

Review

Green Materials for Gel Formulation: Recent Advances, Main Features and Applications

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Abstract: Biogels (hydrogels, oleogels, and bigels) are structured systems used as delivery vehicles for bioactive substances. The objective of this study was to provide an updated view of green materials used as biogels, discussing the different aspects related to their formulation. An overview of the application possibilities of these gels in different areas, such as food, cosmetics, pharmaceuticals, and medicine, is reported. Furthermore, an evaluation of the profile of studies using biogels was carried out in the last decades (1980–2023), showing the advances in knowledge about these materials in different application domains. Additionally, a consideration of future demands regarding studies involving biogels from a technological and process engineering point of view is highlighted.

Keywords: green materials; bigel; hydrogel; organogel; bioactive delivery

1. Introduction

In recent years, the interest in environmentally compatible processes and the use of green products have increased the demand for research in the academic and industrial sectors. In regard to the world's biodiversity, the need to preserve natural resources has driven society and governments to change their way of thinking. Today, biodiversity is no longer a "heritage of humanity" but a "concern of humanity" [1,2]. The sustainable use of biodiversity and awareness of its preservation is fundamental in industrial operations and in the preparation of new products today. The current scenario seeks the smart and sustainable use of products and processes from renewable sources (Figure 1), reducing the environmental impact while helping the global economy.



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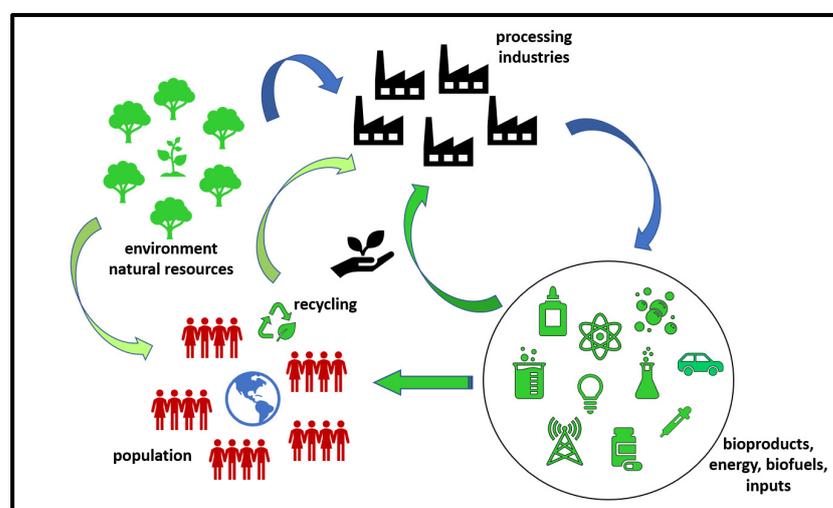


Figure 1. Representation of green logistics.

In this context, green materials have been seen as a viable alternative for many diverse applications in the chemical, food, cosmetic, and pharmaceutical industries. In this class are biogels, which are materials constituted of bioactive compounds derived from food with great health benefits, such as antioxidant, anti-inflammatory, antifungal, antimicrobial, and anticancer properties, among others.

Gels are semi-solid systems consisting of a liquid (nonpolar or polar solvent) and a gelling agent (defined as gelator or organogelator). They have a three-dimensional network of gelator molecules, which allows for the entrapment of the liquid phase, resulting in a viscoelastic gel [3,4]. They are two-phase systems formed by means of covalent crosslinks of network constituents (chemical gels) or by means of non-covalent interactions, amongst them hydrogen bonds, hydrophobic interactions, and ionic interactions of network constituents (physical gels) [5–7]. According to IUPAC [8], a gel is a “non-fluid colloidal network or polymer network that is expanded throughout its whole volume by a fluid”.

In rheological terms, a gel is a material that does not flow and presents elastic attributes of solid and viscous attributes of a liquid. The gel point occurs in the so-called *equilibrium modulus*. The determination of this point is made through monitoring over time of the properties that characterize the elasticity of the material, called *storage modulus*- G' (which represents the stored energy), and the property that characterizes the viscosity of the material, called *loss modulus*- G'' (which represents the strain energy). Generally, before gelation, G'' is greater than G' . The gelation point occurs when the values of G' and G'' become equal. After a certain induction time, the value of G'' becomes negligible, and G' increases rapidly until reaching a steady state level, with its value much larger than G'' , indicating a more elastic response. The value of the G''/G' ratio tends to be <0.1 . The higher the value obtained for the G' modulus, the stronger the gel formed [7].

A gel is called a **hydrogel** when the liquid constituent is a polar solvent (water), and it is called an **organogel** when the liquid constituent is an organic solvent, which includes alcohols or hexane and also oils. In this last case, the system formed is defined as an oleogel. Likewise, a subdivision can be made with organogelators, which may be high molecular weight (HMW) or low molecular weight (LMW) gelling agents (Figure 2). Polymers are the traditionally more common class of gelators. In this group, proteins, polysaccharides, carrageenan, alginate, and starches can also be cited as widely studied gelators. Moreover, among the biopolymers considered GRAS (generally regarded as safe) solvents, there are propylene glycol, pectin, ethyl cellulose, and hydroxypropylmethyl cellulose (HPMC), among others. In parallel, among LWN gelators, special attention has been given to triacylglycerols (TAG), monoacylglycerol (MAG), and fatty acids due to their bioactive characteristics [4,9]. In addition to the bioactive, biofunctional, and bionutritive characteristics, fatty acids are considered renewable sources of chemical products since several products can be obtained from reactions and formulations using these compounds [10–12]. Furthermore, expanding the list of possibilities, there are also the **bigels**, which are a class formulated from the junction of hydrogel and organogel, presenting particular characteristics compared to individual gel systems. The type of interaction between the constituents of the gel acts directly on the formation of the matrix of the gel obtained and, therefore, on the appearance and structure of the gel formed. According to the constituents present in the system, the formed gels will present specific and distinct viscoelastic and thermodynamic characteristics due to the three-dimensional structures resulting from each mixture [9]. Gels obtained through chemical interactions are generally resistant, as they are mainly formed by covalent bonds (primary forces), while gels resulting from physical interactions are less resistant, as they are maintained through different secondary forces, such as hydrogen bonds, hydrophobic interactions, or van der Waals forces. On the other hand, physical gels tend to be thermally reversible, a behavior not observed in chemical gels [13]. Although it is well accepted that physical and chemical forces act and control the structuring of the gel network, a precise description of the mechanism that permeates gel formation, as well as the influence of solvent-gelling agent interactions on gel formation and gel behavior remain poorly understood [14–16]. In the case of hydrogels, different mechanisms aris-

ing from stimuli-sensitive (physical, chemical, and biological/biochemical) to hydrogels can explain the formation of the gel [17]. However, in the case of organogels: (i) the full understanding of the organogelation mechanism; (ii) the knowledge of the behavior and interactions between the gelator and different solvents; (iii) the relationship between the chemical structure of the gelator and the gelation process; and (iv) the effect of process conditions on the physical behavior of the resulting gels are still unknown [14–20].

