Advances in Bioresearch
Adv. Biores., Vol 17 (3) March 2026:163-176

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.17.3.163176

Advances in Bioresearch

REVIEW ARTICLE

Hydrogels In Drug Delivery: A Systematic Review of Their Design, Evaluation, And Therapeutic Potential

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ABSTRACT

Hydrogels are three-dimensional networks made of polymers that can absorb significant quantities of water, which makes them promising materials in pharmaceutical and biomedical applications. This review presents an overview of hydrogels, including their structure, classification, and the various Polymers derived from natural sources and artificially made that are utilized in their production. Approaches to hydrogel synthesis and evaluation techniques are discussed, alongside a compilation of recent advances reported in the literature. The advantages of hydrogels, like biocompatibility and properties, are balanced with challenges like mechanical limitations and stability issues. Drug delivery, wound healing, and tissue engineering applications highlight their versatility. Future outlooks focus on creating hydrogel systems that are responsive to stimuli, targeted, and tailored to individual patients, with emerging technologies like nanotechnology and 3D printing offering significant innovation potential. Continued research in this field is essential for enhancing therapeutic efficacy and advancing personalized medicine.

Keywords: *Hydrogel, Polymer-based hydrogels, Novel Drug delivery system, Evaluation of Hydrogel, Polymers.*

Received 04.02.2026 Revised 24.02.2026 Accepted 21.03.2026

How to cite this article:
Onkar Vilas J, Anuj Jagannath S , Preetam Balakrishna P, Sampada Suresh H , Umesh Dattatray K , Twarita Dilip D , Sandip Ashok M. Hydrogels in Drug Delivery: A Systematic Review of Their Design, Evaluation, And Therapeutic Potential. Adv. Biores., Vol 17 (3) March 2026: 163-176.

INTRODUCTION

In recent times, extensive studies have been concentrated on the advancement of pharmaceutical technologies, particularly novel drug delivery systems (DDS), which offer effective strategies for targeted and/or temporally regulated administration of therapeutic compounds. Among the diverse polymer-based platforms employed as drug carriers or release modulators, hydrogels have emerged as prominent materials of interest [1-3].

Since the early 1960s, Hydrogels have been investigated as novel systems for drug delivery. The research conducted by Wichterle and Lim introduced cross-linked hydroxyethyl methacrylate hydrogels; a form of hydrophobic gel designed for applications in biomedicine. Hydrogels possess several advantageous properties, including excellent biocompatibility, high water affinity, the capability to regulate the rates of

drug release, and respond to environmental cues. These characteristics have spurred widespread interest among scientists from multiple disciplines to develop and refine these delivery platforms [4-6].

Hydrogels consist of three-dimensional networks of hydrophilic polyelectrolyte polymers that can be cross-linked either physically or chemically and can absorb large quantities of water. They exhibit adjustable biocompatibility, sensitive environmental responsiveness, biodegradability, and tailored mechanical characteristics [7-10].

Currently, two main types of hydrogels are available commercially: physical and chemical hydrogels. Physical hydrogels are inherently heterogeneous due to molecular entanglement clusters and ionically associated domains that form within the network. These gels contain transient network imperfections such as free chain ends or loops. Ionotropic hydrogels, a subclass of physical hydrogels, form when a polyelectrolyte engages with multivalent ions that have an opposite charge, for example, calcium alginate hydrogels. Additionally, hydrogels can form through complex coacervation when polyelectrolytes of opposite charges are mixed. These physical interactions are affected by environmental factors like ionic strength, pH, temperature, and mechanical stress, or the presence of competing solutes that can bind to polymeric sites. In contrast, Chemical hydrogels are formed by the covalent cross-linking of water-soluble polymers or by transforming hydrophobic polymers into hydrophilic varieties, followed by cross-linking to create a network. These covalently bonded networks are often referred to as 'permanent' or chemical gels. Similar to physical hydrogels, chemical hydrogels are also heterogeneous, typically featuring cluster areas with high cross-link density and low water swelling, interspersed within regions exhibiting lower cross-link density and higher swelling capacity [11-14].

Hydrogels provide protective environments for drugs against harsh conditions, such as enzymatic degradation and acidic pH in the stomach. Their porous network enables efficient drug loading within the gel matrix and allows for controlled release at predetermined rates. Additionally, hydrogels can modulate drug release by experiencing modifications in their structure as a reaction to various environmental stimuli, including pH fluctuations, temperature variations, ionic strength, and applied electric fields [1].

Hydrogels are utilized in various applications, particularly in the medical and pharmaceutical sectors. Due to their significant water content and soft consistency, they more closely resemble natural living tissues compared to other synthetic biomaterials. This similarity, along with their substantial hydration, enhances their biocompatibility. Consequently, hydrogels are utilized in diverse biomedical devices, such as artificial heart linings, synthetic skin replacements, contact lenses, biosensor membranes, and systems for controlled drug delivery [15].

Review highlights hydrogels as effective carriers for delivering bioactive agents like drugs and proteins, with potential for targeted therapy. It covers the structure and classification of hydrogels, their advantages and drawbacks, and key applications. The polymers used, preparation methods, and evaluation techniques are also discussed. Finally, future prospects and examples of drug formulations involving hydrogels are summarized.

STRUCTURE OF HYDROGELS

Both natural and synthetic polymers can be used to synthesize hydrogels. using monomers that are hydrophilic or hydrophobic. Various cross-linking methods chemical, physical, or ionizing radiation, can be employed to form the hydrogel network. The primary components in hydrogel synthesis include monomers, cross-linkers, and initiators. Hydrogels are categorized into various types according to their preparation methods. (Fig. 1).

1. Homo-polymeric Network

   Homo-polymeric networks consist of one specific type of monomer. Based on the properties of the monomers and the technique used for polymerization, these homopolymers may create cross-linked structures.

2. Co-polymeric Network

These are synthesized from more than one monomer. The inclusion of at least one hydrophilic component is essential in these hydrogels to ensure their swelling capability.

3. Multi-polymeric Network

These consist of two independently cross-linked polymer networks. These dual polymer systems often exhibit enhanced properties compared to individual polymers. A common form of multi-polymeric hydrogels is interpenetrating polymer networks (IPNs), where two polymers are physically intertwined, with at least one being cross-linked or synthesized within the network [4,16,17].

Classification of hydrogel

1. Based on Source

1.1 Natural Source

This hydrogel exhibits excellent cell attachment properties, along with biodegradability and biocompatibility. They are primarily derived from two categories of natural polymers: Polysaccharides, such as hyaluronic acid, alginate, and chitosan, along with proteins like collagen, gelatin, and lysozyme, are commonly used in hydrogel formulation.

1.2. Synthetic Source

These are designed to display a wider array of mechanical and chemical properties than natural hydrogels, improving their adaptability and usefulness. Notably, hydrogels made from polyethylene glycol (PEG) are commonly utilized in biomedical fields because of their non-toxic nature, compatibility with biological systems, and minimal immune response.

1.3. Semi-Synthetic Source

These hydrogels consist of a combination of natural and synthetic polymers. Numerous biopolymers that originate from natural sources, such as dextran, collagen, and chitosan, have been combined with synthetic polymers like poly(N-isopropylacrylamide) and polyvinyl alcohol to merge the benefits of both hydrogel types.

