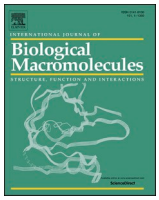
International Journal of Biological Macromolecules 281 (2024) 136398

Contents lists available at ScienceDirect

International Journal of Biological Macromolecules

journal homepage: www.elsevier.com/locate/ijbiomac



Review

In the process of polysaccharide gel formation: A review of the role of competitive relationship between water and alcohol molecules

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ARTICLE INFO

Keywords:
Polysaccharide gels
Alcohol-induced gelation
Monoalcohols and polyols
Hydrogen bonding
Hydrophobic interactions
Polysaccharides biomedical applications

ABSTRACT

Polysaccharides have emerged as versatile materials capable of forming gels through diverse induction methods, with alcohol-induced polysaccharide gels demonstrating significant potential across food, medicinal, and other domains. The existing research mainly focused on the phenomena and mechanisms of alcohol-induced gel formation in specific polysaccharides. Therefore, this review provides a comprehensive overview of the intricate mechanisms underpinning alcohol-triggered gelation of different polysaccharides and surveys their prominent application potentials through rheological, mechanical, and other characterizations. The mechanism underlying the enhancement of polysaccharide network structures by alcohol is elucidated, where alcohol displaces water to establish hydrogen bonding and hydrophobic interactions with polysaccharide chains. Specifically, alcohols change the arrangement of water molecules, and the partial hydration shell surrounding polysaccharide molecules is disrupted, exposing polysaccharides' hydrophobic groups and enhancing hydrophobic interactions. Moreover, the pivotal influences of alcohol concentration and addition method on polysaccharide gelation kinetics are scrutinized, revealing nuanced dependencies such as the different gel-promoting capabilities of polyols versus monohydric alcohols and the critical threshold concentrations dictating gel formation. Notably, immersion of polysaccharide gels in alcohol augments gel strength, while direct alcohol addition to polysaccharide solutions precipitates gel formation. Future investigations are urged to unravel the intricate nexus between the mechanisms underpinning alcohol-induced polysaccharide gelation and their practical utility, thereby paving the path for tailored manipulation of environmental conditions to engineer bespoke alcohol-induced polysaccharide gels.

1. Introduction

Polysaccharides, vital natural polymer compounds, exhibit a broad spectrum of sources, including plants, animals, or microorganisms. Their intricate structures confer diverse properties and functionalities [1], rendering them indispensable across various applications. Leveraging their unique physicochemical attributes, polysaccharides serve as crucial components in the food industry, functioning as thickeners, emulsifiers, and gelling agents, while also facilitating flavor release [2] and enhancing food packaging [3]. Additionally, their commendable stability, non-toxicity, biocompatibility, and biodegradability render polysaccharides highly useful in biomedical and pharmaceutical realms, facilitating the formulation of tissue scaffolds and enabling efficient drug delivery systems [4,5]. Furthermore, certain polysaccharides boast notable bioactivities, such as anti-tumor and antiviral properties, thereby finding widespread utilization in the production of health-oriented products [6,7].

Polysaccharide gels are prevalent in various aspects of daily life, boasting diverse applications across many different fields. For example, polysaccharide hydrogels, renowned for their softness, elasticity, absorption, flexibility, and moisture retention [8], are highly favored in various food-related endeavors. Their hydrophilic nature and non-immunogenic properties further enhanced their utility in food preservation, pharmaceuticals, agriculture, and food packaging [8]. Meanwhile, polysaccharide aerogels, distinguished by their porous structure and extensive surface area, have found widespread adoption in biomedicine and beyond. Their exceptional attributes, including non-toxicity and biodegradability, position them as invaluable functional

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https://doi.org/10.1016/j.ijbiomac.2024.136398
Received 28 July 2024; Received in revised form 1 October 2024; Accepted 5 October 2024
Available online 9 October 2024

materials with substantial application potential [9].

Gels exhibit diverse gelling mechanisms, categorized into chemical crosslinking, physical crosslinking, and biological crosslinking [10]. In the realm of polysaccharide gels, their gelation mechanisms predominantly revolve around physical crosslinking, encompassing hydrogen bonding, ionic interaction, and hydrophobic interaction. Hydrophobic interaction entails the aggregation of polymers containing hydrophobic domains as temperature rises, minimizing contact with water molecules and culminating in gel formation through molecular chain association [10]. For example, carboxymethyl cellulose undergoes gelation via hydrophobic interaction in aqueous solutions [11]. Hydrogen bonding refers to the formation of hydrogen bonds between oxygen and hydrogen atoms in polymer molecular groups, leading to the establishment of a network structure. For instance, pectin, rich in hydroxyl groups, readily forms hydrogen bonds, thereby facilitating gelation [12]. Ionic interaction involves the pairing of anions and cations on polymer molecules or anions and metal cations of polymers to form a gel matrix [13]. For example, when chitosan solution and sodium hydroxide solution are combined, the ammonium ions in chitosan molecules interact with hydroxyl ions in sodium hydroxide crosslink and form a gel [14]. Moreover, certain gels are formed through helix formation, helix association, and junction zone formation. For example, carrageenan undergoes a transition from irregular coil to double-helix aggregates during the gelation process, showcasing distinct molecular states at varying temperatures [15].

Many factors can trigger the gelation of polysaccharides, including salt induction [16], acid induction [17], and alcohol induction [18]. Each induction method engenders distinct polysaccharide gel processes, thereby yielding gels with varied properties and enhancing their utility across diverse fields. For instance, low-methoxy pectin gel induced by sugar exhibits viscoelasticity and plasticity, rendering it suitable as a food ink for 3D printing [19]. Conversely, pectin gel induced by ethanol holds promise as a carrier aerogel [20]. ι-Carrageenan gel induced by salt displays softness and elasticity, coupled with reversible properties upon exposure to heat, making it prevalent in jelly production and 3D printing applications [16]. On the other hand, ι-carrageenan gel induced by alcohol showcases a porous structure [21], offering potential applications in aerogel production.

However, it is important to consider that gel formation through ionic crosslinking and the salting out effect may have certain drawbacks especially for specific applications. For example, pectin achieves gelation through the electrostatic shielding effect of sodium ions and the concomitant hydrogen bonding effect [22]. However, the salt-induced gelation process typically necessitates a substantial quantity of salt, which is undesirable in industries [23] such as food processing due to health concerns. Besides, under acidic conditions, the reduction in intermolecular repulsion among polysaccharide molecules, coupled with decreased hydration, facilitates molecular proximity and subsequent gel formation [22]. *Poria cocos* polysaccharide undergoes gelation via physical entanglement mediated by weak non-covalent interactions like hydrophobic interaction, electrostatic interaction, and hydrogen bonds in an acidic environment [17]. Nonetheless, acid-induced gelation is constrained by a specific pH range, imposing limitations on its applicability. Moreover, small sugar molecules interact with pectin to promote gelation by displacing water molecules around the pectin molecular chain, thus fostering the formation of a three-dimensional network structure [24]. However, akin to salt induction, sugar-induced polysaccharide gelation entails a substantial demand for small-molecule sugars, posing health risks such as obesity and diabetes when utilized in the food sector [25].

In fact, alcohol induction can effectively improve the above problems and be applied in different fields. In the food industry, polysaccharides are commonly paired with ethanol in food and beverage products to enhance uniformity, stability, and viscosity [26,27]. Immersing a polysaccharide gel in an ethanol solution offers the potential to yield a gel containing a high alcohol content [28], presenting significant commercial opportunities. Although alcoholic food products of this nature are currently scarce in the market, their commercial potential remains substantial. Moreover, since polyols are the reduction products of sugars—the aldehyde groups on glucose are reduced to alcohol (hydroxyl) groups through aldose reductase to obtain sorbitol [29], and the hydroxyl groups contribute to gel formation [30], polyols can also induce polysaccharides gelation. Compared with sugar induction, polyols offer lower calorie content and elicit a reduced blood sugar response, rendering them advantageous substitutes in diabetic and low-calorie foods. In the realm of biomedicine, ethanol can be easily eliminated through gel drying and sterilization processes [31]. Ethanol is frequently incorporated with biopolymers in scaffold preparation for tissue engineering, finding widespread application in acellular processes [32]. Furthermore, in materials engineering, polysaccharide-alcohol gels hold promise for producing porous materials via supercritical drying, offering potential advancements in the field [33].

Alcohols are introduced into polysaccharide solutions to establish a three-dimensional network structure through hydrogen bonding and hydrophobic interactions with polysaccharide molecules. Existing studies predominantly concentrate on the phenomena and mechanisms of alcohol-induced gel formation in specific polysaccharides. However, there exists a notable gap in providing a comprehensive overview of the mechanisms governing alcohol-induced polysaccharide gel formation, thereby motivating the inception of this current review. Accordingly, this review article aims to classify polysaccharides according to their different gelation modes (such as temperature-induction, ion-induction, and pH-induction) to explain the potential mechanisms of alcohol-induced formation of different polysaccharide gels (e.g., curdlan, pectin, and chitosan), and look forward to the development prospects of this field.

2. Gelation modes of polysaccharides

The formation of a gel hinges on several key factors: the molecular structure, the intermolecular force that holds the whole network together, and the nature of the junction zones within the polymer's crosslinked structure. These elements collectively determine the conditions under which gelation occurs and the resulting properties of the gel.

A polysaccharide gel's network structure is primarily formed by numerous weak interactions, such as electrostatic attraction and hydrogen bonding [34]. The junction zones within this structure are intricate. Research has shown that polysaccharides can form gels through various mechanisms, but these typically depend on the polymer's specific structure [35]. The different composition of polysaccharide will affect the process and way of gel formation. For example, polysaccharides with high hydrophilicity are easier to absorb water and form gels; polysaccharides containing charged groups can interact with ions to form gels. Gel formation will also be affected by the presence of acidic and alkaline groups on the chains of different polysaccharides in different solvents.