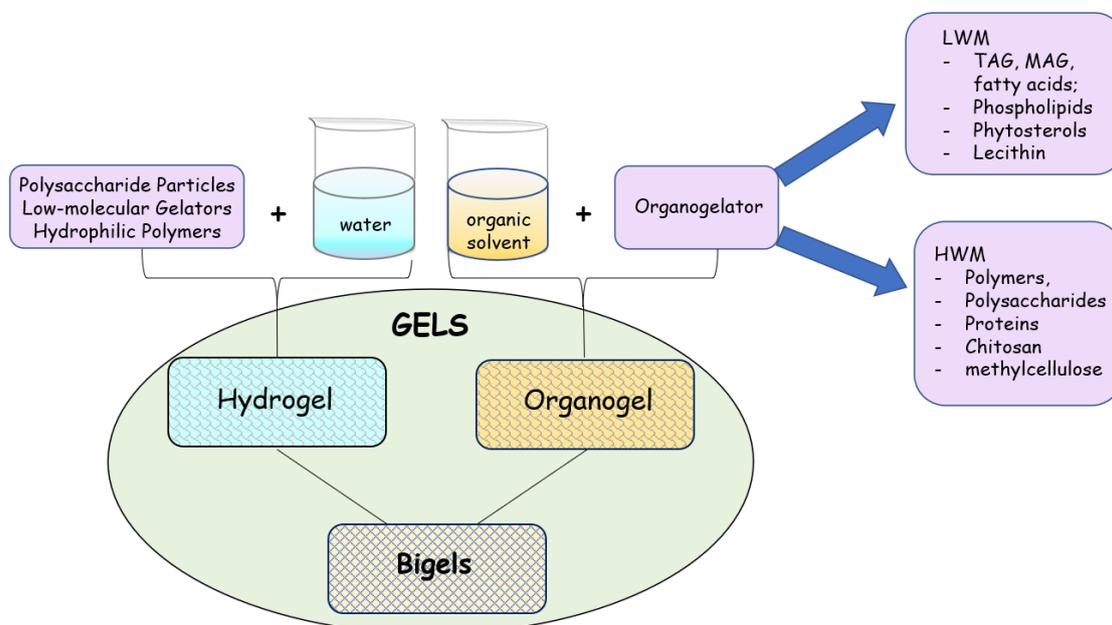


Figure 2. Classification of types of biogels based on solvents and structuring agents used.

Regarding the physical–chemical aspects, the synergy between the gel components is an essential factor since the formation of these systems strictly depends on the particular condition that exists between the solubility vs. insolubility of the gelling molecule within the solvent and the resulting molecular interactions. Without this condition, there is no gel formation. In other words, this particular condition exists because of the possibility of two opposite situations occurring: (i) systems where there is high solubility between the constituents, with high interaction of the solvent with the gelator, resulting in the formation of a solution, instead of a desired gel system, and (ii) systems with low solubility between the constituents where there will be the formation of precipitates [21,22].

Extensive reviews have discussed the formulation of hydrogels/organogels and their applications. They are well reasoned and present relevant information for the sector [2,23–27]. Their contributions are mainly focused on the formulation of gels for drug delivery and specific active ingredients. On the other hand, the comprehensive review of biogels and notable advances for different application sectors from the perspective of green chemistry are still absent. When it comes to green chemistry, green materials are defined as materials derived from renewable sources or from the processing of agricultural crops, non-toxic, which degrade into harmless products, whose processing reduces or eliminates the use and production of hazardous substances [28–30]. In this sense, gels (whether hydrogels, organogels, or bigels) formed from biocompounds of natural or renewable origin, which are non-toxic and have a reduced impact on human health and the environment, can be considered green gels. In this scenario, there are biogels with effective bioactivity and biofunctionality.

When it comes to the industrial production of materials from the perspective of green chemistry, the environmental issue goes beyond reducing toxic waste. In this regard, keeping in mind the environmental impacts of the processes that involve the formulation of new materials and at the same time having the purpose of composing this extremely ordered and

well-defined gel structure, the choice of the ideal gelator, in physical–chemical/rheological terms, which is sustainable and economical, thus becomes an item of fundamental importance. Sagiri and Rao [31] indicate six features that should be considered when choosing an ideal oleogelator (indicated schematically in Figure 3).

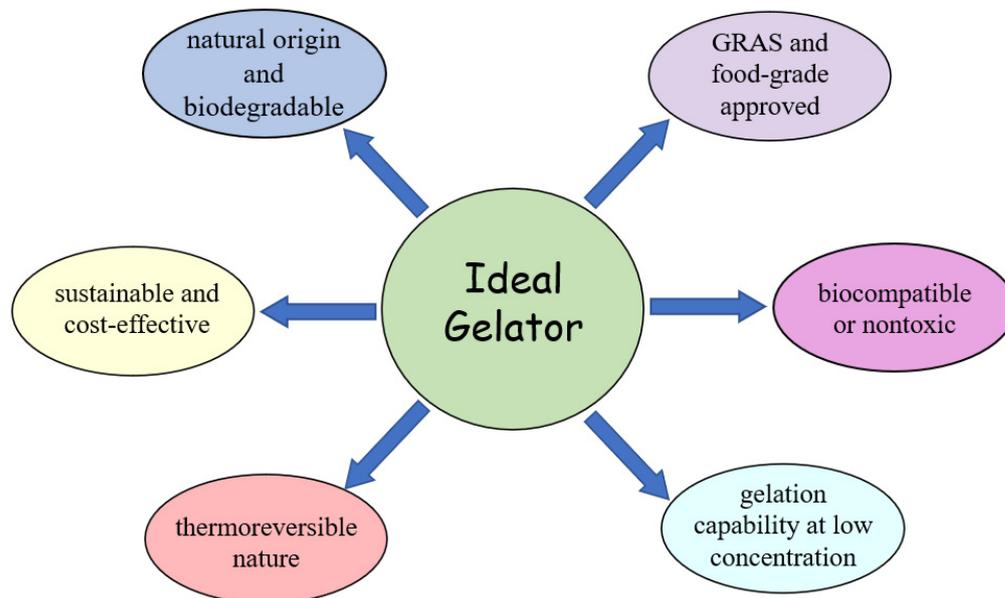


Figure 3. Ideal gelator (according to [31]).

