Chapter 10
Gelling Agents, Micro and Nanogels in Food System Applications

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Abbreviations

DSC	Differential scanning calorimeter
FTIR	Fourier transform infrared spectroscopy
GA	Gelling agent
NMR	Nuclear magnetic resonance
SEM	Scanning electron microscopy
TEM	Transmission electron microscopy
XRD	X-ray diffraction

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C. Egbuna et al. (eds.), *Application of Nanotechnology in Food Science, Processing and Packaging*, https://doi.org/10.1007/978-3-030-98820-3_10

10.1 Introduction

A gel is a material that has both solid and liquid characteristics, as well as elastic and liquid properties. They are made up of polymer molecules that have been covalently bonded to produce a tangled and interlinked molecular network that is submerged in a fluid state, which in the food chain is liquid [1]. When gels develop, a sol to gel transition occurs. Several gel forming components are used carefully to produce food gelling agents of adequate standard, notably the number of textural features that indicate the gelling process. The word "gel" is used by food technologists to characterize meals with a high moisture content that retain their shape after being removed from their vessel [2].

A variety of meals are offered in the form of gels in market, which provides consumers with convenience like jellies, jams, sweets, fruit and vegetable-like products are some examples to obtain the required or targeted parameter, one or more gelling agents are invariably used [1]. Generally, food hydrocolloids are used for this purpose. A wide range of proteins and polysaccharides are generated from natural sources of hydrocolloids. Gelling agents are now used in a wide range of industrial applications to accomplish different tasks such as thickening and stabilizing forms, gelling aqueous dispersions, emulsified suspended particles, limiting or minimizing gel contraction, and rising aqueous dispersions [3].

Gel formation entails the interaction of randomly distributed polymeric chains in suspension to create a 3-dimensional network with solvent in the spaces. Two or more polymer chains can create the related areas known as 'junction zones.' The development of these connection zones is essentially what the gelation process is all about [4]. The clusters of basic inter-chain connections into "junction zones," which forms the basis of a gel's 3-dimensional network which is the most frequent structure involved in hydrocolloid gelation. All these factors like the presence of ions, temperature and the structure of the hydrocolloids all have an effect on the physical configuration of the linking zones in the network. Ionotropic gelation, cold-set gelation and heat-set gelation are three important processes involved in gelation [5]. Alginate, carrageenan, and pectin are examples of such systems [6, 7]. Ionotropic

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gelation can be accomplished by diffusion setting or internal gelling agents. A scattering medium is formed when hydrocolloid particles are dispersed in warm water, which when cooled provides an enthalpically-stabilized chain helix resulting in traces of multiple chains and a 3-dimensional network. This process results in the formation of gel from agar and gelatin. Heat set gels necessitate the heating process to the gel. It is generally only used in meals when a temperature setting is necessary (e.g. the use of starch in sauces).

The heat setting approach includes native starch/protein unfolding/expansion followed by network rearrangement [8]. A food gel that retains its characteristic structural form can be seen as a high moisture 3-dimensional polymeric network that resists flow under pressure. A rigid or hard structure is formed when 3-dimensional structure of polymer chain are interlinked with water molecule inside it that hardens the structure [9].

10.2 Gelling Agents

Gelling agents (GA) are using in thickening and stabilizing the food additives such as jellies and sweets. Heteropolysaccharides and hydrocolloids make up a huge bulk of gelling polysaccharides. These gelling agents are used in sweets, salad dressings, jellies jams, marmalade, jujubes, yogurts, and different items are among the application. Numerous proteins, are utilized in the production of gels. These include numerous animal proteins and zein from maize such as gelling agent and whey proteins [9].

In general, certain colloidal proteins and polysaccharides of microorganism and Plant-derived medium solidifiers or stabilizers create a continuous 3-dimensional structure and serve as medium solidifiers or stabilizers. GA alters its diffusion properties and stiffen the gel medium. The diffusion rate is determined by the medium's viscosity, which is controlled by the concentration of the gelling agent and its physicochemical properties. Some gelling substances may change among liquid and gel forms based on temperature, which contributes to their attraction [10].

GA has a controlled temperature and pH range, and various gelling compounds may be removed by a different group of micro-organisms, requiring the use of various gelling agents. In recent years, traditional gelling agent supplies have been reduced prompting the development of novel gelling agents [11]. New research on gelation that can tolerate a wide range of temperatures and pressures has aided in the cultivation of newer microorganisms, including some extremophiles that could not otherwise be cultivated [11, 12]. Despite their importance in microbiology, essential gelling agents are not synthesized in a single location. Pectin, agar-agar, natural gums, starches and proteins are all commonly used gelling agents that may be generally divided into proteins and poly-saccharides [13].

