



A Closer Look at Herbal Hydrogels; Innovation in Natural Healing

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ABSTRACT:

Herbal medicines have been widely utilized for centuries due to their therapeutic and cosmetic properties, and their integration into modern drug delivery systems has gained considerable attention in recent years. Among various Novel Drug Delivery Systems (NDDS), hydrogels have emerged as promising carriers for herbal bioactive owing to their biocompatibility, biodegradability, high water absorption capacity, and ability to provide controlled and targeted drug release. Hydrogels are three-dimensional cross-linked polymeric networks that can be synthesized from natural, synthetic, or semi-synthetic polymers and are classified based on source, ionic charge, mechanism of cross-linking, responsiveness to stimuli, and physical structure. Herbal hydrogels combine the pharmacological benefits of plant-derived constituents with the advanced delivery characteristics of polymeric systems, thereby enhancing bioavailability, stability, therapeutic efficacy, and patient compliance. These systems have shown significant applications in wound healing, transdermal drug delivery, tissue engineering, anti-inflammatory therapy, antimicrobial treatment, cosmetic formulations, and chronic disease management. The physicochemical properties of herbal hydrogels, including swelling behaviour, mechanical strength, drug loading capacity, rheological properties, and release kinetics, play a critical role in their performance and clinical effectiveness. Various fabrication techniques such as physical and chemical cross-linking, radiation polymerization, and grafting methods are employed for hydrogel preparation, with optimization of formulation parameters being essential for achieving desired therapeutic outcomes. Despite promising advancements, challenges related to stability, large-scale production, standardization of herbal extracts, and regulatory approval remain. This review highlights the classification, formulation strategies, characterization methods, applications, advantages, limitations, and future prospects of herbal hydrogel systems in modern therapeutics.

Keywords: Novel drug delivery system, Evaluation parameters, Physicochemical analysis, Rheology, Herbal hydrogels.

INTRODUCTION:

Hydrogels are cross-linked polymeric networks with three-dimensional (3D) structures capable of absorbing and retaining large amounts of water or biological fluids. Owing to their high-water content, porosity, and soft consistency, hydrogels closely resemble natural living tissues, making them highly suitable for biomedical applications.[1]

The 3D network of hydrogels is primarily formed by chemical or physical cross-linking of natural, synthetic, or semi-synthetic polymers. Their swelling behaviour is attributed to the presence of hydrophilic functional groups such as $-\text{SO}_3\text{H}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{OH}$, $-\text{CONH}_2$, and $-\text{CONH}$, which facilitate water uptake and expansion without dissolution. In some cases, the network structure may also arise from cross-linked colloidal clusters.[2]

Hydrogels are flexible and mechanically tunable materials. Their physicochemical properties—including swelling and deswelling rate, mechanical strength, degradability, and mesh size—can be precisely modulated by altering the hydrophilic–hydrophobic balance, polymer and initiator concentration, cross-linking density, and reaction conditions such as time and temperature. This tunability makes hydrogels versatile platforms for controlled and targeted drug delivery applications.[3]

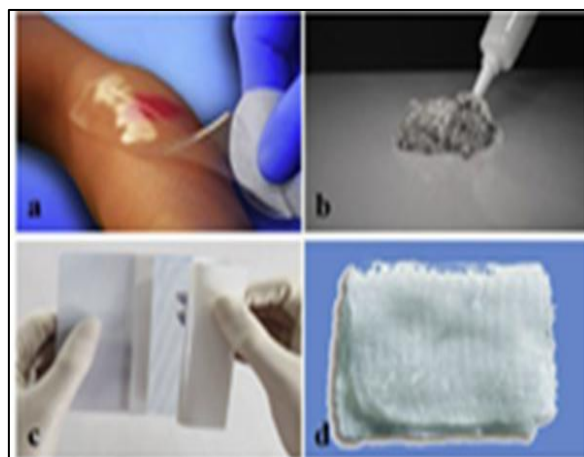
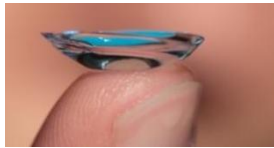


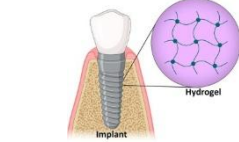




Figure:1 Hydrogels

Different forms of Hydrogels: [4, 5.6]

SI. NO	PHYSICAL FORMS	EXAMPLES	IMAGE
1.	Solid molded forms	Soft contact lenses	
2.	Pressed powder	Pills or capsules	
3.	Microparticles	Bio adhesive carriers	
4.	Coatings	Implants or catheters	
5.	Membrane or sheets	Transdermal patches	
6.	liquids	gels	

Applications of Hydrogels:

Hydrogels are three-dimensional, cross-linked polymeric networks capable of retaining substantial amounts of water while maintaining structural integrity. Owing to their biocompatibility, biodegradability, tunable mechanical strength, and controlled drug



release properties, hydrogels have gained extensive importance in pharmaceutical and biomedical sciences. Based on their site of application, hydrogels can be broadly classified into internal and external applications.

1. Internal Applications [7,8,9]

Internal hydrogels are designed for administration within the body and require high levels of biocompatibility, minimal toxicity, and, in many cases, controlled biodegradability.

