling studies also indicate pH- or temperature-sensitivity in smart hydrogels.<sup>(22)</sup>

#### **Fourier-Transform Infrared Spectroscopy (FTIR)**

FTIR is used to identify functional groups and confirm chemical modifications in hydrogels. Peaks corresponding to -OH, -COOH, -NH<sub>2</sub>, and C=O groups help determine the presence of natural or synthetic polymers. It is particularly useful for verifying crosslinking reactions (e.g., appearance of imine peaks in Schiff base reactions) or incorporation of therapeutic agents like phyto constituents.<sup>(22)</sup>

### **Differential Scanning Calorimetry (DSC)**

DSC measures thermal transitions such as glass transition temperature ( $T_g$ ), melting temperature ( $T_m$ ), and crystallinity. These thermal properties reflect polymer chain mobility, interaction strength, and phase behavior. For example, a shift in  $T_g$  after drug loading may suggest interactions between the polymer matrix and the active agent.

### **Thermogravimetric Analysis (TGA)**

TGA provides insight into the thermal stability and composition of hydrogels by tracking weight loss with increasing temperature. Multi-step degradation profiles can indicate water loss, polymer decomposition, and degradation of embedded agents. This method is useful for assessing residual solvents or moisture content and overall formulation stability.<sup>(23)</sup>

### **Scanning Electron Microscopy (SEM)**

SEM provides micro- and nanoscale images of hydrogel morphology. Cross-sectional images help analyze pore size, shape, and interconnectivity, which are critical for nutrient diffusion, cell infiltration, and drug release. In composite hydrogels, SEM can visualize dispersed nanoparticles or structural reinforcements.

### **Rheological Studies**

Rheology assesses the viscoelastic nature of hydrogels using parameters like storage modulus ( $G'$ ), loss modulus ( $G''$ ), and complex viscosity.  $G' > G''$  indicates solid-like behavior, crucial for shape retention in tissue scaffolds. Time sweep and frequency sweep analyses determine gelation time and stability under physiological conditions.<sup>(24)</sup>

### **Mechanical Testing**

Mechanical strength is critical, especially for load-bearing applications such as cartilage or bone repair. Techniques like tensile, compressive, and shear testing evaluate the hydrogel's elasticity, toughness, and resistance to deformation. Mechanical behavior can be tuned by altering polymer concentration, crosslinking method, or using reinforcement agents like nanofillers.<sup>(24)</sup>

### **In Vitro Biocompatibility**

Evaluating cytocompatibility is vital before in vivo use. Common tests include:

- ✓ **MTT assay:** Measures cell viability based on mitochondrial activity.
- ✓ **Live/Dead assay:** Differentiates viable cells from dead cells via fluorescence staining.
- ✓ **Hemocompatibility testing:** Checks for hemolysis or clotting upon contact with blood. These tests ensure that hydrogels do not elicit cytotoxic or hemolytic responses, a prerequisite for clinical applications.<sup>(25)</sup>

### **In Vivo Evaluation**

Animal models are employed to assess hydrogel biodegradability, biocompatibility, integration with tissues, and therapeutic efficacy. For wound healing studies, parameters such as rate of epithelialization, collagen deposition, angiogenesis, and inflammatory response are typically evaluated through histopathological analysis.<sup>(26)</sup>

### **X-Ray Diffraction (XRD)**

XRD is used to determine the crystalline or amorphous nature of the hydrogel or incorporated agents. The degree of crystallinity affects mechanical strength and drug release behavior. Sharp peaks indicate crystalline regions, while broad humps suggest amorphous characteristics.

### **UV-Vis and Fluorescence Spectroscopy**

These techniques quantify the loading and release of active compounds, especially useful for phytoconstituent-loaded hydrogels. UV-Vis absorbance at characteristic wavelengths can track drug release kinetics, while fluorescence labeling can aid in visualizing distribution or degradation in biological tissues.<sup>(27)</sup>

### **Applications of Hydrogels**

Hydrogels exhibit excellent biocompatibility, high water content, and tunable physical properties, making them versatile materials in a wide range of biomedical and non-biomedical applications. Their soft, tissue-like nature and capacity for controlled drug delivery have especially positioned them as materials of choice in modern therapeutic strategies.

### Wound Healing

Hydrogels provide an ideal moist environment that accelerates wound healing by promoting cell migration, proliferation, and angiogenesis.

