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Preparation Methods and Properties of Hydrogel in Cosmetic and Biomedical Applications: A Mini-Review

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Abstract: This literature review focused on the polymer material source, preparation methods, key properties, and hydrogel application. Hydrogel is a hydrophilic polymer with three-dimensional (3D) cross-linked networks. Hydrogels are classified according to the origin of their polymer: natural or synthetic. Natural sources of polymers include polysaccharides and proteins from plants, animals, and microbial sources, whereas synthetic polymers are made from synthetic monomers via chemical polymerization on a pilot or laboratory scale. The hydrogel preparation methods are chemical or physical cross-linking. Recently, hydrogel has been used in many different applications, such as medicine and cosmetics, as discussed in this review, due to its unique characteristics, such as swelling ability or absorbing huge quantities of water or biological fluid (blood and exudate), controlling the release of drugs, a high level of biocompatibility, and mimicking living human tissues.

Keywords: hydrogel; natural polymer; synthetic polymer; cross-linked; hydrogel preparation.

1. Introduction

Hydrogel is a hydrophilic polymer composed of cross-linked polymer chains to form three-dimensional (3D) networks, which can swell or absorb water or biological fluid in huge quantities and maintain the stability of the 3D network structure in the swollen state but is insoluble in water and this behavior is brought about by the presence of hydrophilic functional groups that are attached to the main chain of a polymer. Some examples of these groups are hydroxyl (-OH), carboxyl (-COOH), amino ($-NH_2$), carboxamides ($-CONH_2$), and sulfonic acids ($-SO_3H$) [1]. Hydrogel is prepared chemically or physically cross-linked from natural sources (plants, animals, and microbial sources) and synthetic polymers (petroleum-based or chemical polymerization of synthetic monomers). Currently, hydrogels from synthetic polymers are widely manufactured due to their excellent physical, chemical, and mechanical properties, but they also have certain disadvantages, such as being non-environmentally friendly, expensive, non-renewable, and non-biodegradable. Therefore, hydrogels made from natural polymers are preferable to synthetic hydrogels due to their nontoxicity, biodegradability, low cost, and abundant availability, especially for biomedical applications [2,3].

Hydrogels have been recognized as highly advantageous materials for a broad range of applications. Many interesting properties, such as swelling ability, soft structure, flexibility, and mimicking soft tissue [4,5], have been observed in the hydrogel, which is excellent for cosmetic and biomedical applications such as sheet masks [6], acne patches [7], wound dressing [8], tissue engineering [9], drug delivery [10], and so on. The key properties of the

hydrogels are swelling ability, mechanical properties, and biocompatibility, which should be assessed to determine the quality of the hydrogel produced for each application. This literature review provides the concept of hydrogel, its classification based on source and preparation methods, key properties, and its applications, focusing on cosmetic and biomedical applications with active ingredients.

2. Classifications of Hydrogel

This review focused on the classification of hydrogels based on the polymer materials used and the preparation methods. Hydrogel polymers can be derived from natural or synthetic sources, and hydrogel preparation methods can be physical or chemical cross-linking.

2.1. Hydrogel polymer material based on sources.

Hydrogels can be classified into natural sources, which are naturally found or known as biopolymers, and synthetic sources, which are non-natural polymer sources. Two types of hydrogel sources are described below.

2.1.1. Natural sources.

Natural sources are easy to obtain, abundant in the environment, nontoxic, biodegradable, inexpensive, and biocompatible. Based on the chemical structure, natural sources are classified into polysaccharides, polyesters, and proteins. Natural sources are also classified into three groups of origin, such as plant source (cellulose, lignin, starch, alginate, agarose, and carrageenan), animal source (chitosan, gelatine, and hyaluronic acid), and microbial source (bacterial cellulose and xanthan gum). Polysaccharides are the most abundant naturally derived biopolymers frequently used in hydrogel synthesis. However, hydrogels derived from natural sources have drawbacks such as limited mechanical robustness and fragility [11]. Several natural sources of polymers for synthesizing hydrogels are described below.

