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A review

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DOI
10.1016/j.msec.2018.12.075

Publication date
2019

Document Version
Accepted author manuscript

Published in
Materials Science and Engineering C

Key Characteristics and Modelling of Bigels Systems: A review

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Abstract

Bigels are interesting semisolid formulations with better properties for different applications like cosmetics and pharmaceutical systems. Due to the mixing of two phases of different nature (polar and apolar), bigels possess some interesting features like ability to deliver hydrophilic and hydrophobic drugs, better spreadability and water washability, improved permeability of drugs, enhanced hydration of stratum corneum and ability to manipulate the drug release rate.

The main objective of this review article is to provide a thorough insight into the important characteristics of bigels together with the discussion on modelling of bigel systems to relate their properties with individual constituents and different parameters. Moreover, some important applications of bigels are also discussed by considering some examples from the literature.

Keywords: bigels, modelling, organogels, hydrogels, drug delivery, cosmetics

Contents

1. Introduction

Gels are semisolid formulations which basically composed of two components, liquid and solid. Liquid component is usually termed as a solvent while solid component is known as a gelling agent/gelator [1, 2]. Gels are typically formed by the ensnarement of solvent phase within the 3-D network of gelling agent [3, 4]. On the basis of polarity of the solvent, gels can be divided into two categories: organogel (apolar solvent) and hydrogel (polar solvent) [5]. Recently, some new classes of gels have also been reported in the literature such as emulgels and bigels [6].

Organogel is usually made by the self-assembly of either polymers or low molecular weight components to entrap the solvent phase [7-9]. Different organogelators have been investigated in the literature, such as fatty acids and fatty alcohols [10], lecithin [11], mixture of physterol and oryzanol [12], waxes [13], steroids and their derivatives [14], 12-hydroxystearic acid (HSA) [15], L-lysine-based gelators [16], cyclodextrins [17], and others. Several solvents have also been studied as a liquid phase for this kind of system such as benzene, hexane, and edible oils including sunflower oil, corn oil, sweet almond oil, cod liver oil, and olive oil [18, 19]. These edible oils are particularly beneficial for health when consumed orally [20] due to their antioxidant and nutritional values and their long shelf-life also make them an ideal candidate to prepare oral and cosmetic commercial formulations [21]. Edible oils are also useful when applied topically, due to its skin moisturizing [22], anti-aging, anti-inflammatory [23], and soothing properties [24]. To modify the physical properties of such edible oils, organogelation is a favorable alternative as compared to chemical modification [25, 26] and crystalline triacylglycerols due to its lower health risks and better nutritional properties [14]. Organogels are easier to prepare and their lipophilic nature can also enhance the drug permeation through stratum corneum [27]. However, the oily nature of organogel systems is the main problem which

creates difficulty in the removal of formulation after application on skin [28]. Organogels cover wide range of applications including production of fat-free food products [29, 30], drug delivery systems [31], self-healing materials [32], pollutant removal [33] and analysis and purification-related systems [34].

Hydrogel is typically formed by the three dimensional network of either natural or synthetic gelling agent (hydrogelator) to immobilize the aqueous phase [35]. These formulations are more patient compliance because of their interesting properties such as easy removal after application, cooling effect, etc. [36]. On the other hand, these systems are not effective in delivering hydrophobic drugs across the stratum cornuem due to their less skin permeability [37]. Emulsion gel/emulgel has been introduced to overcome the drawback of hydrogel system i.e., difficulty in delivering hydrophobic drugs [38]. Emulgel is usually prepared by dispersing the liquid phase within the structured continuum [39, 40]. These formulations can be classified into two categories: emulsion hydrogels and emulsion organogels [41]. Emulgel possesses the characteristics of both, emulsion and gel. However, these systems encounter the problem of less structural stability due to the different mechanical signatures of each phase [42].

The problem of mismatch between the mechanical properties of both phases (continuous and dispersed) and less stability in emulsion gels/emulgels [43] has been solved by structuring both phases, instead of one, which lead towards an interesting system called bigels [44]. Owing to the structured phases of different polarity (aqueous and oily), bigel possesses the advantages of both phases [45] together with the fact that these systems also present better properties than either of the single gel [46]. The key characteristics of bigels include: delivery of both hydrophilic and hydrophobic agents [47], cooling and moisturizing effect [48], spreadability [49], water washability after application [48], easy preparation [6], improved permeability of drugs through

skin [48], better stability at room temperature [50] and ability to manipulate the properties of the system by playing with the fraction and structural distribution of each phase [51, 52]. All these features of bigels make them a suitable and interesting formulation for different applications such as pharmaceutical, cosmetics and food systems [53].

In literature, the term bigels has been used to describe different systems including mixture of hydrogel and organogel [48], combination of two gel strips of different polarity [54], mixture of interpenetrated colloidal gels [55, 56] and bi-continuous type gels having phase separated characteristics [57-59]. Bigels, synthesized by mixing organogel (oil phase) and hydrogel (aqueous phase), have been extensively studied by several researchers in the past decade particularly for drug delivery applications [60] and, therefore, this review will mainly consider this type of bigel system. The schematics of preparation of bigels by mixing hydrogel and organogel is shown in Figure 1.

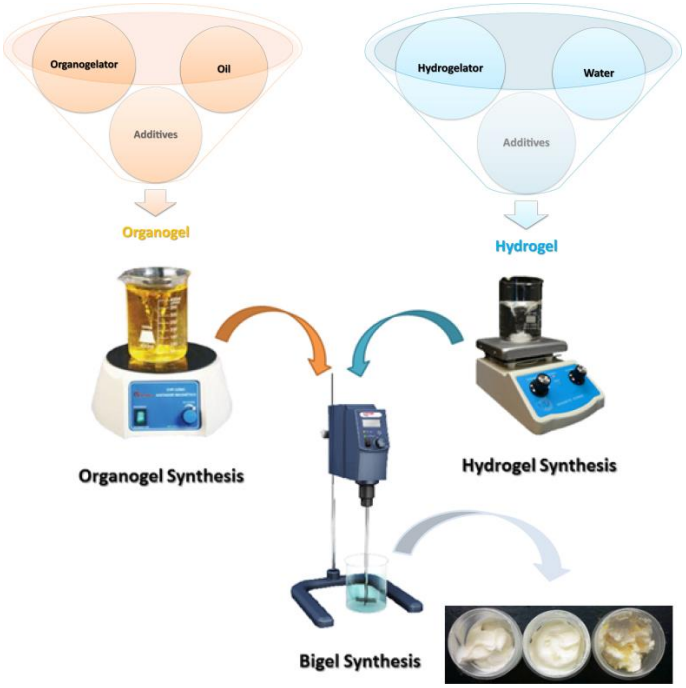


FIGURE 1: Schematics of preparation of bigels by mixing hydrogel and organogel

The three most important parameters for the preparation of bigels, by mixing hydrogel and organogel, are mixing temperature, mixing speed and the storage of bigels. Satapathy et al. [61] reported the preparation of bigels by mixing individual systems at comparatively higher temperature (50^{o}C) whereas room temperature was also used to mix both phases with continuous stirring [62]. Rehman et al. [28] investigated the properties of bigels produced by storing the individual systems (hydrogel and organogel) at a particular temperature and for a specified time period followed by mixing of both systems. In contrast, bigels systems have also been prepared by mixing the individual gels followed by storing the final system [63]. The experimental block diagram for the preparation of bigels using two different methodologies is shown in Figure 2. Recently, Fasolin and Vicente [64] have reported the effect of mixing speed on the rheological and microstructural properties of bigels. Instead of hydrogel, emulgel/emulsion hydrogel was also mixed with the organogel phase in different amounts at room temperature to produce the bigel system [52].

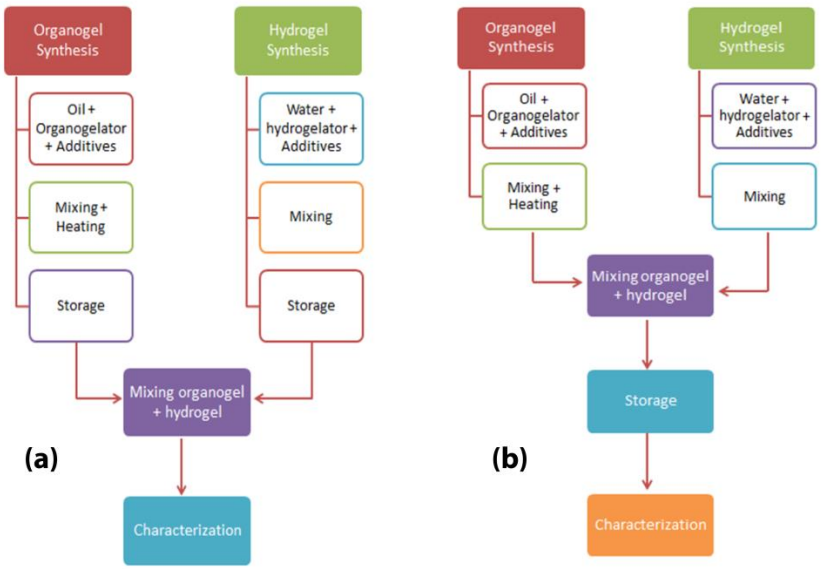


FIGURE 2: Block flow diagram for synthesis of bigels (a) by storing individual gels before bigel preparation and characterization (b) by mixing individual phases and then storing bigel formulations before characterization

Recently, a review article has been published on the considered topic but that was more focused towards the synthesis methods and characterization techniques of bigel systems [65]. However, the aim of this review article is to provide a deep insight into the important and unique characteristics of bigel systems including thermal, mechanical, rheological, electrical, etc. Moreover, several models have been mentioned that can be used to relate the different properties of bigels particularly the rheological models which recently have been proposed in the literature to relate the rheological properties of bigels with the dispersed phase fraction and also with the properties of individual phases (organogel and hydrogel). Furthermore, some important applications of bigel systems have also been discussed through particular examples.