- ✓ **Moisture Retention:** Maintains a hydrated wound bed, enhancing epithelialization and autolytic debridement.
- ✓ **Cooling and Pain Relief:** Their high water content provides a soothing effect on burns and inflamed areas.
- ✓ **Antimicrobial Delivery:** Hydrogels can be loaded with antibiotics, silver nanoparticles, or natural antimicrobial agents to prevent or treat infections.
- ✓ **Phytoconstituent-Loaded Hydrogels:** Botanicals like *curcumin*, *centella asiatica*, *aloe vera*, and *neem* are incorporated into hydrogels to provide anti-inflammatory and antioxidant properties that aid healing.<sup>(28,29)</sup>

### Drug Delivery Systems

Hydrogels serve as carriers for controlled, sustained, or targeted drug delivery:

- ✓ **Controlled Release:** Drug diffusion through the hydrogel matrix or degradation of the polymer allows for prolonged therapeutic action.
- ✓ **Stimuli-Responsive Release:** Smart hydrogels release drugs in response to stimuli like pH, temperature, or enzymes.
- ✓ **Localized Delivery:** Injectable hydrogels deliver drugs directly to the site of action (e.g., tumor, infection, or inflamed tissue), reducing systemic side effects.<sup>(30)</sup>

### Tissue Engineering and Regenerative Medicine

Hydrogels mimic the extracellular matrix (ECM), making them excellent scaffolds for tissue regeneration.

- ✓ **3D Cell Culture:** Support cell adhesion, growth, and differentiation.
- ✓ **Scaffolding Material:** Used for engineering cartilage, skin, bone, neural, and cardiac tissues.
- ✓ **Stem Cell Delivery:** Facilitate localized delivery and differentiation of stem cells in regenerative therapies.

### Ophthalmic Applications

Hydrogels are widely used in eye-related therapies due to their transparency and hydration capacity.

- ✓ **Contact Lenses:** Most soft lenses are hydrogel-based, offering oxygen permeability and comfort.
- ✓ **Ocular Drug Delivery:** Used as inserts, films, or in-situ forming gels to deliver drugs to the anterior or posterior segments of the eye.

### Biosensors and Diagnostic Devices

Hydrogels are used to immobilize enzymes, antibodies, or nucleic acids in biosensing platforms.

- ✓ **Glucose Sensors:** Hydrogel matrices stabilize enzymes like glucose oxidase for diabetic monitoring.
- ✓ **pH or Temperature Sensors:** Smart hydrogels can respond to environmental changes, useful in wearable health devices.<sup>(31)</sup>

### Cancer Therapy

Hydrogels are emerging tools in localized and systemic cancer treatment.

- ✓ **Intratumoral Injection:** Provides high local concentration of chemotherapeutics with reduced toxicity.
- ✓ **Photothermal and Photodynamic Therapy:** Nanoparticle-loaded hydrogels enable light-activated treatments.
- ✓ **Immunotherapy Carriers:** Hydrogels can deliver immune-modulating agents to tumor sites.

### Cosmetics and Personal Care

Used in facial masks, moisturizers, and transdermal patches due to their hydrating and soothing properties.

- ✓ **Hydrogel Facial Masks:** Provide sustained delivery of vitamins and active agents to the skin.
- ✓ **Patch Technology:** Delivers ingredients like hyaluronic acid, caffeine, or herbal extracts through the skin barrier.<sup>(31,32)</sup>

### Dental and Orthopedic Applications

Hydrogels can be used in bone regeneration, periodontal treatment, and as drug carriers in dental care.

- ✓ **Bone Scaffolds:** Serve as carriers for osteoinductive factors and minerals.
- ✓ **Dental Gels:** Used for local delivery of antimicrobials in periodontal pockets.

### Agriculture

Hydrogels are used as **soil conditioners** and **controlled release fertilizers**:

- ✓ **Water Retention:** Improve moisture retention in arid soils.
- ✓ **Nutrient Delivery:** Encapsulate fertilizers or pesticides for slow, sustained release.

### **Environmental Applications**

Hydrogels have potential in **wastewater treatment** and **pollutant adsorption**:

- ✓ **Adsorbents:** Functionalized hydrogels remove heavy metals, dyes, or oil from contaminated water.
- ✓ **Sensor Platforms:** Detect environmental changes or pollutants via embedded sensing agents.<sup>(33)</sup>

### **Future Prospects of Hydrogels**

Hydrogels are poised to revolutionize various scientific and industrial domains due to ongoing advancements in materials science, biotechnology, and nanotechnology. The future development of hydrogels is expected to yield more intelligent, multifunctional, and personalized systems tailored to specific applications.