2.1.1.1. Plant source.

Cellulose is a linear polysaccharide that consists of ß-(1-4) linked D-glucose. Cellulose can be found in a variety of sources, including plants, wood, cotton, bamboo, and microorganisms. Cellulose is insoluble in water but soluble in organic solvents after some treatment. Cellulose can improve hydrogel stability, elasticity, viscosity, and mechanical properties [12]. Lignin is a branched polysaccharide obtained from biomass. It provides cell walls with strength and hydrophobicity, and it protects polysaccharides from attack by microorganisms. Lignin is a complex aromatic biopolymer derived from syringil (S), guaiacyl (G), and hydroxyphenyl (H). Lignin has the potential for antioxidant, antimicrobial, and anti-inflammatory activity, low cytotoxicity, and biocompatibility [13]. Starch is a hydrophilic polysaccharide of the unit α-D-glucose (anhydroglucose), consisting of two structures: a linear structure, which is amylose (approximately 30% in starch), and a branched structure, which is amylopectin (approximately 70% in starch). The proportion of amylose and amylopectin depends on the starch source, such as potatoes, wheat, or maize, and the degree of crystallization of polysaccharides [2].

Alginate ((1,4)-linked ß-D-mannuronate (M) and ((1,4)-linked α-L-guluronate (G)) is a linear polysaccharide obtained from marine brown algae extraction with alkali solutions and

from the biosynthesis of bacteria. Alginate is soluble in water and hydrophilic, and it has a high molecular weight and excellent hydrogel physical properties. Alginate has biological properties such as enhancing injured skin tissue treatment, antimicrobial activity, drug delivery, and wound healing [14]. Agarose (poly-3-β-D-galactopyranosyl-(1-4)-α-L-3,6-anhydrogalactopyranosyl-1) is a linear polysaccharide purified from agar, which is obtained from marine red algae (Gracilariaceae and Gelidiaceae families). Agarose is composed of repeated agarobiose disaccharide units (β-D-galactopyranosyl-(1-4)-α-L-3,6-anhydrogalactopyranose), and it is soluble in water [15]. Carrageenan is a hydrophilic polysaccharide extracted from marine red seaweed. Consisting of linear and highly sulfated galactan composed of repeating 3,6-anhydro-D-galactose and ß-D-galactose-4-sulfated units. Carrageenan is divided into three types based on the seaweed source and functional groups, such as carrageenan with one sulfate group, including kappa (k) carrageenan extracted from *Eucheuma cottonii*, and iota (τ) carrageenan extracted from *Eucheuma spinosum*, and then carrageenan with two and three sulfate groups is lambda (λ) carrageenan extracted from Gigartina and Chondrus genera. Carrageenan is used as a hydrogel for drug-controlled release systems, cell or drug encapsulation, enzyme immobilization, and as a scaffoldn medicine [16,17].

2.1.1.2. Animal source.

Chitosan ((1,4)-2-amino-2-deoxy-ß-D-glucose) is a linear polysaccharide derived from the deacetylation process of chitin ((1,4)-2-acetomido-2-deoxy-ß-D-glucose), which is obtained from crustacean shells like crabs and shrimps, insect cuticles, algae, and fungal cell walls. Chitosan characteristics depend on deacetylation, molecular weight, pH, crystallinity, and temperature. The reactive functional groups in Chitosan are amino ($-NH_2$) in C2, and a hydroxyl group (-OH) in C3 and C6, which can form hydrogen bonds. Chitosan is insoluble in water but soluble in acid-aqueous media because of the presence of amino ($-NH_2$) protonated in large quantities. Chitosan has biological properties, including antimicrobial, hemostatic, anti-inflammatory, and antioxidant effects, or wound healing [18,19].