1.1 Drug Delivery Systems

Hydrogels are widely employed as carriers for controlled and sustained drug delivery. They can be formulated for oral, injectable, implantable, and targeted delivery systems. Stimuli-responsive hydrogels release drugs in response to environmental triggers such as pH, temperature, ionic strength, or enzymatic activity. These systems enhance bioavailability, reduce dosing frequency, and minimize systemic side effects.

1.2 Cancer Therapy

Hydrogels enable localized delivery of chemotherapeutic agents directly to tumor sites, thereby reducing systemic toxicity. Injectable in situ gelling hydrogels are particularly advantageous for post-surgical chemotherapy and site-specific anticancer therapy.

1.3 Gene and Protein Delivery

Hydrogels serve as protective matrices for sensitive biomolecules such as DNA, RNA, peptides, and proteins. Their controlled release behaviour improves stability and therapeutic efficiency of biologics.

1.4 Tissue Engineering and Regenerative Medicine

Due to their structural similarity to the extracellular matrix (ECM), hydrogels are extensively used as scaffolds in tissue engineering. They support cell adhesion, proliferation, and differentiation in applications such as skin regeneration, cartilage repair, bone reconstruction, and cardiac tissue engineering.

1.5 Ophthalmic and Orthopaedic Applications

Hydrogels are used in ocular drug delivery systems, intraocular lenses, and vitreous substitutes because of their transparency and hydration properties. In orthopaedics, they assist in cartilage repair and minimally invasive regenerative procedures.

2. External Applications [10, 11, 12, 13, 14, 15]

External hydrogels are applied topically or on body surfaces and are widely utilized in dermatological, cosmetic, and protective formulations.

2.1 Wound Dressing and Burn Management

Hydrogels are extensively used in wound care due to their ability to maintain a moist environment, absorb exudates, promote autolytic debridement, and reduce pain. Drug-loaded hydrogels, including herbal formulations, enhance antimicrobial and anti-inflammatory activity, making them suitable for chronic wounds such as diabetic ulcers and pressure sores.

2.2 Transdermal Drug Delivery

Hydrogels facilitate controlled drug permeation across the skin and are used in transdermal patches for systemic delivery of hormones, analgesics, and anti-inflammatory agents. Their flexibility and skin compatibility improve patient compliance.

2.3 Dermatological Applications

Hydrogels are incorporated into formulations for the treatment of acne, eczema, psoriasis, fungal infections, and inflammatory skin conditions. Their cooling and hydrating effects enhance skin recovery and therapeutic performance.

2.4 Cosmetic Applications

In cosmetology, hydrogels are used in facial masks, moisturizing gels, anti-aging products, and skin rejuvenation formulations. Their high-water content improves skin hydration, elasticity, and texture.

2.5 Dental and Contact Lens Applications

Hydrogels are employed in periodontal therapy, local drug delivery in oral conditions, and soft contact lenses due to their oxygen permeability, flexibility, and comfort.

Hydrogels and their Classification:

Hydrogels are three-dimensional, hydrophilic polymeric networks capable of absorbing and retaining substantial amounts of water or biological fluids without dissolving. Upon swelling, they become soft and rubbery, closely resembling living tissues and showing excellent biocompatibility. Owing to their physicochemical properties, hydrogels can be systematically classified based on their source, polymeric composition, size, cross-linking mechanism, stimuli responsiveness, and network charge characteristics.

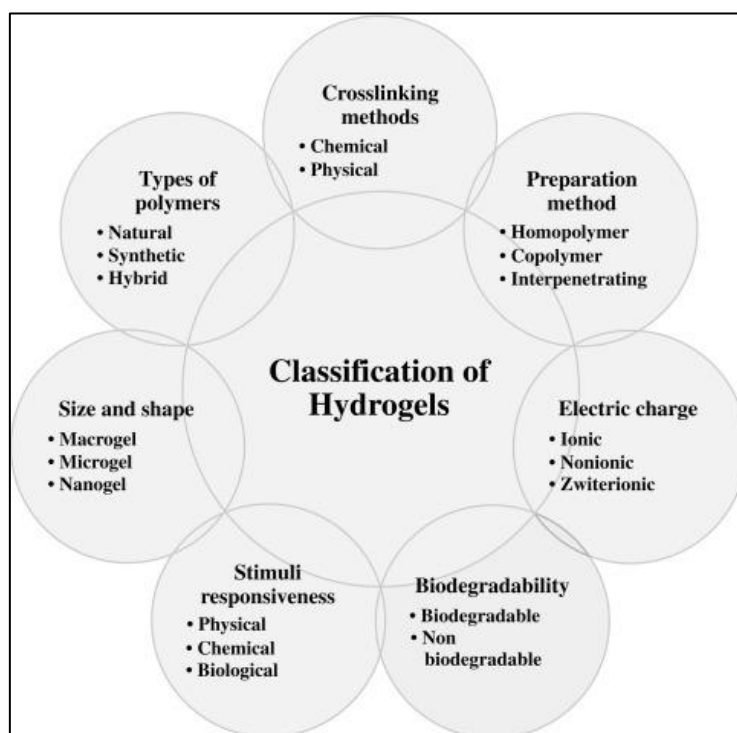


Figure:2 Classification of Hydrogels

1. Classification Based on Source

Hydrogels may be categorized as natural, synthetic, or hybrid systems. [19]

Natural hydrogels are derived from biological polymers and exhibit excellent biocompatibility, biodegradability, and inherent bioactivity. Common examples include protein-based polymers (e.g., collagen, gelatin) and polysaccharides such as hyaluronic acid, alginate, and chitosan.