### **Smart and Responsive Hydrogels**

The next generation of hydrogels will be increasingly responsive to external stimuli such as pH, temperature, magnetic fields, electric fields, light, and biological signals.

- ✓ **Self-Healing Hydrogels:** Capable of autonomously repairing damage to prolong lifespan and function.
- ✓ **Multi-Stimuli Responsive Systems:** Will allow precise, on-demand drug release or sensing based on the biological environment.<sup>(34,35)</sup>

### **Personalized Medicine**

Hydrogels are expected to play a major role in patient-specific therapies.

- ✓ **Tailored Drug Delivery Platforms:** Customized hydrogel formulations based on genetic or physiological profiles.
- ✓ **3D Bioprinting of Organs:** Hydrogels will be critical bioinks in printing tissues and organoids for regenerative medicine.

### **Integration with Wearable and Implantable Devices**

Hydrogels will increasingly merge with electronics and microfluidic technologies.

- ✓ **Hydrogel-Based Biosensors:** Integrated into wearable patches for real-time monitoring of biomarkers.
- ✓ **Implantable Therapeutic Systems:** Hydrogels embedded with electronics for responsive release and long-term monitoring

### **Advances in Regenerative Medicine**

- ✓ **Hybrid Scaffolds:** Combining hydrogels with nanomaterials or synthetic polymers to enhance mechanical strength and biofunctionality.
- ✓ **Neural and Cardiac Tissue Engineering:** Progress in guiding complex tissue regeneration using bioactive and conductive hydrogel scaffolds.<sup>(35,36,37)</sup>

### **Sustainable and Green Hydrogels**

Environmental concerns are driving interest in eco-friendly hydrogel materials.

- ✓ **Biodegradable Hydrogels:** Derived from natural polymers for minimal environmental impact.
- ✓ **Green Synthesis Methods:** Use of water-based, solvent-free, or enzyme-catalyzed reactions for hydrogel preparation.<sup>(38,40)</sup>

### **Agricultural and Environmental Expansion**

- ✓ **Smart Agricultural Systems:** Hydrogels embedded with nutrient sensors or growth regulators.
- ✓ **Pollutant-Responsive Cleanup Systems:** Development of hydrogels that detect and remove emerging contaminants from soil and water.<sup>(38,39,40)</sup>

## **II. Conclusion**

Hydrogels have emerged as one of the most versatile and dynamic classes of biomaterials due to their unique physicochemical properties, biocompatibility, and ability to mimic natural tissue environments. Their high water content, tunable mechanical strength, and responsive behavior have enabled their application in diverse fields ranging from wound healing and drug delivery to tissue engineering, diagnostics, agriculture, and environmental remediation. Advancements in polymer chemistry and crosslinking techniques have led to the development of novel hydrogel systems, including stimuli-responsive, injectable, self-healing, and nanocomposite hydrogels. The incorporation of bioactive compounds, such as phytoconstituents and nanoparticles, has further enhanced their therapeutic efficacy and application potential. Despite significant progress, challenges remain in translating hydrogel-based systems from laboratory research to clinical and industrial practice. These include scalability, long-term stability, regulatory approvals, and cost-effectiveness. Nevertheless, with the continuous integration of materials science, biotechnology, and nanotechnology, hydrogels

hold immense promise for shaping the future of personalized medicine, regenerative therapies, and sustainable technologies.

In conclusion, hydrogels represent a rapidly evolving platform with the potential to address some of the most pressing biomedical and environmental challenges of our time. Future research focused on designing smarter, multifunctional, and patient-specific hydrogel systems will undoubtedly expand their utility and impact across multiple disciplines.