2. Based on Polymeric Composition

2.1. Homo Polymeric Hydrogels

This hydrogel is made up of a network of polymers. formed exclusively from one type of monomer, which serves as the fundamental unit of the polymer structure. The formation of a cross-linked network in homopolymers depends on the monomer's nature and the polymerization technique employed.

2.2. Co-Polymeric Hydrogels

These are composed of more than two different types of monomers arranged randomly, in segments, or throughout the polymer chain. Each monomer type has to include a minimum of one hydrophilic element to ensure the hydrogel's swelling capability.

2.3. Multi-Polymer Interpenetrating Polymeric Hydrogel (IPN)

Hydrogels encompass a broad range of materials featuring cross-linked networks composed of two distinct synthetic or natural polymers. Semi-interpenetrating polymer network (semi-IPN) hydrogels consist of a cross-linked polymer network combined with a non-cross-linked polymer.

3. Based on Biodegradability

3.1. Biodegradable Hydrogels

These materials undergo natural degradation. Biodegradable polymers can be naturally derived, such as chitosan, fibrin, and agar, or synthetically produced, including Poly (N-isopropyl acrylamide), polyanhydrides, and poly (aldehyde guluronate).

3.2. Non-Biodegradable

Various vinyl-based monomers or macromers, including 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, and acrylamide, are used in the synthesis of non-biodegradable hydrogels.

4. Based on Configuration

4.1. Amorphous

These are amorphous and primarily composed of glycerin and water, designed chiefly to maintain wound hydration.

4.2. Semi-Crystalline

A combination of both crystalline and amorphous phases in a complex structure.

4.3. Crystalline

These exhibit enhanced resistance to harsh environmental conditions and possess superior mechanical strength.

5. Based on the Type of Cross-Linking

5.1. Physical Linking

Physical hydrogel networks form transient junctions through hydrogen bonds, hydrophobic interactions, or polymer chain entanglements.

5.2. Chemical Linking

Networks that are chemically cross-linked possess stable and permanent junctions.

6. Based on Physical Appearance

Based on their physical form, hydrogels can exist as films, matrices, or microspheres, depending on the polymerization method used.

6.1. Matrix

6.2. Film

6.3. Microsphere

7. Based on Network Electrical Charges

7.1. Non-Ionic – Neutral

7.2. Ionic - Anionic or cationic
7.3. Zwitter Ionic - Polybetaines containing both anionic and cationic groups.
7.4. Amphoteric Electrolyte – Ampholytic, which has both acidic and basic groups [7, 9,10, 18-21].

Advantages of Hydrogels

1. Shows an elevated degree of flexibility, closely resembling natural tissues.
2. Biocompatible and biodegradable, enabling injectable formulations.
3. Allows localized application, thereby bypassing first-pass metabolism.
4. Delivers drugs in a sustained and prolonged manner, outperforming conventional systems.
5. Reduces the amount of required dosage.
6. Minimizes side effects.
7. Enhances drug bioavailability and utilization.
8. Improves patient adherence to therapy.
9. Supports site-specific drug targeting, including the colon.
10. Protects mucosal tissues from irritating drugs.
11. Prevents drug loss due to extensive first-pass metabolism.
12. Lowers treatment costs by reducing the number of dosage units needed.
13. Allows drug release patterns to align with the body's circadian rhythms.
14. Easily modifiable for various applications.
15. Allows controlled release of growth factors and nutrients to support effective tissue regeneration.
16. Supports the entrapment of microbial cells inside polyurethane hydrogel beads, providing reduced toxicity.
17. Environmentally responsive hydrogels can sense changes in pH, temperature, or metabolite amount and release their payload accordingly.
18. Natural hydrogels like agarose, methylcellulose, and hyaluronan are being explored for tissue engineering applications.
19. Possess favorable transport properties and are readily modifiable.
20. Exhibit superior elasticity and strength compared to other hydrogels with similar softness, exemplified by poly (methyl acrylate-co-hydroxyethyl acrylate) hydrogel implant materials [7, 22-25].

Disadvantages of Hydrogels

1. Movement of maggots can cause discomfort or a sensation in treated areas.
2. In contact lens use, hydrogels may lead to lens deposits, oxygen deprivation (hypoxia), dehydration, and adverse eye reactions.
3. The considerable cost and the sensation associated with maggot activity are key drawbacks.
4. Risks associated with device implantation include clotting at anastomosis locations, along with postoperative complications during insertion or removal.
5. Specific to hydrogel contact lenses, common disadvantages include lens deposition, hypoxia, dehydration, and redness of the eyes.
6. Hydrogels often exhibit poor adherence and may require secondary dressings to stay in place. Additionally, they can cause discomfort due to maggot movement, have low mechanical strength, are challenging to handle, and tend to be costly [7, 23-25].

Benefits of Hydrogels:

1. Biocompatible
2. Biodegradable
3. Suitable for injection
4. Easily modifiable
5. Greater elasticity and enhanced strength
6. Excellent transparency
7. Timely delivery of medications and nutrients [7]

Application of Hydrogel

Different techniques have been designed to improve how efficiently drugs are delivered. Hydrogels have gained significant interest due to their potential in controlled drug release, bioadhesive properties, and site-specific delivery of therapeutic drugs. Their versatility allows hydrogel-based delivery systems to be used through various routes, including ocular, oral, rectal, epidermal, and subcutaneous applications. (Fig. 2) [15, 26-28].

1. Oral drug delivery product

It is extensively utilized for drug delivery due to several benefits, including ease of administration, compatibility with solid dosage forms, sustained and controlled release, and improved patient

compliance. Nevertheless, the intricate anatomy and physiological processes of the gastrointestinal tract play a crucial role in affecting the release, dissolution, and absorption of orally administered drugs.[29–31]

Oral cavity drug delivery provides a flexible platform for the localized treatment of various conditions, including periodontal disease, stomatitis, fungal and viral infections, and oral cancers. To ensure effective local therapy, hydrogels must adhere strongly and persistently to the oral mucosa despite the continuous presence of saliva [15, 32].

First-pass metabolism is minimized through this delivery route. Lidocaine-loaded mucoadhesive formulations have been formulated using a blend of Carbopol 934, hydroxypropyl cellulose, and magnesium stearate. The tablet measured 1 cm in diameter and 2 mm in thickness [33].

2. Buccal drug delivery product

Due to its easy accessibility and the presence of extensive smooth muscle tissue covered by relatively stable mucosa, the buccal region serves as an ideal site for delivering mucoadhesive formulations. Medications absorbed through the buccal mucosa are transported directly into the systemic circulation via the internal jugular vein, circumventing the liver's first-pass metabolic process and thus improving bioavailability. Other benefits include reduced enzymatic degradation, good compatibility with drugs and excipients that cause minimal and reversible irritation to the mucosa, painless application, and straightforward removal of the drug. Therefore, buccal administration offers an efficient alternative pathway for systemic delivery of therapeutics [29, 34].