Although, up to now, little has been explored from this point of view, green gels have great applicability and a range of possibilities that go beyond the mixture of biocompounds. Investigations have been carried out to evaluate biocompatible and efficient materials capable of acting in specific circumstances. Studies have also revealed that biogels, whether originating from bio-sourced materials or renewable products, have great applicability at an industrial level. Being the object of study by several researchers, the formulation and discovery of new biogels have grown in recent years, presenting promising results in several areas of activity. In this sense, this review presents a comprehensive description of different classes of gels, their main applications, and recent discoveries, focusing on the sustainable use of materials and products in obtaining green gels. Technological challenges and issues that still exist in the formulation and production of these materials are also highlighted and discussed.

2. Hydrogels

Hydrogels are hydrophilic, three-dimensional frameworks which are capable of holding large amounts of water and biological fluids [32]. This characteristic makes them an excellent material to be used as drug delivery vectors, biosensors, and carriers or matrices for cells in tissue engineering [33]. Table 1 presents a summary of the main characteristics of hydrogels, a general comparison with organogels and bigels, and highlights the advantages, disadvantages, and molecules involved in each gel.

Table 1. Main aspects, characteristics, and bioconstituents of hydrogels, organogels, and bigels.

Gel Type [Refs]	Hydrogels [5,6,33–37]	Organogels [38–58]	Bigels [38,59–74]
Definition	Water trapped in a 3-D network using a hydrophilic gelling agent (hydrophilic polymer)	Organic liquid trapped in a 3-D network by using an organogelator (LWM and HWM)	Organogel dispersed in hydrogel system (O/W); hydrogel dispersed in organogel system (W/O); or bi-continuous systems

Table 1. Cont.

Gel Type [Refs]	Hydrogels [5,6,33–37]	Organogels [38–58]	Bigels [38,59–74]
Advantages	<ul style="list-style-type: none"> - high hydration ability - cooling effect - good spreadability - high biocompatibility and bioactivity with biological organisms - tunable biodegradability and porous structure - high softness and flexibility 	<ul style="list-style-type: none"> - topical deliveries of hydrophobic drugs - ultra-low adhesion for antifreeze and antifouling uses - last longer than hydrogels due to the boiling point of organic solvents being higher than that of water - greater flexibility as it contains components with adjustable hydrophobicity - thermoreversible 	<ul style="list-style-type: none"> - ability to deliver both hydrophilic and lipophilic actives - easy preparation and easy spreadability - improvement in the permeability of drugs through the skin - cooling, moisturizing, and emollient effects - easily adapted consistency and drug release rate
Disadvantages	<ul style="list-style-type: none"> - the liquid phase (water) can be frozen at temperatures below zero, causing a decrease in softness and bio-affinity - low durability gel in dry environments due to significant evaporation of the liquid phase - low mechanical strength and fragile nature - difficulty in delivering hydrophobic drugs 	<ul style="list-style-type: none"> - difficulty removing after application to the skin due to the oily nature of organogels - lack of precise understanding of the thermodynamic and kinetic factors that control the stability of gelling fibers - more sensitive to microbial proliferation and hydrolysis of systems containing the ester group 	<ul style="list-style-type: none"> - they may not be thermoreversible since, at higher temperatures, they are unstable - need for an emulsifier to avoid phase separation - the formulation procedure and operating conditions influence the gel properties
Bio-sourced Molecules	water, biopolymers (polysaccharides and proteins), natural polymers (such as gelatine or agar)	fatty acid, edible oils, waxes, fatty alcohols, carbohydrates, vitamin derivatives, peptides, steroids, and derivative molecules	Water, edible oils, lipids, biopolymers, others arising from the structures of organogels, and hydrogels
Examples of Biomolecules/ Biomaterials used in gel formation	Gelatin, agar, chitosan, sodium alginate, cellulose, hyaluronic acid, pectin, dextran, and their derivatives	stearic acid, 12-hydroxystearic acid, palm oil, sesame oil, soybean oil, canola oil, rice bran oil, cetyl alcohol, stearyl alcohol, ethylene glycol, propylene glycol, glycerol, among others.	guar gum, gelatin, sodium alginate, xanthan gum, agar, protein, pectin, starch, maltodextrin, olive oil, sunflower oil, castor oil, soybean oil, among others

The networks of hydrogels are composed of homo or copolymers and may present chemical crosslinks (tie-points, junctions), or physical crosslinks, such as entanglements or crystallites [32]. Due to existing interactions, physical hydrogels are not homogeneous systems, as the structures obtained by clusters of molecular tangles or hydrophobically or ionically associated domains create heterogeneous regions [75].

Hydrogels are responsive to various stimuli such as heating, pH, light, ionic strength, electromagnetic radiation, and chemical agents and may also show a swelling behavior dependent on the external environment and chemical composition [76–84]. Depending on the degree of ionization, chemical compound, or any other external stimulus, the behavior, osmotic balance, ionic strength, network structure, and swelling properties of the hydrogel can be changed, making these materials attractive gels to be applied as biosensors, controlled drug release systems, self-healing materials, superabsorbent materials, and hemostasis bandages [85–91].

There are numerous applications of hydrogels in the medical, pharmaceutical, and cosmetic sectors [92–98]. They have been used as drug delivery [99–103], scaffolds [104–108], actuators [109–113], biosensors [114–118], ophthalmic [119–122], tissue engineering [99,123–125], wound dressing [126–128], analytical separation, and detection [129,130] materials, among others. The great differential of these materials is their properties (water solubility, spreadability, miscibility) that make them a highly used gel. In addition to their porosity and soft consistency, the three-dimensional and hydrophilic structure of hydrogels enables the absorption of a large amount of water in their interstitial space, which provides physical characteristics similar to natural living tissue. Moreover, the fact that they are non-toxic, biocompatible, versatile, and easy to handle makes them interesting not only in the administration of nutrients/drugs and tissue engineering but also in food sectors and bioadsorbent systems [92,131,132].