### References:

- [1] Yang D. Recent Advances In Hydrogels. *Chemistry Of Materials*. 2022 Mar 8;34(5):1987-9.
- [2] Revete A, Aparicio A, Cisterna BA, Revete J, Luis L, Ibarra E, Segura González EA, Molino J, Reginensi D. Advancements In The Use Of Hydrogels For Regenerative Medicine: Properties And Biomedical Applications. *International Journal Of Biomaterials*. 2022;2022(1):3606765.
- [3] Pandian M, Reshma G, Arthi C, Måsson M, Rangasamy J. Biodegradable Polymeric Scaffolds And Hydrogels In The Treatment Of Chronic And Infectious Wound Healing. *European Polymer Journal*. 2023 Oct 17;198:112390.
- [4] Liu H, Ai R, Liu BZ, He L. Recent Advances In Hyaluronic Acid-Based Hydrogels For Diabetic Wound Healing. *International Journal Of Biological Macromolecules*. 2025 Feb 7:140797.
- [5] You C, Wang C, Ma Z, Yu Q, Liu S. Review On Application Of Silk Fibroin Hydrogels In The Management Of Wound Healing. *International Journal Of Biological Macromolecules*. 2025 Jan 18:140082.
- [6] Tian X, Wen Y, Zhang Z, Zhu J, Song X, Phan TT, Li J. Recent Advances In Smart Hydrogels Derived From Polysaccharides And Their Applications For Wound Dressing And Healing. *Biomaterials*. 2025 Jan 26:123134.
- [7] Chen S, Xia J, Hou Z, Wu P, Yang Y, Cui L, Xiang Z, Sun S, Yang L. Natural Polysaccharides Combined With Mussel-Inspired Adhesion For Multifunctional Hydrogels In Wound Hemostasis And Healing: A Review. *International Journal Of Biological Macromolecules*. 2024 Oct 28:136965.
- [8] Gong C, Wu Q, Wang Y, Zhang D, Luo F, Zhao X, Wei Y, Qian Z. A Biodegradable Hydrogel System Containing Curcumin Encapsulated In Micelles For Cutaneous Wound Healing. *Biomaterials*. 2013 Sep 1;34(27):6377-87.
- [9] Xu R, Fang Y, Zhang Z, Cao Y, Yan Y, Gan L, Xu J, Zhou G. Recent Advances In Biodegradable And Biocompatible Synthetic Polymers Used In Skin Wound Healing. *Materials*. 2023 Aug 3;16(15):5459.
- [10] Stern D, Cui H. Crafting Polymeric And Peptidic Hydrogels For Improved Wound Healing. *Advanced Healthcare Materials*. 2019 May;8(9):1900104.
- [11] Farasati Far B, Naimi-Jamal MR, Sedaghat M, Hoseini A, Mohammadi N, Bodaghi M. Combinational System Of Lipid-Based Nanocarriers And Biodegradable Polymers For Wound Healing: An Updated Review. *Journal Of Functional Biomaterials*. 2023 Feb 18;14(2):115.
- [12] Da Silva CM, Reis RL, Correló VM, Jahno VD. The Efficient Role Of Sodium Alginate-Based Biodegradable Dressings For Skin Wound Healing Application: A Systematic Review. *Journal Of Biomaterials Science, Polymer Edition*. 2024 Feb 11;35(3):397-414.
- [13] Chelu M, Calderon Moreno JM, Musuc AM, Popa M. Natural Regenerative Hydrogels For Wound Healing. *Gels*. 2024 Aug 23;10(9):547.
- [14] Nguyen MK, Lee DS. Injectable Biodegradable Hydrogels. *Macromolecular Bioscience*. 2010 Jun 11;10(6):563-79.
- [15] Li Y, Rodrigues J, Tomás H. Injectable And Biodegradable Hydrogels: Gelation, Biodegradation And Biomedical Applications. *Chemical Society Reviews*. 2012;41(6):2193-221.
- [16] Deptuła M, Zawrzykraj M, Sawicka J, Banach-Kopec A, Tylingo R, Piśkuła M. Application Of 3D-Printed Hydrogels In Wound Healing And Regenerative Medicine. *Biomedicine & Pharmacotherapy*. 2023 Nov 1;167:115416.
- [17] Gao Y, Li Z, Huang J, Zhao M, Wu J. In Situ Formation Of Injectable Hydrogels For Chronic Wound Healing. *Journal Of Materials Chemistry B*. 2020;8(38):8768-80.
- [18] Bae KH, Wang LS, Kurisawa M. Injectable Biodegradable Hydrogels: Progress And Challenges. *Journal Of Materials Chemistry B*. 2013;1(40):5371-88.
- [19] Tan H, Marra KG. Injectable, Biodegradable Hydrogels For Tissue Engineering Applications. *Materials*. 2010 Mar 10;3(3):1746-67.
- [20] Zhang X, Wei P, Yang Z, Liu Y, Yang K, Cheng Y, Yao H, Zhang Z. Current Progress And Outlook Of Nano-Based Hydrogel Dressings For Wound Healing. *Pharmaceutics*. 2022 Dec 26;15(1):68.
- [21] Gounden V, Singh M. Hydrogels And Wound Healing: Current And Future Prospects. *Gels*. 2024 Jan 5;10(1):43.
- [22] Dimatteo R, Darling NJ, Segura T. In Situ Forming Injectable Hydrogels For Drug Delivery And Wound Repair. *Advanced Drug Delivery Reviews*. 2018 Mar 1;127:167-84.
- [23] Zheng BD, Ye J, Yang YC, Huang YY, Xiao MT. Self-Healing Polysaccharide-Based Injectable Hydrogels With Antibacterial Activity For Wound Healing. *Carbohydrate Polymers*. 2022 Jan 1;275:118770.
- [24] Bertsch P, Diba M, Mooney DJ, Leeuwenburgh SC. Self-Healing Injectable Hydrogels For Tissue Regeneration. *Chemical Reviews*. 2022 Aug 5;123(2):834-73.
- [25] Rizzo F, Kehr NS. Recent Advances In Injectable Hydrogels For Controlled And Local Drug Delivery. *Advanced Healthcare Materials*. 2021 Jan;10(1):2001341.
- [26] Overstreet DJ, Dutta D, Stabenfeldt SE, Vernon BL. Injectable Hydrogels. *Journal Of Polymer Science Part B: Polymer Physics*. 2012 Jul 1;50(13):881-903.
- [27] Mohite PB, Adhav SS. A Hydrogels: Methods Of Preparation And Applications. *Int. J. Adv. Pharm.* 2017;6(3):79-85.
- [28] Thakur S, Thakur VK, Arotiba OA. History, Classification, Properties And Application Of Hydrogels: An Overview. *Hydrogels: Recent Advances*. 2018:29-50.
- [29] Kasai RD, Radhika D, Archana S, Shanavaz H, Koutavarapu R, Lee DY, Shim J. A Review On Hydrogels Classification And Recent Developments In Biomedical Applications. *International Journal Of Polymeric Materials And Polymeric Biomaterials*. 2023 Sep 2;72(13):1059-69.
- [30] Jose J, Athira VP, Michel H, Hafeela AR, Bhat SG, Thomas S, Maria LP. Hydrogels: An Overview Of The History, Classification, Principles, Applications, And Kinetics. *Sustainable Hydrogels*. 2023 Jan 1:1-22.
- [31] Zhu T, Ni Y, Biesold GM, Cheng Y, Ge M, Li H, Huang J, Lin Z, Lai Y. Recent Advances In Conductive Hydrogels: Classifications, Properties, And Applications. *Chemical Society Reviews*. 2023;52(2):473-509.
- [32] Khansari MM, Sorokina LV, Mukherjee P, Mukhtar F, Shirdar MR, Shahidi M, Shokuhfar T. Classification Of Hydrogels Based On Their Source: A Review And Application In Stem Cell Regulation. *Jom*. 2017 Aug;69:1340-7.
- [33] Khansari MM, Sorokina LV, Mukherjee P, Mukhtar F, Shirdar MR, Shahidi M, Shokuhfar T. Classification Of Hydrogels Based On