2. Characteristics

Mechanical, structural, thermal, physical, rheological and electrical properties of bigels are of prime importance for their utilization in different commercial applications [66]. The effect of several parameters on the mechanical properties of bigels has been reported in the literature such as organogel/hydrogel content, polymer structure (linear or branched) and polymer concentration. The increasing organogel content showed significant impact on the cohesiveness, firmness, adhesiveness, stickiness, viscosity, and percent creep recovery of bigels [45, 51]. Likewise, the increase in hardness of bigels was also observed with the increase in hydrogel content [28]. The bigel systems containing branched polysaccharides, as water structuring agent, displayed higher gel strength and better resistance to deformation but poor stress relaxation characteristics as compared to the system containing linear polysaccharides [49]. The concentration of water structuring agent (polymer) has also been observed to have a profound effect on the firmness, stickiness, spreadability, percent stress relaxation and residual stress of the bigel systems [67]. The effect of two different linear polysaccharides (hydroxypropyl

methylcellulose (HPMC) and sodium alginate) on the mechanical properties of resultant bigels has also been investigated in the literature [28]. The incorporation of organogel into hydrogel also resulted in the enhancement of moisturizing effect due to the simultaneous delivery and hold up of water [48]. Sagiri et al. [68] reported the leaching studies of bigels to analyze the leaching of oil phase from the prepared formulations [Fig. 3]. Results showed that the leaching from the bigels was extremely minute as compared to the emulgels. It was also presented that the soybean oil based bigels had lower leaching percent as compared to the sesame oil based bigels.

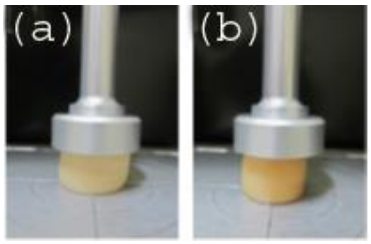


FIGURE 3: Leaching studies of bigels: (a) sesame oil based bigel (b) soy bean oil based bigel [68], "Reproduced with permission, Copyright [2015], [Elsevier]"

Final properties of the bigel system are highly dependent on the structural distribution of each phase within the bigels and droplets size of the dispersed phase and these parameters can easily be measured by the microscopic analysis. The effect of organogel content on the structural features of the bigels has been reported in the literature. The lower amount of organogel resulted in heterogeneous continuous matrix within bigels which comprised of water droplets together with oil droplets [45] while interlinked organogel droplets in a complex system were formed by having higher organogel content [63]. Wakhet et al. [69] also reported, using field emission electron microscope (FESEM) analysis, the existence of two types of globular structures within the continuous matrix of bigels (i) aggregates of hydrogelators and, (ii) globules due to the addition of organogels [Fig. 4].

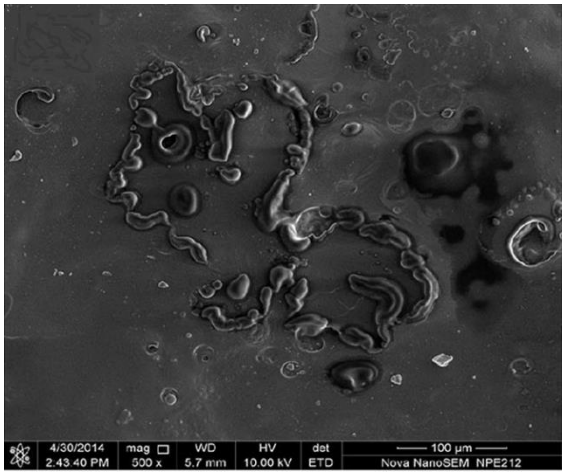


FIGURE 4: FESEM image of gelatin-agar/soybean oil based bigel [69], "Reproduced with permission, Copyright [2015], [Springer Nature]"

The presence of agglomerated globular structures within the continuous matrix of gelatin/sesame oil based bigels was also confirmed by bright field microscopy [61] [Fig. 5]. The organogel fraction also has a profound effect on the droplet size and polydispersity of dispersed phase droplets. Usually, the increase in organogel fraction resulted in larger droplets [51, 63] [Figs. 6 & 7]. On the other hand, a decrease in droplet size was also reported with increasing organogel content [45] [Fig. 8]. This peculiar behavior was associated with the increased stability of bigels due to the closer packing of dispersed droplets.

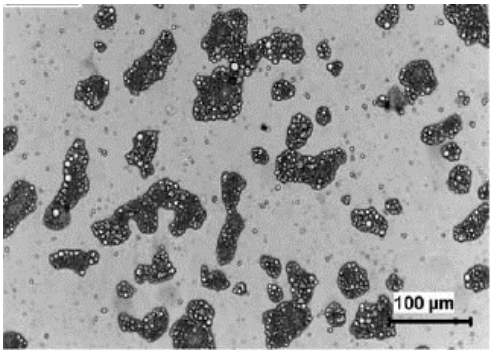
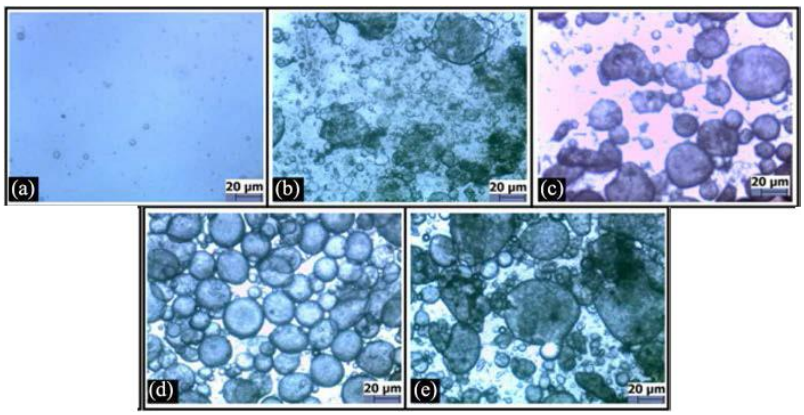


FIGURE 5: Bright field micrograph of gelatin/sesame oil based bigel systems [61], "Reproduced with permission, Copyright [2014], [John Wiley and Sons]"



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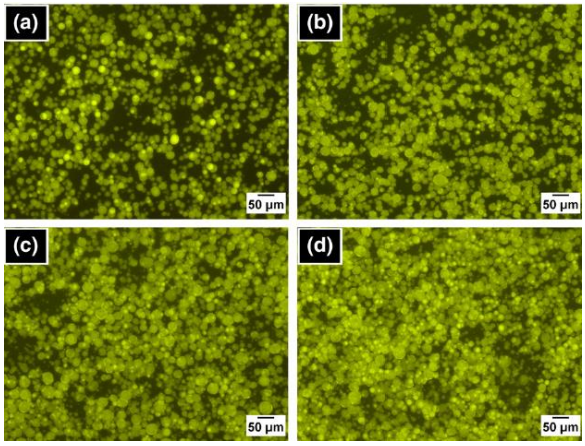
184 **FIGURE 6:** Bright field micrographs of bigels: (a) 0 wt% organogel, (b) 2.5 wt% organogel, (c) 5 wt% organogel,
185 (d) 7.5 wt% organogel, and (e) 10 wt% organogel [70], "Reproduced with permission, Copyright [2017], [Taylor &
186 Francis]"



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188 **FIGURE 7:** Fluorescent micrographs of carbopol/sesame oil based bigels: (a) 11.11 wt% organogel (b) 20 wt%
189 organogel (c) 27.27 wt% organogel (d) 33.33 wt% organogel [51], "Reproduced with permission, Copyright [2014],
190 [Elsevier]"

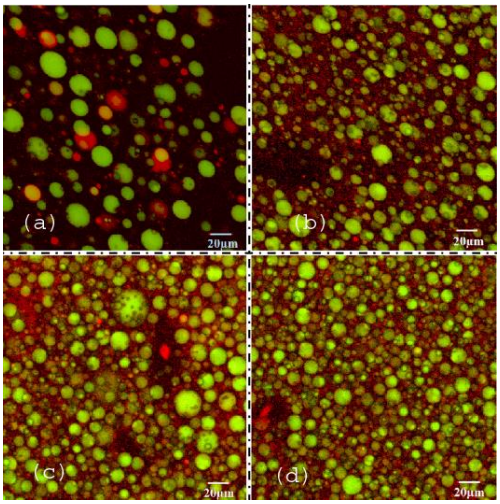


FIGURE 8: Confocal micrographs of guar gum/sesame oil based bigels: (a) 11 wt% organogel (b) 20 wt% organogel (c) 27 wt% organogel (d) 33 wt% organogel [45], "Reproduced with permission, Copyright [2014], [Elsevier]"

Maltodextrin and carboxy methyl cellulose based bigels displayed narrow droplet size distribution as compared to alginate and starch based bigels [Fig. 9] due to the viscosity enhancement effect caused by maltodextrin and carboxy methyl cellulose [49]. The cryo-SEM image of bigel sample showed the existence of porous matrix of polymer dispersed between the solid oil phase [62] [Fig. 10]. The increased organogel fraction can affect the polydispersity of droplets either in enhancing [63] or reducing [45] manner depending upon the constituents of the system. However, polydispersity is not a function of organogelators amount such as samples with different organogelators content displayed a similar droplet size distribution [63]. Microscopic analysis was also used to characterize an interesting and complex bigel system prepared by mixing emulsion gel with the organogel in different fractions. The micrographs showed the presence of oil droplets together with the structured phases [52].

