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A review on hydrogel: Classification, preparation techniques and applications

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Abstract
Hydrogel products are a class of polymeric materials with a hydrophilic structure that allows them to store huge amounts of water in three-dimensional networks. The presence of hydrophilic groups such as NH_2, COOH, OH, $CONH_2$, -CONH-, and $-SO_3H$, as well as the capillary effect and osmotic pressure, contribute to the network's hydrophilicity. Weaker forces, like van der Waals forces and hydrogen bonds, can frequently act as cross-links, resulting in swelling networks that behave like hydrogels. Depending on their physical and chemical structure, hydrogels can be classified in a variety of ways. Material scientists and biological researchers continue to be fascinated by hydrogels today, and significant progress has been made in terms of formulations and applications. However, many articles and technical studies dealing with hydrogel products from an engineering standpoint were investigated to provide a broad overview of the technological features of this rapidly expanding interdisciplinary field of study. The major goal of this paper is to examine the literature on the technologies used in the creation, categorization, and use of hydrogels.

Keywords: Hydrogels, cross-linked networks, preparation techniques, hydrogel classification

Introduction
The materials of interest in this brief overview are hydrogels, which are polymer networks that have been swelled with water. Hydrophilic gels, also known as hydrogels, are polymer chains that are occasionally found as colloidal gels and have water as their dispersion medium (Ahmed *et al*., 2013) [3].

The network's hydrophilicity is attributable to the presence of hydrophilic groups such as NH2, COOH, OH, CONH2, -CONH-, and -SO3H, as well as the capillary effect and osmotic pressure (Dergunov & Mun, 2009) [11]. The hydrophilic functional groups connected to the polymeric backbone give hydrogels their capacity to absorb water, while cross-links between network chains give them their resistance to disintegration. The term "hydrogel" encompasses a wide range of materials, both natural and man-made.

Hydrogels have been characterized in a variety of ways by scientists throughout the years. The most prevalent is a hydrogel, which is a water-swollen, cross-linked polymeric network made by a simple reaction of one or more monomers. Another description is a polymeric substance that can expand and hold a substantial amount of water inside its structure but will not dissolve in water. Due to their remarkable promise in a wide variety of applications, hydrogels have gotten a lot of attention in the last 50 years (Li Yuhui *et al*., 2013).

A variety of "classical" chemical methods can be used to make hydrogels. These include one-step procedures such as polymerization and parallel cross-linking of multifunctional monomers, as well as multi-step procedures involving the synthesis of reactive polymer molecules and their subsequent cross-linking, possibly by reacting polymers with suitable cross-linking agents. The polymer engineer may create polymer networks with molecular-scale control over the structure, such as cross-linking density, and custom attributes, such as biodegradation, mechanical strength, and chemical and biological reaction to stimuli (Burkert *et al*., 2007) [9]

Classification of hydrogels

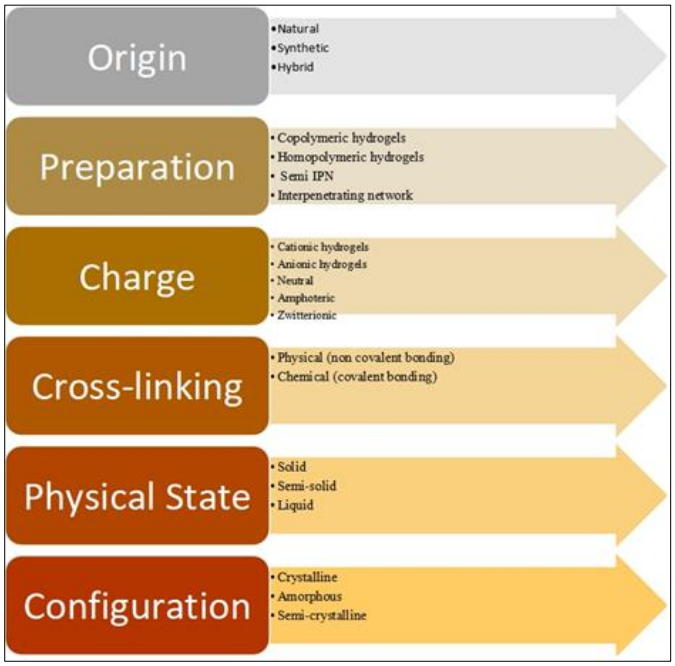

Fig 1: Classification of hydrogels

On the basis of origin

Natural polymers forming hydrogels

These hydrogels are nontoxic, biocompatible, and biodegradable. They do, however, have poor mechanical quality, and batch variation may result in poor reproducibility (Paleos, 2012; Kirchmajer *et al*., 2012) [41, 24].