An ideal polymer for buccal drug delivery should exhibit excellent spreadability, swelling capacity, favorable rheological properties, sufficient bioadhesion in both dry and moist conditions, robust mechanical strength, and be non-toxic, cost-effective, biocompatible, and biodegradable [35, 36].

3. Ocular drug delivery product

The human eye is a spherical and intricate organ, anatomically divided into anterior and posterior sections. Delivering drugs to the anterior segment presents considerable difficulties because of both static and dynamic barriers. Major challenges include the blood-aqueous barrier, the corneal epithelium and stroma, tear turnover, conjunctival blood vessels, and lymphatic drainage. These factors critically influence the design and efficacy of ophthalmic formulations, as drug residence time on the ocular surface is typically limited to 1–2 minutes [29, 37].

It is estimated that approximately 75% of ophthalmic solutions are lost due to precorneal factors such as lacrimal drainage, resulting in reduced drug bioavailability. Additional factors, including blinking and tear turnover, further compromise drug retention on the ocular surface. Hydrogels, which are biocompatible and safe, can be implanted sub-conjunctively to enhance therapeutic efficacy. For example, xyloglucan-based hydrogels have been utilized to provide extended release of pilocarpine and timolol in the eye [33].

4. Transdermal drug delivery product

The skin, being the body's largest and outermost organ, covers roughly 1.8 square meters and constitutes about 20% of total body weight. Using the skin as a drug delivery route presents multiple benefits, such as controlled and sustained release of medication, enhanced patient adherence, and a reduced likelihood of systemic side effects compared to oral or injectable methods. Transdermal delivery is especially beneficial due to the skin's large surface area, minimal enzymatic breakdown, and the ability to provide extended therapeutic effects [29, 38, 39].

Topical transdermal application of hydrogels offers multiple benefits, including the circumvention of hepatic first-pass metabolism, thereby enhancing drug efficacy and systemic bioavailability. Transdermal drug delivery systems are employed to maintain sustained and consistent drug release profiles. Due to their hydrated, tissue-like structure, hydrogels provide better patient compliance and ease of removal compared to conventional formulations such as ointments and patches. Transdermal systems are utilized for both systemic delivery and localized treatment of dermatological conditions. For instance, hydrogels formulated with glucocorticoid budesonide are applied in managing topical disorders. Additionally, Poloxamer 407-based hydrogels loaded with gentamicin have demonstrated superior therapeutic outcomes for skin infections, surpassing the safety and efficacy profile of gentamicin administered parenterally, which is often associated with systemic side effects [33].

Historically, drugs have been applied to the skin primarily for treating local dermatological issues and disinfecting the surface. More recently, however, the transdermal route has gained recognition as a promising alternative for systemic drug administration. This approach provides various benefits, such as sustained and controlled drug release over prolonged durations, the option to easily discontinue treatment by removing the delivery device, and avoidance of hepatic first-pass metabolism, which enhances both bioavailability and therapeutic effectiveness [15, 40].

5. Vaginal drug delivery product

The vagina, a key component of the female reproductive system, is a muscular canal approximately 7.5 cm in length, situated between the urethra, bladder, and rectum. It comprises three distinct layers: the epithelial lining, the muscular layer, and the outer tunica adventitia. The epithelial layer's thickness varies depending on factors such as age, hormonal status, and physiological stage of life. Blood flow to the vagina is chiefly provided by the vaginal branch stemming from the uterine artery. The vaginal route is beneficial for drug delivery because of rich blood flow, bypassing first-pass metabolism, and high permeability to many drugs, including proteins and peptides.[29,41,42]

Pharmaceutical agents intended for vaginal administration are typically formulated as creams, suppositories, gels, foams, or tablets. The vaginal route offers several advantages, most notably the bypassing of hepatic first-pass metabolism. The extensive surface area of the vaginal epithelium enhances systemic drug absorption, including for compounds with high molecular weights. For instance, the bioavailability of natural progesterone is significantly reduced by hepatic metabolism, making the vaginal route a more effective alternative. A flat-faced disc formulation containing the anticancer agent bleomycin, cross-linked with the use of Carbopol 934 and hydroxypropyl cellulose, enabled prolonged drug release exceeding 23 hours. [33]

6. Gastrointestinal Tract

The gastrointestinal (GI) tract remains the most widely used and favored method for drug administration due to its ease of use and adherence by patients. It is also utilized for localized drug delivery within the tract. For example, famotidine, an anti-ulcer agent, is administered for its local effects in the stomach. To improve the clinical effectiveness and systemic availability of pharmaceutical agents, sustained-release gastroretentive hydrogels have been developed. These systems extend the duration of the drug's stay in the stomach and ensure a regulated release at the optimal absorption site. [33]

7. Hydrogels for the Brain

The blood-brain barrier, like other protective parts of the body, makes it hard for medicines to reach the brain and central nervous system. Approximately 98% of newly synthesized drugs are unable to cross the BBB, resulting in a limited number of therapeutic agents available for CNS disorders. However, promising advancements have been made using sustained-release systems. For instance, camptothecin-loaded PLGA (poly(lactic-co-glycolic acid)) microspheres have demonstrated prolonged drug release and significantly increased survival rates in rats with malignant gliomas, highlighting their potential for effective CNS drug delivery.[33]

8. Wound healing

Hydrogels are polymer networks that absorb large amounts of water and drugs. Gelatin or sodium alginate-based hydrogels form a barrier on wounds, prevent infection, and maintain moisture for better healing.[33]

9. Subcutaneous Delivery

Research is actively progressing on hydrogel systems for subcutaneous administration of anticancer drugs. For example, crosslinked poly (2-hydroxyethyl methacrylate) has been utilized for delivering cytarabine (Ara-C). Current trends focus on implantable biodegradable hydrogels that eliminate the need for surgical removal after the drug has been released, enhancing patient comfort and treatment efficiency. [33]

10. Rectal Delivery

Although the rectal route is used to administer a range of drugs, patient acceptance is often reduced because of discomfort associated with the dosage forms. It is primarily utilized for the local treatment of rectal conditions such as hemorrhoids. Importantly, Medications absorbed through the lower rectum directly enter systemic circulation, avoiding hepatic first-pass metabolism, which makes this route beneficial for drugs that undergo extensive liver metabolism. [43–45]

POLYMERS USED IN THE HYDROGEL PREPARATION

Polymers are widely found both in nature and as synthetic materials. The human body itself comprises polymers such as proteins and enzymes. The word ‘polymer’ originates from Greek, where ‘poly’ means ‘many’ and ‘meros’ means parts, collectively signifying “made up of many parts.” Christian F. Schunbein made the first semi-synthetic polymer, cellulose nitrate, in 1845. [46]

1. Water-soluble synthetic polymers

It contains hydrophilic groups like esters, amides, or pyrrolidone in its structure. They are usually safe for the body and do not cause toxicity. Examples of such polymers include polyethylene glycol, polyacrylic acid, and polyvinyl alcohol.

I. Poly acrylic acid

Carbomer, or polyacrylic acid, is a synthetic polymer made up of high molecular weight acrylic acid units. Carbomers are available in different grades such as 934, 934P, 940, and 910. When used in hydrogel formulations, these polymers can absorb water several times their own weight. Due to their exceptional water-retention capacity, they are classified as superabsorbent polymers.