A great variety of hydrophilic polymers have been used in the formulation of hydrogels. The main classes consist of natural polymers (polysaccharides and proteins) and synthetic polymers containing hydrophilic functional groups (such as $-\text{COOH}$, $-\text{OH}$, $-\text{CONH}_2$, SO_3H , amines, and R_4N^+ and ether) [75]. Depending on the intrinsic properties of the polymers, a synergistic effect of properties is observed in the hydrogel formed [133–136]. This characteristic can be addressed to modify or adjust the formulation of materials with specific needs, mainly with regards to the medical and pharmaceutical areas. Carvalho et al. [137] present an interesting review of the use of polysaccharides as biomaterials for tissue engineering, focusing on advances involving technologies and materials for the repair and regeneration of an injured brain. In contrast, the use of hydrogels is not limited to medical and pharmaceutical applications. Yang et al. [138] report the use of mixed polysaccharide–protein systems in the manufacture of multistructured food gels, including hydrogels. As noted in the examples cited, a wide variety of biopolymers have been employed in the formulation of hydrogels, some of which are illustrated in Figure 4.

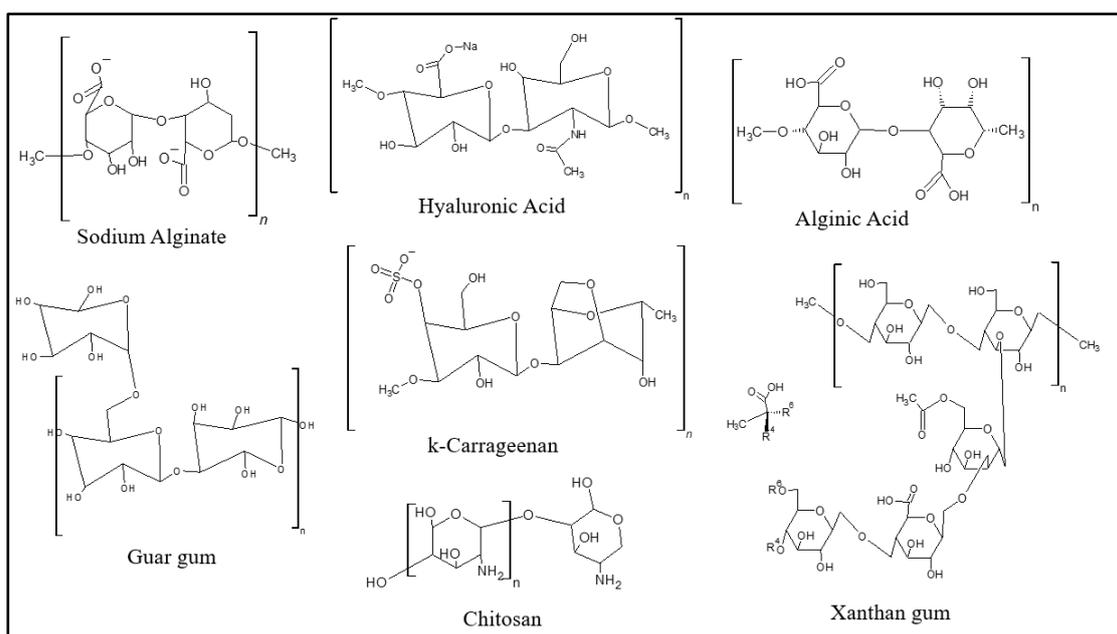


Figure 4. Molecular structure of some biopolymers used for hydrogel preparation.

3. Organogels

Organogels are defined as semi-solid systems whose organic liquid phase is entrapped within a thermoreversible three-dimensional gel network. In these systems, gelator molecules are present in low concentrations (lower than 15 wt%), which makes them interesting from an industrial point of view [9,139,140].

Organogels have structuring bonds similar to those observed in hydrogels, including weak interactions, such as Van der Waals forces and hydrogen bonds [141–143]. Nonethe-

less, the intrinsic properties of organic solvents and gelators make them more stable systems in thermodynamic and kinetic terms. These characteristics are assigned to two events: (i) the interaction of opposing forces related to the partial solubility of the organogelator in the continuous phase [144] and (ii) the spontaneous formation of a fibrous structure that has a low energy state [145].

In practical terms, these systems appear to be quite multifunctional, with applicability in several sectors, such as the food industry, where organogelation is favorable for inhibiting the migration of oils and fats, trapping these components in the matrix, reducing their movement and thus decreasing the occurrence of the fat bloom phenomenon. In addition, because they exhibit behaviors that reproduce the texture of trans fat, they are of great importance in this replacement, as they can also act in the encapsulation of bioactive and functional lipophilic components such as carotenoids, flavorings and essential unsaturated fatty acids, with the aim of increasing their stability, since they are commonly susceptible to oxidation in foods [21]. Moreover, studies of organogels applied to food are the most varied [133,146–149] due to the large number of food-derived compounds that enable their use in the formulation of these gels and also due to the bioactivity and biofunctionality of these biocompounds, as is the case of TAG/MAG/fatty acids, proteins, carbohydrates, applied in the formulation of different matrices.

In the pharmaceutical industry, their use refers to the placement of drugs as delivery vehicles, which may occur through different routes of administration, such as topical, transdermal, parenteral, and oral [31]. Diverse literature can be found on the application of organogels in the pharmaceutical sector. Tankov et al. [150], for instance, developed systems containing two types of mesoporous silica particles incorporated in oleogel for dermal delivery of quercetin. Among the results obtained by the authors, the formulated oleogels presented excellent biocompatibility and a lack of hypersensitivity to quercetin. In another study, Wang et al. [151] formulated oleogels derived from glycerol monostearate for lipophilic bioactive delivery and observed that oleogels formed with 10% GMS showed denser network structures and high stability, preventing the degradation of astaxanthin. In another study, organogels formulated with lecithin were evaluated for the delivery of anti-inflammatory drugs against sprains, strains, and contusions [152]. In this study, the authors observed that the presence of lecithin in the new gel formulation promoted a faster and significantly more marked therapeutic effect compared to that of gel without lecithin.

At the same time, in the cosmetic industry, organogels play an important role both in the thickening and structuring of hydrophobic liquids in formulations to minimize syneresis on the surface (thus improving their rheological properties) and in the distribution of functional ingredients conveyed in moisturizers and coloring agents (improving the delivery profiles to the skin's surface). In this application, organogels are presented precisely to accommodate and maximize the partition of the active ingredient in the skin tissue for the best delivery of bioactives due to better chemical stability since when using the same ingredients, the organogels promote skin permeation to a greater degree [21,153]. This type of application is quite common in anti-aging formulations or in creams intended for cellulite treatments, where permeation of the gel containing the active ingredient is desired and where a modulation of structures and rigidity more appropriate for each case is necessary [153].