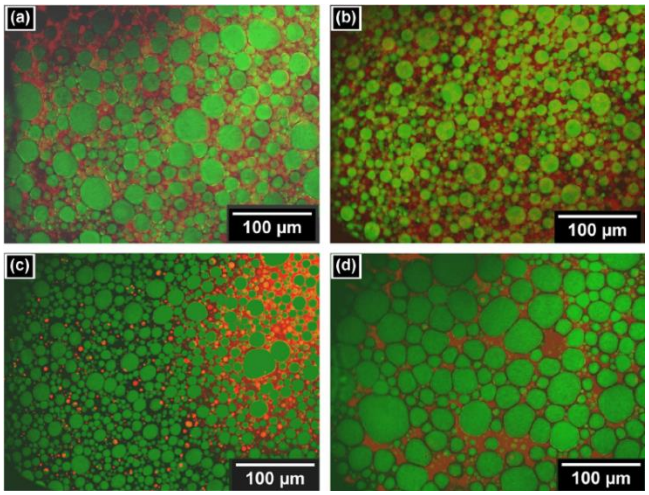


FIGURE 9: Fluorescent micrographs: (a) sodium alginate based bigels (b) sodium carboxy methyl cellulose based bigels (c) maltodextrin based bigels (d) starch based bigels [49], "Reproduced with permission, Copyright [2014], [John Wiley and Sons]"

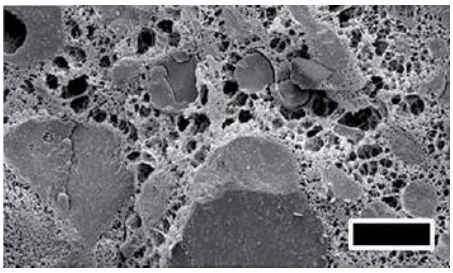
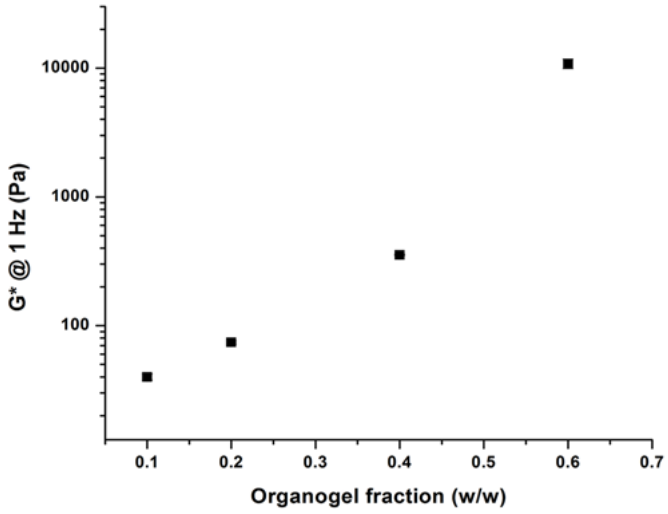


FIGURE 10: cryo-SEM image of bigel sample having 60 wt% of organogel captured after sublimation of water (scale bar = 10 µm) [62] "Reproduced with permission, Copyright [2015], [The Royal Society of Chemistry]"

The efficiency of gelled systems for commercial applications can be directly linked with their rheological properties. Therefore, dynamic rheological methods are particularly useful in analyzing and optimizing the rheological properties of formulations [71]. Rheological characterization of different bigel systems has been reported in the literature by using strain controlled rheometer [49, 72] and stress controlled rheometer [52, 63].

Stress sweep tests of bigels [49] showed that the critical stress, before which the moduli remain constant, was 10 Pa for linear polysaccharides based bigels whereas for branched polysaccharides based bigels the value was 100 Pa. A sudden decrease in moduli after this critical value of stress was linked with the destruction of the structure. Results of frequency sweep tests within linear viscoelastic regime (non-destructive regime) revealed that all the formulations were strong bigels. This fact was evidenced by the higher storage modulus than the loss modulus and also by the independency of moduli as a function of frequency. The storage modulus of branched polysaccharides based bigels was higher as compared to the linear polysaccharides based bigels which was attributed to the enhancement in the elastic character of the system due to the incorporation of branched chain polymers.

Strain sweep tests of natural gums based bigels [72] showed that below critical strain (linear viscoelastic regime), bigels displayed higher elastic character as compared to their viscous counterpart. The highest values of critical strain for guar gum based bigels were associated with the interaction between the gum and organogelator (span 40) molecules whereas the lowest values of xanthan gum based bigels were linked with the weak interaction between gelator molecules. Frequency sweep tests of pectin/olive oil based bigels [63] revealed a non-linear increase in complex modulus [Fig. 11] and a non-linear decrease in phase angle [Fig. 12] as a function of increasing organogel amount. This behavior suggested the enhancement in consistency (related to complex modulus) and degree of structuration (related to phase angle) of bigels.



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239 **FIGURE 11:** Complex modulus at 1 Hz as a function of organogel fraction for pectin/olive oil based bigels [63]

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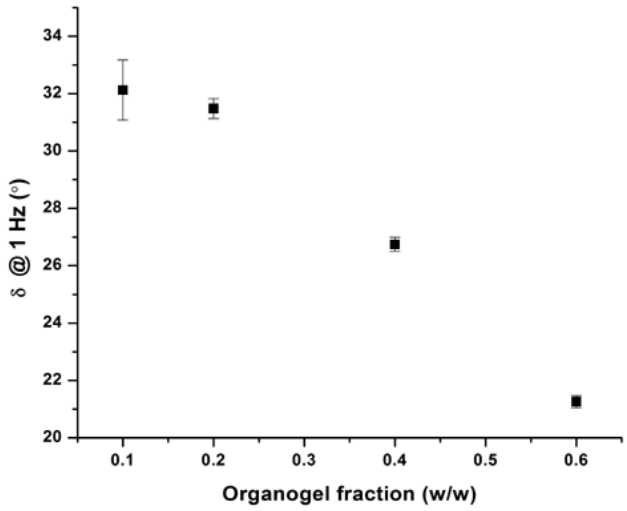

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242 **FIGURE 12:** Phase angle at 1 Hz as a function of organogel fraction for pectin/olive oil based bigels [63]

243 "Reproduced with permission, Copyright [2016], [Elsevier]"

244 Viscosity and swelling behavior of bigel systems are also important features to consider for their
245 commercial applications particularly for drug delivery. The molecular weight, concentration and
246 structure of polymer (water structuring agent) together with organogel, organogelator and
247 hydrogel fraction have significant effect on the viscosity of bigel systems. More viscous systems

were obtained by using higher molecular weight polymer, branched chain polymer [49] or higher fractions of polymer [67], organogel [45], organogelators [63] and hydrogel [28]. In contrast, Patel et al. [62] reported a decrease in the viscosity of bigels with the increasing hydrogel content. The organogel fraction can also affect the yield stress of bigels, for example, higher values of yield stress were observed for the bigels containing higher organogel content [45, 51].

Sol-gel/gel-sol transition as a function of temperature and thermal stability are interesting and important attributes of bigel systems for their successful commercial utilization. Thermal analysis of proteins/sunflower oil based bigels [47] revealed that the broad endothermic peak, linked with the evaporation of moisture, was observed at higher temperature for bigels. Furthermore, bigels also displayed higher values of change in enthalpy (ΔH), associated with the evaporation of water. These two behaviors were attributed to the increased thermal stability of bigels due to the interaction between protein molecules and OH groups of water molecules in bigels.

The thermal properties of organogel phase after its incorporation into the bigel system remained same as the pure organogel sample [61, 69]. Thermal stability of bigel system can be improved by increasing the organogel fraction [51] or organogelators amount [63]. Gel-sol transition of cosmetic system/olive oil based bigels [52] was reported for which at lower temperatures the complex modulus was constant while after certain temperature a sudden decrease in complex modulus was observed. The formulation displayed a solid-like behavior during the whole temperature ramp test by having the loss tangent value lower than 1. This fact was attributed to the non-thermoreversible character (only softening without melting) of starch gel. Patel et al. [62] also reported an increase in the storage modulus of bigels during heating cycle, which was linked with the interaction between polymer chains and silica particles.