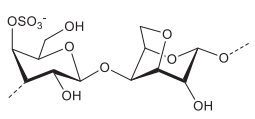
In the presence of alcohols, these compounds can induce polysaccharide gelation or enhance their gel-forming behavior through hydrophobic interactions or hydrogen bonding. The nature and structure of the polysaccharide itself also influence the formation of their alcohol-induced polysaccharide gels.

This article aims to elucidate the mechanisms underlying the alcohol-induced gelation of polysaccharides, organized according to the different gelation mechanisms. Table 1 provides an overview of these gelation methods, the alcohol used, the interactions involved, the resulting gel properties, and the potential applications of these polysaccharide gels. Fig. 1 illustrates two major classes of polysaccharides that form gel, either by combining specific groups or gel by interaction between chains, in the presence of an alcohol. Fig. 2 shows the molecular structural formulas of the relevant alcohols.

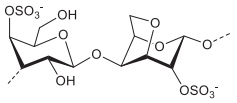
Table 1
Summary of gelation methods, alcohol used, interactions involved, gel properties, and applications of different polysaccharides.

Polysaccharide	Structural feature responsible for gelation	Gelation method	Alcohol	Interaction	Gel properties	Application
Carrageenan	Cation-induced gelation: Crosslinking of thickener chains with ions (e.g., K^+ and Na^+). The formation process of thermo-reversible gel: the molecular chain presents an irregular curl in hot water, turns into single helices after the temperature drops, and finally turns from single helices to double helices to form a gel.	Cooling-induced gelation (reversible) Cation-induced gelation (reversible)	Ethanol	Hydrogen bonding and hydrophobic interactions	Gel strength and gelling point temperature are increased.	Alcoholic foods
			Sorbitol/xylitol	Hydrophobic interactions	Gel strength and gelling point temperature are increased.	
β-Glucan	Thermoreversible gel has a high content of single helices, and the micelles are connected by hydrogen bonding; Thermal irreversible gel has a high content of triple helices, which forms a three-dimensional network structure through hydrophobic crosslinking.	Heating-induced gelation (reversible/ irreversible)	Sorbitol	Hydrophobic interactions	The elasticity and thermal stability of the gel are enhanced.	Production of healthy food
Curdlan	Thermoreversible gel has a high content of single helices, and the micelles are connected by hydrogen bond; The thermal irreversible gel has a high content of triple helices, which forms a three-dimensional network structure through hydrophobic crosslinking.	Hitting-induced gelation (irreversible) cooling-induced gelation (reversible)	Erythritol	Hydrogen bonding	The strength and freeze-thaw stability of the gel are improved.	Production of healthy food (good for diabetes patients)
Gellan gum	Cooling-induced gel: during heating, the nonaggregating spiral of gellan gum dissociates, and during cooling, the double spiral of gellan molecule aggregates. Cation-induced gel: Cations shield the electrostatic repulsion between carboxyl groups.	Cooling-induced gelation (reversible) Cation-induced gelation (reversible/ irreversible)	Ethanol, 1-propanol, 2-propanol/ isopropanol	Hydrogen bonding	Gel strength is increased.	Alcoholic gelling agent
Pectin	Low-methoxy pectin: Carboxyl groups on molecular chains interact with ions. High-methoxy pectin: A portion of the molecular chains form hydrogen bonds, while a portion of the methoxy groups on the chains interact with water.	Low-methoxy pectin: cation-induced gelation (reversible) High-methoxy pectin: pH-induced gelation (irreversible)	Ethanol (acid)	The hydrogen bonds of polysaccharide molecular chains are disrupted; hydrophobic interactions	Gel strength is increased.	Anti-counterfeiting and information storage; Improving the bioavailability of antagonists
Tamarind seed polysaccharide	The disruption of hydrogen bonds between polysaccharide molecules and water molecules and the aggregation of molecular chains due to hydrophobic interactions	Ethanol-induced gelation (reversible)	Ethanol	The hydrogen bonds between polysaccharide molecules and water molecules are disrupted; Hydrophobic interaction	Gel strength and gelling point temperature are increased.	Drug-carrying water gel
Chitosan	Amino and hydroxyl groups are neutralized, or NH^{3+} is crosslinked with phosphate ions.	pH-induced and ion-induced gelation (irreversible)	Ethanol	Hydrophobic interaction	Gel strength is increased, and the gel becomes more resistant to high temperature.	Bone tissue engineering materials
			1,2-Propanediol	Hydrogen bonding and hydrophobic interactions		
Sodium alginate	Sodium ions on the G unit are replaced with multivalent ions through ion exchange	Ion-induced gelation (irreversible)	Ethanol			3D Printing
Xanthan gum	Metal ions form coordination complexes with xanthan gum.	Metal ion-induced gelation (irreversible)	Ethanol	Hydrophobic interaction	Gel strength is increased.	Drug delivery; cosmetics
Konjac glucomannan	Acetyl and hydroxyl groups interact to induce changes in molecular structure (deacetylation). Hydrogen bonds and hydrophobic interactions are formed between KGM molecular chains.	Modification-induced gelation (irreversible)	Ethanol	The hydrogen bonds between polysaccharide molecules and water molecules are disrupted; Hydrophobic interaction	Gel strength is increased.	Preparation of low-salt foods
Codonopsis pilosula polysaccharides	Molecular chains undergo hydrophobic interactions	Ethanol-induced gelation (reversible)	Ethanol	Hydrophobic interaction	The gel has shear-thinning and self-healing properties.	Injectable drug-loaded gel

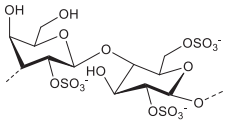
Gelation by linking specific functional groups:



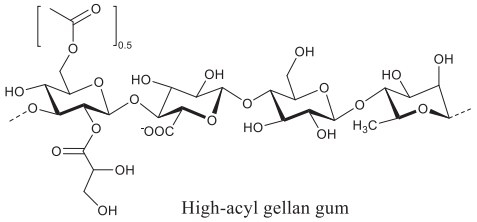
κ-Carrageenan



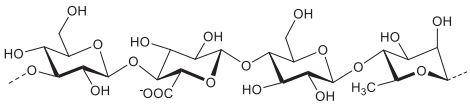
ι-Carrageenan



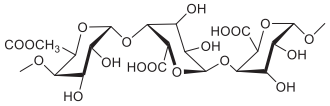
λ-Carrageenan



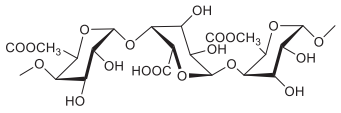
High-acyl gellan gum



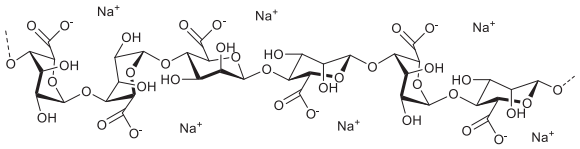
Low-acyl gellan gum



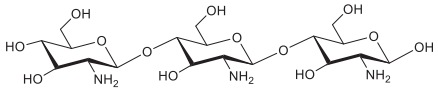
Low-methoxy pectin



High-methoxy pectin

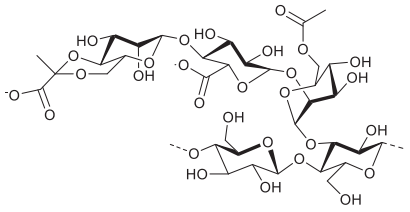


Sodium alginate

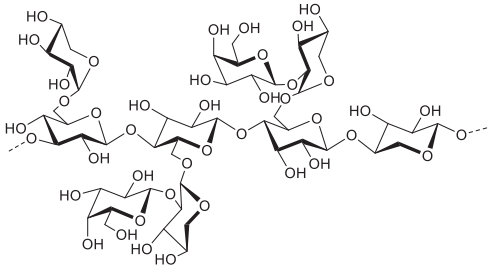


Chitosan

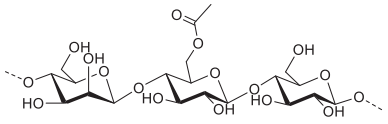
Gelation by enhanced chain interactions:



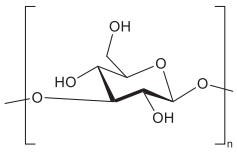
Xanthan gum



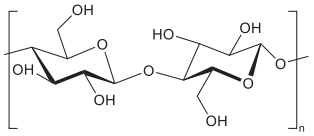
Tamarind seed polysaccharide



Konjac glucomannan



Curdlan



β-Glucan

Fig. 1. Molecular structures of different polysaccharides.