This primordial structuring ability based on organic nature, chain symmetry, and molecular weight, as well as characteristics that take into account issues of saturation and molecular chain length, result in distinct microstructures, as well as different physicochemical characteristics. Some examples of well-known and widely used structuring agents are polyethylenes, polyalkylene glycols, polyesters, those of synthetic/mineral origin, and commonly those of natural origin, for example, fatty acids and alcohols such as 12-hydroxystearic acid, wax esters such as carnauba wax and candelilla wax, phospholipids such as lecithin, monoacylglycerols (glyceryl monopalmitate and monostearate), and phytosterols such as β -oryzanol and ceramides [154,155].

Table 2 shows organogel systems reported in the literature with examples of solvents and structuring agents used for their formation. This table also presents the use of some constituents that allow for the incorporation of water-insoluble bioactives, generating greater bioaccessibility and bioavailability of these assets, as is the case of the system explored by Yu et al. [156] who developed an oleogel with high-loading and bioavailability of curcuminoids for use in food grade.

Table 2. Examples of organogel systems formed from different pairs of organic solvents and structuring agents.

Solvent	Organogelator	Oil Content % (w/w)	Ref.
Amaranth oil	mixture of palmitic and stearic acid	88–93	[157]
Canola oil	candelilla wax (CDW) and glycerol monostearate (GMS)	90	[158]
Canola oil	Ethylcellulose	90	[159]
Canola oil	hydroxypropylmethyl cellulose (HPMC)	94	[160]
Coconut and peanut oil	whey protein isolate	95	[161]
Coconut, canola and corn oil	Monostearin	95	[156]
Grapeseed oil	GMS, palmitic acid, Compritol 888, and stearic acid	85	[162]
Macadamia oil	GMS	>85	[163]
Palm oil	Beeswax	>95	[164]
Palm oil	whey protein isolate	12–20	[165]
Peanut oil	stearic acid/stearic alcohol	75–95	[166]
Soybean oil	sugarcane wax (SCW) and candelilla wax (CLW)	96–99	[42]
Soybean oil	carnauba wax (CRW)	85–95	[167]
Soybean oil	Ethylcellulose	88	[168]
Sunflower oil	lecithin and α -tocopherol	75	[169]
Sunflower oil	Gelatin (pork skin)	20	[170]

The literature also describes that, like sugars, substances such as ethylene glycol, diethylene glycol, propylene glycol, 1,4-butane diol, and 1,6-hexane diol for example (group of polyols), have interesting properties such as resistance to tension, tearing, cutting, abrasion, adhesion, and dimensional stability [171]. Such mechanical properties can be explained by the greater compatibility of the flexible polar polyester segments with the rigid polar segments, which causes a slower phase separation, making them relevant in the composition and distribution of the polymeric matrix [171]. However, the disadvantages of this system configuration refer to the ester group being more sensitive to hydrolysis and microbial proliferation. An alternative is the use of glycols or longer chain diacids such as palmitic acid (C16) to increase resistance to hydrolysis, resulting in a greater hydrophobic portion of the polyester polyol, also leading to the formation of the desired oil gel.

In order to minimize the resistance to hydrolysis, additives, such as dispersions of vinyl polymers like polyvinylpyrrolidone in the polyester polyol mass, can be used in order to obtain greater hardness at the same density, more uniform cellular structure, and better dimensional stability [171]. An alternative has been proposed by Gandolfo et al. [172] to adjust the physical–chemical, rheological, thermal, and textural properties of oleogels. These authors mixed stearic acid with fatty alcohols of different chain length (C16 to C22) at a concentration of 5% (w/w) in sunflower oil, producing an oleogel of better quality than the oleogels formed by individual gelators. Another example of the use of gelator blends was studied by Kamali et al. [156], in which amaranth oil oleogel was formulated with a mixture of palmitic and stearic acid. In this work, the use of the mixture of fatty acids as a gelator promoted the creation of a structured gel richer in solid contents than the reference sample. Kim et al. [157] studied blends of candelilla wax (CDW) and glycerol monostearate (GMS) in the preparation of canola oil oleogels and verified that the ratio of

60:40 of CDW:GMS presented better results, producing oleogels with a harder texture and lower melting temperature.

4. Bigels

The idea of elaborating defined materials to obtain bigels is quite new compared to other gel structures. The literature mentions the work by Almeida et al. [72] as the first study on the elaboration of these materials with pharmaceutical applications. In this study, the authors evaluated formulations of the hydrogel/organogel mixture using different oleogels mixed with polyacrylic acid hydrogel, and found bigels with an improved moisturizing effect, making them promising candidates for topical formulations. Bigels are uniform semi-solid systems obtained by mixing hydrogel and organogel at a given temperature and appear as a single gel when visually observed [173,174]. The peculiarity of bigels comes from their ability to deliver hydrophilic and lipophilic active agents at the same time.

Bigels bring together in a single gel interesting properties of each original gel; that is, they have characteristics arising from both aqueous and oily phases and have better properties than gels in their original forms [68]. The great advantage of bigels is their greater stability, in addition to being easy to prepare and not requiring large amounts of surfactants to be formed [69]. The greater stability of the bigels is associated with the formation of extra-fine colloidal dispersions, which are the result of the immobilization of the original gel phases in a three-dimensional gel structure [72]. In addition, among other advantages of these gels, the following can be mentioned: they are easy to spread and absorb through the skin, they have refreshing, emollient, and moisturizing effects due to the enrichment of hydration in the stratum corneum, as well as easy washability after administration on the skin [38,60,70–72,74,175,176] (other qualities are listed in Table 1). Depending on the method of preparation, structural organization, characteristics of the original gel, and organogel/hydrogel ratios, the bigels can be presented as (i) organogel dispersed in a hydrogel system (O/W); (ii) hydrogel dispersed in an organogel system (W/O); or (iii) a bi-continuous system [38] (Figure 5). The latter may have greater structural complexity depending on the organogel/hydrogel ratio and methodology for obtaining the bigel [69]. The preparation method has a strong influence on the type and structure of the bigels due to intrinsic factors in gel formation, such as oleogel content, homogenization temperature, shear level and time, and gelling state of each phase [177]. The balance between these factors will promote the most appropriate training for a given application.