II. Polyethylene glycol (PEG)

Polyethylene glycol (PEG) is a water-soluble polymer frequently utilized in hydrogels because of its biocompatibility, non-toxicity, and superior solubility in water. Hydrogels based on PEG are often called "smart polymers" or "intelligent gels" due to their responsiveness to various stimuli. These triggers can be physical, such as changes in solvent, temperature, light, radiation, or pressure, or chemical, including shifts in pH or the presence of specific ions. These properties make PEG-based hydrogels ideal for applications involving controlled drug release.

III. Polyvinyl alcohol (PVA)

This polymer dissolves in water and is recognized for its excellent ability to retain moisture. making PVA hydrogels ideal for wound dressing applications. Additionally, PVA is used as a scaffold material due to its excellent hydrophilicity and chemical stability.

2. Cellulose derivatives

Cellulose, found in plants, doesn't dissolve in water because of strong hydrogen bonds. However, its water-soluble forms, like HPMC, HEC, and CMC, are commonly used in medicines.

3. Hydrocolloids

Most gums are hydrophilic, which makes them widely used in pharmaceutical formulations. They possess excellent thickening and gelling properties.

I. Alginate

Alginate is a linear polysaccharide derived from brown seaweed and algae, consisting of (1→4)-linked β-D-mannuronic acid and (1→4)-linked α-L-guluronic acid units. Stomach-targeted hydrogels for famotidine delivery have been developed by grafting sodium alginate with polyacrylamide.

II. Carrageenan

Carrageenan, a hydrocolloid derived from red seaweed, consists of galactose and anhydrogalactose units. It is commonly used in sustained-release dosage forms. Gels are typically prepared using 0.5–1% carrageenan concentration. Besides pharmaceuticals, carrageenan is also used in products like toothpastes.

III. Chitosan

It is a natural polymer produced mainly by deacetylating chitin, which is sourced from the shells of shrimp, crab, and lobster. Its biodegradability, biocompatibility, and non-toxic nature make it popular in pharmaceutical use. Thermo and pH-responsive chitosan-based hydrogels have been formulated with doxorubicin hydrochloride as a model drug to investigate drug release under varying pH conditions.

IV. Hyaluronic acid

Hyaluronic acid (HA), also called hyaluronan or sodium hyaluronate, is a natural polymer made up of N-acetyl-D-glucosamine and beta-glucuronic acid units. It is present in the tissues of higher animals. Due to its viscoelastic characteristics, HA-based hydrogels are extensively used for delivering therapeutic agents in tissue repair. These hydrogels can be engineered into various forms, such as rigid or flexible gels, non-woven meshes, sheets, and targeted drug delivery platforms.

4. Natural polymers

I. Gelatin

Gelatin is a natural, water-soluble polymer obtained through the hydrolysis of collagen from animal connective tissues and bones. Wound dressing hydrogels created by crosslinking gelatin with sodium alginate using agents like sodium chloride or glutaraldehyde are non-toxic and exhibit enhanced performance when both polymers are combined in equal ratios.

II. Dextran

Dextran, made from sucrose, is a water-soluble, biocompatible polymer used to extend the effects of proteins and drugs like interleukin-2. Dextran-based hydrogels, which are pH-sensitive, have been developed with the anticancer drug paclitaxel for targeted colon delivery.

III. Xanthan gum

Xanthan gum, a cream-colored powder made by fermenting Xanthomonas campestris, dissolves in both hot and cold water and remains stable between pH 4 and 10. Super porous hydrogels were synthesized through graft copolymerization of xanthan gum with acrylic acid and 2-hydroxyethyl methacrylate (HEMA).

5. Starch based polymers

Starch

Starch, a biodegradable plant energy storage molecule, forms pH-sensitive hydrogels with methacrylic acid, used to deliver ketoprofen. [47–55]

METHODS OF PREPARATION OF HYDROGELS

1. Homopolymer hydrogel

Homopolymers are polymers made from only one kind of monomer. Hydrogels can be crosslinked or non-crosslinked based on the monomer type and polymerization method used. Crosslinked homopolymer hydrogels are often utilized in applications requiring sustained drug release, such as transdermal delivery systems and ophthalmic devices like contact lenses. Crosslinked homopolymers, such as poly (glycerol methacrylate) (PGMA) and poly (3-hydroxypropyl methacrylate) (PHPMA), form stable hydrogel networks. Non-crosslinked homopolymers like polyvinyl alcohol (PVA) and poly(N-vinyl-2-pyrrolidone) (PNVP) are valued for their water solubility and broad applications in medicine and agriculture. Poly (2-hydroxyethyl methacrylate) (PHEMA) is often polymerized using polyethylene glycol Di methacrylate as a crosslinker and benzoin isobutyl ether as a photo initiator, commonly in contact lens production. Other commonly used polymers include polyvinyl pyrrolidone, polyacrylic acid, and polyethylene glycol.[56–62]

2. Co-polymeric hydrogel

Copolymeric hydrogels consist of two monomers, with at least one having hydrophilic properties. Numerous significant copolymeric hydrogels have been developed through the combination of compatible monomers, including examples such as poly (N-vinyl pyrrolidone-co-hydroxyethyl methacrylate) (poly (NVP-co-HEMA) and poly (hydroxyethyl methacrylate-co-methyl methacrylate) (poly (HEMA-co-MMA). Additionally, triblock copolymers composed of polyethylene glycol (PEG), poly(ε-caprolactone) (PCL), and polyethylene glycol have been prepared. The formation involves combining ε-caprolactone through a copolymerization process.[63–66]

3. Semi-interpenetrating networks (semi-IPN)

In these hydrogels, a linear polymer blends into the crosslinked network without chemical bonding. This configuration allows for modification of the pore size and facilitates sustained drug release. Semi-IPN hydrogels are made by blending a linear polymer with a crosslinked network. Examples include alginate with poly (N-isopropyl acrylamide) using calcium chloride, showing temperature and pH sensitivity. PHEMA hydrogels use N, N-methylenebisacrylamide, ammonium persulfate, and trisodium citrate in their preparation. Gum Arabic with silver nitrate shows antibacterial activity, and polyallyl ammonium chloride is used in acrylic-based semi-IPNs. [56,67–69]

4. Interpenetrating networks (IPN)

These hydrogels contain two polymers, with one formed or crosslinked in the presence of the other using monomers and an initiator in solution, followed by immersion of a pre-polymerized hydrogel to complete the reaction. Hydrogels produced by this technique exhibit enhanced mechanical properties such as increased stiffness and toughness, along with improved drug-loading efficiency compared to conventional hydrogel preparation methods. For example, poly (ethylene glycol) diacrylate (PEGDA) hydrogels can be enhanced with β-chitosan by mixing PEGDA and chitosan solutions, then crosslinking them under UV light. The resulting hydrogel typically contains 77–83% water. IPN hydrogels swell and shrink faster than single-network gels, making them useful in biomedical fields.[20,38,55]