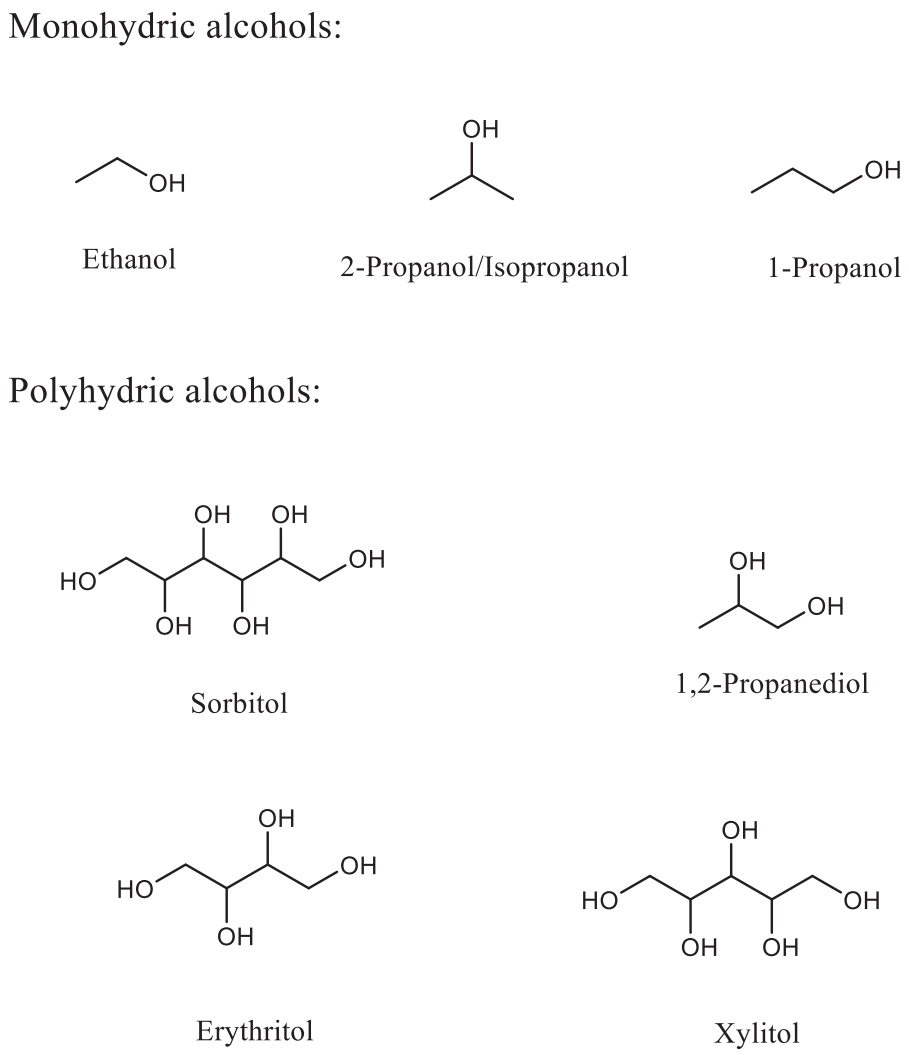


Fig. 2. Molecular structures of different alcohols.

2.1. Temperature-induced polysaccharide gelation

Within a specific temperature range, some polysaccharides transition from a solution state to a gel state due to temperature changes. These gels are categorized into cooling-induced gels and heat-induced gels. For cooling-induced gels, polysaccharide molecules exist as clusters in solution. When the temperature drops, hydrogen bonding causes the molecules to form a helical structure, resulting in gelation. Conversely, for heat-induced gels, heating causes hydrophobic interactions between molecules and substituents, leading to gelation. Upon cooling, some of these polysaccharides retain their gel state, while others can revert to the original solution state. Typical temperature-induced polysaccharides include curdlan, β-glucan, and gellan gum.

Curdlan is a water-insoluble glucan produced by microorganisms, characterized by β-1,3-glycoside bonds and a unique triple-helix structure [36]. This polysaccharide exhibits two distinct types of gelation behavior: 1) Heat-induced gelation: At temperatures of 80 °C or higher, curdlan undergoes an irreversible gelation process; 2) Cool-induced gelation: Upon cooling to about 55 °C, curdlan forms a reversible gel [37].

β-Glucan is a polysaccharide composed of β-glucose molecules connected by β-1,3- and β-1,6-bonds, forming a distinct triple-helix structure [38]. Depending on heating temperature, β-glucan can form gels with markedly different properties: 1) Cooling-induced gelation: Heating to about 55 °C and subsequently cooling below 40 °C yields a low-strength, thermally reversible gel; 2) Heat-induced gelation: Heating above 80 °C results in a high-strength, thermally irreversible gel [39].

Gellan gum is a high-molecular-weight linear polysaccharide composed of four repeating monosaccharide units: two glucose residues, one glucuronic acid residue, and one rhamnose residue. It forms a distinct double-helix structure and is commonly used as a thickener and stabilizer. Gels made of gellan gum are known for their excellent flavor-release properties [40]. Gellan gum is soluble in hot water and forms a hydrogel after cooling, undergoing two main transitions during this process. During heating, the non-aggregated helices of gellan gum dissociate, while during cooling, the double helices of gellan gum molecules aggregate. The resulting gel properties depend on the degree of acetylation: high acetyl gellan gum forms soft, elastic gels while removing the acetyl group yields more rigid gels [41]. In addition to temperature-induced gelation, gellan gum can also form transparent gels through complexation with multivalent cations, such as Ca^{2+} and Mg^{2+} [41]. While being discussed here, the ion-induced gelation of gellan gum will not be repeated later. In the presence of cations, the gel mechanism is considered to involve crosslinking between the double helices initiated by cations. The carboxyl side chains of gellan gel molecules repel each other due to electrostatic interactions, hindering tight helix aggregation, while the presence of cations shields this electrostatic repulsion [41].

2.2. Ionically induced polysaccharide gelation

Certain polysaccharides can reinforce gel formation through the synergistic interplay of ion-induced crosslinking and salting out. That is, in the presence of univalent or bivalent cations, polysaccharides can gelate, such as pectin, carrageenan, and xanthan gum. Monovalent cations reduce intermolecular electrostatic repulsion and promote intermolecular aggregation by masking the negative charges on polysaccharide chains. Divalent or multivalent cations directly bond with the dissociated carboxyl groups in polysaccharide molecules to form intermolecular crosslinking. When the concentration of cations is too high, the polarity environment of the solution is changed, which may cause the "salt out" effect of polysaccharide branching. Examples of polysaccharides where ionically induced gelation can be applied include pectins, carrageenan, xanthan gum and sodium alginate.

Pectins are acidic heteropolysaccharides mainly composed of D-galacturonic acid linked by α-1,4-glycosidic bonds, forming a triple-helix structure [42]. They are classified as high-methoxy or low-methoxy based on their degree of esterification. While low-methoxy pectins have a large number of hydroxyl groups and can form gels by interacting with divalent ions like Ca^{2+} and Mg^{2+}, high-methoxy pectins more readily form irreversible gels when the soluble sugar content exceeds 60 % and the pH is between 2.6 and 3.4 [43].

Carrageenan is a widely used thickener and gelling agent in the food industry, composed of alternating sulfated or non-sulfated galactose and dehydrated galactose units connected by α-1,3-glycosidic and β-1,4-glycosidic bonds. It forms a distinct double-helix structure. Depending on the type of sulfate ester bonding, different varieties of carrageenan can be produced, including κ-carrageenan, ι-carrageenan, and λ-carrageenan [44]. κ-Carrageenan and ι-carrageenan form gels in the presence of K^{+} and Ca^{2+}, respectively [45].

Xanthan gum is a non-toxic, biodegradable, and high-performance natural polymer material with a primary structure consisting of a β-D-glucose main chain and trisaccharide side containing glucuronic acid and mannose units. It forms a distinctive double-helix structure [46]. In aqueous solutions or extremely low salt concentrations at room temperature, xanthan gum exhibits an ordered helical conformation. However, in the presence of high salt concentrations or upon heat treatment, the ordered structure becomes disordered, and the xanthan gum molecular chains transform into a double-helix conformation. The side chains dissociate from the main chain and interact with each other or other macromolecular chains, forming a network structure [47].

Sodium alginate is a byproduct of extracting iodine and mannitol from brown algae such as kelp or seaweed. Its molecule is composed of β-D-mannuronic and α-L-guluronic acid connected by (1 → 4) bonds, making it a natural polysaccharide with the stability, solubility, viscosity, and safety required for pharmaceutical excipients. The formation mechanism of sodium alginate gel is that sodium ions on the G unit in the molecule are replaced with divalent or multivalent ions through ion exchange (the most common type of ion used is Ca^{2+}), leading to the formation of a gel with thermal irreversibility, and locks a large amount of water in the gel structure [48].

2.3. pH-induced polysaccharide gelation

The effect of pH value on the gel of polysaccharides is to change the molecular conformation of charged polysaccharides and the interaction between molecules. Changing the pH value of the solution can induce gelation of some polysaccharides, or contribute to gel formation induced by other factors, such as chitosan and Konjac glucomannan.

Chitosan is a disaccharide composed of two glucosamine units connected by β-1,4-glycosidic bonds, forming a distinctive double-helix structure [49]. It is a highly nitrogen-rich polysaccharide obtained by deacetylation of chitin, which is abundant in nature. The numerous amino and hydroxyl groups in chitosan molecules endow them with various chemical activities, particularly excellent film-forming ability, crosslinking potential, and biocompatibility in alkaline media [49]. Chitosan forms intramolecular and intermolecular hydrogen bonds through the interactions of hydroxyl, amino, and *N*-acetylamino groups distributed along the macromolecular chains. Chitosan is readily soluble in weak acid solvents, and the dissolved solution contains amino groups [50]. When the chitosan solution is mixed with a sodium hydroxide solution, the amino groups in the chitosan molecules neutralize with the hydroxyl ions from NaOH, forming a gel [51]. Additionally, since chitosan is positively charged above its isoelectric point, the NH_2 groups on the glucosamine residues convert to NH_3^+ groups, enabling crosslinking with phosphate ions upon heating to form a gel [52].

Konjac glucomannan is a non-ionic water-soluble polymer polysaccharide composed of D-mannose and D-glucose linked by β-1,4-glycosidic bonds [53]. It forms an irregular cluster state and can develop a three-dimensional network structure through deacetylation and heat treatment, involving molecular stretching, physical interactions, and irregular aggregation [54].