Electrical characterization is an important tool to quantify different parameters of the bigel formulations such as electrical conductance, electrical resistance, impedance, etc. and these parameters are directly linked with their efficacy for the controlled delivery of drugs. Secondly, electrical conductivity is also a key parameter in order to understand the distribution of individual phases within the multiphase systems and the microenvironment of the systems. Phase inversion phenomenon (interchange of continuous and dispersed phase) is usually encountered during production, mixing, processing and handling of multiphase systems, which also resulted in abrupt change of electrical conductance of the system [73]. Therefore, this phase inversion phenomenon can also be predicted by analyzing electrical conductance as a function of weight/volume fraction of any single phase within the multiphase system. The sol-gel transformation has also been investigated in the literature using electrical conductivity analysis [74]. Hence, the understanding of electrical characteristics of the formulations is vital to consider them for different applications. The investigation of electrical properties of different bigel formulations has been reported using phase sensitive multimeter by injecting AC voltage with variable frequency at room temperature [60, 75, 76]. Lupi et al. [63] also reported the electrical characterization of pectin/olive oil based bigel samples prepared with NaCl by using parallel copper plates with LCR meter.

Results of electrical characterization of proteins/sunflower oil based bigels [47] revealed a lower bulk resistance (i.e. higher conductivity) and smaller relaxation time as compared to the emulgels which was attributed to the charged groups or free charges present in the protein molecules incorporated in the bigel systems. Similarly, guar gum based bigels displayed higher bulk resistance as compared to acacia gum based bigels which was linked with the uncharged character of guar gum. The conductivities of bigels were approximately constant within the

frequency range of 0-1200 KHz, but after this range an increase in the conductivities of the bigels was observed due to the polarization at the interface between sample and measuring electrode [75].

According to Satapathy et al. [61] and Wakhet et al. [69], hydrogel displayed lowest bulk resistance and impedance followed by emulgel and then bigel. This behavior was associated with the incorporation of insulating material, oil and organogel within emulgel and bigel respectively. Furthermore, an increase in the bulk resistance of bigels was also observed with the increase in organogel content due to the non-conducting nature of organogel [60, 76]. Similarly, Lupi et al. [63] reported a decrease in the conductivity of bigels with the increase in organogel amount [Fig. 13], which was linked with the incorporation of electrical insulant (organogel). The organogel-in-hydrogel type morphology of bigel systems was also confirmed by the conductivity analysis [63]. Lupi et al. [52] reported an irregular behavior of conductivity of bigels as a function of organogel fraction, which suggested the complex changes in phase distribution of bigels instead of phase inversion phenomenon.

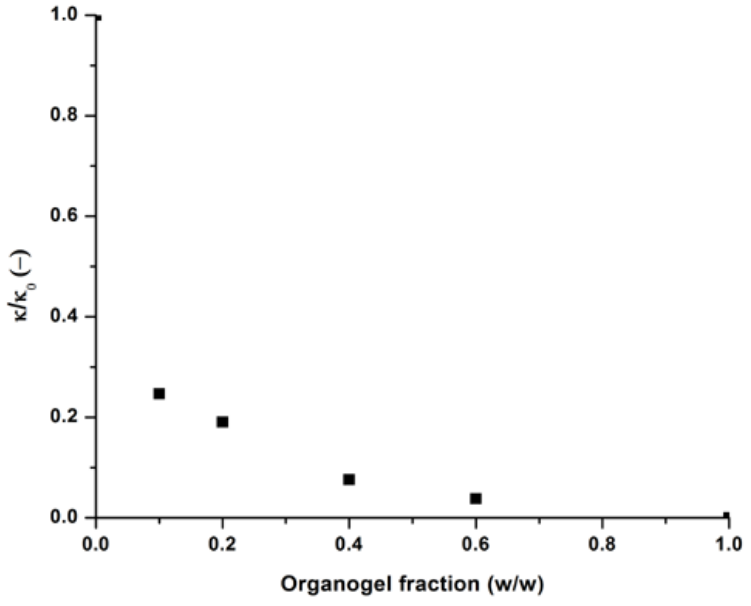

FIGURE 13: Electrical conductivity as a function of organogel fraction for pectin/olive oil based bigels [63] "Reproduced with permission, Copyright [2016], [Elsevier]"

The cytocompatibility or biocompatibility of bigel systems has been reported by exposing the formulations to the human keratinocyte cell line (HaCaT cells). The variation in the proliferation indices of bigel formulations and the control was insignificant [Fig. 14] which showed that the bigel formulations were cytocompatible or biocompatible [45, 51, 69]. Therefore, bigel system is a potential candidate for biomedical applications particularly for drug delivery.

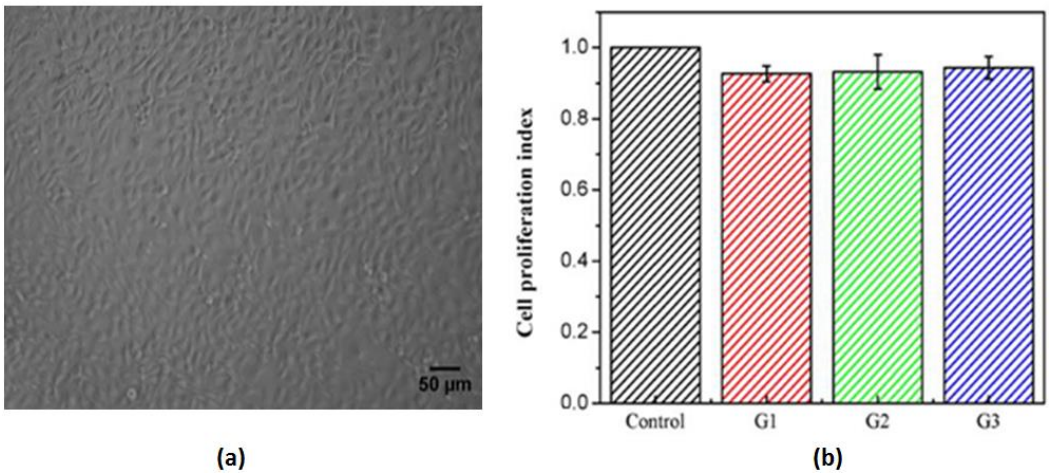

FIGURE 14: Biocompatibility studies: (a) cell morphology of bigel (b) HaCaT cell proliferation index (G1 = hydrogel, G2 = emulgel and G3 = bigel) [61] "Reproduced with permission, Copyright [2014], [John Wiley and Sons]"

The Mucoadhesive properties of bigels including mucoadhesive strength and mucoadhesive time have been studied by using static mechanical testing and in vitro wash-off method, respectively [68]. The mucoadhesivity (strength and time) of bigels was higher than the emulsion gels [68] but lower than hydrogel [61] and this behavior was linked with the composition of the dispersed phase. The incorporation of oil or organogel into the hydrogel was the main reason for reduction

in mucoadhesivity due to the leaching of oil phase, which was more pronounced in emulsion gels [61].

In summary, bigel systems have exciting thermal, rheological, structural and electrical characteristics due to the combination of two different gelled phases, i.e. hydrogel and organogel. Another appealing fact, for these kind of systems, is to manipulate the above mentioned properties by varying different parameters such as organogel/hydrogel ratio, nature and structure of gelling agents, amount of gelators (organogelator and hydrogelator), incorporation of additives/emulsifiers and type of organic solvent/oil. In literature, a lot of research has been done so far to analyze the behavior of resultant bigels as a function of organogel/hydrogel ratio and nature of hydrogelator. Therefore, further research should be directed towards analyzing the influence of nature of organogelators, amounts of gelling agents, addition of different additives/emulsifiers and type of oil on the characteristics of these exciting systems. Furthermore, the effect of synthesis parameters including mixing speed, storage temperature and mixing temperature on the final properties of bigels should also be investigated.

3. Modelling

In this section, different theoretical, semi-empirical and empirical models have been discussed that can be utilized to predict several properties of bigels specifically rheological properties as a function of dispersed phase fraction and characteristics of individual phases.

Weak gel model was used to fit the rheological data in terms of complex modulus (combination of storage and loss modulus) of bigels as a function of frequency, given as follows: [77]

$$G^*(\omega) = \sqrt{(G')^2 + (G'')^2} = A \cdot \omega^{\frac{1}{z}} \quad (1)$$

According to the "weak gel model", the parameter 'z', also called coordination number, is related to the number of interacting rheological units within the three dimensional network of system, and the parameter 'A' is the strength of these interactions. Weak gel model parameters for cosmetic system/olive oil based bigels displayed an irregular behavior as a function of organogel fraction. This peculiar behavior was linked with the formation of bi-continuous type bigel or with the phase inversion phenomenon [52].