Synthetic hydrogels

Synthetic hydrogels are cross-linked polymers produced under controlled conditions using the addition reaction or ring-opening polymerization. Polyacrylic acid and its derivatives (Pan *et al*., 2019) [42], polyvinyl alcohol (Guo *et al*., 2019) [17], polyethylene glycol and its copolymers (Guo *et al*., 2019) [17], and polyvinylpyrrolidone (Ma *et al*., 2016), among others, are commonly utilised as skeletons in the manufacture of synthetic hydrogels.

On the basis of composition

Hydrogels are categorised into four types based on their polymer composition: (1) homopolymeric hydrogels, (2) copolymeric hydrogels, (3) semiinterpenetrating networks (semi-IPNs), and (4) IPNs (Ahmed, 2015) [2].

Homopolymeric hydrogel

Homo-polymers are polymer networks formed from a single monomer species. It serves as the fundamental structural unit in any polymer network (Lizawa *et al*., 2007). Among natural polymers, cellulose hydrogel is an example of a homopolymeric hydrogel produced using a one-step polymerization procedure in which cellulose is dissolved in a urea/NaOH solution. As a cross-linker, epichlorohydrin is added, resulting in a translucent hydrogel.

Copolymeric hydrogel

Co-polymeric hydrogels are made up of two types of monomers, one of which is hydrophilic. For the development of drug delivery systems, Gong *et al*., (2009) [16] created a biodegradable triblock poly (ethylene glycol)-poly (caprolactone)-poly (ethylene glycol) (PECE) co- polymeric hydrogel.

Semiinterpenetrating network

A semi-IPN is formed when one polymer is linear and penetrates another cross-linked network with no additional chemical linkages between them (Ahmed, 2015) [2]. In this case, one polymer is crosslinked while the other is not. Polymer blends are formed when the component linear or branched polymers can be isolated from the constituent polymer networks without breaking chemical connections.

Interpenetrating network IPNs

Conventionally, this is described as the intimate combination of two polymers in which at least one monomer is polymerized or cross-linked in the presence of the other. A common process is immersing a prepolymerized hydrogel in a monomer and initiator solution. The interlocking structure of the cross-linked IPN components increases the bulk and surface morphology stability. IPN creation may be used to create moderately dense hydrogel matrices with stiffer and harsher mechanical characteristics. IPN hydrogels distribute drugs more efficiently than traditional hydrogels (Singh *et al*., 2017; Ullah *et al*., 2015; Paleos, 2012; Garg & Garg, 2016; Manya *et al*., 2016; Das, 2013; Morkhande, 2016) [41, 46, 48, 35, 10].

On the basis of charge

Hydrogels are classified into five categories based on the sort of charges present on the polymer network (Paleos, 2012; Mahinroosta *et al*., 2018) [41].

1. Nonionic (neutral) substances such as dextran, agarose, and pullulan;
2. Anionic substances like carrageenan
3. Cationic substances, such as chitosan;
4. Amphoteric electrolyte collagen
5. Polybetaines with zwitterionic properties, such as polyanionic xanthan and polycationic chitosan (Ahmed, 2015; Singh *et al*., 2017) [2, 46]

On the basis of cross linking

Physical hydrogels

Physical hydrogels are three-dimensional networks created by noncovalent interactions (secondary bonds) between linear molecules that generate physical cross-linking joints, such as electrostatic contact, hydrogen bonding, chain entanglement, and hydrophobic interaction (Pan *et al*., 2019; Lin *et al*. 2019) [42]. Physical hydrogels frequently exhibit reversible solgel conversion because relatively low energies are required to disrupt the physical connections between the molecules (Feng *et al*., 2018) [14]. There is no chemical reaction required in their manufacture, and the circumstances are generally moderate, making them suitable for biological applications (Liu *et al*., 2019).