2.4. Alcohol-induced polysaccharide gelation

In addition to the aforementioned gel polysaccharides, many polysaccharides are not sensitive to factors like temperature and ions, but are sensitive to alcohols, and can form gel with the induction of alcohol molecules. Examples include tamarind seed polysaccharides and *Codonopsis pilosula* polysaccharides (CPP).

Tamarind seed polysaccharide (TSP) is a neutral polysaccharide extracted from the seed endosperm of the leguminous plant Tamarindus. It has a main chain composed of β-D-1,4-linked glucose and side chains of α-D-1,6-linked xylose and β-D-1,2-linked galactose [55], forming a double-helix structure [56]. It is a widely used edible gum with thickening, coagulation, and other functions, and is also an ideal source of dietary fiber with potential benefits for hypertension and diabetes [57]. TSP can interact with ethanol to form high-strength gels within a certain range of ethanol concentrations [58].

CPP, vital components of *Codonopsis pilosula*, possess diverse properties including anti-swelling, antioxidant effects, and enhancement of cellular immunity. The main chain comprises 1,2-linked β-D-furan fructose [59]. In the current research, CPP can interact with ethanol to form a gel.

The polysaccharides mentioned above that can form gel in different ways have one thing in common: they can all form gel through the induction of alcohol molecules. In the following, the role of alcohol molecules in alcohol induced polysaccharide gel system will be described from two major mechanisms.

In addition to the above-mentioned gelation mode of polysaccharides, in fact, enzymes, small molecule sugars, phenols and other substances can also induce some polysaccharides to form gel.

3. Formation mechanism of alcohol-induced polysaccharide gels

3.1. Role of alcohol in disrupting polysaccharide–water hydrogen bonding and enhancing polysaccharide interchain hydrophobic interactions

Hydrophilic polysaccharides interact with water molecules in aqueous solutions through hydrogen bonds to maintain stability and achieve uniform dispersion. However, the addition of alcohols, like ethanol, can disrupt this arrangement by altering the hydration shell around the polysaccharide molecule. This disruption weakens the hydrogen bonds between the polysaccharide and water. Furthermore, alcohol molecules may establish new hydrogen bonds with water or directly interact with hydroxyl groups or specific functional groups on polysaccharides, exposing hydrophobic groups. This exposure enhances interchain hydrophobic interactions or hydrogen bonding within polysaccharides, leading to increased aggregation (refer to Fig. 3). On a larger scale, changing water as a solvent for polysaccharides into alcohol reduces their solubility. The mechanisms regarding how alcohol induces

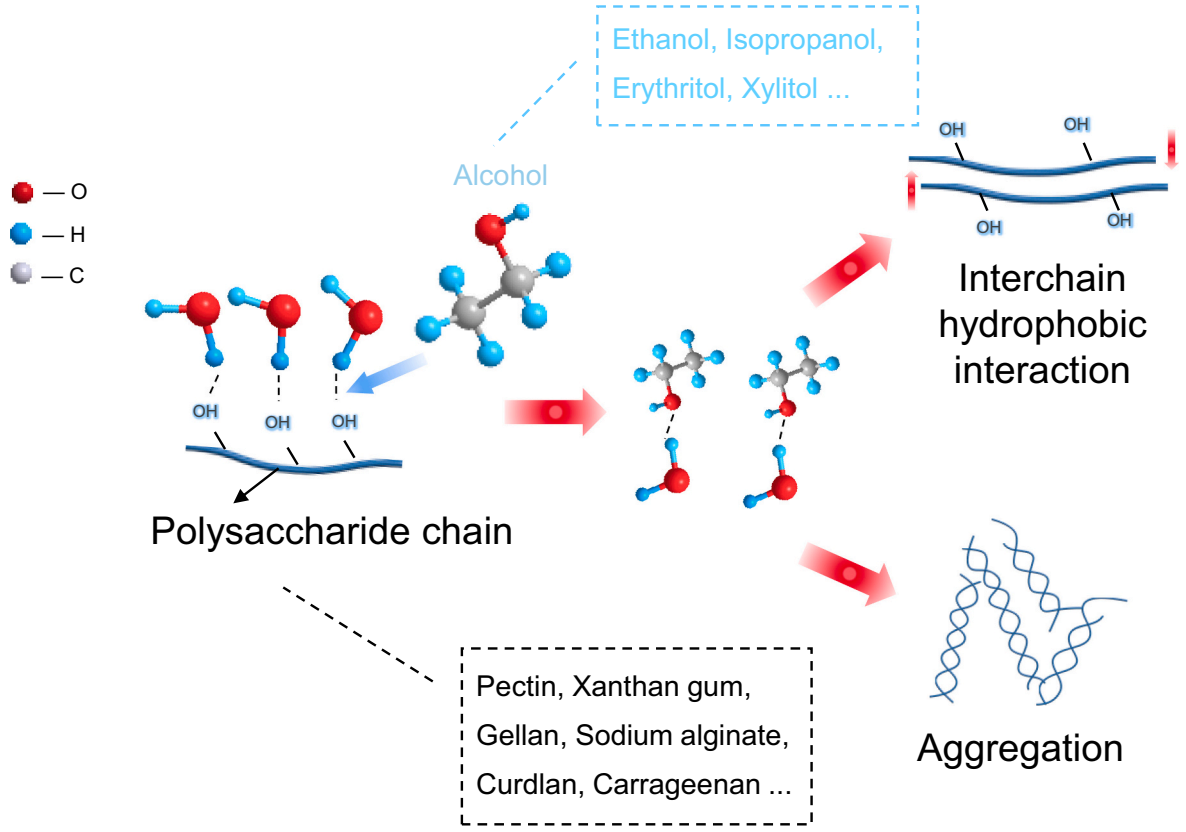


Fig. 3. Mechanism diagram of alcohol molecules inducing polysaccharide to form gel.

the gelation of various polysaccharides are discussed in detail below.

3.2. Tamarind seed polysaccharide

The addition of alcohols to form gels has greater potential for future product development, such as the creation of alcohol jelly products. TSP can interact with ethanol (monohydric alcohol) to form high-strength gels within a certain range of ethanol concentrations [60]. The mechanism of gel formation between TSP and ethanol is primarily due to the disruption of hydrogen bonds between TSP chains and water molecules [58], as well as an increase in hydrophobic interactions between TSP chains [60].

Ethanol molecules can form stronger bonds with the molecular chains of TSP than water molecules, and the interaction between ethanol molecules and TSP chains tends to be hydrophobic. Ethanol molecules quickly break the hydrogen bonds between TSP chains and water molecules, bonding to TSP chains to slow their expansion and contraction movements. TSP chains then aggregate with each other in certain structural domains, enveloping water within the formed gel network, ultimately resulting in a water-rich gel [58]. The formation of these structural domains may also be attributed to the irregular aggregation of TSP chains due to their poor solubility in ethanol [60,61].

During the gelation process, TSP gels undergo a certain degree of shrinkage. This is due to the competition for water between the polysaccharide and ethanol, ultimately leading to a shrinkage of the polymer hydration shell and local polymer association in the crosslinking zone [62].

The type and concentration of alcohols are crucial factors affecting the gelation process. Gels formed in the presence of polyols consist of smaller aggregation domains or crosslinking points, which are more likely to promote aggregation and form more extended "suture" regions than monohydric alcohols [62]. TSP may only be able to form gels within a certain range of ethanol concentrations, as excessive ethanol can lead to the polysaccharide's precipitation [63].

Additionally, the concentration of the TSP aqueous solution also affects the gel properties. Paul et al. [64] prepared ethanol-induced TSP gels with varying TPS concentrations and found that the degree of hydrogen bonding and electric resistance component in the gels decreased with increasing TSP content. However, gels with high TSP content exhibited highly stable mechanical properties [64].

Sharma et al. [65] reported that, compared to TSP gels containing ionic liquids (1-butyl-3-methylimidazolium chloride or 1-butyl-3-methylimidazolium bromide) gels or bio-based ionic liquids (choline acrylate, choline caproate, or choline caprylate) prepared by a heating-cooling method, ethanol-induced TSP gels displayed inferior gumminess, viscoelasticity (elastic modulus, viscous modulus, and viscosity), thermal stability, and thixotropy. Due to the excellent adhesion of Sharma et al.'s gels to human finger muscles and skin, they can be applied in fields such as electrochemistry and sensors [65]. Therefore, improving the overall properties of ethanol-induced TSP gels remains an area for further exploration.

3.3. Pectin

In high-methoxy pectin gels, the gel structure is formed through hydrogen bonding and hydrophobic interactions of the methyl ester group. Traditionally, these gels are prepared by acid gelation, which is a time-consuming process taking up to 48 h to produce a strong solid gel structure [20]. Tkalec et al. [20] proposed an alternative method by adding 10 % (*v*/v) ethanol (monohydric alcohol) to an aqueous high-methoxy pectin solution, forming an "alcohol gel" that can subsequently be supercritically dried to obtain high-methoxy pectin aerogels, potentially due to hydrogen bonding and hydrophobic interactions [20].

Due to ethanol' higher activity compared to water, when a high-methoxy pectin solution contacts ethanol, interactions between the high-methoxy pectin and water are minimized, while hydrophobic

interactions increase [33]. Oakenfull et al. [66] calculated that hydrophobic interactions between methyl groups contribute only half as much as hydrogen bonding to the overall gelation process, but are essential for overcoming the entropy barrier of gelation. Gel strength is maximized when hydrophobic interactions are strongest [66].