The storage modulus (G') is an important parameter of gelled systems to analyze their elastic character (solid-like behavior) and, therefore, G' is usually used to model their characteristics. The type of the bigel (physical or chemical) was identified by relating the storage modulus (G') of the bigels with the frequency using the following relation: [72]

$$log\ G' = n\ log\ \omega + k \quad (2)$$

where n and k are constants. The parameter n can be calculated by the slope of logarithmic plot of G' vs ω. On the basis of the value of n, bigels can be classified into either physical ($n > 0$) or chemical ($n = 0$) gels. For example, the n values for natural gum based bigels were higher than 0 which suggested the formation of physical gels. This means that either chain entanglements or secondary forces (i.e. hydrogen bonding) were responsible for the network formation [72].

Modified Palierne model [63] was used in the literature to relate the complex modulus of bigels in the form of G_r^* (ratio of complex modulus of bigel (G^*) at 1 Hz and the complex modulus of hydrogel (G_c^*) at 1 Hz) with the volume fraction (φ) of the dispersed phase (organogel) given as follows:

$$G_r^* = \frac{G^*}{G_c^*} = \frac{1 + {}^3/_2\,\alpha H\varphi}{1 - \beta H\varphi} = \frac{1 + a \cdot \varphi}{1 - b \cdot \varphi} \quad (3)$$

where fitting parameters α and β represent deviation from the ideal behavior. Parameters H and M were calculated by the following equations:

$$H = \frac{2(M-1)}{2M+3} \quad (4)$$

$$M = \frac{G_d}{G_c} \quad (5)$$

where G_d is the dispersed phase modulus. The volume fraction (φ) of the dispersed phase was estimated by the following expression:

$$\varphi = \frac{m_{og}}{m_{og} + m_{hyd} \cdot \frac{\rho_{og}}{\rho_{hyd}}} \quad (6)$$

where m_{og} and m_{hyd} represent the mass of organogel and hydrogel respectively, whereas ρ_{og} and ρ_{hyd} are the densities of organogel and hydrogel, respectively. The values of a and b for pectin/olive oil based bigels were 17.0 ± 0.9 (−) and 1.627 ± 0.001 (−), respectively. This empirical model was proposed to remain valid within the particular range of volume fractions ($0 \leq \varphi \leq 0.601$) [63].

Recently, Lupi et al. [78] proposed another semi-empirical model, based on the theoretical models presented in the literature for such systems, to effectively relate the complex modulus of

bigels with the volume fraction (φ) of dispersed phase by incorporating two extra parameters k and ψ, given as follows:

$$G_r{}^* = \frac{1 + M^k \cdot \varphi}{1 - \psi\varphi} \tag{7}$$

where three equations were used to calculate the crowding factor ψ, given as:

$$\psi = \frac{1}{\emptyset_m} \tag{8}$$

$$\psi = \frac{1}{\varphi}\left(1 - \exp\left(\frac{-\emptyset}{1 - \frac{\emptyset}{\emptyset_m}}\right)\right) \tag{9}$$

$$\psi = 1 + \left(\frac{1 - \emptyset_m}{\emptyset_m{}^2}\right)\emptyset \tag{10}$$

where $\emptyset_m$ is the maximum packing fraction of the dispersed phase. The value of parameter k for pectin/olive oil bigels system was 0.24 ± 0.01 whereas the values of maximum packing fraction $\emptyset_m$ for the abovementioned system were 0.576 ± 0.009, 0.664 ± 0.003 and 0.553 ± 0.002 from all three equations, respectively [78]. Although the proposed semi-empirical model showed quite good agreement with the experimental values, further research is needed to analyze the dependence of complex modulus on particle size distribution (in terms of $\emptyset_m$).

Jonscher power law model was proposed to fit the data of conductivity of bigels as a function of frequency, given as follows: [76]

$$\sigma_{ac} = \sigma_{dc} + B\omega^{s} \tag{11}$$

and

$$\sigma_{dc} = (l/R_b) \cdot (l/A) \tag{12}$$

where B = pre-exponential constant, ω = angular frequency, s = power law constant, σ_{ac} = AC conductivity, σ_{dc} = DC conductivity, l = thickness of sample, A = area of the sample and R_b = bulk resistance. A monotonic decrease in AC and DC conductivity of bigels was observed with the increase in organogel fraction [60].

The stress relaxation behavior of bigels can be analyzed by normalizing the stress profile i.e., calculating the decaying parameter Y(t) given as: [79]

$$Y(t) = \frac{\sigma_0 - \sigma(t)}{\sigma_0} \tag{13}$$

where $\sigma(t)$ is the stress measured after certain time t during relaxation. Another relation between the decaying parameter $Y(t)$ and time t was given by Mickley et al. [80] as follows:

$$Y(t) = \frac{abt}{1 + bt} \tag{14}$$

where a represents the extent of relaxation and b shows the rate at which stress relaxes. The stress relaxation data of bigel systems was modelled by combining above two equations (Eqs. 13 & 14), resulted in modified Peleg's model, as follows: [69]

$$\frac{\big(\sigma_0 - \sigma(t)\big)t}{\sigma_0} = k_1 + k_2 t \tag{15}$$

where k_1 and k_2 are the initial rate and extent of relaxation, respectively and σ_0 is the obtained maximum force after the loading phase. The overall stress relaxation behavior of bigels is usually described by the parameter k_2.

The creep data of the bigel systems was fitted by using the four element Burger's model, given as follows: [61]

$$J_c(t) = J_0 + J_1[1 - \exp(-t/t_1)] + t/\eta_0 \quad (16)$$

where $J_c(t)$, J_0, J_1, t_1, and η_0 are creep compliance at any time t, instantaneous compliance, retarded creep compliance, retardation time and viscosity of material, respectively. Martins et al. [81] also reported the use of Burger's model to describe the creep and stress relaxation behaviors of poly lactid acid (PLA) and poly ε-caprolactone (PCL) composite fibres. The result showed that the model was not appropriate to accurately describe the stress relaxation behavior of the considered system. However, investigation of this model to predict the stress relaxation behavior of bigels needs more attention.

During the recovery cycle of creep, developed strain was partially recovered for bigel systems. Percent strain recovery of the formulations was calculated for each cycle by using the following equation: [68]

$$\gamma_{rec} = \frac{(\gamma_c - \gamma_r)}{(\gamma_c - \gamma_0)} \times 100 \quad (17)$$

where γ_0 is the strain at the start of creep cycle, γ_c is the strain at the end of creep cycle and γ_r is the strain at the end of recovery phase of creep cycle. An initially higher value and a decrease in creep recovery of bigels were observed with the increase in number of cycles. The initial rise in

creep recovery was linked with the loss of viscous character in bigels whereas the decrease in creep recovery was attributed to the failure of structure [45].

Ostwald-de wale power law model and Herschel-Bulkley model have been used in the literature to study the flow characteristics of bigel systems, given as follows: [47]

$$\eta = k \cdot \dot{\gamma}^{n-1} \tag{18}$$

$$\tau = \tau_0 + k \cdot \dot{\gamma}^{n} \tag{19}$$

where η, k, $\dot{\gamma}$, n, τ, and τ_0 are the viscosity, consistency index, shear rate, flow index, shear stress and yield stress, respectively.

The data of thermal analysis of bigels, given by differential scanning calorimetry (DSC), was also fitted by using the Avrami equation given as follows: [45]

$$\ln\left(ln\left({}^{1}/_{1} - X_t\right)\right) = lnK + nlnt \tag{20}$$

where X_t and K are the volume fraction of gelator at any time t and rate constant for crystallization, respectively.

In short, different theoretical, empirical and semi-empirical models have been used so far to relate the properties of bigels with different important parameters. Several empirical and semi-empirical rheological models have already been proposed in the literature but these models are limited to the particular hydrogel/organogel ratios and structural distribution within the bigels. Therefore, further insight is needed to completely understand the relation between different

parameters and the end-use characteristics of bigels and, hence, to propose a more generalized rheological model applicable for all kinds of bigels.

4. Applications

Different applications of bigel systems have been proposed in the literature particularly in the field of drug delivery and cosmetics. Controlled delivery of different drugs including metronidazole [47], ciprofloxacin [68] Tenofovir [82] or diltiazem hydrochloride [83] using bigel systems has been reported in the literature. According to Sagiri et al. [68] bigels displayed lower drug release as compared to emulsion gel which was attributed to the structuration and aggregation of internal phase (oil phase) resulted in reduced permeability and lower dissolution of drugs. Satapathy et al. [61] also reported the highest drug release from hydrogel followed by emulsion gel and then bigel which was associated with the conductivity and swelling behavior of formulations. Similar results of higher drug release rate from hydrogel as compared to bigels were reported by Ibrahim et al. [83] with the help of permeability studies of diltiazem hydrochloride using abdominal skin of rabbits.

In contrary, higher drug release rate from bigels has also been reported as compared to hydrogel which was linked with the existence of fatty acids in fish oil [28]. Drug release rate from bigels can be manipulated by varying the polymer fraction [67], the organogel content [45, 51] or the backbone structure of polymer chains (linear or branched) [49]. Recently, Andonova et al. [84] reported the delivery of ketoprofen incorporated into polymer carriers which were basically embedded within the bigel formulation. Results revealed that the prepared formulation provided better drug photostability and controlled release together with an effective and safer formulation for dermal application.