Synthetic hydrogels are chemically engineered polymers designed to provide superior mechanical strength, controlled degradation, and reproducible properties. These systems allow precise modulation of network architecture and functionality. Polyethylene glycol (PEG)-based hydrogels are widely used in biomedical applications.



Hybrid hydrogels combine natural and synthetic polymers to integrate the biological advantages of natural materials with the mechanical robustness of synthetic counterparts. Examples include systems incorporating dextran, collagen, or chitosan with polymers such as poly (N-isopropyl acrylamide) or polyvinyl alcohol.

2. Classification Based on Polymeric Composition [20]

Hydrogels can be classified according to the nature of the polymer network.

Homopolymeric hydrogels are formed from a single monomer species and represent the simplest polymer network structure.

Copolymeric hydrogels consist of two or more different monomers, with at least one hydrophilic component. These monomers may be arranged in block, alternating, or random configurations, enabling tailored physicochemical properties.

Interpenetrating polymer network (IPN) hydrogels comprise two or more independent cross-linked polymer networks that are physically interlaced but not covalently bonded. In semi-IPN systems, one polymer is cross-linked while the second remains linear, enhancing flexibility and swelling behaviour.

3. Classification Based on Size [21]

Depending on particle dimensions, hydrogels are categorized into Macrogels, with dimensions in the micrometer range, Microgels, in the micrometer range and Nanogels, in the nanometer range. Nanogels, in particular, have gained significant interest in drug delivery due to their enhanced permeability and controlled release capabilities.

4. Classification Based on Type of Cross-Linking

The nature of cross-linking significantly influences hydrogel properties.

Chemically cross-linked hydrogels contain permanent covalent bonds between polymer chains, resulting in stable and mechanically strong networks.

Physically cross-linked hydrogels are formed via non-covalent interactions such as hydrogen bonding, ionic interactions, hydrophobic associations, or chain entanglements. These networks are reversible and often exhibit stimuli-responsive behaviour.

5. Classification Based on Stimuli Responsiveness [22]

Stimuli-responsive hydrogels, also known as “smart” hydrogels, are advanced polymeric systems capable of undergoing reversible physicochemical changes in response to specific environmental triggers. These hydrogels can alter their swelling behavior, sol–gel transition, permeability, or mechanical properties when exposed to external or internal stimuli. Due to their dynamic responsiveness, they are widely explored in controlled and targeted drug delivery systems.

Based on the type of stimulus, smart hydrogels are classified as follows:

1. Physical Stimuli-Responsive Hydrogels: These hydrogels respond to physical factors such as temperature, light, electric fields, or magnetic fields. For example, thermos responsive hydrogels exhibit sol–gel transitions at specific temperatures (e.g., body temperature), making them suitable for injectable drug delivery systems. Photo responsive hydrogels change their structure upon exposure to light, while electrically or magnetically responsive hydrogels alter their properties under applied fields.

2. Chemical Stimuli-Responsive Hydrogels: These systems respond to changes in chemical conditions such as pH, ionic strength, or redox environment. pH-sensitive hydrogels swell or shrink depending on the surrounding pH, making them ideal for site-specific drug release in different regions of the gastrointestinal tract or infected wounds. Redox-responsive hydrogels react to oxidative or reductive conditions within biological systems.

3. Biological Stimuli-Responsive Hydrogels: These hydrogels respond to specific biological signals such as enzymes, glucose, or other biomolecules. Enzyme-responsive hydrogels degrade in the presence of particular enzymes, enabling targeted drug release. Glucose-responsive hydrogels are particularly useful in insulin delivery systems for diabetes management.



6. Classification Based on Network Electrical Charge [23]

Hydrogels may also be categorized according to the presence of charged functional groups:

1. **Non-ionic (neutral) hydrogels**, which lack ionizable groups and swell without generating electrostatic interactions.
2. **Ionic hydrogels**, containing either cationic or anionic functional groups that facilitate ion exchange and electrostatic interactions.
3. **Amphoteric hydrogels**, possessing both acidic and basic groups, enabling pH-dependent charge variation.
4. **Zwitterionic hydrogels**, containing equal positive and negative charges within the same polymer chain, resulting in overall electrical neutrality with high hydrophilicity and antifouling properties.

Properties of Hydrogels: [24, 25]

Hydrogels possess unique physicochemical and biological characteristics that make them highly suitable for biomedical and pharmaceutical applications. Their key properties include swelling behavior, mechanical performance, biocompatibility, biodegradability, and stimuli responsiveness.

1. Swelling Properties: Swelling is a fundamental characteristic of hydrogels and refers to their ability to absorb large quantities of water or biological fluids without dissolving. Upon hydration, the polymer network expands due to osmotic pressure differences and polymer-solvent interactions. The swelling behaviour is influenced by factors such as cross-linking density, polymer composition, ionic content, and environmental conditions (e.g., pH and temperature). Swelling capacity directly affects drug loading, release kinetics, and mechanical performance.