Congo red, which chelates with the triple-helix structure of high-methoxy pectins, undergoes a redshift in its λ_{max}. Jiang et al. [67] found that in the presence of acid, this redshift gradually disappears with increasing ethanol concentration, potentially due to the disruption of hydrogen bonds and the triple-helix structure by ethanol. The conformational transformation and aggregation behavior of high-methoxy pectins correlated positively with ethanol concentration [67].

Different from systems in which only ethanol exists, in acidic ethanol-induced high-methoxy pectin gels, hydrogen bonding, and electrostatic repulsion, rather than hydrophobic interactions, are the decisive forces [67]. Ethanol may cause chain contraction, hindering hydrophobic interactions, while reducing the solvation of high-methoxy pectins, preventing carboxyl group ionization, lowering the ζ-potential, and ultimately promoting the aggregation of high-methoxy pectins [67].

3.4. Xanthan gum

The solubility and intermolecular association ability of xanthan gum aqueous solutions can be affected by various factors, especially alcohols, which promote conformational structure changes and lead to gelation [68]. Similar to chitosan, the formation of xanthan gum aerogels by adding ethanol (monohydric alcohol) does not require washing or solvent exchange before supercritical drying, shortening the production time. In addition, xanthan gum water gels obtained in the presence of ethanol are highly effective hydrophobic drug encapsulation agents with good biocompatibility [69].

In xanthan gum aqueous solutions, the presence of ethanol reduces the solvent's thermodynamic properties and increases polymer contact, leading to association. In high-concentration xanthan gum solutions, the turbidity curve exhibits multiple maximum values, corresponding to the critical ethanol concentration that causes xanthan gum's phase transition [70].

At low ethanol concentrations, the addition of ethanol reduces the interaction between xanthan gum and water, promotes polymer–polymer interactions, and forms a weak gel [69]. At high ethanol concentrations, the solubility of xanthan gum decreases rapidly, and the interaction between macromolecules becomes dominant. The weak gel begins to aggregate, forming two distinct phases: a xanthan gum-poor phase and a xanthan gum-rich phase with gel-like behavior. Furthermore, the repulsive effect between xanthan gum and ethanol becomes significant, and the trapped solvent is discharged from the aggregates. Finally, xanthan gum separates from the bulk mixture in the form of a swelling gel [69].

3.5. Sodium alginate

Adding ethanol (monohydric alcohol) to sodium alginate precursor solutions can enable them to gelate in a temperature-sensitive manner. Ethanol makes the microstructure of sodium alginate changes from a layered structure to a network structure. The pore size of the network structure decreases with increasing ethanol concentration. Zhou et al. [71] showed that as the ethanol concentration increased from 0 % to 40 %, the scattering intensity in the low q range increased, indicating that ethanol promoted the formation of polymer clusters.

Without ethanol, the hydrophilicity of alginate chains makes alginate highly water-soluble, forming hydrogen bonds with water molecules. Ethanol molecules can disrupt the hydrogen-bonded network formed between alginate chains and water molecules, leading to local dehydration and effectively reducing the intermolecular separation distance between alginate chains. Therefore, the alginate chains are close enough to each other to form a relatively stronger hydrogen-bonded network, especially for the G block of alginate. However, excessive ethanol ($\geq$ 40 % v/v) can force alginate chains to form large aggregates, leading to macroscopic phase separation [71].

3.6. Codonopsis pilosula polysaccharides

The gelation of CPP inethanol (monohydric alcohol) solution may arise from random aggregation due to the limited solubility of CPP chains in ethanol. The interaction between CPP chains and ethanol induces a reduction in the hydration shell, promoting hydrophobic interactions between CPP chains within the crosslinking domain, eventually forming a three-dimensional network structure [72].

Adding ethanol to a low-concentration aqueous solution of CPP at room temperature results in the instant formation of a physical hydrogel with shear-thinning behavior and viscoelasticity, with reversible gelation behavior [72]. Throughout the gelation process, CPP maintains its original molecular chain chemical structure. Moreover, viscoelastic testing demonstrated minimal dependence of the gel on oscillation frequency, time, and temperature, ensuring a stable gel state and mechanical properties.

The gel formed from a low-concentration aqueous solution of CPP exhibited an irregular porous network structure under SEM observation, accompanied by significant viscoelasticity. With increasing concentration, the gel's viscosity rose, leading to a tighter, denser network and smaller pore size [72].

Furthermore, heightened concentrations of CPP enhanced the hydrophobic bonding effect, promoting increased aggregation and entanglement of CPP chains. This constrained the movement of CPP chains within the gel matrix, resulting in a continuous elevation of storage modulus and loss modulus. As concentration increased, the loss factor value increased, while the viscoelasticity (elastic modulus and viscous modulus) of the gel system decreased [72].

3.7. Gellan gum

Research has shown that the addition of ethanol (monohydric alcohol) can alter the water network in deacetylated gellan (containing carboxyl groups) gels, irreversibly affecting their performance at molecular and macroscopic levels. Ethanol replaces water in deacetylated gellan gel, dehydrating and shrinking the gel network [18].

On the molecular scale, this mechanism is evidenced by a reduction in the absorbance of the hydroxyl peak in infrared spectra [18]. Simultaneously, the characteristic peak of ethanol shifts from that of pure ethanol, indicating an interaction between ethanol and the deacetylated gellan molecular chains. The addition of ethanol promotes gel formation by destabilizing the hydrogen bonds between the hydrophilic groups of deacetylated gellan gel and water, disrupting the water network and altering the thermal behavior of the gel, as observed in differential scanning calorimetry (DSC) measurements [18].

Macroscopically, the presence of ethanol causes gellan gum gels to shrink, potentially due to increased network stacking and chain entanglement, deforming the gel network. Compared to the direct addition of high-concentration ethanol, the gradual addition of low-concentration ethanol can better retain the volume and shape of gellan gels [27].

Similar phenomena have been observed when treating gellan gels treated with 1-propanol (polyhydric alcohol), 2-propanol (polyhydric alcohol), or isopropanol (polyhydric alcohol), and other polyols, although their impact on mechanical properties is slightly reduced compared to ethanol, possibly due to differences in chain length and fluidity [27]. A new peak observed in the infrared spectra of polyols compared to ethanol may indicate effective interactions between the gellan gel and these polyols [18].

3.8. Chitosan

In the process of preparing chitosan aerogel by reacting with NaOH,

supercritical drying involving water-ethanol (monohydric alcohol) exchange is necessary [73]. Therefore, the use of ethanol facilitates this process, allowing the transformation of chitosan gels into aerogel products.

Pantić et al. [73] compared ethanol-induced chitosan gels and ethanol/NaOH-induced chitosan gels, finding that chitosan aerogels prepared in pure ethanol exhibited a dense, uniform, open-porous surface, and the gels were more stable and resistant to high temperatures. As a non-solvent for chitosan, ethanol causes polymer aggregation and the formation of a three-dimensional network. In the presence of ethanol, the hydrophobic domain of chitosan molecules begins to aggregate to minimize contact with ethanol, leading to the formation of chitosan gel [73].

Throughout the gel formation process, the balance between hydrophilic and hydrophobic interactions plays a crucial role. Zhang et al. [74] found that in the ethanol/water system, even at lower concentrations, chitosan could form a gel, and the crosslinking strength did not increase with increasing crosslinker agent content. This indirectly indicates that ethanol as a co-solvent can indeed increase the crosslinking density and promote gel formation [74].

As illustrated in Fig. 4, chitosan molecules tend to spontaneously aggregate in good solvents or acidic aqueous solutions. The addition of ethanol promotes aggregation by changing the solvent's thermodynamic properties, reducing the dielectric constant and charge density. When the ethanol concentration is below a critical value, chitosan aggregates and free chitosan molecules can remain in equilibrium in the solution for an extended period. However, when the ethanol concentration exceeds the critical value, the hydrogen bonding between chitosan and the solvent weakens, while the hydrogen bonding between chitosan molecules is enhanced. Eventually, the interactions between chitosan molecular chains lead to gel formation [75].

Montembault et al. [76] prepared chitosan (containing amino groups)-based hydrogels by adding acetic acid and 1,2-propanediol to a chitosan aqueous solution, followed by neutralization with NaOH and thorough washing to remove excess reagents. The gelation mechanism was attributed to hydrophobic interactions and hydrogen bonding between polymer chains. The role of 1,2-propanediol was to reduce the medium's dielectric constant and potentially participate in the formation of hydrophobic interactions between polymer chains [76].

With the initial water content increased, the time required for chitosan gel formation also increased. This behavior demonstrates the effect of water and 1,2-propanediol on the kinetics of physical crosslinking formation [76]. Due to the solubility of polar and ionized groups in water, it is not conducive to the formation of complexes through hydrophobic interactions and hydrogen bonding. Due to its high dielectric constant, water also facilitates the amine ionization of glucosamine residues, resulting in electrostatic repulsion between ion sites. In contrast, 1,2-propanediol is responsible for a decreased dielectric constant and then a reduction in electrostatic repulsions between glucosamine residues. [76]. A hydrophobic/hydrophobic complex could be formed between acetyl groups of two different NAGs with a molecule of alcohol in between. The OH group of the alcohol would therefore contribute to maintaining a certain hydrophily and thus preclude any precipitation [76].

3.9. Konjac glucomannan

Konjac glucomannan gels prepared under highly alkaline conditions suffer from issues like dehydration shrinkage and an alkaline odor [77], making the development of alkali-free konjac glucomannan gels desirable.

Reports indicate that konjac glucomannan in ethanol can improve its gel strength, potentially related to ethanol (monohydric alcohol)-induced dehydration, with higher ethanol concentrations enhancing this effect [78]. Ethanol acts as a fixative, causing the gel network to contract and densify as its concentration increases, as confirmed by a denser network structure as shown by SEM and increased gel hardness. Molecularly, the ethanol-treated samples exhibited spectra similar to that of konjac glucomannan, but with peak shifts at higher ethanol concentrations (e.g., 1633 cm^{-1} band shifting to lower wavenumbers), indicating effective solvent interaction [78].