Due to some exciting properties of bigels such as good spreadability, cooling effect, emollient and moisturizing effect, these are potential candidates for transdermal applications especially for cosmetics [48]. Lupi et al. [52] reported the synthesis of cosmetic formulation in the form of bigels. The effect of increasing organogel fraction on the rheology and microstructure of cosmetic bigels was investigated. Table 1, 2 and 3 provide the critical analysis of the bigel systems reported in the literature for drug delivery, cosmetics and other applications.

Bigel systems were found to have quite interesting properties for drug delivery applications. However, it was observed in bigel systems that the mechanical and drug release properties were inversely related to each other. Bigels possessing superior mechanical properties were observed to exhibit lower drug release rate as compared to the commercial formulations. Therefore, future studies should be focused on the development of bigel systems having better drug release ability in addition to the excellent mechanical properties. Moreover, the utilization of bigel systems in food applications have not been explored yet, which can be an interesting field of research for further studies.

467 **TABLE 1.** Different bigel systems investigated in the literature for drug delivery applications.

Oil Phase	Organogelator	Hydrogelator	Total Concentration of Gelators	Additives	Drug Employed	Structural Distribution	Objective(s) of Study	Key Findings	Analysis	Ref
Sunflower oil	Span 40	Gelatin, Whey protein	10 wt%	NaOH, Potassium dihydrogen phosphate	Metronidazole	Organogel-in-hydrogel type	Comparative analysis of bigels (either based on gelatin or whey protein) for iontophoretic drug delivery	• Whey protein based bigels displayed higher stability as compared to other system. • Gelatin based bigels showed higher spreadability, firmness, stickiness and drug release than whey protein based bigels.	Gelatin based bigel seems more suitable system for drug delivery applications specifically when higher thermal stability is not required.	[47]
Sunflower oil	Span 40	Guar gum, Acacia gum, Xanthan gum	9.6 wt%	-	Metronidazole	Organogel-in-hydrogel type	Comparative analysis of bigels based on different biopolymers (guar gum, acacia gum, or xanthan guma) for antimicrobial agents delivery	• Guar gum based bigel showed highest firmness and strength as compared to other bigel systems. • Xanthan gum and guar gum based bigels displayed the diffusion controlled release of drugs and this drug release was slower than the drug release from acacia gum based bigels and commercial formulation. • All the prepared bigels were stable, viscoelastic in nature together with the shear thinning behavior.	Acacia gum based bigel shows comparatively better mechanical, rheological and drug release properties making them suitable candidate for drug delivery.	[72]
Sunflower oil	Tween 80, Span 80	Guar gum, Acacia gum	40.3 wt%	-	Metronidazole	Organogel-in-hydrogel type	To study the effect of ionic (gum acacia) and non-ionic (guar gum) gums on the properties of bigels, synthesized using fluid-filled organogels, for drug delivery application	• Aggregated structure was evident for guar gum based bigels while a de-flocculated structure was present in the case of acacia gum based bigels. • The mechanical properties of guar gum based bigels were superior than the acacia gum based bigels whereas the acacia gum based bigels displayed better conductivity and drug release properties.	A compromise has to be made between the mechanical and drug release properties of two systems for the selection of suitable system for drug delivery.	[75]
Sunflower oil	Span 40	Sodium carboxy methyl cellulose, Sodium alginate, Starch, Maltodextrin	9.5 wt%	-	Metronidazole, L. Platarum	Organogel-in-hydrogel type	To compare the properties of linear (sodium alginate and sodium carboxy methyl cellulose) and branched (starch and maltodextrin) polysaccharide based bigels for antibiotics and probiotics delivery	• The produced bigels showed shear thinning behavior, diffusion mediated drug release, good antimicrobial efficiency, better strength and stability over a long period of time. • Furthermore, the branched polysaccharide (starch and maltodextrin) based bigels showed higher firmness and better probiotics viability but lower drug release rate as compared to linear polysaccharides (sodium alginate and sodium carboxy methyl cellulose) based bigels.	This study also presents two types of systems, one having better mechanical but poor drug release properties while other with opposite behavior. Therefore, selection of suitable system, will depend upon the application specific requirements, by making a compromise between different properties of the selected system.	[49]

Sunflower oil	Span 40	Polyvinyl pyrrolidone (PVP), Polyvinyl alcohol (PVA)	10-14 wt%	-	Metronidazole	Organogel-in-hydrogel type	To compare the properties of bigels containing water soluble synthetic polymers (PVP and PVA) and to analyze their suitability for drug delivery	• The results showed an increase in the viscosity of bigels and a decrease in the drug release rate with the increase in polymer concentration. • PVA based bigels displayed higher gel strength, better biocompatibility and lower drug release as compared to the PVP based bigels. • The drug containing bigels displayed resistance against Escherichia coli making them potential candidate for controlled delivery of active agents.	PVP based bigels can be good option for drug delivery application if their mechanical properties can further be enhanced, without disturbing their drug release properties, by playing with the concentration of PVP in bigels.	[67]
Sesame oil	Span 60	Guar gum	2.5-5.7 wt%, 4.8-5.6 wt%	Propyl paraben	Ciprofloxacin, Metronidazole	Organogel-in-hydrogel type	To investigate the effect of increasing organogel content on the properties of resultant bigel systems, used for drug delivery application	• Bigels having higher organogel fraction displayed smooth texture, better stability and biocompatibility, higher viscosity and firmness and lower drug release as compared to the bigels containing lower fraction of organogels.	A balance between mechanical and drug release properties can be made for bigels by manipulating the organogel/hydrogel ratio in bigels.	[45, 76]
Sesame oil	Span 60	Carbopol	2.5-5.7 wt%	-	Metronidazole	Organogel-in-hydrogel type	To analyze the influence of varying organogel/hydrogel ratio on the characteristics of resultant bigels, used for drug delivery application	• Results showed an increase in the size and number of dispersed phase droplets, viscosity, stability, firmness, enthalpy and entropy of the bigels with the increase in organogel content. • The produced bigels also showed smooth texture, biocompatibility, shear thinning behavior, diffusion mediated drug release and better antimicrobial efficiency against E. coli.	Better mechanical, thermal and drug release properties of bigels can be obtained by playing with the organogel content within the bigels.	[51, 60]
Almond oil	Span 60	Carbopol	5.2 wt%, 3.8-6.6 wt%	Propylene glycol, Ethanol, Triethanolamine	Ketoprofen	Organogel-in-hydrogel type	• To understand the effect of organogel/hydrogel ratio on the viscosity, stability and spreadability of prepared bigels. • To investigate the suitability of a selected bigel formation for enhancing the photostability of drug incorporated in polymeric carrier	• Results showed that the bigels prepared with 80/20 and 70/30 organogel/hydrogel ratio were stable with similar viscosity, spreadability and droplet size. The system prepared with 60/40 organogel/hydrogel ratio was unstable during storage. • Results revealed an improvement in the photostability of drug after incorporation of drug carriers into the bigel formulations. • The drug carriers containing bigels also showed homogeneous microstructure, sustained release of drugs, better rheological properties, biocompatibility, anti-inflammatory, analgesic and anti-hyperalgesic effects.	Rheology, spreadability and stability of a bigel system can be controlled by manipulating the organogel/hydrogel ratio.	[84, 85]
Liquid paraffin	Polyethylene	Poloxamer 407	*32.2-54.7 wt%	-	Ciclopirox olamine (CPO), Terbinafine	Organogel-in-hydrogel type	• To study the effect of increasing organogel content on the thermal stability and	• Results revealed a decrease in viscosity and consistency index as a function of increasing	The thermal stability and drug release properties of studied bigels can be	[86]

					hydrochloride (TFH)		drug release properties of resultant bigel systems. • To analyse the effect of adding antifungal substances on the drug release properties of prepared bigels.	oleogel content. • Reported bigels were stable at room temperature for six months and four months at 40 °C. • The amount of drug release from prepared bigels decreased with increasing organogel concentration. • The amount of drug release was enhanced by adding ciclopirox olamine in both phases, in equal quantity, and terbinafine hydrochloride in organogel or in hydrogel.	enhanced by decreasing the organogel content in the investigated bigels. This study is quite interesting because both, mechanical and drug release, properties have inverse relation with the organogel fraction.	
Isopropyl palmitate	Mixture of Soya lecithin and Pluronic	Hydroxypropyl-methylcellulose	9.8-13.5 wt%	Potassium sorbate, Sorbic acid, Water	Flurbiprofen	**N.A	To examine the impact of organogel/hydrogel ratio on the viscosity, consistency and drug release properties of investigated bigel systems	• Prepared bigels showed extended drug release and bigel having equal fraction of both phases (50/50) was selected as the optimum formulation. • In vitro permeation release was observed to be 89.99% after 8 hrs. • The prepared bigels were found to be stable and biocompatible.	The formulation having 50/50 organogel/hydrogel ratio shows good consistency, good visual appearance, required viscosity and neutral pH which makes this system a suitable option for drug delivery.	[87]

*Including the weight fraction of oil as well

**Microscopic analysis of bigels is not reported

TABLE 2: Comparison of bigels with organogels, hydrogels and emulgels for drug delivery applications.