2. Mechanical Properties: The mechanical properties of hydrogels are critical for their structural integrity and biomedical performance.

Elasticity: Hydrogels can exhibit significant extensibility and recover their original shape after deformation, depending on the network structure.

Viscoelasticity: Many hydrogels demonstrate time-dependent mechanical behavior, combining both elastic and viscous responses under applied stress.

Strength and Stiffness: Conventional hydrogels often possess limited mechanical strength; however, these properties can be enhanced through strategies such as double-network formation, fiber reinforcement, or nanocomposite incorporation.

Toughness: Resistance to crack initiation and propagation is an important parameter, particularly for load-bearing applications. Toughness can be improved by introducing interpenetrating networks or energy-dissipating structures.

3. Biocompatibility and Biodegradability: Hydrogels are widely valued for their compatibility with biological systems.

Biocompatibility: It refers to the ability of hydrogels to interact with biological tissues without eliciting adverse immune or inflammatory responses.

High water content provides a hydrated microenvironment that mimics natural extracellular matrices.

Minimal irritation and inflammation can be achieved through appropriate material selection and purification.

Cell adhesion and proliferation can be promoted by functionalizing hydrogels with bioactive moieties.

Hydrogels derived from natural polymers such as chitosan and alginate exhibit inherent biocompatibility.

Biodegradability: Biodegradable hydrogels are designed to degrade into non-toxic by-products that can be metabolized or eliminated by the body.



Controlled degradation enables sustained drug release.

Tissue integration is facilitated as the material gradually resorbs.

The **degree of cross-linking** significantly influences degradation rate.

Degradation products must be biocompatible and non-toxic.

4. Stimuli Responsiveness: Stimuli-responsive (smart) hydrogels undergo reversible changes in their physical or chemical properties upon exposure to external triggers. These stimuli may include temperature, pH, light, electric fields, ionic strength, or specific biomolecules. Such responsiveness enables controlled drug release, site-specific delivery, and dynamic tissue engineering applications.

Advantages and Disadvantages of Hydrogels: [26]

Advantages: Hydrogels possess a high-water content, which imparts flexibility and softness similar to natural tissues, making them suitable for biomedical applications. They enable controlled and timely release of drugs or nutrients and can be engineered for injectability. Their inherent biocompatibility and biodegradability further enhance their clinical utility. Additionally, certain hydrogels exhibit stimuli-responsive behaviour, allowing them to respond to changes in pH, temperature, or metabolite concentration and release their therapeutic payload accordingly. Hydrogels also demonstrate favourable transport properties and can be readily modified to tailor their physicochemical and biological characteristics.

Disadvantages: Despite their benefits, hydrogels present certain limitations. They can be costly and difficult to handle due to their soft, highly hydrated structure. Conventional hydrogels often possess low mechanical strength, restricting their application in load-bearing systems. In wound care, their non-adherent nature may require secondary dressings. Additionally, efficient drug loading can be challenging depending on the network structure and drug compatibility.

Table:1 Raw Materials Used in Herbal Hydrogels and Their Functions

Category	Function in Hydrogel Formulation	Common Examples
Gel-forming polymers	Form the three-dimensional network structure; responsible for swelling, viscosity, elasticity, and drug release behaviour.	Carbopol 934/940, Sodium alginate, Hyaluronic acid, Polyvinyl alcohol (PVA)
Solvents	Act as dispersion medium; facilitate polymer hydration, dissolution, and uniform distribution of ingredients.	Purified water, Ethanol, Methanol, Acetone
Cross-linking agents	Create covalent or ionic bonds between polymer chains to stabilize the network and enhance mechanical strength and swelling control.	Glutaraldehyde, Calcium chloride, Genipin, N, N'-methyl enebisacrylamide (MBA)
Initiators	Generate reactive species to initiate polymerization or cross-linking reactions in chemically prepared hydrogels.	Ammonium persulfate (APS), Redox systems, Photo initiators
pH adjusters / Buffers	Regulate pH to control polymer ionization, viscosity, swelling behaviour, and formulation stability.	Triethanolamine, Sodium hydroxide, Hydrochloric acid, Phosphate buffer, Citrate buffer
Emollients	Provide moisturizing effect; improve skin hydration and formulation acceptability in topical applications.	Glycerin, Mineral oil, Petroleum jelly, Aloe vera gel
Wetting agents / Surfactants	Reduce surface tension; improve dispersion of polymers and herbal extracts; enhance spreadability.	Polyethylene glycol (PEG), Polyvinylpyrrolidone (PVP), Polysorbates
Preservatives	Prevent microbial growth; enhance shelf life and product stability.	Methylparaben, Propylparaben, Sorbates, Essential oils
Herbal extracts (Active component)	Provide therapeutic activity through bioactive phytoconstituents (e.g., anti-inflammatory, antimicrobial, antioxidant, wound healing).	Aloe vera extract, Moringa oleifera extract, Curcuma longa extract