Ethanol disrupts the three-dimensional network formed by konjac glucomannan and water but enhances the hydrophobic effect of konjac glucomannan, thereby increasing gel strength [78]. During soaking, ethanol molecules push water molecules to gather around the konjac glucomannan chains, reducing free water. This promotes larger entanglements and aggregates of the konjac glucomannan chains, resulting in increased gel strength. However, excessively high ethanol concentrations can lead to overly strong hydrophobic interactions, causing excessive chain aggregation and a decrease in gel strength [78]. Thermogravimetric analysis (TGA) indicated that ethanol hinders chain mobility and thermal decomposition, resulting in a higher initial thermal decomposition temperature for the gels [78].

Furthermore, for deacetylated konjac glucomannan, ethanol similarly enhances the aggregation of konjac glucomannan chains and creates a more anisotropic gel network. The random aggregation of deacetylated konjac glucomannan aggregates leads to structural reorganization, enabling the formation of low-alkaline konjac glucomannan

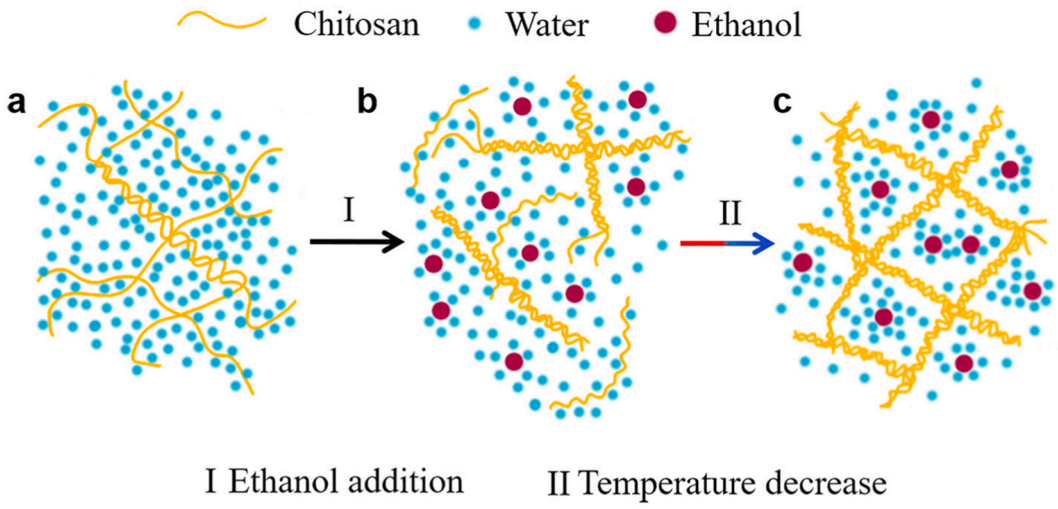


Fig. 4. Schematic illustration of chitosan sol formation with increasing ethanol concentration (ϕ_{EtOH}) and the sol-gel transition with reducing temperature. Reprinted from [75] with permission from Elsevier, Copyright 2022.

gels through ethanol soaking [79].

3.10. Curdlan

Research by Tao et al. [80] has demonstrated that incorporating erythritol (polyhydric alcohol) can improve the properties of curdlan gels. Their findings revealed that the gel hardness initially increased and then decreased as the erythritol concentration rose [80]. At low concentrations, erythritol weakens the interaction between curdlan and water, promoting the aggregation of curdlan molecular chains into a denser network structure with higher gel strength. However, excessive erythritol at high concentrations can hinder the aggregation of curdlan chains, impeding the formation of the gel network [80].

From a macroscopic perspective, scanning electron microscopy (SEM) images showed that the addition of erythritol altered the structure of curdlan gels [80]. Erythritol molecules formed hydrogen bonds with curdlan molecules, resulting in a denser network structure. Microscopically, the infrared spectrum of the erythritol-containing curdlan gel was consistent with that of the pure curdlan gel, indicating no change in the chemical composition. However, a redshift in the O—H vibration peak at 3268 cm^{-1} for the gel and a blueshift of erythritol indicated there is an interaction between erythritol and curdlan [80].

In addition, incorporating a certain concentration of erythritol improved the freeze-thaw stability of curdlan gels. This enhancement is attributed to the intermolecular crosslinking hydrogen bonds formed between the hydroxyl groups of curdlan and erythritol, reinforcing their freeze-thaw stability [80].

3.11. β-Glucan

Due to its excellent freezing-thaw stability, β-glucan gels are often used as carriers for proteins [81] or in the production of frozen foods [82]. Interestingly, the gel strength can be enhanced through freeze-thaw cycles, although excessive cycling may lead to dehydration and shrinkage [83].

Research by Lazaridou et al. [84] revealed that the addition of sorbitol (polyhydric alcohol) improved the freeze-thaw cycle stability of β-glucan gel. As the sorbitol concentration increased, the fibrous network structure of the frozen β-glucan gel became less pronounced and even disappeared at high concentrations. This suggests that sorbitol promoted the formation of a smoother and more uniform gel structure with nodal points, resulting in a more elastic gel [84].

Furthermore, with higher sorbitol concentrations, the thermal stability of the gels significantly improved. As the number of freeze-thaw cycles increases, the number and length of crosslinked bonds potentially increase, forming a network with higher-density ordered bonding regions. Consequently, the β-glucan gel acquired a more heat-resistant structure [84].

3.12. Carrageenan

Carrageenan is a water-soluble polysaccharide with excellent stability and gel-forming performance [44]. To expand its applications, researchers have explored the behavior of carrageenan in other solvents.

Sason et al. [28] investigated the changes in κ-carrageenan gels after soaking in different concentrations of ethanol (monohydric alcohol) solutions. Their study found that κ-carrageenan gel exhibited gel-like characteristics in both low-concentration (more effective solvent) and high-concentration (ineffective solvent) ethanol solutions. In low ethanol concentrations (<50 %), the counter ions of carrageenan were trapped within the gel, generating positive osmotic pressure that caused the gel to swell. In high ethanol concentrations (≥50 %), the low dielectric constant of these polar media promoted the formation of ion pairs between the ionized negative ions and counter ions due to dipole–dipole interactions [85], causing the gel to shrink and increase in strength. This type of change was not only related to the changes in the concentration of colloids but also to the nature, type, or quantity of system interactions, as well as the concentration of ethanol [28].

For ι-carrageenan, Yang et al. [21] confirmed through Kirkwood Buff's theory that ethanol promotes gelation by participating in the exclusion effect and combining with ι-carrageenan molecules. At low ethanol concentrations, the fractal dimension is large, allowing molecular freedom and decreasing gel strength [21]. Conversely, high ethanol levels reduce the fractal dimension and promote more rigid gel assembly via hydrophobic interactions [21]. Infrared spectroscopy indicated that hydrogen bonding between ethanol and carrageenan molecules, potentially at the sulfate positions [21].

As illustrated in Fig. 5, at high ethanol concentrations, ethanol addition induced the sol-gel transition in carrageenan by further promoting molecular aggregation and increasing gel strength [86]. Ethanol disrupts carrageenan–water interactions due to its high hydration ability, allowing carrageenan chains to aggregate. Hydrogen bonding between ethanol hydroxyls and carrageenan may also occur [86]. Moreover, increasing ethanol raises the critical gelling temperature from 50.8 °C to 61.3 °C [86]. Unlike acetone [87], ethanol does not cause gel collapse, likely due to its hydroxyl groups of ethanol participating in hydrogen bonding [86].

For κ-carrageenan, Nishinari et al. [88] explored gelation mechanisms with sorbitol (polyhydric alcohol) or xylitol (polyhydric alcohol) using DSC. Increasing sorbitol concentration raised the gelling temperature while decreasing the gel enthalpy change. In aqueous solutions, the hydrogen bonding between κ-carrageenan chains replaces that between κ-carrageenan and water, leading to double helix formation. Sorbitol molecules, by interacting with κ-carrageenan molecules through hydrogen bonding, weaken the hydrogen bonding between κ-carrageenan chains. Meanwhile, due to the stronger ability of sorbitol to interact with water, the addition of sorbitol also increases the chemical potential of hydrophobic groups in κ-carrageenan, resulting in enhanced hydrophobic interactions [88].

3.13. Other polysaccharides

In addition to the above-mentioned polysaccharides, there have been also studies exploring the impact of alcohols on complex polysaccharides. Sodkouieh et al. [89] used ethylene glycol, a polyhydric alcohol, as a crosslinking agent to facilitate the formation of a gel using tragacanth gum in an acidic environment. The presence of acidic protons in the reaction medium enhances the electrophilic properties of carbon in the carbonyl groups (ester and carboxylic acid carbonyl groups) in tragacanth gum. The oxygen atoms in ethylene glycol molecules, with their non-bonded electron pairs, react with the active carbonyl group. As alcohol molecules depart, a new ester group is formed. Similarly, another oxygen atom from the same ethylene glycol molecule reacts with another carbonyl group on the framework of tragacanth gum, resulting in crosslinking between tragacanth chains. Meng et al. [90] found that maltitol, another polyhydric alcohol, can enhance the formation of a curdlan/gellan gum composite gel. Maltitol effectively improved the gel strength and increased the gel temperature of the curdlan/gellan gum composite system, which can be attributed to the reduction in relaxation time and the stretching movement of hydroxyl groups. In addition, the involvement of maltitol led to a denser microstructure of the composite gel system.