Chemical hydrogels

Chemical cross-linking between molecules forms chemical hydrogels, and this cross-linking is irreversible. Chemical hydrogels often feature stable qualities, adjustable architectures, excellent mechanical properties, and so forth (Nada *et al*., 2019; Matsumoto *et al*., 2015) [36, 34].

On the basis of physical state

Solid hydrogels

Solid hydrogels are generally chemically cross-linked and solid at ambient temperature, but they may swell in aqueous environments such as water, buffer solutions, and biological fluids. Because they can imitate the physical, chemical, electrical, and biological characteristics of most biological tissues, they may be employed to make hydrogels for biomedical, environmental, and ecological purposes. The inclusion of nanoparticles into the polymer matrix improves mechanical characteristics. For example, methacrylate gelatin reinforced with multiwalled COOH-functionalized carbon nanotubes (CNTs) and gelatin-collagen modified with bioactive glass nanoparticles for cardiac tissue engineering are two examples (Varaprasad *et al*., 2017; Shin *et al*., 2011) [49, 45].

Semisolid hydrogels

Semisolid hydrogels are distinguished by their adhesive interactions with interfacial (van der Waals, hydrogen bonds, and electrostatic) forces and soft-tissue networks. Because of their bioadhesive feature, these hydrogels are also known as bioadhesive or mucoadhesive hydrogels. They have applications in the biomedical field for extended medication administration and effective dosing (Varaprasad *et al*., 2017; Nep *et al*., 2011) [49, 37]. This category includes hydrogels made from the natural polysaccharide sterculia gum and poly (vinylpyrrolidone) (both of which are biological in nature). A hydrogel based on starch nanocrystals was recently created for transdermal application (Nep *et al*., 2011) [37].

Liquid hydrogels

Liquid hydrogels, as the name implies, are in a liquid phase at normal temperature but have a soft tissue-like elastic phase with acceptable functionality at a particular temperature. These hydrogels are injectable and have a wide range of biomedical applications. This category includes high mannuronic alginate hydrogels used for wound dressing in cutaneous wound healing. A smart injectable hydrogel made of microbial TG and human-like collagen could be used as a soft material for skin tissue creation. Keratinsilica hydrogel can be used as a dressing material (Varaprasad *et al*., 2017) [49].

Technologies adopted in hydrogel preparation

Bulk polymerization

For the synthesis of hydrogels, a variety of vinyl monomers can be used. With one or more kinds of monomers, bulk hydrogels may be made. Because of the large number of monomers available, it is possible to make a hydrogel with the appropriate physical qualities for a particular application. Any hydrogel formulation typically contains a tiny amount of cross-linking agents. Radiation, UV, or chemical catalysts are commonly used to start the polymerization reaction.

Bulk polymerization is the most straightforward method, requiring only monomer and monomer-soluble initiators. The high concentration of monomer results in a high rate and degree of polymerization. However, when the conversion produces heat during polymerization, the viscosity of the process increases significantly. Controlling the response at low conversions can help to avoid these difficulties (Kiatkamjornwong *et al*., 2007) [23].

Solution polymerization/cross-linking

The ionic or neutral monomers are combined with the multifunctional cross-linking agent in solution copolymerization/cross-linking operations. UV irradiation or a redox initiator system are used to start the polymerization process. The existence of a heat sink in the form of a solvent is the primary benefit of solution polymerization versus bulk polymerization.

To eliminate the monomers, oligomers, cross-linking agents, initiator, soluble and extractable polymers, and other contaminants from the produced hydrogels, wash them with distilled water. When the amount of water added during polymerization is greater than the water content corresponding to equilibrium swelling, phase separation occurs and a heterogeneous hydrogel is created.

Water, ethanol, water-ethanol mixes, and benzyl alcohol are common solvents for the solution polymerization of hydrogels. After the gel has been formed, the synthesis solvent can be eliminated by swelling the hydrogels in water.