EVALUATION PARAMETERS OF HYDROGEL

1. Visual and Sensory Inspection of Prepared Formulations

Visual assessment of the prepared hydrogel formulations included two main categories: appearance and color, as well as uniformity, consistency, stickiness, greasiness, and adhesive properties.[70,71]

2. pH Determination

The pH values of the gels were recorded three times using a properly calibrated pH meter

3. Spreadability Test

A sterile syringe was used to place 1 mL of the prepared hydrogel onto a glass plate, which was then covered with a calibrated plate where weights were gradually added (20, 50, 100, 200, 300, 400, 500, and 600 g) sequentially applied. The radius of the hydrogel spread was measured 20 seconds after placing each weight. The area covered by the hydrogel was determined using the following formula.:

$$P=\pi r2$$

where P is the surface area occupied by the hydrogel (cm^2) and r is the radius of the hydrogel (cm). Spreadability tests were conducted three times at room temperature.[72]

4. Rheology Measurements

The rheological behavior of the hydrogel formulations was assessed using a rotational rheometer equipped with parallel plate geometry (35 mm diameter, 1.0 mm gap) and temperature regulation. Flow and viscosity data were collected under controlled shear rates between 5.0 and 100.0 s^1 over 100 seconds. Each measurement was repeated six times at 32 ± 0.5 °C. The flow and viscosity curves were obtained through the hysteresis loop test.

5. Texture Analysis

Texture profile analysis and compression properties of hydrogels were measured using a texture analyzer with an 8 mm diameter hemispherical probe. The probe compressed samples at 1 mm/s to a 5 mm depth, with pre- and post-test speeds of 0.1 mm/s and a trigger force of 0.05 N. Two compression cycles were applied with a 20-second pause between them. Hardness was recorded as the peak force during the first compression, while cohesiveness, adhesiveness, and elasticity were calculated from the compression data. Tests were performed at 25 °C with six replicates per formulation.[73]

6. Stability Test

Six hydrogel formulations were stored in polyethylene containers at refrigerated temperatures (2–8 °C) for 28 days. Following this period, the samples were visually assessed and analyzed for chemical stability (including pH and drug content) as well as physical properties such as color, spreadability, texture, and viscosity.

7. Ex Vivo Skin Permeation Experiments

Skin permeation studies were performed using Franz diffusion cells with porcine skin (1.1 × 1.1 cm) prepared by removing fat and hair. The skin was mounted between donor and acceptor compartments, maintained at 37 ± 0.2 °C. A hydrogel sample of 0.2 g was applied to the donor side. The acceptor compartment contained 5 mL of ethanol-PBS (40:60 v/v). Samples (2 mL) were taken at 1, 2, 4, 8, 12, and 24 hours and replaced with fresh fluid. Drug concentration was measured spectrophotometrically using a calibration curve. Each test was done in six replicates.

To measure drug retained in the skin, residual hydrogel was removed, the skin washed with PBS and ethanol, then dried. The skin was cut, soaked in ethanol for 4 hours, and analyzed. Blank skin was used as control to ensure cleaning effectiveness.

8. Statistical Analysis

Statistical analysis was done using software. Data are shown as mean ± standard deviation. One-way ANOVA with Tukey's test was used to compare groups, and p-values below 0.05 were considered significant.

FUTURE PROSPECTS

Studies on polymer-based hydrogels for drug delivery are progressing rapidly, with efforts centered on solving current limitations and exploring novel methods. Upcoming trends and main research areas are likely to include:

1. Advanced Drug Release Mechanisms

Advanced drug delivery systems are being developed to precisely control how and when drugs are released. This includes creating hydrogels that respond to environmental changes like pH, temperature, enzymes, or light. Efforts also focus on designing hydrogels that provide sustained, pulsatile, or on-demand drug release.

2. Targeted and Site-Specific Delivery

Improving the precision of drug delivery to targeted cells, tissues, or organs continues to be a key focus. Hydrogels are being engineered to include specific molecules like antibodies, peptides, or aptamers for improved delivery to targeted sites. Researchers are also exploring the use of external methods, including magnetic fields and ultrasound, to steer these hydrogels precisely where needed.

3. Combination Therapy Platforms

Hydrogels made from polymers offer promising platforms for the co-delivery of multiple therapeutic agents, enabling effective combination therapies. This method allows the simultaneous administration of drugs with varied mechanisms or the inclusion of biological molecules such as growth factors and gene therapies, which can improve treatment outcomes, lower side effects, and help overcome resistance to drugs.

4. Bioactive Hydrogels for Tissue Regeneration

Hydrogels with bioactive ingredients like peptides help heal and regenerate tissues by supporting cell growth and attachment, useful in wound care and tissue repair.

5. Integration of Nanotechnology

Embedding nanoparticles including liposomes, polymeric, or inorganic nanoparticles, within hydrogel matrices increases drug loading, improves stability, and allows controlled release. Nanoparticles protect

drugs from breakdown and help deliver them to a specific target, improving overall therapeutic performance.

6. 3D Printing and Additive Manufacturing

Additive manufacturing advances, like 3D printing, enable the creation of complex, patient-specific hydrogel drug delivery devices with precise control over shape and drug placement for personalized treatment.

7. Smart Hydrogels Coupled with Sensor Technologies

New studies are exploring smart hydrogels that can sense and react to biological or environmental changes like pH, enzymes, or biomarkers. These hydrogels enable real-time tracking of drug release, treatment effects, and disease progress.

8. Biodegradability and Sustainability

Research is focused on creating hydrogels that degrade in a controlled way, avoiding surgery after treatment. Priority is given to biocompatible, eco-friendly materials like natural and biomimetic polymers to reduce environmental impact.

In short, polymer-based hydrogel research is moving toward advanced, targeted, and personalized drug delivery systems. Combining various technologies and new materials will drive innovations that enhance treatment effectiveness and support personalized medicine.[74]

Table No.1 Compilation of Reported Works on Hydrogel

Drug	Category	Route of administration	Application
Diclofenac Sodium	Anti-inflammatory	Oral	Sodium alginate
Silymarin	Antioxidant	Oral	Sodium alginate
Bovine Serum	Protein	Oral	HPMC
Nicotine	Stimulant	Transdermal	Agar
Prazocine Hydrochloride	Antihypertensive	Transdermal	Sodium alginate
Loratadine	Antihistamine	Topical	Carbopol 1980
Curcumin	Antimicrobial agent	Topical	Antimicrobial and wound healing
Letrozole	Non-steroidal Aromatase Inhibitor	Inject	Endometriosis
Doxorubicin	Antineoplastic Agent	Inject	Triple-negative breast cancer.
Nap-FFKK	Peptide-based Hydrogelator	Ocular	Ocular disorders
Cu2-xse nanoparticles.	Anti-inflammatory	Ocular	Dry eye disease