Gelatin is a protein that is soluble in water. Gelatine is obtained from the partial hydrolysis of collagen protein found in animal sources such as bones, cartilage, tendons, ligaments, and animal skin from cattle, pigs, fish, or poultry. However, continuous exposure to temperatures over 40°C may denaturate proteins [20]. Hyaluronic acid is a linear polysaccharide that is present in the extracellular matrix of several soft connective tissues, such as vertebrate tissues. It is composed of N-acetyl-D-glucosamine and glucuronic acid. Hyaluronic acid is soluble in water and has specific viscoelastic properties [21,22].

2.1.1.3. Microbial source.

Bacterial cellulose is a polysaccharide produced from bacteria such as *Agrobacterium*, *Aerobacter*, *Achromobacter*, *Sarcina*, *Acetobacter*, *Rhizobium*, *Salmonella*, *Azotobacter*, and *Gluconacetobacter xylinus*. Bacterial cellulose is produced via a biosynthetic pathway that involves polysaccharide secretion, which occurs using carbon sources in culture media such as glucose, fructose, mannose, glycerine, ethanol, and pyruvate. Both bacterial and plant-derived cellulose have similar chemical structures, but bacterial cellulose has high crystallinity (69-84%), excellent mechanical properties, a 3D nanofibrous structure, the water retention capacity of bacterial cellulose is one hundred times greater than its dry weight, and it is also free of

lignin and hemicellulose [23]. Xanthan gum is a polysaccharide obtained from *Xanthomonas campestris* bacteria with a fermentation process in aerobic conditions. The monomer consists of glucose, mannose, and glucuronic acid repeated units with a molecular ratio of 2:2:1. Glucose is attached by α-1,3 linkages on C3, composed of a D-glucuronic acid (β−1,2), which is located between two D-mannose units (β−1,4) [24,25].

2.1.2. Synthetic sources.

Synthetic sources are non-natural polymers generated by the chemical polymerization of synthetic monomers on a pilot or laboratory scale. They can be produced with long-chain structures and high molecular weight. Synthetic polymers possess superior mechanical, physical, and chemical properties compared to natural polymers due to their high level of controllability. However, they exhibit lower biological activity than hydrogels derived from natural sources and are not environmentally friendly because they are non-biodegradable, non-renewable, and high-st [2]. Synthetic polymers are frequently used in the synthesis of hydrogels such as poly (vinyl alcohol)/(PVA), poly (ethylene glycol)/(PEG), poly (acrylic acid)/(PAA), and poly (acrylamide)/(PAAm), and so on [1]. Several synthetic polymers used to synthesize hydrogels are described below.

Poly(vinyl alcohol), often known as PVA, is a vinyl polymer linked by carbon-carbon bonds and is the most commonly used in hydrogel synthesis [26]. Poly(ethylene glycol) (PEG) is a polymer that can be linear or branched and has hydroxyl groups at its ends. PEG is produced through the anionic polymerization of ethylene oxide; the process is initiated by the nucleophilic attack of a hydroxide ion on the epoxide ring [27]. Poly (acrylic acid) or PAA, often called a carbomer, is a polymer composed of acrylic acid (AA) monomers. Each monomer unit of PAA contains a carboxylic group (-COOH) attached to the vinyl group [28]. Poly (acrylamide), also known as PAAm, is a water-soluble polymer and can be generated through the polymerization of either acrylamide monomers or N, N′-methylene bis (acrylamide) [29]. PMMA or Poly (methyl methacrylate) with IUPAC name [1-(methoxycarbonyl)-1-methyl ethylene] is an odorless polymer prepared from methyl methacrylate ($C_5O_2H_8$) as a monomer through free radical addition and polymerization [30]. Poly (vinyl-pyrrolidone) or PVP, known as povidone, is prepared from monomer N-vinylpyrrolidone through radical polymerization [31].

2.2. Hydrogel preparation method.

There are two types of hydrogel preparation methods: physical cross-linking and chemical cross-linking. Physical cross-linking is a non-covalent, reversible interaction; chemical cross-linking is a covalent, irreversible interaction. Those types are described below.