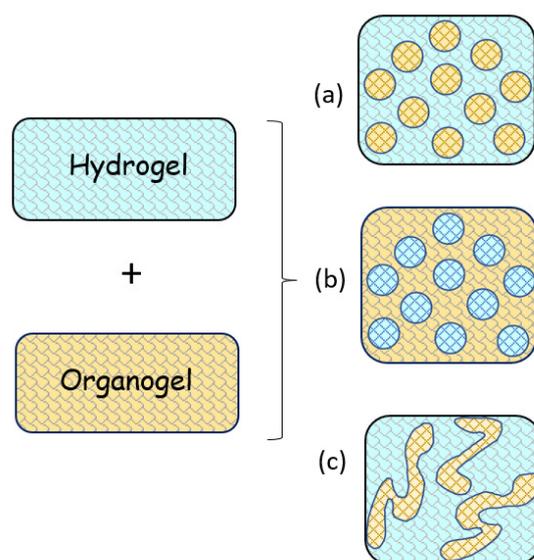


Figure 5. Representative illustration of different types of bigels: (a) organogel-in-hydrogel, (b) hydrogel-in-organogel; (c) bi-continuous.

The literature cites several studies of the applications of bigels in the food, cosmetics, pharmaceutical, and medical sectors. Some of them are listed in Table 3. This is due to certain functional characteristics of bigels, such as greater thermal stability, firmness, electrical insulation, and greater ease of permeation of the bioactive due to its emollient properties [38,69,70,177].

Table 3. Some bigel systems developed for the food, cosmetic, pharmaceutical, and medical sectors.

Solvent	Oleogel Organogelator	Hydrogel Hydrogelator	Incorporated Active	Application	Ref
Almond oil	Sorbitan monosterate	Carbopol	Ketoprofen	drug delivery	[66]
Caprylic + capric triglycerides	Compritol	Carbopol	Ibuprofen [47]	periodontitis	[178]
Castor oil	Tween 80	Sodium alginate	Essential oil of <i>Bidens tripartita</i>	antifungal treatment	[179]
Corn oil	glycerol monoglyceride	Dispersion of κ -carrageenan	β -Carotene	food bioactive delivery	[180]
Fish oil	Beeswax	Carbopol	Coenzyme Q10	cosmetic	[181]
Fish oil	Beeswax	Carbopol	Imiquimod	transdermal	[182]
Fish oil	Beeswax	Sodium alginate, Hydroxypropyl-methylcellulose	Imiquimod	drug delivery	[59]
Linseed oil	Tween 80	Sodium alginate	Metronidazole	periodontitis	[183]
Liquid paraffin	Cholesterol	Carbopol	-	cosmetic	[72]
Olive oil	Beeswax	Hydroxyethyl-cellulose	Povidone-iodine	transdermal	[184]
Rapeseed oil	glycerol monoglyceride + beeswax	Xanthan	Curcumin	food bioactive delivery	[185]
Rice bran oil	Stearic acid	Tamarind gum	Moxifloxacin	drug delivery	[186]
Rice bran oil	Stearyl alcohol	Agar	Ciprofloxacin hydrochloride	drug delivery	[187]
Sesame oil	Sorbitan monostearate	Carbopol	Metronidazole	drug delivery	[74,188]
Sesame oil	Sorbitan monostearate	Gelatin	Ciprofloxacin	drug delivery	[189]
Sesame oil	Sorbitan monostearate	Guar gum	Ciprofloxacin	drug delivery	[190]
Soybean oil	Sorbitan monostearate, cetyl alcohol, lecithin-pluronic	Hydroxypropyl-methylcellulose	Diltiazem hydrochloride	drug delivery	[64]
Soybean oil	Stearic acid	Agar + gelatin	Metronidazole	drug delivery	[67]
Soybean oil	glycerol monoglyceride + beeswax	Gellan gum	Lycopene	food bioactive delivery	[191]
Sunflower oil	Sorbitan monopalmitate	Gelatin, whey protein	Metronidazole	drug delivery	[60]
Sunflower oil	Sorbitan monopalmitate	Guar gum, acacia gum, xanthan gum	Metronidazole	drug delivery	[192]
Sunflower oil	Sorbitan monopalmitate + tween 80	Guar gum, acacia Gum	Metronidazole	drug delivery	[193]
Sunflower oil	Sorbitan monopalmitate	Polyvinyl alcohol, polyvinyl pyrrolidone	Metronidazole	drug delivery	[194]
Sunflower oil or mineral oil	candelilla wax or 1,2-hydroxystearic acid	Sodium polyacrylate	Vitamin E	food bioactive delivery	[195]
Sweet almond oil	Sorbitan monosterate	Alginate	Cetavlon	drug delivery	[196]
Sweet almond oil	Sorbitan monosterate	Carbopol	-	Cosmetic	[72]
Isopropyl palmitate + soya lecithin	pluronic lecithin	Hydroxy propyl methyl cellulose	Ketoprofen	drug delivery	[62]

Interesting studies have been developed for the investigation of the physical–chemical characteristics of these systems. Loza-Rodríguez et al. [197] formulated a bigel consisting of oil-beeswax oleogel and hydrogel, with a high potential for drug delivery through the skin. In this work, differences in each type of gel produced were pointed out, with the evidence that the bigel, although visually presented as a homogeneous phase, in reality, is a heterogeneous system. Analyses performed by fluorescence microscopy indicated the presence of two phases in the bigel structure, with the hydrogel phase incorporated into a continuous matrix of oleogel (Figure 6).

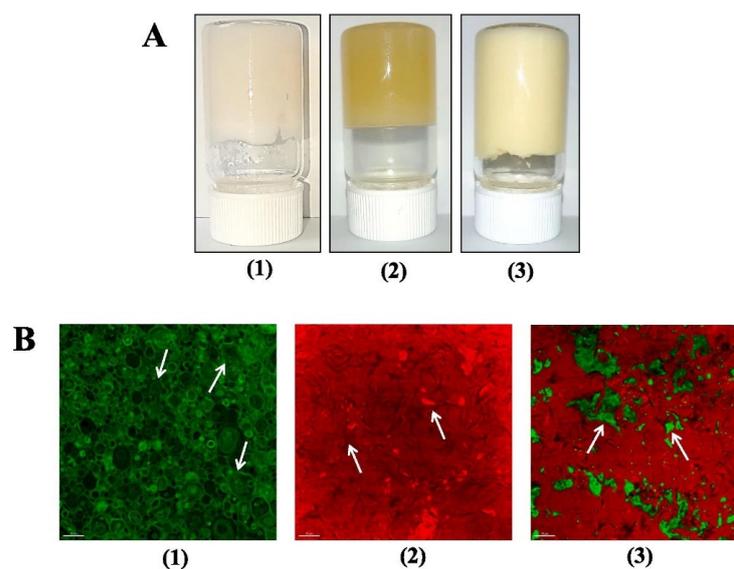


Figure 6. Hydrogel (1), oleogel (2), and bigel (3) obtained using hydrogenated soy phosphatidylcholine, olive oil, beeswax, and α -tocopherol as constituents. (A) Visual appearance of the materials, (B) Fluorescence micrographs (10 μ m) [197], with permission from Elsevier Ltd., Copyright 2023 Elsevier.