**Table 2: Medicinal Plants Commonly Used in Herbal Hydrogel Formulations for Dermatological Applications**

Sl. No.	Herb (Botanical Name; Family)	Part Used	Major Dermatological Uses
1	Aloe vera (<i>Aloe barbadensis</i> ; Liliaceae)	Leaf gel	Wound healing, sunburn relief, acne, anti-inflammatory, moisturization, psoriasis, insect bites
2	Turmeric (<i>Curcuma longa</i> ; Zingiberaceae)	Rhizome	Antimicrobial, acne, anti-inflammatory, hyperpigmentation, psoriasis, eczema
3	Indian Pennywort (<i>Centella asiatica</i> ; Umbelliferae/Apiaceae)	Leaves	Wound healing, scar reduction, burns, anti-aging, skin repair
4	Marigold (<i>Calendula officinalis</i> ; Asteraceae)	Flowers, leaves	Wound healing, dermatitis, acne, soothing and anti-inflammatory effects
5	Chamomile (<i>Matricaria recutita</i> ; Asteraceae)	Flowers	Skin irritation, wound healing, anti-inflammatory, redness reduction
6	Red Ivy (<i>Strobilanthus alternata</i> ; Acanthaceae)	Leaves	Wound healing, anti-inflammatory, treatment of minor skin disorders
7	Drumstick Tree (<i>Moringa oleifera</i> ; Moringaceae)	Leaves	Wound healing, acne, moisturizing, anti-aging, anti-inflammatory
8	Yarrow (<i>Achillea millefolium</i> ; Asteraceae)	Flowers	Wound healing, eczema, dermatitis, skin repair
9	Rosemary (<i>Rosmarinus officinalis</i> ; Lamiaceae)	Leaves	Acne, anti-inflammatory, redness reduction, dry skin management
10	Myrrh (<i>Commiphora molmol</i> ; Burseraceae)	Oleo-gum resin	Wound healing, acne, soothing irritated skin, anti-aging
11	Neem (<i>Azadirachta indica</i> ; Meliaceae)	Leaves, seeds	Antimicrobial, acne, psoriasis, eczema, wound healing, anti-inflammatory
12	Amla (<i>Phyllanthus emblica</i> ; Phyllanthaceae)	Fruit	Antioxidant, anti-aging, pigmentation reduction, skin hydration
13	Lotus (<i>Nelumbo nucifera</i> ; Nymphaeaceae)	Roots, seeds	Anti-inflammatory, acne, skin hydration, anti-aging
14	Ashwagandha (<i>Withania somnifera</i> ; Solanaceae)	Roots, leaves	Anti-inflammatory, anti-aging, hyperpigmentation, acne management

Methods of Preparation of Hydrogels [27, 28, 29, 30]

Hydrogels are typically synthesized from three essential components: a monomer or polymer precursor, a cross-linking agent, and, in chemically initiated systems, an initiator. These components are used in specific ratios to establish a stable three-dimensional network structure. Following synthesis, hydrogels are purified by washing to remove unreacted monomers, initiators, or by-products. Hydrogel systems may be prepared via homopolymerization (single monomer), copolymerization (two or more monomers, at least one hydrophilic), or graft polymerization techniques. Both natural (e.g., polysaccharides, proteins) and synthetic monomers (e.g., acrylic acid derivatives) are commonly employed.

Hydrogel formation is primarily achieved through physical, chemical, or radiation-induced cross-linking methods, each influencing the structural and mechanical properties of the final system.

1. Physical Cross-Linking Methods: Physically cross-linked hydrogels are formed through non-covalent interactions such as ionic bonding, hydrogen bonding, hydrophobic interactions, or chain entanglement. These systems avoid the use of chemical cross-linking agents, thereby enhancing biocompatibility and reducing toxicity. Additionally, they are generally simple and cost-effective to produce.

1.1 Heating and Cooling (Thermal Gelation): Thermally induced gelation occurs when polymer solutions undergo conformational changes upon heating or cooling. For example, gelatin and carrageenan form gels upon cooling due to helix formation and junction zone development. Certain block copolymers (e.g., polyethylene oxide–polypropylene oxide systems) exhibit sol–gel transitions upon temperature changes, enabling injectable hydrogel formation.

1.2 Ionic Interaction: Ionic cross-linking involves the interaction between oppositely charged polymers or multivalent ions. A common example is the gelation of sodium alginate in the presence of divalent calcium ions (Ca^{2+}), forming an ionically cross-linked network. Similar systems include chitosan-based ionic hydrogels.



1.3 Complex Coacervation: Complex coacervation occurs when oppositely charged polyelectrolytes interact to form a polymer-rich phase. For instance, mixtures of polyanionic xanthan gum and polycationic chitosan form hydrogels through electrostatic interactions. Protein–polysaccharide systems may also form polyionic complex hydrogels depending on pH and concentration.

1.4 Hydrogen Bonding: Hydrogels may form via intermolecular hydrogen bonding, particularly in polymers containing carboxyl or hydroxyl groups. For example, carboxymethyl cellulose (CMC) can form hydrogen-bonded networks under acidic conditions. Similarly, poly (acrylic acid)–polyethylene oxide systems form pH-dependent hydrogen-bonded hydrogels.

1.5 Heat-Induced Aggregation (Maturation): Certain natural polymers containing protein fractions (e.g., gum Arabic) undergo structural aggregation upon heat treatment. This process increases molecular weight and enhances water-binding capacity, leading to hydrogel formation with improved mechanical properties.