4. Application

Research on the application of alcohol-induced polysaccharide gels is still in its early stages, primarily grounded in theoretical frameworks, thus paving the way for future applications. However, a significant portion of current research has already explored various industrial uses for alcohol-induced polysaccharide gels. In the food industry, the combination of polysaccharides and ethanol serves to impart functional

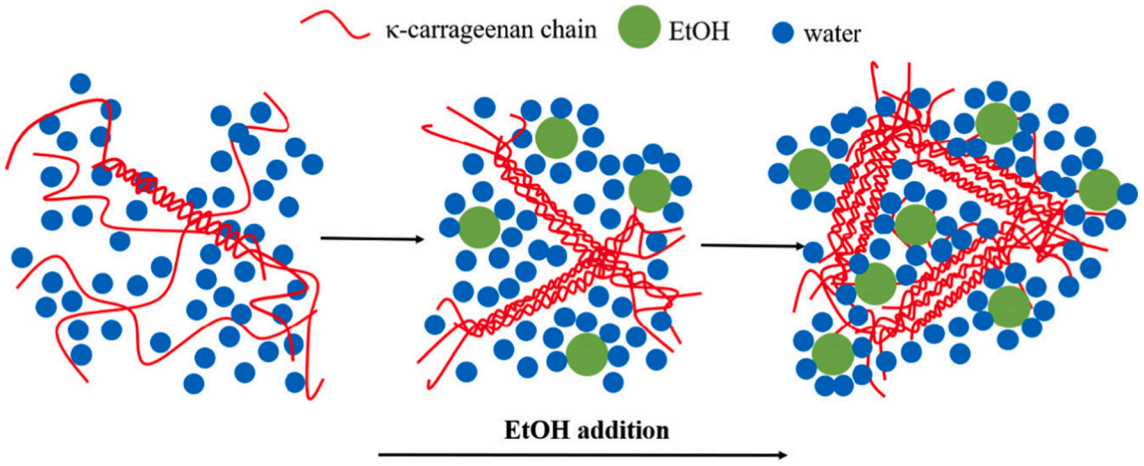


Fig. 5. Schematic illustration of the sol-gel transition of κ-carrageenan hydrogels as affected by ethanol addition. Reprinted from [86] with permission from Elsevier, Copyright 2018.

properties to products like beverages, enhancing stability and uniformity within food systems. Within the pharmaceutical sector, ethanol plays a crucial role in disinfection and sterilization processes. Furthermore, alcohol-induced polysaccharide gels can serve as effective drug carriers for drug delivery applications. Moreover, these gels can be transformed into aerogels through supercritical drying methods, finding applications in the material industry. The applications of alcohol-induced polysaccharide gels are exemplified below.

4.1. Medical applications

Alcohol-induced polysaccharide gels have been mostly explored in biomedical applications. Paul et al. [64] demonstrated that an ethanol-induced TSP gel exhibited potential as a drug-carrying hydrogel, showcasing notable antibacterial activity against *Escherichia coli*. Their study revealed that drug release from the gel increased proportionally with increasing TPS content, laying a foundation for its pharmaceutical application. Similarly, the ethanol-induced CPP gel is expected to be developed into injectable and self-healing drug-loaded gels with good mechanical strength, high shear thinning sensitivity and fast and efficient self-healing characteristics. As shown in Fig. 6, relevant data indicates that this gel has been proved to have the ability to encapsulate and transport hydrophobic and hydrophilic drug small molecules, which not only realizes the effective delivery of drugs, but also enhances the

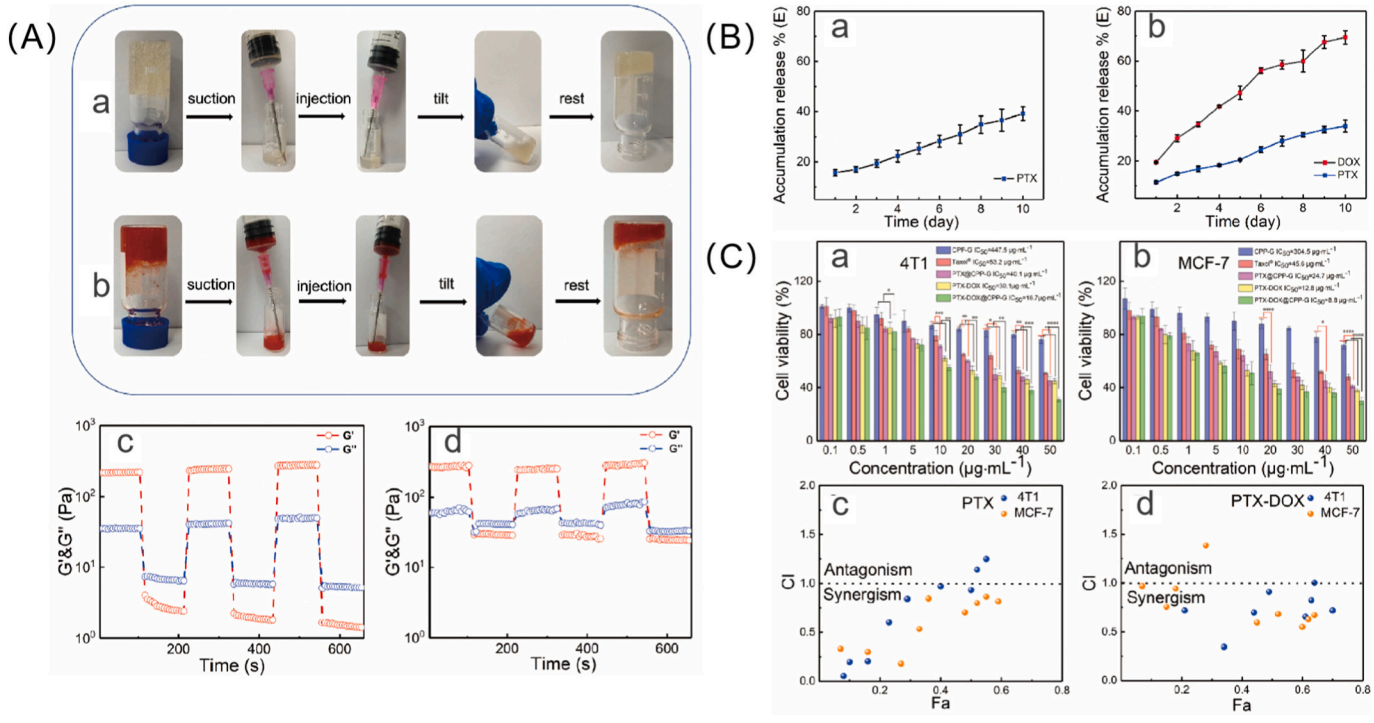


Fig. 6. (A) Injectability and extrudability of PTX@CPP-G (a) and PTX-DOX@CPP-G (b). Step-strain time sweep test of PTX@CPP-G (c) and PTX-DOX@CPP-G (d) under alternating high- and low-strain conditions (shear rate between 0.001 s^{-1} and 5 s^{-1}, 0.1 Hz, 37 °C; PTX-Hydrophobic paclitaxel; DOX-hydrophilic doxorubicin). (B) PTX release from PTX@CPP-G (a), PTX and DOX release from PTX-DOX@CPP-G (b) in PBS (pH = 7.4), at 37 °C. (C) In vitro antitumor activity of PTX@CPP-G and PTX-DOX@CPP-G on 4T1 cells (a) and MCF-7 cells (b) determined by MTT assays (The data are shown as mean ± SD, $n = 6$, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$); combination index (CI) analysis of CPP-G with PTX (c) and PTX-DOX (d) on two cells. Reprinted from [72] with permission from Elsevier, Copyright 2023.

anti-tumor effect of drugs [72]. Brunchi et al. [69] produced xanthan gum/chitosan nanofibers via electrospinning from a formic acid solution, offering a novel avenue for drug delivery applications. Employing a mixture of water and ethanol mitigated the need for direct exposure to formic acid. It is noteworthy that formic acid while possessing low toxicity, can elicit adverse effects such as optic nerve damage, skin irritation, renal dysfunction, or respiratory and circulatory impairment when present in significant quantities. Koop et al. [91] deeply studied the gel behavior of xanthan gum and guar gum in the dispersion containing buffer solution (potassium dihydrogen phosphate, potassium hydrogen phosphate), 1,2-propanediol, and ascorbic acid. The stability evaluation showed that after 12 weeks of storage, the concentration of ascorbic acid decreased by about 36.5 %, and the pH value stabilized between 4.5 and 4.7, which is reflected in the potential of this gel as the matrix of ascorbic acid preparations in medicine (antioxidant, stabilizing drugs and enhancing efficacy) and cosmetics (promoting collagen synthesis and antioxidant). Tkalec et al. [20] demonstrated that a high-methoxy pectin aerogel holds promise as a potent drug carrier, enhancing the bioavailability of nifedipine. The solubility of nifedipine in ethanol is higher than that in water. Therefore, after nifedipine is infiltrated into the ethanol-containing hydrogel, the aerogel obtained by supercritical drying can achieve high drug loading.

4.2. Food applications

Besides, biomedical applications, alcohol-induced polysaccharide gels have demonstrated their potential in food applications. Sason et al. [28] observed that immersing a carrageenan gel in ethanol alters the interactions within its gel system. This phenomenon offers a pathway for the creation of innovative alcoholic foods by regulating the concentrations of polysaccharides and ethanol. Additionally, Jiang et al. [67] revealed that the dissolution and gelation of high-methoxy pectin within an ethanol (acid) system contributed synergistically to the freeze-thaw stability of high-methoxy pectin lotion. As shown in Fig. 7, ethanol plays an important role in the stability of pectin lotion gel with different molecular weights, and endows pectin lotion gel with shear thinning behavior. Compared with urea, adding ethanol will prevent lotion from delaminating after three freeze-thaw cycles (Φ represents molecular weight; H/L represents high-methoxy pectin and low-methoxy pectin respectively; W/E represents water and ethanol respectively; 3/6 represents pH). This discovery is of great significance for improving the freeze-thaw stability of food-grade Pickering lotion stabilized by protein particles, and this lotion has potential applications in frozen food or functional food formulations.