Figure No. 1 Structure of hydrogels

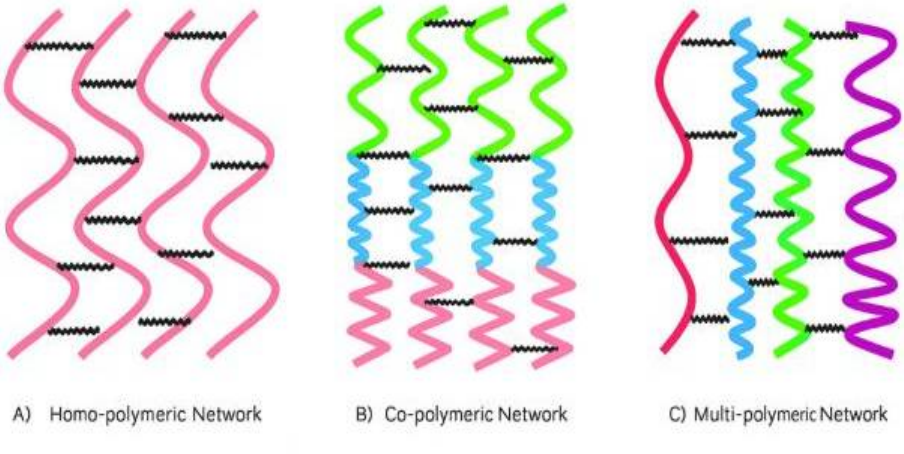
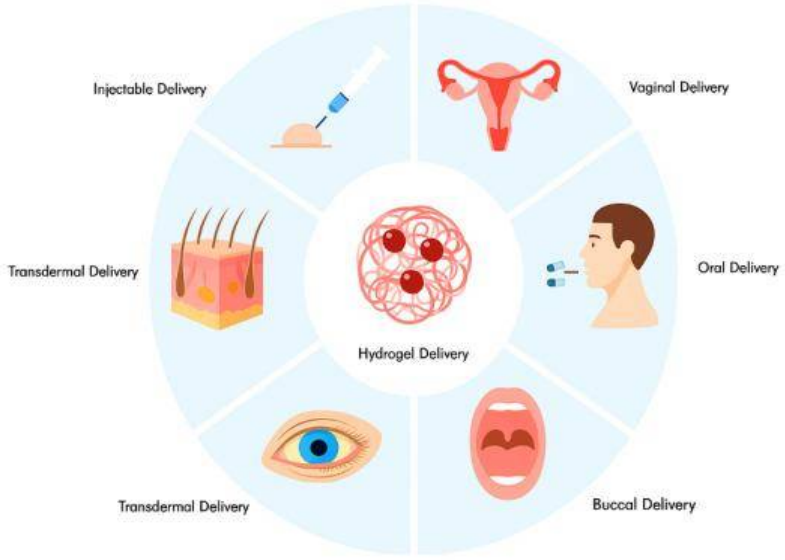


Figure No. 2 Application of hydrogel for drug delivery based on route of administration



CONCLUSION

Hydrogels are adaptable polymer structures that hold large amounts of water, which makes them important materials for applications such as delivering drugs, repairing tissues, and treating wounds. Their structure and classification allow for customization using various natural and synthetic polymers, enabling tailored mechanical and biological performance. Despite some limitations like mechanical weakness and scalability challenges, ongoing advancements in preparation techniques and polymer chemistry have significantly enhanced their functionality and applicability.

Looking ahead, the future of hydrogel research is focused on developing smart, stimuli-responsive, and targeted systems that can deliver drugs more effectively and safely. The integration of emerging technologies such as nanotechnology, 3D printing, and biosensing will further expand their applications and improve patient-specific treatments. With ongoing innovation and teamwork across fields, hydrogels are set to be key in advancing personalized medicine and enhancing treatment results.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

ACKNOWLEDGEMENT

The authors would like to acknowledge their collective efforts and contributions toward the preparation of this review article. No external financial or technical assistance was received

REFERENCES

1. Ganji F, Vasheghani-Farahani E. (2009). Hydrogels in controlled drug delivery systems. Iranian Polymer Journal. ;18(1):63-88.
2. Ris, M. M., Deitrich, R. A., & Von Wartburg, J. P. (1975). Inhibition of aldehyde reductase isoenzymes in human and rat brain. Biochemical Pharmacology, 24(20), 1865–1869. https://doi.org/10.1016/0006-2952(75)90405-0
3. Pfister, M., Schaub, M. C., Watterson, J. G., Knecht, M., & Waser, P. G. (1975). Radioactive labeling and location of specific thiol groups in myosin from fast, slow and cardiac muscles. Biochimica Et Biophysica Acta, 410(1), 193–209. https://doi.org/10.1016/0005-2744(75)90220-x
4. Ghasemiyeh, P., & Mohammadi-Samani, S. (2019). Hydrogels as drug delivery systems; pros and cons. Trends in Pharmaceutical Sciences, 5(1), 7–24.
5. Pogodina, V. V. (1975). Elizaveta Nilolaevna Levkovich-75th birthday. Acta Virologica, 19(6), 509.
6. Mekler, L. B. (1975). On the problem of oncogene of tumour viruses. Acta Virologica, 19(6), 501–508.
7. Sakshi B Bhalerao, Vijay R. Mahajan, & Rahul R Maske. (2022). Hydrogel based drug delivery system: A review. World Journal of Biology Pharmacy and Health Sciences, 12(3), 039–053. https://doi.org/10.30574/wjbphs.2022.12.3.0227