10.3 Gel Formation Conditions

A basic polymer dispersion or particle suspension coupled with an externally controlled temperature or solution composition causes gel formation. The process of sol gel conversion generally includes particle or macromolecule aggregation, culminating in the creation of a network that spans the whole container volume [14]. Gelation processes can be generally categorized as physically or chemically induced. In the case of protein gels, to unwind the natural structure of proteins, a driving force is required which will be followed by an agglomeration process that indicates a 3-dimensional structure of clustered molecules connected by covalent or non-covalent bonds. The conditions for gel formation are primarily determined by the many physicochemical variables discussed in the following sections [15].

10.3.1 Temperature

Heat-induced gelling agents is most likely the significant and widely used procedure for producing gels. Gelation is a two-stage process in which molecules unfold or dissociate owing to energy input in the first step, exposing reactive sites. The second phase involves the interaction and aggregates of extended substances to produce greater molecular mass complexes. The initial stage of the Gel might be reversible, and the other stage is particularly irreversible [13].

10.3.2 Presence of Enzyme

The insertion of artificial covalent cross-links into dietary proteins is the basis for enzyme-induced gelation. Protein cross-linking reactions include those mediated by trans-glutaminase, polyphenol oxidase and peroxidase amongst many others [16].

10.3.3 Pressure

Because higher pressure may be used as a different process or in combination with another, significantly greater temperature; it allows for greater flexibility in changing the functional properties of molecules. High pressure encourages reactions that lower the total capacity of the medium and the pH of the medium becomes acidic under high pressure and water disassociate into the medium [17].

10.3.4 pH

Changes in pH caused by acid addition or microbial fermentation affect the net charge of the molecule, altering the attractive and repulsive forces between molecules as well as the interactions among molecules and solvent, i.e., hydration characteristics. Furthermore, salt solubility varies with the pH, which lead to formation of the gel. The fractal aggregation hypothesis might explain the mechanism of acid gel production [18].

10.4 Gel Formation Methods

There are two types of gel formation mechanisms: chemical cross-linking and physical cross-linking because of the creation of covalent bonds, the chemical cross-linking process enables persistent connection between chains. Because these inter-linked gelling agents are not treated after synthesis, they are referred to as irreversible gels [19].

Irreversible gels can be created by using two techniques either cross-linking throughout the polymerization stage or cross-linking the polymer chain helix. Cross-linking may be produced throughout polymerization by several polymerization methods such as condensation polymerization, free radical polymerization, photopolymerization, and plasma polymerization [20, 21]. In the process of cross-linking polymer chains, however, gel structures inter-link by the reactivity of side chain connected to molecular chains, which can also be done through radiation, cross-linking or photo and plasma cross-linking [22].

Physical cross-linking results in reversible gel with transient bonding within chains when temperature, pH, and solvent level alters. Transient connections such as hydrogen, ionic, hydrophobic association, coordination bonding hydrophobic association, helix formation and are widely known for creating reversible gels [23].

10.4.1 Gelatin and Carrageenan

While heating gelatin, it melts and solidified again after cooling down while with liquid/water addition it makes semi-solid colloidal gel by fractional reorganization of triple helices present in collagen while cooling by two steps orientation and condensation [24]. In order to prompt a reactive site polypeptide chain grosses an orientation that condense more chains to create a triple chain helix near the reaction site [25]. In the presence of potassium ions on cooling, carrageenan forms gels which promote both gelation and helix formation [26].

10.4.2 Whey and Soy Proteins

Whey proteins is basically globular proteins by following events: denaturation of proteins, aggregation of denatured proteins, strand formation by aggregates and finally network formation from strands [27]. Gel is formed via heating soybean flour in the presence of calcium and magnesium which introduces clusters of denatured molecules of protein [28].

10.4.3 Milk and Egg Proteins

Casein protein in milk is bonded together via hydrophobic bonds and salt conduits. Casein is hydrolyzed into gelation in the presence of caseino macro-peptide [29]. While heating egg protein (albumen and yolk), gelation occur by denaturation of egg proteins and after that aggregation of denatured proteins [30]. Table 10.1 shows different gelling agents and their applications.

10.4.4 Alginates and Pectins

Alginate gel formed at low pH (less than 4) by the adding polyvalent cations. Guluronic acid gives active binding site for the attachment of cations. The type of polyvalent cations defines the strength of gel such as Barium ion > Strontium ion > Calcium ion > magnesium ion [36]. The properties of gel from pectin defines by the degree of esterification. High methoxyl pectin gels are formed only in the presence of sugars and polyols at pH from 3.0 to 4.5 while High methoxyl pectin gels are formed only in the presence of Calcium ions [37] (Fig. 10.1 represents the Food applications of proteins).