4.3. Other applications

There has also been research carried out to expand the application spectrum of hydrogels wider than biomedical and food domains. Chen et al. [18] leveraged the solubility variance of TMG in diverse solvents to create TMG-hydrogels capable of modulating transmittance. These hydrogels exhibit distinct response profiles to ethanol, offering potential utility in areas such as anti-counterfeiting measures and information storage.

5. Conclusion and outlook

Polysaccharides, abundantly found in nature, serve diverse roles as constituents of biological structures, energy storage, protective agents, and regulators of protein structure and function, as well as cell-to-cell interactions and information transfer. Gelation represents a prevalent characteristic of polysaccharides, and polysaccharide gels offer remarkable properties such as elasticity and plasticity, which find wide-ranging applications.

Alcohol-induced polysaccharide gelation represents a promising avenue for the evolution of polysaccharide gels. This review aims to elucidate the role of alcohol in polysaccharide gelation and explore related mechanisms. From the examination of alcohol-induced polysaccharide gelation mechanisms, it becomes evident that alcohols within a specific concentration range can promote gelation or enhance gel strength, yielding elastic gels irrespective of polysaccharide gelation pathways.

Hydrophilic polysaccharides maintain stability in aqueous solutions by forming hydrogen bonds with water molecules, ensuring even

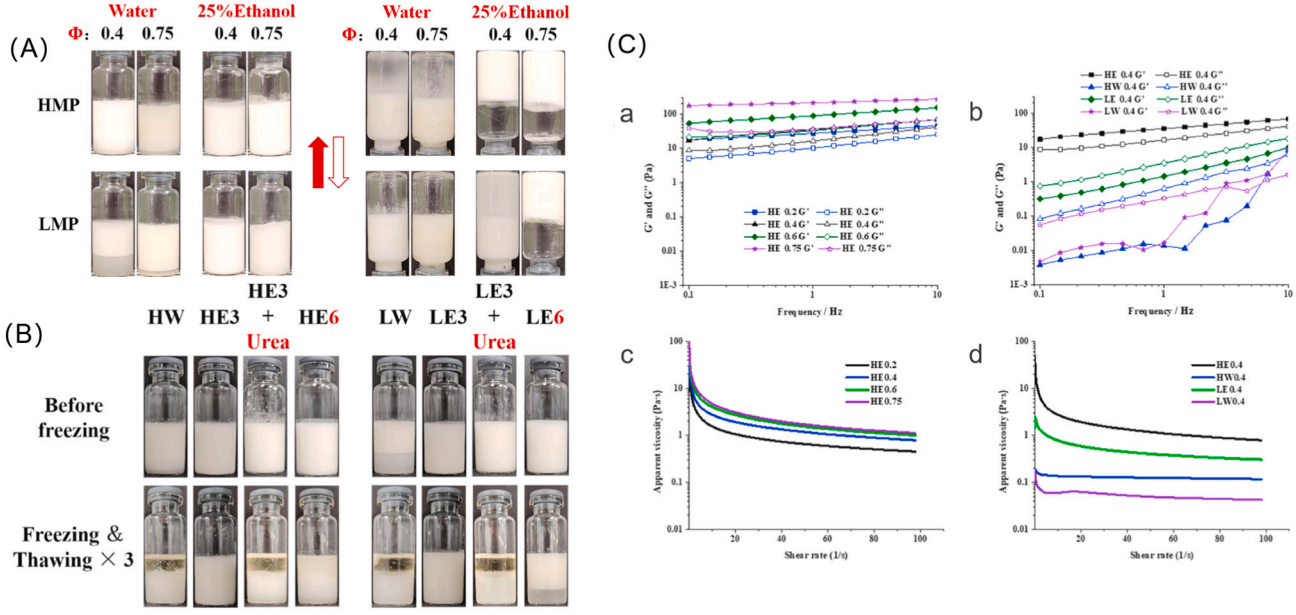


Fig. 7. (A) Visual appearance of upright and inverted HW, HE, LW, and LE, emulsions (only Φ 0.4 and 0.75 were presented). (B) Visual appearance of pectin emulsion (Φ 0.4) before and after 3 × freeze-thaw cycles. (C) Frequency sweeps for (a) HE emulsions with different Φ value (0.2–0.75), and (b) Pectin emulsion (Φ 0.4) of different pectin type with or without 25 % (*v*/v) ethanol (HW0.4, HE0.4, LW0.4, and LE0.4). G' and G'' are shown as filled and open symbols, respectively. Viscosity curves for (c) HE emulsions with different Φ value (0.2–0.75), and (d) Pectin emulsion (Φ 0.4) of different pectin type with or without 25 % (v/v) ethanol (HW0.4, HE0.4, LW0.4, and LE0.4). Reprinted from [67] with permission from Elsevier, Copyright 2021.

dispersion. However, the addition of alcohols like ethanol can disrupt this stability by altering the arrangement of water molecules due to solvent effects. This disruption may break the hydrogen bonds between polysaccharide and water molecules, and new hydrogen bonds can form between the alcohol and water molecules. This exposes the hydrophobic groups of the polysaccharides and enhances their hydrophobic interactions.

In the presence of high concentrations of alcohols, such as ethanol, alcohol molecules can interact with hydroxyl groups on polysaccharide molecules via hydrogen bonding, displacing water molecules surrounding the polysaccharides. This induces a change in the conformation of the polysaccharide molecules, facilitating closer proximity of their hydrophobic groups. Simultaneously, polysaccharide molecules transition from the aqueous phase to the ethanol phase, thereby decreasing their solubility.

The concentration of alcohol, and the method of alcohol addition, play pivotal roles in shaping the gelation process of polysaccharides. When alcohols facilitate the stacking of polysaccharide chains to form a network structure, there is likely a critical concentration threshold beyond which this effect is maximized. The immersion of polysaccharides in alcohols tends to enhance the properties of the resulting polysaccharide gel. Conversely, the direct addition of alcohols more commonly exerts a catalytic effect on gelation processes for polysaccharides. On the other hand, research into the effect of different types of alcohol has been extremely limited. Specifically for gellan gum, variations in alcohol chain lengths (ethanol, 1-propanol, 2-propanol/isopropanol) result in different flowability, with polyols often exhibiting a greater propensity to induce gel formation compared to single hydroxyl group-containing molecules.

Furthermore, the introduction of alcohols in alcohol-induced polysaccharide gelation has facilitated its widespread use, including applications such as reducing the production time of aerogels, developing novel food products, and expanding the utilization of polysaccharide gels in the medical field. However, current research on translating these theoretical concepts into practical production methods remains insufficiently comprehensive and detailed. There is a notable lack of exploration regarding practical applications.

Future research efforts should prioritize investigating the intricate relationship between process parameters and gel properties. Specifically, it is important explore a wide range of parameters (e.g., the type and concentration of alcohol and the way of alcohol addition, the structural variations of polysaccharides themselves such as the methoxy content of pectin, the type of carrageenan, and the deacetylation degree of chitosan, and the G/M-block composition of alginate, as well as process conditions such as temperature) and study more extensively based on these parameters to achieve desired alcohol-induced polysaccharide gels with desired properties for targeted applications. Accompanying this, it is also important to ensure that alcohols used in the development of alcohol-induced polysaccharide gels be cost-effective and non-toxic.

In addition, future research aims to enhance gel network structures through alcohol induction, such as in double-network (DN) hydrogels [92]. DN hydrogels consist of two interpenetrating polymer networks exhibiting significantly enhanced mechanical properties especially toughness [93]. Moreover, DN hydrogels can exhibit versatility functionalities, such as the regulation of inflammatory processes, promotion of collagen deposition, enhancement of angiogenesis, and accelerated wound healing [94]. Natural polysaccharides are increasingly employed in the synthesis of DN hydrogels considering dynamic bonds formed between polysaccharide chains [95], but the research on the use of alcohols to modify the gelation behavior and gel characteristics (e.g., pore size, structural compactness, and mechanical properties) of polysaccharide-incorporating DN hydrogels has been limited. Additionally, how alcohol induction can modify the gel network structure and provide more functionalities, such as realizing anisotropic structures and enhancing its energy dissipation mechanism, remains to be explored.

CRediT authorship contribution statement

Kexin Li: Writing – original draft, Visualization. **Xizhong Liu:** Writing – original draft, Visualization. **Fatang Jiang:** Resources. **Binjia Zhang:** Writing – review & editing, Resources, Conceptualization. **Dongling Qiao:** Writing – review & editing, Visualization, Supervision, Resources, Project administration, Funding acquisition, Conceptualization. **Fengwei Xie:** Writing – review & editing, Visualization, Supervision, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Dongling Qiao reports financial support was provided by National Natural Science Foundation of China. Dongling Qiao reports financial support was provided by Key Research and Development Project of Hubei Province. Fengwei Xie reports financial support was provided by Engineering and Physical Sciences Research Council. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgment

The authors would like to acknowledge the National 1Natural Science Foundation of China (32172240), Key R & D Project of Hubei Province (2022BBA004). F. Xie acknowledges the financial support provided by the Engineering and Physical Sciences Research Council (EPSRC) [grant number EP/V002236/3].

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