2. Chemical Cross-Linking Methods

Chemical cross-linking involves the formation of permanent covalent bonds between polymer chains, resulting in mechanically stable hydrogels. This process typically occurs via reactions between functional groups such as –OH, –COOH, and –NH₂ and suitable cross-linking agents.

Common cross-linkers include aldehydes (e.g., glutaraldehyde), carbodiimides, and dihydrazides. Chemical hydrogels may also be prepared through Free radical polymerization using initiators such as ammonium persulfate, Graft polymerization, where monomers are polymerized onto a pre-existing polymer backbone and Interpenetrating polymer network (IPN) formation, where one polymer network is synthesized within another. Chemically cross-linked hydrogels exhibit enhanced mechanical strength, structural stability, and controlled degradation compared to physically cross-linked systems.

3. Radiation-Induced Cross-Linking: Radiation cross-linking involves exposure of polymer solutions to high-energy radiation, such as gamma (γ) rays or electron beams. Irradiation generates free radicals on polymer chains as well as hydroxyl radicals from water radiolysis. Recombination of these macroradicals results in covalent cross-link formation and hydrogel network development.

Radiation-induced polymerization offers several advantages, including absence of chemical initiator residues, simultaneous sterilization and cross-linking, formation of highly pure hydrogels.

Hydrogels such as poly (2-hydroxyethyl methacrylate) (poly (HEMA)) have been prepared using this method for controlled delivery of antibiotics, anticancer agents, peptides, and proteins. Drug release from radiation-synthesized hydrogels depends largely on swelling behaviour, which is influenced by polymer composition and environmental condition.

Evaluation Parameters of Hydrogels [31, 32, 33, 34]

Hydrogel formulations are evaluated using physicochemical, phytochemical (in the case of herbal hydrogels), and biological assessment methods to ensure quality, stability, and therapeutic efficacy.

1. Physicochemical Evaluation

1.1 Visual Inspection

Visual examination is performed to assess the physical appearance and homogeneity of the hydrogel formulation. Parameters evaluated include color, clarity or transparency, consistency, uniformity, firmness, presence of particulate matter, stickiness, and greasiness. Any phase separation, air entrapment, or visible defects are also recorded.

1.2 pH Determination

The pH of the hydrogel is a critical parameter, particularly for topical formulations, as it should be compatible with skin pH to avoid irritation. pH may be determined using a calibrated digital pH meter.

Procedure: The pH of the hydrogel is determined by first calibrating the pH meter using standard buffer solutions. The electrode is then rinsed with distilled water and gently blotted dry to remove any residual moisture. It is immersed directly into the hydrogel sample, and the reading is allowed to stabilize before recording the value. The measurement is performed in triplicate to ensure accuracy and reliability of the results.



The pH of hydrogels may influence swelling behaviour, stability, and drug release characteristics, particularly in pH-sensitive systems.

1.3 Spreadability Test

Spreadability determines the ease of application of the hydrogel on the skin surface. A specified quantity of hydrogel is placed on a glass plate within a pre-marked circle. Another glass plate is carefully placed over it, followed by the application of a known weight (e.g., 500 g) for a fixed duration (e.g., 5 minutes). The diameter or area of spread is measured. Greater spreadability indicates better patient compliance and ease of application.

1.4 Rheological Studies

Rheological analysis evaluates the flow behaviour and viscoelastic properties of hydrogels, which are essential for stability and performance.

Viscosity measurement: Performed using a viscometer by measuring resistance to spindle rotation within the gel.

Viscoelastic properties: Assessed using a rheometer, which applies controlled stress or strain and measures the resulting deformation.

These studies help determine whether the hydrogel exhibits Newtonian or non-Newtonian (commonly pseudoplastic) behaviour.

1.5 Swelling Studies

Swelling behaviour is commonly evaluated using a gravimetric method to determine the swelling ratio.

Procedure: The swelling study is performed by accurately weighing the dried hydrogel (W_0) and then immersing it in a suitable swelling medium, such as distilled water or a buffer solution, until equilibrium swelling is achieved. After reaching equilibrium, the hydrogel is removed from the medium, excess surface liquid is carefully blotted off, and the swollen hydrogel (W_t) is weighed to determine the extent of swelling.

The swelling ratio (SR) is calculated as:

$$SR = \frac{W_t - W_0}{W_0}$$

Swelling studies provide insight into the network structure, cross-linking density, and drug release potential of the hydrogel.

Evaluation Parameters of Hydrogels:

Hydrogels are three-dimensional, hydrophilic polymeric networks capable of absorbing and retaining large amounts of water or biological fluids. Evaluation of hydrogels is essential to ensure their quality, stability, performance, and suitability for pharmaceutical and biomedical applications. The evaluation parameters can be broadly classified into:

1. Physicochemical Analysis
2. Preliminary Phytochemical Analysis (for herbal hydrogels)
3. Biological Evaluation

Physicochemical Analysis

1.1 Visual Inspection

Visual inspection is a primary and essential quality assessment method used to evaluate the physical characteristics and homogeneity of hydrogels. During this evaluation, parameters such as colour and overall appearance, uniformity, consistency, transparency or clarity, firmness, presence of air bubbles or particulate matter, as well as stickiness and greasiness are carefully observed to ensure formulation quality and batch-to-batch consistency. This step helps in detecting visible defects and ensures batch-to-batch consistency.