2.2.1. Physically cross-linked hydrogels.

Physically cross-linked hydrogel is easy to prepare and has lower toxicity than chemically cross-linked hydrogel due to the absence of a chemical cross-linking agent. The hydrogels formed by physical cross-linking, also referred to as thermoplastic or supramolecular hydrogels, exhibit high water sensitivity, thermoreversibility, and reversible solids with viscosity and elasticity, making them compatible with applications at room temperature [1,32]. Physical cross-linking refers to the formation of bonds between polymer chains via non-

covalent interaction, including hydrogen bonding, amphiphilic graft and block polymers, crystallization, ionic interactions, and protein interactions [33].

2.2.2. Chemically cross-linked hydrogels.

Chemical cross-linking occurs when functional groups in the polymer interact covalently with cross-linking agents, an irreversible process that can enhance the physical properties of hydrogels, including swelling behavior, mechanical strength, and biodegradability. The cross-linking agents should contain functional groups, such as amino, carboxyl, and alcoholic groups, including citric acid and glutaraldehyde. Chemically cross-linked hydrogel networks have advantages over physically cross-linked hydrogels because their synthesis and applications are independent of pH levels [32]. Chemical cross-linking techniques include Schiff base reactions (complementary groups chemical reaction), high-energy radiation (photocrosslinking), hybrid polymer networks, small-lecule cross-linking, enzymes, and free radical mechanisms [1,33].

3. Key Properties of Hydrogel

Hydrogels have become more popular in cosmetic and biomedical fields due to their advantageous characteristics, including biocompatibility and their physical, chemical, and mechanical properties, which must be assessed to define the quality of the hydrogel produced for specific applications. Some of the key properties of some hydrogels are listed below.

3.1. Swelling ability.

Swelling refers to the capacity of hydrogels to absorb water or biological fluids such as blood or exudate and is facilitated by the porosity network of the hydrogel due to the existence of a functional group that is hydrophilic which connected to the main chain of a polymer, such as hydroxyl (-OH), carboxyl (-COOH), amino ($-NH_2$), carboxamides ($-CONH_2$), and sulfonic acids ($-SO_3H$). Water might be firmly bound or free to move inside the polymer network. Since hydrogels can swell, they are particularly well-suited for biomedical applications such as wound treatment, drug delivery, and tissue engineering. This is because hydrogels can absorb a significant amount of water or other fluids, which allows them to resemble human body tissues. Hydrogels can have water concentrations ranging from around 70% to over 99%, similar to, or even higher than, those found in biological tissues that contain substantial water. Hydrogels exhibit significant swelling behavior in both dynamic and equilibrium states [22,34]. The weight ratio between the swollen gel and the dry gel denotes the weight ratio. The swelling ratio is influenced by various biological and environmental factors, including the cross-linking ratio (structures with high cross-linking exhibit a reduced swelling ratio), the chemical composition of polymers (hydrogels with a higher proportion of hydrophilic groups experience greater swelling compared to hydrogels with hydrophobic groups), temperature, and pH (changes in pH influence the ionization of hydrophilic groups, which causes pH-sensitive hydrogels to expand) [1,32].

3.2. Mechanical properties.

Evaluation of the mechanical characteristics of hydrogels is essential for good physiological functioning from multiple perspectives. There are two ways to determine the mechanical analysis of hydrogels: compression and tension analysis [34]. The hydrogel must

retain its physical texture for a specified period while therapeutic drugs are released. Involves their behavior under stress, including tensile strength, percent elongation at break, toughness, and young modulus. The mechanical properties depend on the degree of cross-linking; increasing it can yield a more robust hydrogel. As the degree of cross-linking increases, the percent elongation of the hydrogels decreases, leading to a more brittle hydrogel structure [32].