8. Korelitz, B. I., & Sommers, S. C. (1975). Responses to drug therapy in ulcerative colitis. Evaluation by rectal biopsy and histopathological changes. The American Journal of Gastroenterology, 64(5), 365–370.
9. Narayanan A, Ashok K, Prasanth B, Saravanan S. Analysis and Optimization of Hybrid Soil Properties for Gel Based Roof Tiles. Indian Journal of Structure Engineering (IJSE). 2021;1(2):17-24.
10. Singh A, Sharma PK, Garg VK, Garg G. Hydrogels: a review. International Journal of Pharmaceutical Sciences Review and Research. 2010;4(2):97-105.
11. Kalshetti, P. P., Rajendra, V. B., Dixit, D. N., & Parekh, P. P. (2012). Hydrogels as a drug delivery system and applications: A review. Int. J. Pharm. Pharm. Sci, 4(1), 1–7.
12. Fiddian-Green, R. G., & Silen, W. (1975). Mechanisms of disposal of acid and alkali in rabbit duodenum. The American Journal of Physiology, 229(6), 1641–1648. https://doi.org/10.1152/ajplegacy.1975.229.6.1641
13. A.S. Hoffman. Hydrogels for biomedical applications. Advanced Drug Delivery Reviews. 2002; 43: 3–12. (n.d.).
14. P. Drumheller, J.A., Hubbell Densely. Crosslinked polymer networks of PEG in trimethylolpropane triacrylate for cell adhesion-resistant surfaces, J. Biomed. Mater Res., 1995; 29: 201–215. (n.d.).
15. Peppas, N. A., Bures, P., Leobandung, W. S., & Ichikawa, H. (2000). Hydrogels in pharmaceutical formulations. European Journal of Pharmaceutics and Biopharmaceutics, 50(1), 27–46.
16. Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. J Adv Res. 2015 Mar;6(2):105-21. Doi: 10.1016/j. Jare.2013.07.006. (n.d.).
17. Das N. Preparation methods and proper ties of hydrogel: A review. Int J Pharm Pharm Sci. 2013;5(3):112-7. (n.d.).
18. Enas M. Ahmed. (2013). Hydrogel: Preparation, characterization, and applications. Journal of Advanced Research. (n.d.). https://doi.org/10.1016/j.jare.2013.07.006
19. Malpure PS, Patil SS, More YM, Nikam PP. (2018). A review on-hydrogel. American Journal of PharmTech Research. 8(3):41-61.
20. Sowjanya P, Komali BV, Ajay Babu CH. (2013). A review article on hydrogels. International Journal of Research in Pharmaceutical and Nano Sciences.2(5):548-553.
21. Madan, Yadav S, Jitender. (2020). Hydrogels: a review. International Journal of Pharmacy & Life Sciences. 11(6):6711-6717.
22. Ahmed, E. M. (2015). Hydrogel: Preparation, characterization, and applications: A review. Journal of Advanced Research, 6(2), 105–121. https://doi.org/10.1016/j.jare.2013.07.006
23. Muhammad Z, Waqar S, Sadaf W, Rai MS, Asif M, Junaid Q, Javed I, Fazal RS, Muhammad SR, Usman K, Hydrogels, Their Applications and Polymers Used For Hydrogels: A Review, International journal of pharmacy and allied science, (2015); 4(12): 6581 6603. (n.d.).
24. Nilimanka D, Preparation Methods and Properties of Hydrogel: A Review, International Journal of Pharmacy And Pharmaceutical Sciences, (2013); 5(3):112-117. (n.d.).
25. Sandeep C, Harikumar SL, Hydrogels: A Smart Drug Delivery System, International Journal Of Research In Pharmacy And Chemistry, (2012); 2(3): 2231 2781. (n.d.).
26. Lefkowitz, R. J. (1975). Identification of adenylate cyclase-coupled beta-adrenergic receptors with radiolabeled beta-adrenergic antagonists. Biochemical Pharmacology, 24(18), 1651–1658. https://doi.org/10.1016/0006-2952(75)90001-5
27. T. Nagai, Y. Machida, Buccal delivery systems using hydrogels, Adv. Drug Deliv. Rev. 11 (1993) 179±191. (n.d.).
28. Järvisalo, J., & Saris, N. E. (1975). Action of propranolol on mitochondrial functions—Effects on energized ion fluxes in the presence of valinomycin. Biochemical Pharmacology, 24(18), 1701–1705. https://doi.org/ 10.1016/0006-2952(75)90009-x
29. Raeisi, A., & Farjadian, F. (2024). Commercial hydrogel product for drug delivery based on route of administration. Frontiers in Chemistry, 12, 1336717.
30. Homayun, B., Lin, X., and Choi, H.-J. (2019). Challenges and recent progress in oral drug delivery systems for biopharmaceuticals. Pharmaceutics 11 (3), 129. Doi:10.3390/ pharmaceutics 11030129. (n.d.).
31. 31. Shah, H. P., Prajapati, S. T., and Patel, C. (2017). Gastroretentive drug delivery systems: From conception to commercial success. J. Crit. Rev. 4 (2), 10. Doi:10.22159/jcr. 2017v4i2.16717. (n.d.).
32. T. Nagai, Y. Machida, Y. Suzuki, H. Ikura, U.S. Patent No. 4226848, 1980. (n.d.).
33. Mohite, P. B., & Adhav, S. S. (2017). A hydrogels: Methods of preparation and applications. Int. J. Adv. Pharm, 6(3), 79–85.
34. Sudhakar, Y., Kuotsu, K., and Bandyopadhyay, A. (2006). Buccal bioadhesive drug delivery—A promising option for orally less efficient drugs. J. Control. Release 114 (1), 15–40. Doi:10.1016/j.jconrel.2006.04.012. (n.d.).
35. Jacob, S., Nair, A. B., Shah, J., Sreeharsha, N., Gupta, S., & Shinu, P. (2021). Emerging role of hydrogels in drug delivery systems, tissue engineering and wound management. Pharmaceutics, 13(3), 357.
36. Nair, A.B.; Al-Dhubiab, B.E.; Shah, J.; Jacob, S.; Saraiya, V.; Attimarad, M.; SreeHarsha, N.; Akrawi, S.H.; Shehata, T.M. Mucoadhesive buccal film of almotriptan improved therapeutic delivery in rabbit model. Saudi Pharm. J. 2020, 28, 201–209. (n.d.).
37. Torres-Luna, C., Fan, X., Domszy, R., Hu, N., Wang, N. S., and Yang, A. (2020). Hydrogel-based ocular drug delivery systems for hydrophobic drugs. Eur. J. Pharm. Sci. 154, 105503. Doi:10.1016/j.ejps.2020.105503. (n.d.).
38. Brown, M. B., and Williams, A. C. (2019). The art and science of dermal formulation development. Florida, United States: CRC Press. (n.d.).