Table 10.1 Proteins that are utilized as gelling agents

Gelling agents	Gelling agent source	Binding blocks of Gelling agents	Applications of gelling agents	Ref.
Gelatin	Animal skin and bones	Proline and glycine	Gelling agent in jelly and jam	[31]
Whey protein	Casein curd	Lactoglobulin	Gelling agent and thickener in food industry	[32]
Soya proteins	Soybeans	Conglycinin	Heat set gel	[33]
Egg proteins	Egg	Albumen	Gelling and thickening agent	[34]
Zein	Corn	Prolamin	Gel coated candy and nuts	[35]

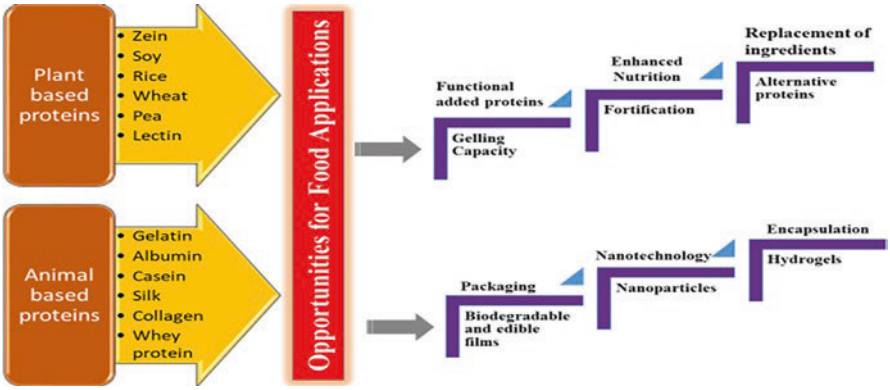

Fig. 10.1 Food applications of proteins

10.4.5 Agar and Starch

Agar gelation is a reversible process because of hydrogen bond. Hot agar on cooling turn into gel by aggregation of helices while starch heated above the limit in the presence of large water cause solubilization of amylose and after cooling this gel is formed [38].

10.4.6 Guar and Gellan Gum

Guar gum has mannose and galactose and form gels by cooling in the presence of salts via aggregation of helices [39]. At high temperature gellan gum turned into disordered coil while after cooling turns into double helix [40].

10.5 Characterization of Gel

Formation of gel is primarily conversion from a solid to a gel form in which elasticity altered rapidly while solid characteristics develop simultaneously. In many other words, during gel formation, continuous and discontinuous stages interact. As a consequence, assessing the viscoelastic (rheological) properties of materials is required, which is frequently achieved through a variety of experiments. Table 10.2 shows the non-rheological ways to evaluating characteristics of gel [9].

The geometry of the sample or the instrument used have no effect on the essential tests. Parameters such as stress/strain are commonly assessed at large deformations and are generally examined by uni-axial density and tension. To identify the basic factors and mechanisms involved in gelling and to define gel texture, features and

Table 10.2 Methods for the measuring the characteristics of gel

Measurement Type	Used Instrument	Measurement parameters	Applications	Ref.
Structural characterization	DSC	Rate of heat flow	Polyvinyl alcohol and gellan blend film	[41]
	XRD	Analysis of particle size	Food nano delivery system	[42]
Microscopic characterization	SEM	Components structural arrangement.	The size, number and distribution of particles in gel	[43]
	TEM	Structural distribution of particles.	Studies of mixed gel characteristic	[44]
Molecular characterization	NMR	Conformation changes.	Determination of particles structural features.	[42]
	FTIR	Molecular structure/ functional group identification	Determine components	[43]
			Infrared spectra	

rheological aspects of starch gels have been researched generally on functional studies [45]. Rayleigh scattering is a technique for determining the size of molecules in suspension. It can enlighten about the various agglomeration mechanisms that happen in gel formation. Dynamic light diffraction may be used to analyze the rheology of gelatin dispersion by measuring the diffusion co-efficient of dispersed molecules and the efficient viscosity of the gel [46].

The presence of a molecular network affects rheological properties. Measurements may be made on a gel under compression to demonstrate the correlation among strain and stress. Gel rheological measurements are commonly divided into small and big deformation testing small deformation tests commonly indicate structure, whereas huge deformation trials examine the condition and properties of a gel [47].