3.3. Biocompatible properties.

Biocompatibility is a property that determines the cytotoxicity of the biomaterial [1]. Biocompatibility is found to be higher in biomaterials or natural polymers compared to synthetic polymers. Biocompatibilities refer to the capacity of a substance to perform a specific function, which is developed of two components: bio-functionality (the ability of substances to carry out their intended function via interacting with the body during cellular regeneration, healing, and scaffold breakdown) and biosafety (not causing cancer, mutagenesis, or cytotoxicity). Biocompatibility can be evaluated using two types of tests: *in vivo* (within living organisms, such as rats) and *in vitro* (outside living organisms, such as agar diffusion, elution, and direct contact) [32].

4. Applications of Hydrogel

Some active substances are unstable and susceptible to environmental factors such as temperature, pH, light, and oxidation. They need to encapsulate the active substances to effectively reach target areas without inducing adverse effects or irritation during topical or transdermal delivery. The use of hydrogel polymers as encapsulation materials offers several advantages over other encapsulation materials, as hydrogel polymers possess a porous network, especially those derived from natural sources, which can increase drug efficacy and bioavailability [35]. This review focuses on hydrogel polymers as encapsulation materials for cosmetic and biomedical applications, which are described below.

4.1. Cosmetic applications.

Hydrogel in cosmetic applications contains active cosmetic ingredients. Hydrogel can be synthesized using synthetic and natural polymers for cosmetic applications. Natural polymers are also utilized extensively in the formulation of moisturizers and thickening agents for cosmetics [22]. Several applications of hydrogels in cosmetics are described below.

4.1.1. Contact lens.

Contact lenses are customized, transparent-thin layers that are placed directly on the cornea to improve eye vision. A hydrogel for contact lenses was developed by Childs *et al.* (2016) and formed by poly (methyl methacrylate). Several tests are used to assess the quality of contact lenses and compare them to commercial contact lenses. The result showed a high optical refractive index of 1.42-1.45, transmission spectra in 400 nm to 800 nm wavelength, young modulus of 1.47 MPa (commercial contact lens has value between 0.3 to 1.9 MPa), sessile drop contact angle value of 40.5° (commercial contact lens has a value between at 15 to 80°), and then *in vivo* retinal examination revealed no apparent corneal damage and shown excellent compatibility with optical coherence tomography (OCT) imaging techniques [36].

4.1.2. Acne treatment.

Hydrogel for acne treatment from carboxymethyl cellulose for acne treatment loaded with salicylic acid and herbal extract consisting of green tea, ginger, and Phyllanthus emblica fruit extract as active ingredients developed by Lin *et al*. (2021); the result showed that the hydrogel can reduce skin inflammation and heal 50% of acne from moderate to severe acne severity within 14 days [37].

4.1.3. Sheet mask.

Hydrogel sheet mask developed by Ghosh *et al*. (2022): the hydrogel was produced by combining synthetic polymers (poly(ethylene glycol)) and natural polymers (chitosan, pectin, and carboxymethyl cellulose), with tea tree essential oil as the active ingredient. Hydrogel-encapsulated tea tree oil exhibits superior antibacterial efficacy compared to standalone tea tree oil [6]. Therefore, it is advantageous to provide a lower concentration of tea tree oil topically to minimize skin irritation while maintaining the antibacterial efficacy of the oil. The hydrogel exhibits excellent porosity and demonstrates a significant capability for swelling in water, with a swelling ratio of 94%. Other hydrogel sheet masks were also developed by Akl *et al*. (2023); carboxymethyl cellulose was used as a natural polymer material, citric acid was used as a chemical cross-linking agent, and clove buds were used as active ingredients [38]. The hydrogel sheet mask produced has antioxidant activity up to 60%, shows excellent cytocompatibility at an IC_{50} value of 259 µg/ml, and has strong antifungal and anti-microbial activity against microbial (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Bacillus subtilis*) and fungi (*Candida albicans* and *Aspergillus niger*).