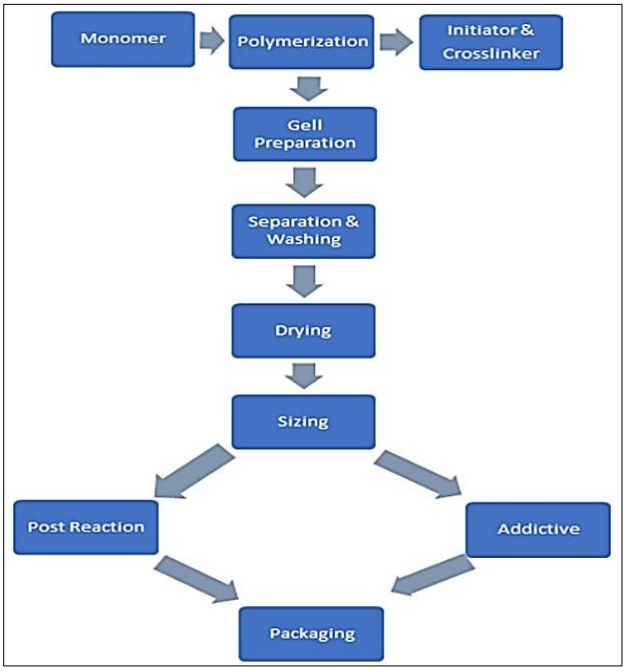

Fig 2: Hydrogel synthesis by solution polymerization

Suspension polymerization or inverse-suspension polymerization

Because the products are produced as powder or microspheres (beads), dispersion polymerization is a convenient process because it eliminates the need for grinding. The polymerization is known as "inverse suspension" because it uses the water-in-oil (W/O) method rather than the more typical oil-in-water (O/W).

In this approach, the monomers and initiators are disseminated as a homogeneous mixture in the hydrocarbon phase. The resin particle size and form are primarily determined by the viscosity of the monomer solution, agitation speed, rotor design, and dispersant type (Ogata *et al*., 2006) [39]. There have already been some comprehensive talks on heterophase polymerizations published. Because the dispersion is thermodynamically unstable, it requires constant agitation as well as the inclusion of a low hydrophilic-lipophilic–balance (HLB) suspending agent