1.2 pH Determination

The pH of a hydrogel is a critical parameter, especially for topical and transdermal formulations, as it must be compatible with the physiological pH of the skin (approximately 5.5–7.0). The pH of hydrogels can be influenced by polymer composition, crosslinking density, ionic strength, temperature, and the presence of specific ions or molecules.

Methods for pH Determination:

- Colorimetric analysis using acid-base indicators
- Optical sensor-based methods
- Digital pH meter (most commonly used method)

Procedure: The pH measurement of the hydrogel is carried out by first calibrating the pH meter using standard buffer solutions. The pH electrode is then rinsed with distilled water and gently blotted dry before being immersed into the hydrogel sample. The reading is allowed to stabilize, after which the pH value is recorded. The measurement is repeated to ensure accuracy, and the average of the readings is calculated and reported.

1.3 Spreadability Test

Spreadability determines the ease with which a hydrogel spreads over a surface, which is important for patient compliance and uniform drug distribution.

Procedure:

The spreadability test is performed by placing a known quantity of hydrogel at the center of a glass plate marked with a pre-determined circle. Another horizontal glass plate is carefully placed on top of the sample. A specific weight, for example 500 g, is then applied on the upper plate for a fixed duration such as 5 minutes to allow uniform spreading. After removing the weight, the diameter or area of the spread hydrogel is measured to evaluate its spreadability. Greater spreadability indicates better ease of application.

1.4 Rheological Study

Rheological evaluation is performed to assess the viscoelastic properties of hydrogels, which influence their stability, application behaviour, and drug release characteristics.

Rheometers are used to apply controlled stress or strain to the hydrogel and measure deformation.

Viscometers measure viscosity by determining resistance to flow when a spindle rotates within the sample.

Rheological analysis helps in determining important flow and deformation characteristics of hydrogels, including viscosity, shear-thinning or shear-thickening behaviour, elastic modulus (G'), and viscous modulus (G''). These parameters provide insight into the viscoelastic nature of the hydrogel and are essential for predicting its stability, ease of application, and drug release performance. These parameters are essential for predicting performance during storage and application.

1.5 Swelling Study

Swelling behaviour is a key characteristic of hydrogels and directly influences drug release and absorption properties.

Gravimetric Method:

The swelling behavior of the hydrogel is determined using the gravimetric method. The hydrogel is first weighed in its dry state (W_d) and then immersed in a suitable solvent, such as distilled water or a buffer solution. It is allowed to remain in the medium until equilibrium swelling is achieved. After reaching equilibrium, the hydrogel is removed, excess surface solvent is carefully blotted off, and the swollen hydrogel is weighed (W_s).



The swelling ratio is calculated using the following formula:

$$\text{Swelling Ratio (SR)} = (W_s - W_d) / W_d$$

Swelling studies are essential for evaluating the water uptake capacity, volume expansion, and structural integrity of the hydrogel network, which directly influence drug release and overall performance. Swelling studies also help in determining volume expansion and structural integrity of the hydrogel network.

Table: 3 Physical analysis of Hydrogels

S. No	Parameter	Method	Purpose
1	Visual Inspection	Direct observation	To assess color, appearance, homogeneity, clarity, and presence of defects
2	pH Determination	Digital pH meter	To ensure compatibility with physiological pH
3	Spreadability Test	Glass plate method	To evaluate ease of application
4	Rheological Study	Rheometer/Viscometer	To determine viscosity and viscoelastic behavior
5	Swelling Study	Gravimetric method	To determine water uptake capacity and swelling ratio

Chemical analysis

1. **Spectroscopic analysis:** These analyses include various methods to determine the structure, composition and properties of hydrogels. Spectroscopic techniques include Raman spectroscopy, Fourier transform (FT-IR) spectroscopy and terahertz spectroscopy and also NMR, and UV-visible spectroscopies are also used. This helps to understanding their water structure behavior, gelation process, crosslinking and dehydration etc.

2. **SEM and TEM analysis:** Scanning electron microscopy (SEM) used for surface analysis, visualizing external morphology and topography of hydrogel. It provides a 3D review of surface, revealing details like pore size, surface roughness and network structures. Transmission electron microscopy (TEM) provides internal structure, visualization of internal features like fibers nanoparticles and other Nano scale features.

2. Preliminary Phytochemical Analysis (For Herbal Hydrogels)

In herbal-based hydrogels, preliminary phytochemical screening is performed to identify and confirm the presence of bioactive phytoconstituents responsible for therapeutic activity. Qualitative chemical tests are carried out to detect major classes of secondary metabolites such as alkaloids, flavonoids, tannins, saponins, glycosides, and terpenoids.

The identification of these phytoconstituents is essential, as they contribute significantly to the pharmacological properties of the formulation. Alkaloids are known for their antimicrobial and analgesic activities; flavonoids exhibit antioxidant and anti-inflammatory effects; tannins possess astringent and wound healing properties; saponins demonstrate antimicrobial activity; glycosides show diverse therapeutic actions; and terpenoids are recognized for their anti-inflammatory and antimicrobial potential. Thus, preliminary phytochemical analysis ensures the presence of active constituents and supports the therapeutic efficacy of herbal hydrogel formulations.