Two of the questions involved in the formulation of all these gels (hydrogels, organogels, and bigels) are (i) knowing the proportion of the constituents and (ii) what structure one wants to obtain and for a given purpose of application. In this sense, the study of phase equilibrium is presented as an important tool in the analysis of the different possibilities of gel elaboration [9]. The importance of knowing the phase behavior of these systems lies in defining the application of the gel as a function of the amount of the constituent used, together with the functionality of the product obtained. Literature involving the study of the phase equilibrium of these systems is still very scarce. In a recent study, Corredor-Chaparro et al. [198] showed the formation of HPMC bigels formed by organogelator system (sorbitan monostearate: polysorbate 80), sesame oil, and hydrogel. In this work, the authors illustrate the region of existence of the bigel (Figure 7) and describe the bigel as a uniform and brilliant color system, without lumps, and smooth and creamy to the touch. In another study, Cortés et al. [199] evaluated the use of two non-ionic surfactants derived from castor oil (Kolliphor ELP and Kolliphor RH40) that are commonly used in pharmaceutical formulations in the evaluation of phase diagrams with water, sunflower oil, and ethanol as cosurfactant. In the study, the use of Kolliphor RH40 exhibited a larger microemulsion (ME) area than that formulated with Kolliphor ELP, along with other regions of emulsion (E) and phase separation (2P), with a region of gel-like behavior similar to lipogels and gel microemulsion, characterized by the region indicated as L9 in Figure 8. In both cases, without studying the phase's behavior for the entire range of compositions, knowledge of the limits and existing possibilities for a given mixture of solvent (s) + structuring agent (s) + bioactive (s) would be restricted to the range of pre-prepared compositions, and perhaps it would not be possible to visualize the biphasic regions so clearly.

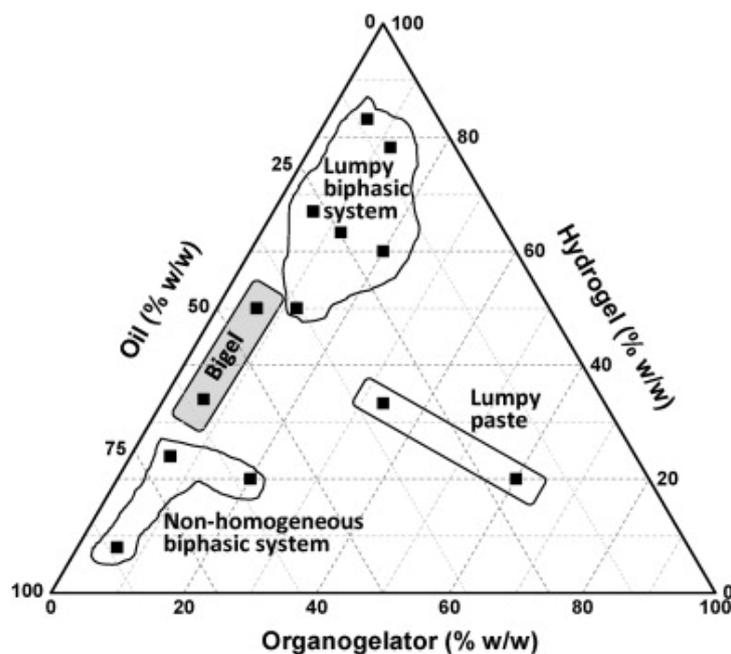


Figure 7. Ternary diagram for the hydrogel system (constituted by HPMC 10% aqueous dispersion), organogelators (sorbitan monostearate/polysorbate 80), and sesame oil [198], with permission from Elsevier Ltd., Copyright 2023 Elsevier.

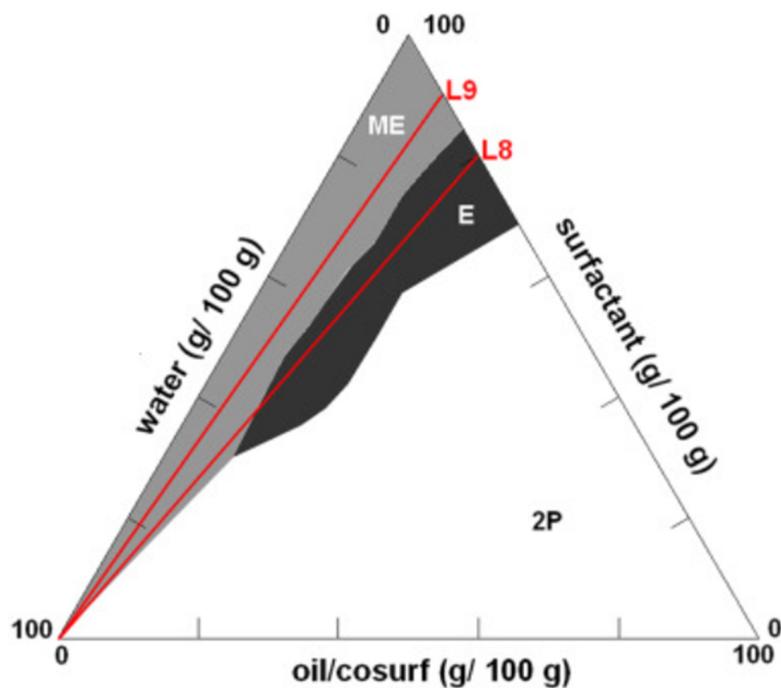


Figure 8. Pseudo-ternary phase diagrams for systems Kolliphor RH40-water-oil, where the lines L9 and L8 are indications of the ratio 9:1 and 8:2 of surfactant: (oil + cosurfactant), respectively, and ME, E, and 2P correspond to microemulsion, E: emulsion, 2P: two phases [199], with permission from Elsevier Ltd., Copyright 2023 Elsevier.

5. Concluding Remarks and Future Challenges

In recent years, the concern and need to use biocompatible products have increased the search for new materials and processes. The use of clean technologies with green materials has been the basis of several research groups. Linked to this, there are biogels,

made up of biomaterials with great applicability in the food, cosmetics, pharmaceutical, and medical sectors (some of which are listed in Tables 1–3. Bioactive raw materials play a crucial role in the design and synthesis of multifunctional gels for applications in the various production axes.