10.6 Nanotechnological Application of Gelling Agents

The most important thing for the food industry is to deliver quality, soft food and healthy foods. Foodstuffs with texture modification tends to be more demanding. In the production of soft foods, nanotechnology offer an appreciable input [48]. In order to soften the food, some conventional techniques can be used such as freeze-thawing, enzyme impregnation [49], high-pressure processing, pulsed electric fields and sonication [50] while some unique techniques are used to preserving the color and flavor such as microfluidics, 3D printing electrospinning and electro-spraying [51]. Moreover, lipids, proteins and carbohydrates are simple constituents in texture modified food. While heating, globular proteins unfold and denature and increase the viscosity of fluids while further heating, globular proteins assemble and form aggregates, fibrils and network chains of gels [52]. Polysaccharides are used to condense and stabilize the fluids as gelling agents [40] while gums and starches are used as thickening agents in enzymes and colorants [53].

10.7 Microgels and Nanogels

Microgels and nanogels are among the three types of hydrogels, the third being macrogels according to their size.

Microgels are polymer chains intra-molecularly crosslinked in small dimensions (from hundreds of nanometers to some micrometers) dispersed in colloidal solutions. Their structure is very close to solid particles, once their surface is well established [53, 54]. These kinds of gels have a high capacity for water content, large surface area, and an interior network useful for drug delivery systems. Biopolymer-based microgels are of great interest for food, drug delivery and tissue engineering systems because of its roles such as biodegradability, nontoxicity, and relatively low cost, beyond being abundant in nature.

Nanogels are innovative systems on the nanometer-scale of great potential in nanomedicine, nutraceutics, pharmaceutics, and bionanotechnology. Their internal structure is similar to that of microgels; however, there is variation in size (up to 100 nm) and responsiveness leading to several advantages. The nanoscale size improves the solubility of hydrophobic drugs, increases drug accumulation in tumors, makes the therapeutic agents very stable against enzymatic and chemical degradation, and decreases cytotoxic side effects. The nanogels helps in drug encapsulation, large surface area, and stable interior network structure [55].

10.7.1 Methods of Synthesis of Microgels and Nanogels

10.7.1.1 Methods of Synthesis of Microgels

Essentially, microgels may be prepared by physical or chemical crosslinking of hydrophilic polymers. Physical crosslinking is reversible upon external stimuli once it involves non-covalent attractive forces such as ionic and hydrophobic interactions. Biodegradable physically crosslinked microgels can encapsulate drugs, cells, and proteins and release them by their degradation process.

The production of microgels can be divided into homogeneous nucleation and polymerization, emulsification, or complexation methods. Basically, microgel is obtained from homogeneous solutions; in the second, aqueous droplets are dispersed in an oil phase followed by crosslinking; and, in the last, two water-soluble polymers are put together to form complexes with each other [56]. Homogeneous nucleation and polymerization methods are important to describe because of their relevance. These methods consist of mixing water-soluble monomers with crosslinking agents and an initiator. This type of process can be performed by emulsion polymerization using a water-soluble monomer, a radical initiator, and surfactants in an aqueous medium. To produce core-shell microgels, this emulsion step is followed by a second polymerization to form the shell. Microgels can also be made

by water-in-oil heterogeneous emulsifications from the combination of a continuous oil phase, with oil-soluble surfactants and droplet emulsions of water-soluble polymers.

10.7.1.2 Methods of Synthesis of Nanogels

Different synthetic routes have been used for the development of nanogels that can be classified into two main categories: Chemically crosslinked nanogels and physically crosslinked nanogels, according to their crosslinked structure. The chemically-cross-linked nanogels present covalent bonds linking the polymer network and making them stable, rigid, and permanent, while the physically crosslinked nanogels present non-covalent bonds, which are weaker linkages, thus allowing sol-gel phase transitions as a result of the environmental stimuli [57]. The main methods of synthesis of nanogels are divided into two groups, one of which is known as crosslinking polymerization and involves techniques based on simultaneous polymerization and crosslinking, using monomers or their mixtures as substrates. The other group covers methods based on the crosslinking of macromolecules from polymer precursors which are polymers such as amphiphilic copolymers capable of forming nanogels by self-assembly or polymers with many reactive sites which can be directly used for chemical crosslinking.

Apart from these two groups, nanogels can also be prepared by controlled aggregation by physical self-assembly of hydrophilic polymers and template-assisted fabrication of nanogel particles.

The first method is a simple, and low-cost process conducted in dilute aqueous media that implies controlled association of hydrophilic or amphiphilic polymers linked by hydrogen bonds, van der Waals forces, hydrophobic forces, and/or electrostatic interactions.