Oil Phase	Organogelator	Hydrogelator	Total Concentration of Gelators	Additives	Drug Employed	Structural Distribution	Objective(s) of Study	Key Findings	Analysis	Ref
Soya-bean oil	Span 60, Cetyl alcohol (CA)	Hydroxypropyl-methylcellulose	10 wt%	Span 80, Tween 20, Tween 80	Diltiazem HCl (DH)	Organogel-in-hydrogel type	• To analyze the effect of incorporating different surfactants (Span 80, Tween 20 and Tween 80) on the properties of bigels. • To investigate the effect of using different organogelators (Span 60 and Cetyl alcohol) on the characteristics of resultant bigels. • To compare the properties of different gelled systems i.e., hydrogel, organogel and bigel.	• The results revealed the existence of needle shaped clusters of Span 60 which became fiber-like structures by adding surfactants in the gels. • The viscosity of prepared gels increased whereas the amount of drug release decreased by adding surfactants. • Cetyl alcohol based bigels showed better mechanical and drug release properties as compared to the bigels having Span 60 as an organogelator. • Hydrogels and Bigels showed higher drug release and permeation rates as compared to organogels.	Cetyl alcohol based bigel shows promising mechanical and drug release properties, as compared to other bigel system and organogel, which can further be enhanced by playing with the amounts of organogelator and surfactant. Although hydrogel displays highest drug release but also have lowest viscosity. Therefore, CA based bigel seems suitable option for drug delivery application.	[83]
Fish oil	Beeswax	Sodium alginate, Hydroxy	3.7-6.5 wt%	Benzalkonium chloride, Butylated hydroxyanisole	Imiquimod	Hydrogel-in-organogel type	• To see the influence of increasing organogel content on the properties of prepared	• The outcome of the study showed an increase in the thermal stability while a decrease	Sodium alginate based bigel system, having 10/90 organogel/hydrogel	[28]

		propyl methyl cellulose (HPMC)					bigels. • To compare the characteristics of sodium alginate and hydroxy propyl methyl cellulose based bigels. • To compare the properties of prepared bigels with the hydrogel.	in apparent viscosity and drug release rate of prepared bigels with the increase in organogel content. • Bigels prepared from sodium alginate displayed higher apparent viscosity, hardness, peak stress, drug permeation and drug release rate as compared to the HPMC based bigels. • Hydrogels showed higher apparent viscosity, adhesiveness, hardness, and peak stress values as compared to bigels. • Bigels having sodium alginate or hydroxypropyl methylcellulose together with the fish oil showed higher drug permeation and release rate as compared to hydrogels which was attributed to the incorporation of fish oil.	ratio, seems to be the most suitable candidate for drug delivery applications with enhanced mechanical properties, as compared to hydrogel and other bigel system.	
Sesame oil	Span 60	Gelatin	19 wt%	Tween 80	Ciprofloxacin	Organogel-in-hydrogel type	To compare the characteristics of different gelled systems i.e., hydrogel, emulgel and bigel	• XRD and FTIR analysis of bigels revealed an increase in the crystallinity of bigels due to the addition of organogel within the hydrogel phase which in turn results the enhanced mechanical properties of bigel as compared to hydrogel and emulgel. • Bigel and emulgel also displayed higher impedances and lower swelling indices as compared to hydrogel. • The drug release rate was highest from hydrogel followed by emulgel and then bigel.	Bigel shows better mechanical properties as compared to hydrogel and emulgel but the drug release characteristics needs to be improved for this system.	[61]
Fish oil	Beeswax	Carbopol	3.7-6.5 wt%	Benzalkonium chloride, Butylated hydroxyanisole, Triethanolamine	Imiquimod, Coenzyme Q10 (CoQ10)	Hydrogel-in-organogel type	• To check the influence of increasing organogel content on the properties of prepared bigels. • To compare the behavior of different gelled systems i.e., organogel, hydrogel and bigel. • To develop an immune-modulatory role of imiquimod and fish oil against skin cancer and inflammation resulted from carcinogenesis.	• The output of the study showed a decrease in viscosity, hardness and firmness while an increase in drug permeation of prepared bigels by increasing organogel content. • Hydrogel displays highest viscosity, adhesiveness and lowest drug permeation than organogel and bigel. • Results revealed the higher drug release through diffusion mechanism in the case of drug loaded bigels as compared to drug loaded hydrogel and organogel. • Drug loaded bigels displayed better antitumor effects together with reduction in pro-inflammatory cytokine levels and an increase in anti-	Bigel having 50/50 organogel/hydrogel ratio displays better mechanical, rheological and drug release properties as compared to organogel and hydrogel.	[88, 89]

								inflammatory cytokine levels, both of which helped in the antitumor activity against skin cancer.		
Rice bran oil	Stearyl alcohol	Agar	2.4-6.5 wt%	-	Ciprofloxacin hydrochloride	• Organogel-in-hydrogel type at lower organogel fractions • Complex bi-continuous type at highest organogel fraction	• To investigate the effect of increasing organogel fraction on the properties of prepared bigels. • To compare the properties of hydrogel and bigel.	• Results showed an increase in the mechanical properties of bigels with the increase in the organogel content up to a certain critical concentration and after that a sudden decrease in the properties of bigels was observed. • Bigels also showed lower electrical stability as compared to hydrogels which was further reduced by the increase in organogel content. • The drug release mechanism from the bigel formulations was diffusion mediated.	The bigel formulation having 37.5 wt% organogel displays interesting mechanical and drug release properties making it suitable candidate for drug delivery application.	[70]
Soya-bean oil	Stearic acid	Mixture of Agar and Gelatin	12 wt%	Glutaraldehyde, Ethanol, Hydrochloric acid	Metronidazole	Organogel-in-hydrogel type	• To develop a bigel system based on organogel and phase separated gelatin-agar co-hydrogel • To analyze and compare the properties of co-hydrogel, emulgel and bigel.	• XRD and FTIR analysis showed an increase in the crystallinity of bigel and emulgel due to the addition of organogel or oil, respectively within the co-hydrogel phase. • Bigel and emulgel also displayed higher electrical impedances and better mechanical properties as compared to the co-hydrogel while drug release profiles of all the formulations were similar.	This study reported the preparation of bigels with co-hydrogel. The bigel formulation displays better mechanical characteristics as compared to emulgel and co-hydrogel, making it a good option for drug delivery application.	[69]
TegoSoft® CT(Caprylic/ capric triglyceride)	Compritol® (lipid excipient of glyceryl behenate)	Carbopol	10.5 wt%	Transcutol® P (diethylene glycol monoethyl ether), Triethanolamine (TEA)	Ibuprofen	Organogel-in-hydrogel type	To compare the characteristics of organogel, hydrogel and bigel for drug delivery application, to treat periodontitis	• All the studied formulations showed elastic (solid-like) behaviour in frequency sweep tests. • Organogel displayed highest viscosity and better viscoelastic properties followed by bigel and then the hydrogel. • After 6 hours, bigel exhibited highest drug release as compared to organogel and hydrogel.	This is the first study reporting the use of Compritol® as an organogelator. Bigel is a potential candidate to treat periodontitis because of possessing comparable mechanical properties and excellent drug release properties as compared to organogel and hydrogel.	[90]
Rice bran oil	Stearic acid	Tamarind gum	4.2 -5.4 wt%	Ethanol	Moxifloxacin HCl	• Organogel-in-hydrogel type at lower organogel fraction • Hydrogel-in-organogel type at higher organogel fraction	• To study the influence of different organogel/hydrogel ratio on the properties of prepared bigels. • To compare the characteristics of resultant bigels with the individual gels, i.e., hydrogel and organogel.	• A decrease in electrical impedance together with an increase in molecular interactions and drug diffusion was observed for prepared bigels as a function of increasing hydrogel content. • The firmness of organogel and hydrogel was quite similar and higher than the prepared bigels. • Bigels displayed highest drug release followed by hydrogel and then the organogel.	Bigel having higher amount of hydrogel (organogel-in-hydrogel type) displays excellent drug release properties together with better mechanical and electrical properties, making it an idea candidate for drug delivery applications.	[91]

Sesame oil, Soy bean oil	Stearic acid	Gelatin	20 wt%	Tween 80, Glutaraldehyde, Ethanol, Hydrochloric acid	Ciprofloxacin	Organogel-in-hydrogel type	• To investigate the effect of different oils on the properties of resultant bigels. • To compare the behaviour of bigels with the emulgels.	• The effect of using different vegetable oils on the mechanical properties of the bigels was not significant. • The drug release was bit higher from soy bean oil based bigel as compared to the bigel having sesame oil. • The output of microscopic analysis showed the existence of organogel aggregates within the bigels while the oil droplets were dispersed inside the emulgel. • The bigels showed the resistance towards leaching of dispersed phase (organogel) whereas the leaching of oil phase from emulgels was bit higher. • Bigels displayed higher mechanical and mucoadhesive properties whereas lower deformation and drug release rate as compared to emulgels.	The drug release characteristics of prepared bigels can be manipulated, by using different vegetable oils, without affecting their mechanical properties. Soy bean based bigel seems an interesting option for drug delivery applications because of its excellent mechanical properties together with comparative drug release behaviour.	[68]

472

473 **TABLE 3.** Different bigel systems reported in the literature for cosmetics and other applications