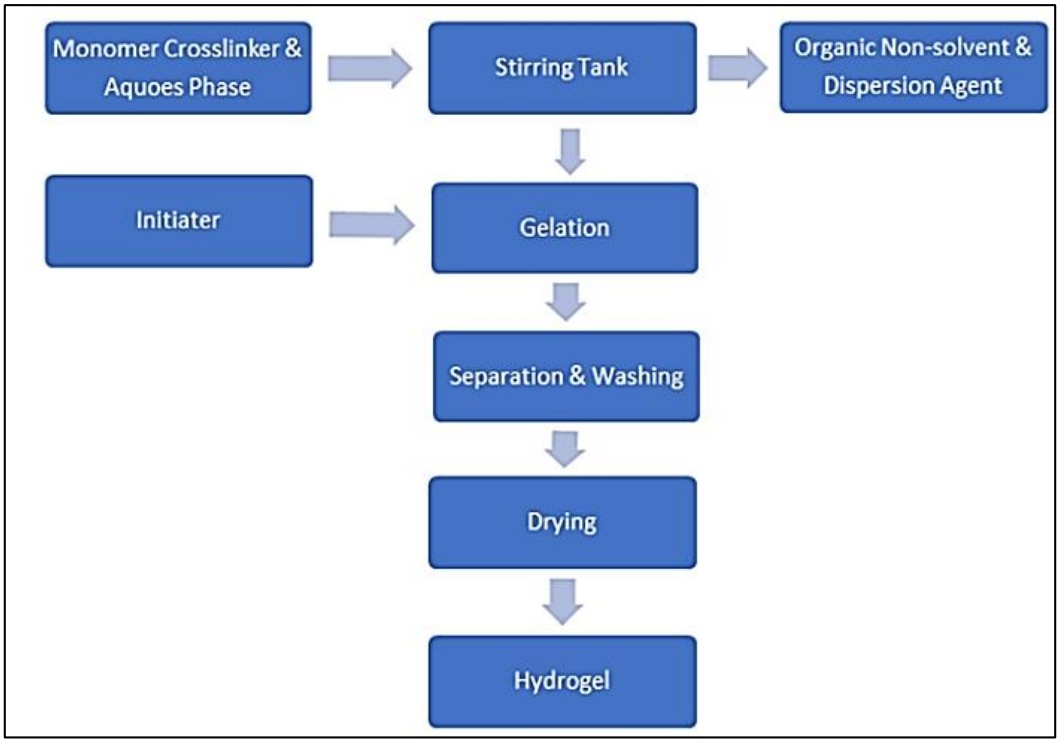

Fig 3: Hydrogel synthesis by suspension polymerization

Grafting to a support

Hydrogels made by bulk polymerization have a fragile structure by nature. A hydrogel's mechanical characteristics can be improved by grafting it onto a stronger support surface. This process includes generating free radicals on a stronger support surface and then polymerizing monomers directly onto it, resulting in a covalently bound chain of monomers. Through grafting procedures, a variety of polymeric supports have been employed to synthesize hydrogels (Talaat *et al*., 2008; Qunyi *et al*., 2005) [47, 43].

Polymerization by irradiation

High-energy ionizing radiation, such as gamma rays (Karadao *et al*., 2001) and electron beams (Ajji *et al*., 2008) [5], has been employed as an initiator to generate unsaturated chemical hydrogels. Irradiating an aqueous polymer solution causes radicals to develop on the polymer chains. In addition, the radiolysis of water molecules produces hydroxyl radicals that attack polymer chains and produce macro-radicals.

Applications of hydrogels

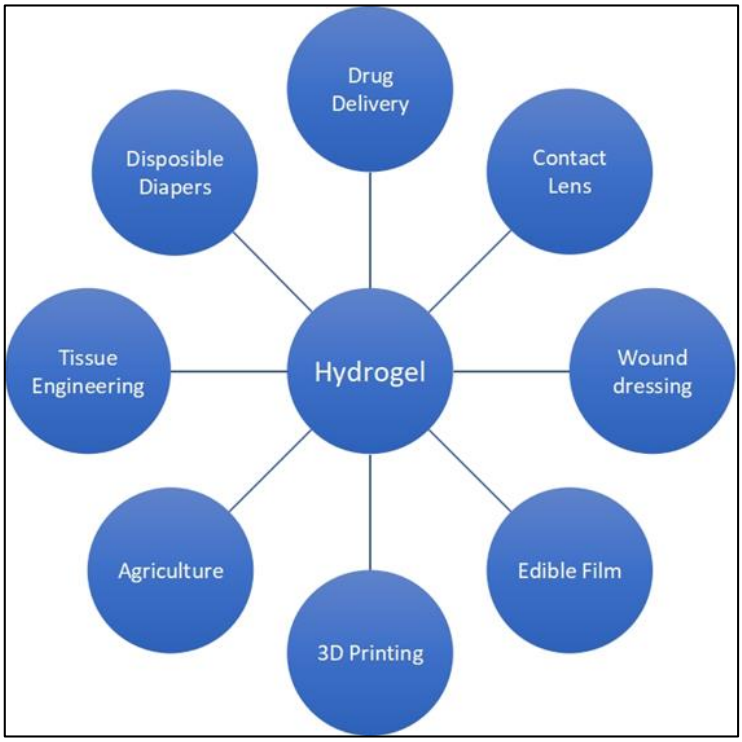

Fig 4: Hydrogel applications

Wound dressings

A wound is an injury that occurs in human tissues, either inside or outside, primarily in the skin, as a result of trauma, cutting, or other damage (Basu *et al*., 2017) [7]. Hydrogels are excellent wound dressings because they provide a moist environment at the wound site, aid in the removal of wound exudates, prevent infection, and promote tissue regeneration (Gupta *et al*., 2011) [19]. Anti-bacterial and anti-inflammatory hydrogels have a positive influence in wound dressing applications. A wound healing multifunctional and pH-responsive composite hydrogel consisting of carboxylated agarose and tannic acid that is ionically crosslinked using zinc salts (Ninan *et al*., 2016) [38].