4.1.4. Nail fungal treatment.

Onychomycosis is a fungal chronic infection caused by dermatophytes, yeast, and non-dermatophyte molds that affect nails. Some materials have been developed to cure onychomycosis. Bozoğlan *et al*. (2020) developed a hydrogel for topical medication from chitosan and carboxymethylcellulose containing oxiconazole nitrate as the antifungal active ingredient [39]. The result showed that the hydrogel has a maximal compression value at 200 kPa, can release oxiconazole nitrate up to 70%, and has strong antifungal activity against Trichophyton mentagrophytes and Trichophyton rubrum, dermatophytes.

4.2. Biomedical applications.

Hydrogel has a very big potential for biomedical applications, including wound healing treatment, tissue engineering, and drug delivery. Hydrogels are a novel material compared to other materials because they have porous structures that can absorb water or biological fluids, such as blood and exudate, and exhibit good permeability and biocompatibility, which can lead to improved biological therapy performance inopical and transdermal systems [35]. Several biomedical applications of hydrogels are described below.

4.2.1. Wound treatment.

Wound treatment has three phases: the inflammation phase, the proliferation phase, and the tissue remodeling phase in the healing of skin epidermal damagesuch as burns, ulcers, and acute or chronic wounds [26]. Hydrogel is excellent for wound dressing because of its

biocompatibility, porous network, high swelling ability, and permeability, which can provide a moist environment, develop a new epidermis, and heal the wound rapidly [40]. Chopra *et al*. (2022) developed a hydrogel as a wound dressing for wound treatment from chitosan polysaccharide as a polymer material and honey as an active ingredient [26]. The result showed that the hydrogel exhibited potential for wound dressing, that the *in vitro* release of honey as the active ingredient is controllable, and that the antimicrobial was successful against Staphylococcus aureus bacteria. Mali *et al*. (2023) developed a hydrogel from carboxymethyl tamarind gum and polyvinyl alcohol with moxifloxacin hydrochloride as active ingredients through chemical cross-linking using citric acid and solvent casting techniques. Hydrogels containing polyvinyl alcohol and citric acid at high and low concentrations showed excellent swelling ratios in phosphate buffer, simulated wound fluid [41]. Feketshane *et al*. (2023) developed a hydrogel from sodium alginate and carboxymethyl cellulose as a polymer and cephalexin monohydrate as an active ingredient through the solvent casting evaporation technique [42]. The result showed *in vitro* assay for drug release is 47-80% in 48 hours and effectively inhibits bacteria in wounds such as *Staphylococcus aureus* and *Escherichia coli* and has good tensile strength, flexibility, good biodegradability, and minimal moisture absorption to inhibit microbial growth.

4.2.2. Tissue engineering.

Hydrogels have great potential as an alternative in tissue engineering, as they can grow and regenerate damaged structures by mimicking and serving as scaffolds for various tissues in the body. Scaffolds act as substrates, cellular matrices, and drug-delivery media to support cell attachment, formation, migration, proliferation, and differentiation [9]. The porosity in hydrogel through cellular networks may facilitate the transport of oxygen, nutrients, and extracellular fluids. To avoid adverse effects during the healing process, the scaffolds should have high biocompatibility and be non-immunogenic [23]. Several applications of hydrogel in tissue engineering are described below.

4.2.3. Fibroblast cell growth.

Hydrogel for fibroblast cell growth from keratin and poly (ethylene glycol) through photo cross-linking was developed by Yue *et al*. (2018); several *in vitro* assays were conducted, such as cell culture, cell encapsulation, cell viability, cell adhesion, spreading, and cell metabolic activity. The NIH/3T3 fibroblast cell type was utilized as a model in this study. It was cultured on both two-dimensional (2D) and three-dimensional (3D) substrates made of keratin-PEG hydrogel tissue engineering system. These substrates effectively facilitated cell attachment [43].

4.2.4. Cartilage scaffold.

A hydrogel for cartilage scaffold was developed by Davachi *et al*. (2022) from chitosan and hyaluronic acid via enzymatic cross-linking with horseradish peroxide, which establishes a stable hybrid microenvironment for cell encapsulation and tissue engineering [44]. The results demonstrated that the hydrogel composed of chitosan and hyaluronic acid is highly capable of replicating the cellular environment and can be useful for the further development of cartilage scaffold fabrication.