Oil Phase	Organogelator	Hydrogelator	Total Concentration of Gelators	Additives	Structural Distribution	Objective(s) of Study	Key Findings	Analysis	Ref
Sweet almond oil, Liquid paraffin	Cholesterol, Span 60, Zinc stearate, Silicic acid	Carbopol	0.8-2.5 wt%	Triethanolamine	*N.A	• To study the influence of different organogels on the properties of resultant bigels. • To investigate the effect of varying organogel/hydrogel ratio on the behavior of prepared bigels. • To compare the characteristics of organogel, hydrogel and bigel.	• Bigels prepared from organogels having zinc stearate or silicic acid were heterogeneous and non-smooth while other two organogelators resulted in homogenous and smooth bigel systems. • The adhesiveness and firmness of the bigels showed an increase with the increase in organogel content. • Results of stability analysis showed no change in the texture and appearance of gels for the period of six months whereas after six months changes were observed in the color and texture of the formulations. • Bigels also showed moisturizing effect, cooling effect and good spreadability, without the need of any additives, which made them a potential candidate for cosmetic applications as a moisturizer.	This was the first study to report the synthesis and characterization of bigels. Span 60 based bigel (10 wt% organogel content) shows interesting mechanical and moisturizing properties as compared to other reported systems.	[48]
Extra virgin olive oil	Mixture of policosanol and glyceryl monostearate	LM pectin	3.63-15.5 wt%	Tocopherol, Citric acid, Tribasic sodium citrate, Glycerin, Calcium chloride dihydrate	• Organogel-in-hydrogel type at lower organogel fractions • Complex bi-continuous type at highest	• To analyze the effect of increasing organogel fraction and organogelators amount on the rheological properties and phase inversion phenomena • To develop a semi-empirical model to fit the rheological properties of bigels.	• The outcome of the study showed an increase in the consistency, degree of structuration and thermal stability of bigels with the increase in organogel fraction or the amount of organogelators due to the thermally stable nature of organogel. • The microscopic and conductivity analysis of bigels confirmed the oil-in-water type system	This study first time reported the semi-empirical model to fit the rheological data of bigels. This model shows the dependence of bigel properties on the dispersed phase fraction and also on the properties of	[63]

					organogel fraction		which became more complex matrix-in-matrix type at the highest organogel fraction (60 wt%). • A semi-empirical rheological model was also proposed which displayed a reasonably good agreement with the experimental data. • The resultant bigel system is an interesting option for sustained release of hydrophilic/hydrophobic active agents for cosmetics and pharmaceutical applications.	individual phases.	
Virgin olive oil	Mixture of policosanol and glyceryl monostearate	LM pectin	4-16 wt%	Tocopherol, Citric acid, Tribasic sodium citrate, Glycerin, Calcium chloride dihydrate	• Organogel-in-hydrogel type at lower organogel fractions • Complex bi-continuous type at highest organogel fraction	• To investigate the influence of increasing organogelator, hydrogelator and organogel amount on the microstructural and rheological properties of bigels. • To develop a model by relating the bigel properties with the amount and properties of individual phases.	• The increasing consistency of the individual phase within bigel system did not show much effect on the structural distribution of the individual phases within the resultant bigels. • The increasing organogelator and hydrogelator amounts displayed an increase in the consistency and degree of structuration of the prepared bigels. The effect of modifying consistency of hydrogel phase (continuous) on the rheological properties of bigels was more pronounced as compared to the manipulating the amount of organogelator. • The results of the rheological model fitting on the experimental data showed that the Palierne model modified with crowding factor was not able to fit the experimental data accurately which was linked with the non-ideal behavior of bigels due to the presence of non-spherical and polydisperse droplets. • Due to the absence of theoretical model for such a complex system, an empirical model, based on Palierne model, was proposed. • The proposed model showed a quite good agreement with the experimental data and can be used to the predict the complex modulus of bigels if moduli of individual phases are known and the maximum packing fraction can be safely assumed.	The proposed model is an interesting tool to predict the complex modulus of bigels by using the information of moduli of individual phases and the maximum packing fraction of the considered system. This study also shows that the hydrogel phase is more important to influence the properties of resultant bigels.	[78]
Extra virgin olive oil	Monoglycerides of fatty acids	Potato starch	4.8-7.3 wt%	Ascorbyl palmitate, Algae, α-Tocopherol, Glycerin, Sodium ascorbyl phosphate, Phenoxyethanol, Cethyl alcohol	Complex matrix-in-matrix system	• To develop a bigel system by mixing emulgel (cosmetic formulation) and organogel. • To analyze the effect of increasing organogel content on the properties of resultant complex bigel system.	• The prepared bigel formulations showed satisfying results for the stability due to the presence of starch hydrogel. • Bigel formulations showed an increase in the consistency with the increase in organogel fraction up to a certain level and after that a decrease in consistency was observed followed by a new increase and this was attributed to the transition of O/W system to a more complex bicontinuous type arrangement as also confirmed by NMR self-diffusion, microscopic and conductivity analysis of bigels.	This is the first and only study which presents the synthesis of bigel system by mixing emulgel, instead of hydrogel, with the organogel phase. The reported bigel is an interesting system because it possesses organogel, hydrogel and oil phase in a single system.	[52]
Sunflower oil	Hydrophilic fumed silica	Mixture of Locust bean gum and Carrageenan	9.4-13.6 wt%	-	Hydrogel-in-organogel type	• To develop a bigel system by using colloidal silica particles as an organogelator. • To check the effect of increasing hydrogel fraction on the behavior of resultant bigel systems. • To compare the characteristics of organogel, hydrogel and bigel.	• Results revealed a completely different rheological behavior of bigels as compared to organogel and hydrogel. • Bigels also displayed higher gel strength and lower structure recovery as compared to organogel and hydrogel. • Furthermore, hydrogel/organogel ratio also showed a significant effect on the rheological	This is the first study reporting the gelation of vegetable oil by using colloidal silica particles and also incorporating that organogel into hydrogel to prepare bigel systems. The resultant bigel system shows	[62]

							properties of the bigel formulations.	synergistic effect and displays better properties than either of the single gel i.e., hydrogel and organogel, which makes them an interesting system for cosmetic and pharmaceutical applications.	
Vegetable oil	Beeswax	Sodium alginate	2-4 wt%	-	Organogel-in-hydrogel type	To study the behavior of bigels by increasing the organogel fraction within the bigel system	• Results showed a non-homogeneous distribution of organogel droplets within bigels at the highest fraction of organogel. • Bigels showed a decrease in firmness, spreadability and adhesivity with the increase in organogel content which was attributed to the de-flocculated structure. • X-ray diffraction analysis showed that once poly-crystallinity was reached the results remained same for all tested ratios.	This study presents the critical fraction of organogel after that the properties of the resultant system is not much affected by the increase in organogel fraction.	[92]
High oleic sunflower oil	Glycerol monostearate	Gellan gum	**N.A	-	Hydrogel-in-organogel type	To evaluate the effect of process variables (organogel/hydrogel ratio and mixing speed) on the properties of bigels through multivariate analysis	• Results revealed that the smaller droplets size resulted in higher cohesiveness, modulus, adhesiveness, consistency and spreadability. • Mixing speed and organogel/hydrogel ratio was pointed out the most important parameters to influence the properties of bigels.	This is the first and only study reporting the effect of processing variables on the properties of resultant bigel systems. Organogel-hydrogel ratio and mixing speed are quite important parameters to manipulate the properties of bigel systems.	[64]

*Microstructural analysis of bigels is not reported

**Hydrogel/organogel ratio is not mentioned in the paper

5. Conclusion and Future Perspective

In recent times, different bigel systems have been produced and manipulated according to the needs of different applications. This review presented the literature regarding the important characteristics of bigels and also demonstrated the detailed discussion on the modelling of these systems. Moreover, utilization of these systems for pharmaceutical and cosmetics applications has also been discussed.

Bigels are emerging class of materials and, therefore, extensive analysis of these systems is required for commercial applications. Different parameters, which are important in the synthesis of bigels include: storage of bigels, mixing speed, mixing temperature, amount of organogelator and hydrogelator, organogel/hydrogel ratio, addition of emulsifiers and incorporation of emulgels instead of either organogel or hydrogel. The effect of above mentioned parameters on the final properties of prepared formulation requires more attention from the researchers. Organogel-in-hydrogel type bigels have been investigated much in the literature while other two types, hydrogel-in-organogel and bi-continuous type are less studied which require more focus from the researchers in future.

From literature, it was observed that the systems with better mechanical and rheological properties displayed lower drug release rate. Therefore, further investigation is required in this area to prepare a system with better properties together with enhanced drug release rate. Discussion on the rheological modeling of bigels revealed that the existing models are not enough to accurately predict the rheological properties of bigels. Therefore, further investigation is necessary to understand the dependence of rheological properties of bigels on the moduli of dispersed and continuous phase and also on the particle size distribution, with the aim of

498 proposing a better model to accurately predict the properties of such a complex system.
499 Furthermore, simulation of such systems can also be performed to compare the results with real
500 time response. Moreover in future, along with pharmaceutical and cosmetics applications, bigel
501 formulations can be prepared and analyzed for food applications.

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