3. **Biological Evaluation:** Biological tests are performed to assess safety and efficacy. These may include:

1. Antimicrobial activity studies
2. In vitro drug release studies
3. Skin irritation tests
4. Wound healing studies
5. Cytotoxicity evaluation



Biological tests of hydrogel formulations are essential to evaluate their safety, biocompatibility, and therapeutic effectiveness before clinical application. These studies help determine whether the hydrogel is non-toxic, non-irritant, and capable of delivering the intended pharmacological action.

1. Antimicrobial activity studies are performed to determine the ability of the hydrogel formulation to inhibit the growth of pathogenic microorganisms. Commonly used methods include the agar well diffusion method, disc diffusion method, and broth dilution technique. In the agar diffusion method, a standardized microbial suspension (e.g., *Escherichia coli*, *Staphylococcus aureus*, or *Pseudomonas aeruginosa*) is spread uniformly on sterile nutrient agar or Mueller–Hinton agar plates. Hydrogel samples or discs are placed on the inoculated surface and incubated at 35–37°C for 18–24 hours. After incubation, the zone of inhibition around the hydrogel is measured in millimeters. A larger zone indicates stronger antimicrobial activity. In broth dilution methods, microbial growth inhibition is assessed by measuring turbidity, allowing determination of minimum inhibitory concentration (MIC).

2. In vitro drug release studies are conducted to evaluate the release profile and kinetics of the drug incorporated within the hydrogel. Typically, the hydrogel is placed in a suitable dissolution medium such as phosphate buffer (pH 5.5 or 7.4) maintained at 37°C to simulate physiological conditions. The study may be performed using a dialysis membrane method or a USP dissolution apparatus. At predetermined time intervals, aliquots of the medium are withdrawn and replaced with fresh medium to maintain sink conditions. The amount of drug released is analysed using UV–Visible spectroscopy or high-performance liquid chromatography (HPLC). The cumulative drug release data are plotted to determine release kinetics and mechanism (e.g., zero-order, first-order, Higuchi model).

3. Skin irritation tests are carried out to evaluate the dermal safety of topical hydrogel formulations. These tests may be performed on animal models (such as rabbits or rats) or on reconstructed human epidermal models. A measured amount of hydrogel is applied to a shaved area of skin and covered for a specified duration (usually 24 hours). The application site is observed for signs of erythema (redness), oedema (swelling), or inflammation at specific intervals. The irritation score is calculated based on standardized grading scales. A low or zero irritation score indicates that the formulation is safe for topical use.

4. Wound healing studies assess the therapeutic potential of hydrogels in promoting tissue repair. In vivo wound models, such as excision or incision wound models in animals, are commonly used. A standardized wound is created under aseptic conditions, and the hydrogel formulation is applied daily. The rate of wound contraction is measured periodically by calculating the reduction in wound area over time. Histopathological examination may also be performed to evaluate re-epithelialization, collagen formation, and tissue regeneration. In vitro scratch assays using cultured fibroblasts or keratinocytes can also be used to assess cell migration and wound closure ability.

5. Cytotoxicity evaluation is performed to determine the biocompatibility of the hydrogel with living cells. This is typically assessed using cell viability assays such as the MTT assay, XTT assay, or trypan blue exclusion test. Cultured cells are exposed to the hydrogel extract or direct contact with the hydrogel for a defined period. After incubation, cell viability is measured spectrophotometrically. A high percentage of viable cells (usually above 70–80%) indicates that the hydrogel is non-toxic and suitable for biomedical application.

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Conclusion

Herbal hydrogels represent an advanced and promising approach in the field of novel drug delivery systems, combining the therapeutic potential of medicinal plants with the unique physicochemical properties of hydrogel networks. Structurally, hydrogels are three-dimensional, cross-linked polymeric systems capable of absorbing and retaining substantial amounts of water, thereby maintaining a moist environment that is highly beneficial for wound healing and skin applications. Their inherent properties, including high water absorption capacity, biocompatibility, flexibility, and controlled drug release behavior, make them ideal carriers for both pharmaceutical and cosmetic applications.

The incorporation of herbal ingredients into hydrogel matrices enhances therapeutic efficacy while minimizing toxicity and adverse effects commonly associated with synthetic drugs. Medicinal herbs possessing wound healing, antimicrobial, antifungal, antioxidant, and anti-inflammatory activities further strengthen the clinical and cosmetic relevance of these formulations. The preparation of herbal hydrogels through physical, chemical, or radiation cross-linking techniques allows the development of stable and efficient delivery systems tailored for specific applications.



Comprehensive evaluation through physicochemical, chemical, phytochemical, and biological studies ensures the quality, safety, and effectiveness of the final formulation. Based on the available evidence, herbal hydrogels can be regarded as a versatile and innovative platform for wound management, transdermal drug delivery, skin regeneration, and cosmetic care products such as face masks, serums, and under-eye patches.

In conclusion, herbal hydrogels offer a synergistic integration of natural therapeutics and advanced polymer technology, making them a promising and sustainable solution for future biomedical and cosmetic applications.

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