The second method involving photolithography or micro-molding techniques, photolithography, uses exposure to ultraviolet (UV) radiation of UV cross-linkable polymers with direct collect of fabricated particles by the dissolution of the substrate in water.

The crosslinking of polymer precursors provides excellent properties relevant to many applications, especially when using ionizing radiation for crosslinking. It is known that the reaction of intra-molecular crosslinking can be obtained by using water-soluble polymers in dilute solutions and a cross-linker capable of reacting with the chain's functional groups. The ionizing radiation is an alternative method of intra-molecular crosslinking initiation which avoids the addition of any additives, allowing the reaction to be carried out in a pure polymer-solvent system, and in this way, one can produce nanogels for biomedical applications free from monomers, crosslinking agents, or surfactants, eliminating the purification step [58].

10.7.2 Applications of Microgels and Nanogels in the Food Industry

10.7.2.1 Application of Microgels

There are many important application of microgels in food system depending on intended goal. Some of their usefulness include for texture control, encapsulation, as delivery system and protection agent [59, 60]. Microgels have the ability to increase their viscosity properties by swelling in an appropriate solvent [61]. With the need to replace excess fats from food, microgels have seen application in the food industry as it helps improve texture and mouth feel of foods [61]. As an emerging encapsulation agent, microgels have in recent years been experimented for their ability to protect and release bioactive compounds such as macronutrients, phytochemicals, nutraceuticals, vitamins, minerals, antimicrobials, antioxidants, enzymes, probiotics and flavors, in a controlled manner [61]. Microgels importance as an encapsulating agent is arguably because of some negative sensory properties linked to many bioactives such as unstable chemical nature with potentials to undergo physical or chemical changes in the gastrointestinal tract that may negatively impact bioavailability and bioactivity of the bioactive compound. In other words, microgels can be designed to serve as good delivery system or also designed to prevent food spoilage.

In biomedical or pharmaceutical applications, microgels can be explored when stability is of concern or degradation, or even their ability to dissolve according to the purpose of the application that may be for wound dressings, tissue engineering, contact lenses, drug delivery systems, and others [62]. Among the several applications of microgels, delivery of chemotherapy for cancer treatment is one of great research interest. Although chemo treatments are effective in treating tumors, they have many limitations such as low specificity which is the main reason for their toxicity [63].

10.7.2.2 Application of Nanogels

Just like microgels, nanogels have found application in the food industry for food/nutrient encapsulation, delivery and protection of bioactive compounds. One of the widely used nanogel is protein nanogel obtained from milk proteins such as casein and whey proteins. The use of nanogels is on the rise because of the need to develop products that will resist degradation/spoilage or products with enhanced property of controlled release of bioactives for target delivery. Nanogels are used for the delivery of poorly water-soluble substance due to their single construction formed by a hydrophobic core, micelles, and hydrophilic exterior. A study by Hu et al. [64] explored the encapsulation of curcumin using acylated ovalbumin nanogels (AOVA) produced through acylation modification and heat-induced self-assembly as novel delivery system. Their study found that at gastrointestinal conditions, curcumin

encapsulated in AOVA nanogels displayed 93.64% higher encapsulation efficiency with slower sustained release compared to native ovalbumin (NOVA) nanogels [64]. This exploration is necessary because curcumin is hydrophobic in nature and poorly absorbed [65, 66].

In biomedical and pharmaceutical applications, nanogels present a great potential of use in chemotherapy, diagnosis of diseases, the release of bioactive substances and vaccines, antimicrobials [64, 65], cell culture systems, contrast agents, biocatalysis, in the generation of bioactive scaffolds in regenerative medicine [65], besides being able to act as sensors, nanoreactors, nanodevices, superabsorbents, and biomimetic mechanical devices, such as artificial muscles. The interpenetrating network structure of the nanogels allows better encapsulation of drugs that can be delivered by various routes of administration such as oral, nasal, intraocular, and pulmonary pathways. It is also possible that nanogels entrap two drugs simultaneously, an important feature for the co-administration of two or more anticancer drugs.

10.8 Conclusion

Gels are elastic material, and the stability of food gelling agents is important for commercial application. As a result, recognizing the solid to the gel conversion is important for creating gelled materials. A number of elements, including as material type, concentration, time, pH, temperature, and so on, can greatly impact the gel formation process and, as a consequence, its consistency, which is the most essential feature for customer approval. The presence of cations, as well as the presence of hydrocolloids and proteins, influences the structure of gel. Gelling agents are used in the manufacture of restructured foods and innovative forms of foods products that have acceptable mechanical integrity, a prolonged storage value, good nutrient content, and customer acceptance.

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