39. Akbarian, M., Chen, S. H., Kianpour, M., Farjadian, F., Tayebi, L., and Uversky, V. N. (2022). A review on biofilms and the currently available antibiofilm approaches: Matrix destabilizing hydrolases and anti-bacterial peptides as promising candidates for the food industries. Int. J. Biol. Macromol. 219, 1163–1179. Doi:10.1016/ j.ijbiomac.2022.08.192. (n.d.).
40. Y.-M. Sun, J.-J. Huang, F.-C. Lin, J.-Y. Lai, (1997). Composite poly(2- hydroxyethyl methacrylate) membranes as rate-controlling barriers for transdermal applications, Biomaterials 18. 527±533. (n.d.).
41. Aka-Any-Grah, A., Bouchemal, K., Koffi, A., Agnely, F., Zhang, M., Djabourov, M., et al. (2010). Formulation of mucoadhesive vaginal hydrogels insensitive to dilution with vaginal fluids. Eur. J. Pharm. Biopharm. 76 (2), 296–303. Doi:10.1016/ j.ejpb.2010. 07.004. (n.d.).
42. 42. Valenta, C. (2005). The use of mucoadhesive polymers in vaginal delivery. Adv. Drug Deliv. Rev. 57, 1692–1712. (0169-409X (Print)). Doi:10.1016/j.addr.2005.07.004. (n.d.).
43. Ryu, J.-M., Chung, S.-J., Lee, M.-H., Kim, C.-K., & Chang-Koo Shim. (1999). Increased bioavailability of propranolol in rats by retaining thermally gelling liquid suppositories in the rectum. Journal of Controlled Release, 59(2), 163–172. https://doi.org/10.1016/S0168-3659(98)00189-8
44. S. Miyazaki, F. Suisha, N. Kawasaki, M. Shirakawa, K. Yamatoya, D. Attwood, thermally reversible xyloglucan gels as vehicles for rectal drug delivery, J. Control. Release 56 (1998) 75±83. (n.d.).
45. J.-M. Ryu, S.-J. Chung, M.-H. Lee, C.-K. Kim, C.-K. Shim, Increased bioavailability of propranolol in rats by retaining thermally gelling liquid suppositories in the rectum, J. Control. Release 59 (1999) 163±172. (n.d.).
46. Andrade, J. D. (Ed.). (1976). Hydrogels for Medical and Related Applications (Vol. 31). American Chemical Society. https://doi.org/10.1021/bk-1976-0031
47. Amiraev, U. A. (1975). Functional characteristics of teeth after tooth root apex resection]. Zdravookhranenie Kirgizii, 3, 40–42.
48. Moroff, G., & Brandt, K. G. (1975). Yeast glutathione reductase. Studies of the kinetics and stability of the enzyme as a function of pH and salt concentration. Biochimica Et Biophysica Acta, 410(1), 21–31. https://doi.org /10.1016 /0005-2744(75)90204-1
49. Megerman, J., & Murphy, R. A. (1975). Myosin from arterial smooth muscle: Isolation following actin depolymerization. Biochimica Et Biophysica Acta, 412(2), 241–255. https://doi.org/10.1016/0005-2795 (75)90038-0
50. Wu, J., Su, Z.-G., & Ma, G.-H. (2006). A thermo- and pH-sensitive hydrogel composed of quaternized chitosan/glycerophosphate. International Journal of Pharmaceutics, 315(1–2), 1–11. https://doi.org/10.1016 /j.ijpharm.2006.01.045
51. Burdick, J. A., & Prestwich, G. D. (2011). Hyaluronic Acid Hydrogels for Biomedical Applications. Advanced Materials, 23(12). https://doi.org/10.1002/adma.201003963
52. Ribeiro, M. P., Morgado, P. I., Miguel, S. P., Coutinho, P., & Correia, I. J. (2013). Dextran-based hydrogel containing chitosan microparticles loaded with growth factors to be used in wound healing. Materials Science and Engineering: C, 33(5), 2958–2966. https://doi.org/10.1016/j.msec.2013.03.025
53. Gils, P. S., Ray, D., & Sahoo, P. K. (2009). Characteristics of xanthan gum-based biodegradable superporous hydrogel. International Journal of Biological Macromolecules, 45(4), 364–371. https://doi.org/10.1016/ j.ijbiomac.2009.07.007
54. Ismail, H., Irani, M., & Ahmad, Z. (2013). Starch-Based Hydrogels: Present Status and Applications. International Journal of Polymeric Materials, 62(7), 411–420. https://doi.org/10.1080/00914037.2012.719141
55. Zaman, M., Siddique, W., Waheed, S., Sarfraz, R., Mahmood, A., Qureshi, J., Iqbal, J., Chughtai, F., Rahman, M. U., & Khalid, U. (2015). Hydrogels, their applications and polymers used for hydrogels: A review. Int. J. Biol. Pharm. Allied Sci, 4, 6581–6603.
56. 56. Singh, G., A. Lohani, and S.S. Bhattacharya, Hydrogel as a novel drug delivery system: A review. (n.d.).
57. Iizawa, T., et al., Synthesis of porous poly (N-isopropylacrylamide) gel beads by sedimentation polymerization and their morphology. Journal of applied polymer science, 2007. 104(2): P. 842-850. (n.d.).
58. Andrade, J.D., Hydrogels for medical and related applications. Vol. 31. 1976: American Chemical Society Washington, DC. (n.d.).
59. Lai, Y.C., Effect of crosslinkers on photocopolymerization of N-vinylpyrrolidone and methacrylates to give hydrogels. Journal of applied polymer science, 1997. 66(8): P. 1475-1484. (n.d.).
60. Güner, A. and M. Kara, Cloud points and temperatures of aqueous poly (N-vinyl-2-pyrrolidone) solutions in the presence of denaturing agents. Polymer, 1998. 39(8): P. 1569-1572. (n.d.).
61. Lopérgolo, L.C., A.B. Lugão, and L.H. Catalani, Direct UV photocrosslinking of poly (N-vinyl-2 pyrrolidone)(PVP) to produce hydrogels. Polymer, 2003. 44(20): P. 6217-6222. (n.d.).
62. Lugão, A.B., S.O. Rogero, and S.M. Malmonge, (2002). Rheological behaviour of irradiated wound dressing poly (vinyl pyrrolidone) hydrogels. Radiation Physics and Chemistry, 63(3): P. 543-546. (n.d.).
63. Gong, C., et al., (2009). Synthesis and characterization of PEG-PCL-PEG thermosensitive hydrogel. International Journal of Pharmaceutics, 365(1): P. 89 99. (n.d.).
64. Korsmeyer, R.W. and N.A. Peppas, (1989). Solute and penetrant diffusion in swellable polymers. III. Drug release from glassy poly (HEMA-co-NVP) copolymers. Journal of Controlled Release,. 1(2): P. 89-98. (n.d.).
65. Brazel, C.S. and N.A. Peppas, (1999). Mechanisms of solute and drug transport in relaxing, swellable, hydrophilic glassy polymers. Polymer, 40(12): P. 3383-3398. (n.d.).

66. Am Ende, M.T. and N.A. Peppas, (1997). Transport of ionizable drugs and proteins in crosslinked poly (acrylic acid) and poly (acrylic acid-co-2 hydroxyethyl methacrylate) hydrogels. II. Diffusion and release studies. Journal of controlled release, 48(1): P. 47-56. (n.d.).
67. Zhang, J.-T., R. Bhat, and K.D. Jandt, (2009). Temperature-sensitive PVA/PNIPAAm semi-IPN hydrogels with enhanced responsive properties. Acta Biomaterialia, 5(1): P. 488-497. (n.d.).
68. Ganesh, T.A., S.D. Manohar, and S. Ravindra, (2013). Hydrogel-A Novel Technique For Preparation of Topical Gel. WJPS.10;90-97.
69. Gils, P.S., D. Ray, and P.K. Sahoo, (2010). Designing of silver nanoparticles in gum arabic based semi-IPN hydrogel. International journal of biological macromolecules, 2010. 46(2): P. 237 244. (n.d.).
70. Daniels, L. K. (1976). Rapid in-office and in-vivo desensitization of an injection phobia utilizing hypnosis. The American Journal of Clinical Hypnosis, 18(3), 200–203. https://doi.org/10.1080/00029157.1976.10403798
71. Siemiradzka, W., Franczyk, A., Bułaś, L., & Dolińska, B. (2023). Somatotropin Penetration Testing from Formulations Applied Topically to the Skin. Applied Sciences, 13(4), 2588. https://doi.org/10.3390 /app13042588
72. Lee, I.S.; Yang, H.M.; Kim, J.W.; Maeng, Y.J.; Lee, C.W.; Kang, Y.S.; Rang, M.J.; Kim, H.Y. (2005). Terminology development and panel training for sensory evaluation of skin care products including aqua cream. J. Sens. Stud. 20, 421–433. (n.d.).
73. Siemiradzka, W.; Franczyk, A.; Buła´s, L.; Doli´nska, B. (2023). Somatotropin penetration testing from formulations applied topically to the skin. Appl. Sci. 13, 2588. (n.d.).
74. Szulc-Musioł, B., Siemiradzka, W., & Dolińska, B. (2023). Formulation and Evaluation of Hydrogels Based on Sodium Alginate and Cellulose Derivatives with Quercetin for Topical Application. Applied Sciences, 13(13), 7826. https://doi.org/10.3390/app13137826