- Their Source: A Review And Application In Stem Cell Regulation. *Jom*. 2017 Aug;69:1340-7.
- [34] Akhtar MF, Hanif M, Ranjha NM. Methods Of Synthesis Of Hydrogels... A Review. *Saudi Pharmaceutical Journal: SPJ*. 2015 Mar 21;24(5):554.
- [35] Ahmed EM. Hydrogel: Preparation, Characterization, And Applications: A Review. *Journal Of Advanced Research*. 2015 Mar 1;6(2):105-21.
- [36] Bashir S, Hina M, Iqbal J, Rajpar AH, Mujtaba MA, Alghamdi NA, Wageh S, Ramesh K, Ramesh S. Fundamental Concepts Of Hydrogels: Synthesis, Properties, And Their Applications. *Polymers*. 2020 Nov 16;12(11):2702.
- [37] Caló E, Khutoryanskiy VV. Biomedical Applications Of Hydrogels: A Review Of Patents And Commercial Products. *European Polymer Journal*. 2015 Apr 1;65:252-67.
- [38] Aswathy SH, Narendrakumar U, Manjubala I. Commercial Hydrogels For Biomedical Applications. *Heliyon*. 2020 Apr 1;6(4).
- [39] Slaughter BV, Khurshid SS, Fisher OZ, Khademhosseini A, Peppas NA. Hydrogels In Regenerative Medicine. *Advanced Materials*. 2009 Sep 4;21(32-33):3307-29.
- [40] Mandal A, Clegg JR, Anselmo AC, Mitragotri S. Hydrogels In The Clinic. *Bioengineering & Translational Medicine*. 2020 May;5(2):E10158.