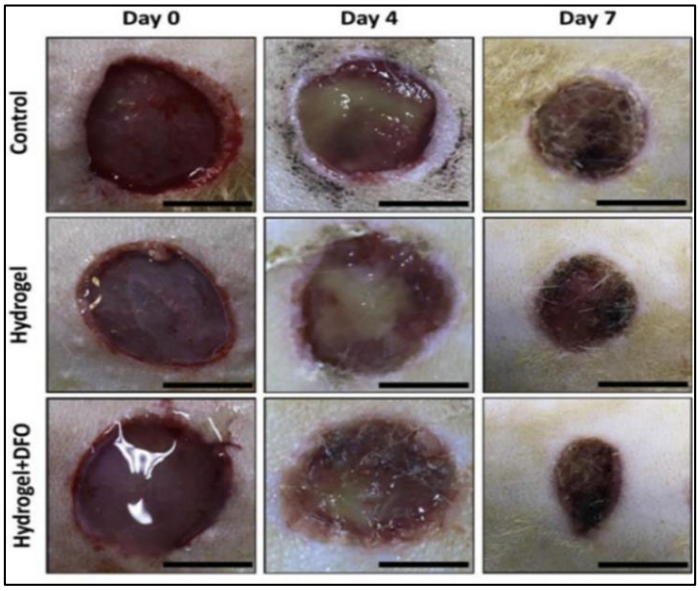

Fig 5: In comparison to the control, drug-loaded thiolated PEG hydrogel improved diabetic skin wound healing (Ninan *et al*., 2016) [38]

Biotechnology application

Hydrogels have been employed in sensors to achieve desired hardness, elasticity, selective analyte diffusion, and refractive indices. Smart hydrogels have been used to concentrate dilute aqueous solutions of macromolecular solutes, such as proteins and enzymes, without disrupting the enzyme's function by altering the temperature or pH of the environment based on the size and net charge of the macromolecular solutes (El-Mohdy *et al*., 2008) [1]. Smart hydrogels in solutions can work as purification devices because they can reversibly expand and contract in response to a tiny change in the environment. The use of hydrogels like agarose and calcium alginate gels to immobilize adsorbents prevents fouling by colloidal pollutants. By modifying their swelling behavior, hydrogels have been used to modulate substrate reactions with immobilized enzymes (Overstreet *et al*., 2013) [40].

Potential food applications

Table 1: Applications of Protein-Polysaccharide combinations

Hydrogels	Form	Application	References
Pectin/Chitosan	coatings	Coating for crop protection	Aider *et al*.,2010 [4]
Cane bagasse/ Gelatin	Films	Self-fertilizing biofilms	Farris *et al*.,2009 [13]
Cellulose/Starch	Films	Food packaging	Muller *et al*.,2009
Starch/Zein	Films	Inner packaging	Leroy *et al*.,2012 [25]
Whey protein/Methylcellulose	Films	Moisture sensitive packaging	Baldwin *et al*.,2011 [6]
Pectin/Beta-lactoglobulin	Films	Food wrapping	Scrinis *et al*.,2013 [44]

Edible films

The traditional edible films prepared by SNs usually have low mechanical strength, weak hindrance against gases and vapors, as well as poor water resistance properties (Yadav *et al*., 2019) [50]. To solve this problem, IPN-based edible films such as KGM-CS (Du, Yang, Ye, & Li, 2013) [12], and GA-SA (Ye *et al*., 2019) have been developed, which possess superior physical characteristics (mainly mechanical strength) and functional characteristics (resistance to gases, vapors, and water).