4.2.5. Drug delivery.

Hydrogel is one of the most exciting and promising materials for drug delivery because it enables controlled release or degradation and protects unstable drugs from premature degradation. Because of their high biocompatibility, natural polymers are the primary building blocks of hydrogels used for drug delivery. Hydrogels have the unique ability to hold drugs within their porous structure and release them gradually over an extended period. This helps maintain therapeutic drug concentrations within the desired range, thereby increasing the drug's bioavailability. By controlling their swelling behavior, hydrogels can also reduce the frequency of dosing, which is convenient for patients and helps to avoid sudden adverse effects [45,46]. Several applications of hydrogel as a drug delivery system are described below.

4.2.6. Antibiotic drug delivery.

Fugueroa *et al*. (2020) developed a hydrogel for amoxicillin drug delivery using polycrylamide) and starch as polymers at different ratios [47]. The results showed the hydrogel's potential for controlled drug delivery in topical and gastrointestinal systems, with water uptake and swelling ratio increasing as the starch content increased. The in vitro assay showed amoxicillin was successfully active against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* after 24 hours of incubation.

4.2.7. Gastro-retentive drug delivery.

Hydrogels for oral drug delivery developed by Ulfah *et al*. (2023), hydrogels formulated by mixing polyvinyl alcohol, calcium alginate, hydroxyl propyl methylcellulose, acrylic acid, and chondroitin sulfate as polymers and esomeprazole as an active ingredient through the solvent casting technique [48]. The result showed that the hydrogels produced are potential candidates for the controlled delivery of esomeprazole with an encapsulation efficiency of up to 80%. It has stability in appearance, color change, and grittiness when kept at 40 °C at 75% relative humidity for 60 days. An *in vivo* assay in albino rabbits demonstrated a regulated, sustained release of esomeprazole compared with drugs available for commercial use.

4.2.8. Periodontal drug delivery.

Periodontitis, caused by pathogenic plaque microorganisms, is a chronic infection of the tooth surface that destroys gingival tissue, the periodontal ligament, and alveolar bone. Treatment for periodontitis by local or systemic delivery, one of the most promising treatments, is hydrogel-loaded antimicrobial ingredients. Research by Wu *et al*. (2022) developed a hydrogel from hyaluronic acid, hydroxypropyl methylcellulose, and glycerol with bomidin (a new recombinant antimicrobial peptide) as the active ingredient [49]. The result showed that the hydrogel loaded with bomidin exhibited strong antimicrobial activity against *Porphyromonas gingivalis*, *Staphylococcus aureus*, and *Escherichia coli*, with a wound-healing rate up to 40%.

4.2.9. Anti-cancer drug delivery.

A hydrogel from poly (vinyl pyrrolidone) loaded with tamoxifen as the anti-cancer drug was developed by Kupiec *et al*. (2023). The result showed that the hydrogel was a more

effective prolonged-release drug in an acidic environment and has potential as a cytostatic carrier, as it cancels cells at acidic pH, is stable for0 days of incubation, and has a high swelling ratio [50]. It can be concluded that the hydrogel developed in this research has excellent properties as an anti-cancer drug delivery.

5. Conclusions

Hydrogel is a three-dimensional polymer network widely used in many applications, such as cosmetics and biomedical, as described in this review. Hydrogels can mimic human tissues, encapsulate active compounds, control drug release, and be used in tissue engineering alternatives due to their key properties, including swelling capacity, mechanical properties, and biocompatibility. Hydrogels are made from natural and synthetic polymers via cross-linking methods, including chemical (irreversible) and physical (reversible) processes. Nowadays, hydrogels from natural polymers, known as biomaterials, have gained significant attention because they exhibit greater biocompatibility than synthetic polymers. However, hydrogels derived from biomaterials have some shortcomings, such as poor mechanical properties.

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Conflicts of Interest

The authors have declared that they have no competing interests.

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