Research in different databases (Science Direct and SciELO) was performed to evaluate the advance in knowledge of these materials using the terms bigel, hydrogel, and organogel as keywords, considering the main sectors of application: food, pharmaceutical, cosmetic, and medical (simple and combined search). Figures 9 and 10 illustrate the distribution of literature by application area and the annual evolution of scientific papers, respectively. A total of 20,066 scientific papers were found in the 1980–2023 period (until July), with great advances in the last decades.

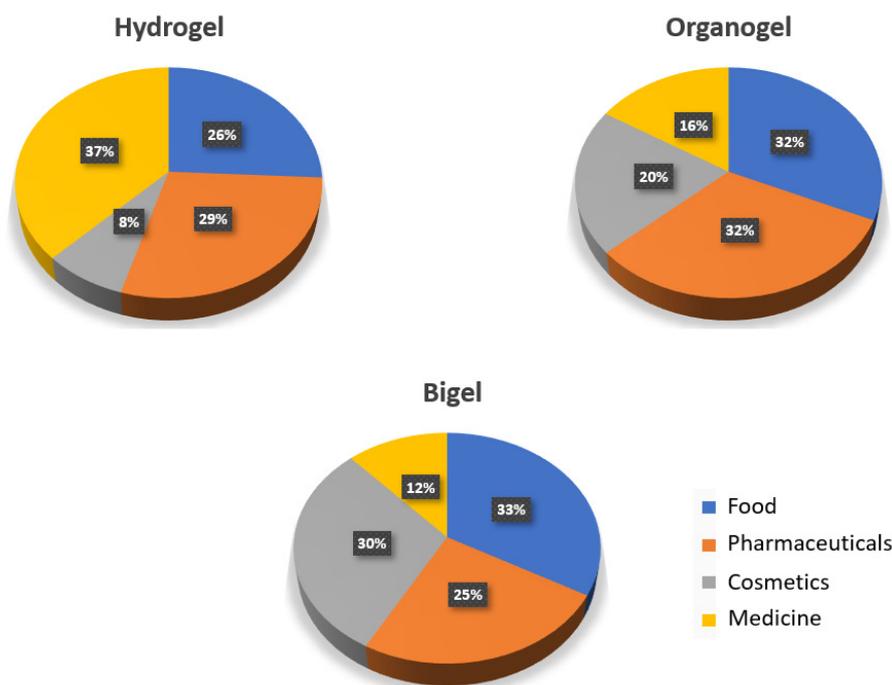


Figure 9. Distribution of scientific papers by application area between 1980 and 2023 (until July).

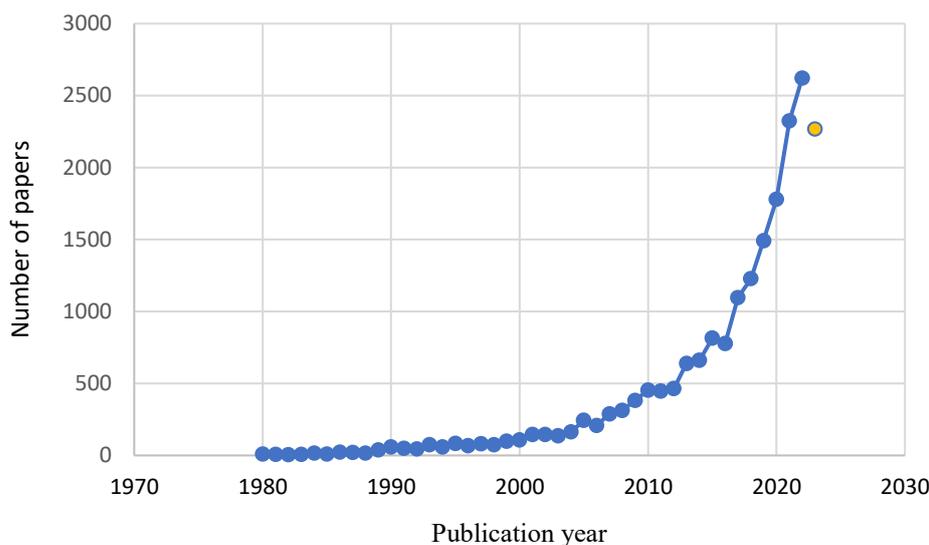


Figure 10. Annual evolution of scientific papers on biogels between 1980 and 2023 (until July, last circle in yellow).

The vast majority of works were focused on the elaboration of hydrogels (96.5%), which is expected since the discovery of the others is more recent. Among the scientific papers evaluated, separated by area (Figure 9), most of the papers are related to the medical sector (12–37%), followed by the pharmaceutical (25–32%), food (25–33%) and cosmetic (8–30%) sectors. In recent years, research involving gels has increased exponentially, increasing from 815 in 2015 to 2267 papers published in the first seven months of 2023 (Figure 10). The increase in studies focused on the formulation of biogels broadens the possible applications, and the results obtained so far are quite encouraging.

Although the growth observed in studies with green gels is evident, knowledge of fundamental and specific points in the formulation of these materials is still the key to their implementation in the industrial sector. In general, studies are still needed in the design of new multifunctional molecules with specific applications, mainly regarding the issue of simultaneous delivery of bioactive substances with synergistic or non-synergistic effects.

In specific terms, while presenting numerous studies and reviews on hydrogels, due to the great importance and applicability of these materials, investigations still need to be carried out regarding the issue of stability and mechanical strength. New hydrogels that are more stable and have better mechanical strength are needed and remain an important direction for research. Furthermore, although a wide variety of polymers have been used for hydrogel formulations, among the constant concerns are the biocompatibility and biodegradability of the polymers used and that their networks make new systems effective and easy to obtain. In addition, special attention must also be paid to the synergistic behavior that may result from the combination of two polysaccharide networks, requiring fundamental studies to better understand the physicochemical, mechanical, and biological properties of each system. As far as organogels are concerned, one of the important points to be unraveled concerns the clear description of the mechanism of gel formations, as well as the effect of solvent–gelator interactions on the formation process and behavior of the gel formed. Furthermore, because there is a wide variety and structures of gelators that have been used in the formation of organogels, the complete and interconnected knowledge of the thermodynamic and kinetic factors that control the stability of gelling fibers continues to be a question that needs to be answered by researchers in the field.

Another important aspect to be highlighted is the characterization of biogels not only in rheological terms but also in physical–chemical and thermodynamic terms, including phase equilibrium (which is very scarce). This information is essential from the industrial point of view since knowledge of thermophysical and thermodynamic properties of materials plays an important role in simulating and designing new products and processes. Moreover, there is a great lack of studies involving the optimization and techno-economic analysis of the process, which may make the production of these materials on an industrial scale unfeasible. Nonetheless, the performance of engineering, science, and technology together can fill these gaps.

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