Three-dimensional (3D) printing

The food sector has shown a lot of interest in 3D printing technology, and it has a lot of potential in the food industry. With free collocation, it can enhance food styles, vary food forms, increase food quality, and balanced nutrition, as well as meet the demands of niche consumer groups, including the elderly, children, and athletes. Food products such as dough, minced meat, cheese, chocolate, and other items have been created using 3D printing technology. Extrusion is currently the most popular method of 3D printing for food applications, owing to its ease of use and wide range of "inks." Cold extrusion, hot-melt extrusion, and gel-forming extrusion are the three varieties based on the extrusion modes (Hospodiuk *et al*., 2017) [20]. Various biopolymers have been widely employed in 3D printing, including SA, κ-car, cellulose, LMP, and GA. When these biopolymers are utilized separately, however, they have limited shape-forming

capacity, and the resulting products have poor mechanical qualities (Li *et al*., 2017). Because of their improved printability, excellent extrudability, and high form fidelity, IPNs are more useful as starting materials for 3D printing than single biopolymers. Furthermore, the rheological characteristics of hydrogels (such as shear thinning and thixotropic behavior) are important in determining the resolution and form fidelity of 3D- printed objects (Li, Wang, *et al*., 2018) [28]. For 3D printing, many IPNs have been used, including SA-κ-car (Kim, Lee, Jung, Oh, & Nam, 2019), SA-MC (Li *et al*., 2017), and GA-κ-car (Li, Tan, & Li, 2018). Kim *et al*., (2019) discovered that solo SA gels were too weak for successful printing, but that when combined with κ-car and 1% CaSO4, the resulting SA-κ-car IPNs had a remarkable shear-thinning capability, allowing them to be used in 3D printing.

Encapsulation and controlled release of bioactive/aroma compounds

Incorporating various bioactive components (e.g., probiotics, hydrophobic and hydrophilic chemicals) or fragrance compounds might improve the nutritional, antibacterial, and organoleptic aspects of food items. Due to their instability, low bioavailability, solubility, and release properties in the small intestine, as well as intermittent unpleasant odors, bioactive/aroma compounds are limited in their applicability in food systems (Abae *et al*., 2017).

Fat-replaced products

Chronic illnesses have become more common as a result of increased intake of fat-rich meals (e.g., obesity, diabetes, and coronary heart disease). As a result, developing fat-reduced food products like ice cream and mayonnaise is critical. However, lowering fat in meals results in undesired features such as a hard texture, reduced hydration retention, and an unusual taste. Fat removal, for example, makes cakes and bread crumbs drier and firmer. The adherence of salad dressing to vegetables may be harmed by a lower fat level (Liu, Wang, Liu, Wu, & Zhang, 2018) [31]. Fortunately, IPNs based on proteins and/or polysaccharides can be used to partially replace fat droplets since their high WHC allows them to preserve food texture and provide a lubricity similar to that of full-fat products (Yang *et al*., 2020) [51]. The first stage in using IPNs as fat replacers is to develop IPNs with acceptable rheological characteristics, particularly thixotropy and viscoelasticity. Several IPN systems, including whey protein-pectin (Sun *et al*., 2018) and SA-KGM, have been successfully manufactured to achieve this purpose (Yang *et al*., 2020) [51]. Whey protein-pectin IPNs were used to replace 20% of the fat in the mayonnaise during manufacture. The resulting products had similar rheological characteristics (viscosity, elasticity, and thixotropy) to the originals, and the inclusion of up to 60% fat replacements might greatly improve mayonnaise storage stability by avoiding fat droplet coalescence and flocculation (Sun *et al*., 2018). Several pure biopolymers, such as starch, CMC, and MCC, have also been reported to be used as fat-replacers, hence IPNs based on these biopolymers serving as fat-replacers are worth investigating further (Diamantino *et al*., 2019; Gibis *et al*., 2015; Li *et al*., 2018; Sun *et al*., 2018).

Conclusion

Many hydrogel-based networks have recently been created and adapted to fulfill the requirements of various applications. The capacity of these hydrogels to expand when exposed to an aqueous solution is one of their most appealing features. The way of making hydrogels and the design process have an impact on the manufacturing of hydrogels using various procedures, which necessitate a high level of sensitivity. IPNs are essential for increasing the functional characteristics of food items. Heating-cooling, ionic, and enzymatic crosslinking techniques can all be used to create IPNs. IPNs have a denser and more compact microstructure than SNs, which means they have better mechanical strength, thermal stability, and water-holding capacity, as well as a lower swelling rate.

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