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A rheological and microstructural characterisation of bigels for cosmetic and pharmaceutical uses

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ABSTRACT

Bigels are biphasic systems formed by water-based hydrogels and oil-based organogels, mainly studied, in the last few years, for pharmaceutical and cosmetic application focused on the controlled delivery of both lipophilic and hydrophilic active agents. The rheological properties of bigels depend on both the amount and the rheological characteristics of single structured phases. Moreover, it can be expected that, at large fractions of one of the starting gels, systems more complex than oil-in-water or water-in-oil can be obtained, yielding bicontinuous or matrix-in-matrix arrangement. Model bigels were investigated from a microstructural (i.e. microscopy and electrical conductivity tests) and rheological point of view. The hydrogel was prepared by using a low-methoxyl pectin whereas the organogel was prepared by using olive oil and, as gelator, a mixture of glyceryl stearate and policosanol. Model bigels were obtained by increasing the amount of organogel mixed with the hydrogel, and microstructural characterisation evidenced an organogel-in-hydrogel behaviour for all investigated samples, even though at the highest organogel content a more complex structure seems to arise. A semi-empirical model, based on theoretical equations developed for suspensions of elastic spheres in elastic media, was proposed to relate bigel rheological properties to single phase properties and fractions.

1. Introduction

Bigels are biphasic systems, with enhanced mechanical and controlled delivery properties, very interesting for food, but also very promising for cosmetics and pharmaceutical uses. The main characteristic, with respect to other multiphase systems (such as emulsions, emulgels, or filled gels), is that both phases (internal and external one) are semi-solid in nature [1–3]. In fact, they are mainly produced by mixing, at high shear rates, an organogel and a hydrogel leading to the development of complex matrices [2,4–7].

In the case of topical use in cosmetic/pharmaceutical field, organogels are commonly considered oily and not easy to be removed after application, even though they are interesting for their ability to dissolve lipophilic agents. In contrast, hydrogels have high market worth due to their patient compliance nature such as non-oily, cooling effect and capability to be washed with water, but they can be used only as carriers of hydrophilic components [8,9].

Owing to their nature, bigels have the features of both gels, for example, the improvement of hydration of the stratum corneum, the moisturising effect and good spreadability, emollient properties and water washability upon application to the skin, the ability to deliver both hydrophilic and lipophilic agents [2,5,6,10]. The contemporary use of two gel systems in bigels can give a synergetic effect such as improvement of drug permeation due to the existence of both water phase and oil phase [7]. Since bigels have the combined characteristics and advantages of organogels and hydrogels, they may, possibly, be used as a topical drug delivery carrier on the skin in pharmaceutical and cosmetic industries [5,6,11]. Moreover, owing to the structuration of both phases of which they are composed, bigels do not display separation of the two phases on storage at room-temperature for the duration of up to 6–12 months [7]. As known, gels are stabilised by ensnarement of the mobile phases through a 3-D network, and showing this microstructure in both phases, bigels are made of an extra-fine dispersion of a phase into the other [3,4,7]. Bigel systems may have some disadvantages, like they are not thermo-reversible as they may become destabilised at high temperatures [7].

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On the basis of the mutual disposition of organogel and hydrogel, bigels can be divided into three categories:

i. Organogel in hydrogel system (O/W)
ii. Hydrogel in organogel system (W/O)
iii. Bi-continuous system

The first category of bigels includes the systems in which the oil phase is dispersed within the aqueous phase and these systems are, probably, the most investigated in the literature, where the hydrogel was prepared by using different kind of hydrogelators such as starch, sodium alginate, sodium carboxy methyl cellulose [12], guar gum [7], hydroxypropyl-methylcellulose [13], gelatin [1,8], gelatin-agar mixture [1] or water soluble synthetic polymers (e.g. polyvinyl alcohol and polyvinyl pyrrolidone) [2]. In the same way different organogels were used as dispersed structured phase: Behera et al. [2,12] used sunflower oil and Span 40 (Sorbitan Monopalmitate), the group of Singh [1,7] investigated a sorbitan monostearate-sesame oil based organogel. Ibrahim et al. [13] proposed organogels based on soya-bean oil as a solvent and span 60, cetyl alcohol or lecithin-pluronic as organogelators, mixed with other surfactants, and Sagiri et al. [8] and Wakhet et al. [3] prepared organogels based on soya-bean oil as a solvent and stearic acid as organogelator.

Bigels were characterised with different techniques aiming at investigating the material microstructure and the mutual position of the structured phases. Rheological methods were used by Behera et al. [2, 12], Singh et al. [7], Satapathy et al. [1]. Additional techniques were also used such as fluorescence microscope [12], confocal laser scanning microscope [7], compound optical microscopy [13], bright-field microscopy [1,3,8], XRD, FTIR and DSC [8].

As far as hydrogel-in-organogel biphasic systems are concerned, a lower number of works is available. Patel et al. [14] reported the characterisation of bigels made by mixing fumed silica-sunflower oil organogel and polysaccharides (locust bean gum-carrageenan) based hydrogel at different oil-water ratios. The bigel was studied with confocal microscopy to understand the distribution of organic and aqueous phases, and a discontinuous distribution of water phase in the oil phase was found.

Finally, Lupi et al. [15] investigated bigels produced by mixing a cosmetic formulation (oil in water) for skin care with increasing fractions of monoglycerides of fatty acids/olive oil organogels. NMR-self diffusion analysis, contrast phase microscopy and electric conductivity confirmed that a complex matrix-in-matrix structure was present at the highest fractions of added organogel.

Therefore, it seems evident that oil in water bigels at constant phase ratio are more common, whereas less data are available on the effects of increasing the organogel fraction and on potential transitions occurring in O/W systems with increasing organogel content.

Starting from this point, the aim of the present work is the investigation of model O/W bigels for potential cosmetic or pharmaceutical applications based on the controlled delivery of hydrophilic/lipophilic active agents. These systems were prepared with different phases ratios to understand their rheological properties and the relationship between their mechanical characteristics with single phase properties.

Bigels were made with an organogel based on extra virgin olive oil and a mixture of policosanol (a fatty alcohol mixture) and glyceryl monostearate (a monoglyceride of fatty acids) as the organogelators. Different amounts of organogels were added to a low methoxyl (LM) pectin hydrogel, and a rheological and microstructural analysis was carried out (Small amplitude oscillation tests, Steady State Flow Curve Tests, Electric conductivity tests, contrast phase microscopy). It was chosen to design new model bigels starting from ingredients as much natural as possible (for example pectin as hydrophilic gelling agent [16,17], and olive oil [18,19] as lipophilic solvent), obviously chosen among those admitted for topical applications. In fact, the increasing demand for clean label excipients [20] should be taken into account when designing new formulations. In this framework, biopolymers currently used in the food field to stabilise biphasic systems could be promising candidates in cosmetic/pharmaceutical field too [20].

2. Materials and methods

Bigels were produced by preparing, separately, the hydrogel and the organogel, and mixing them with a mechanical (rotor-stator) homogeniser at room temperature. Samples with different organogel/hydrogel ratios were prepared and their properties investigated.

2.1. Organogel and hydrogel materials

The organogels were prepared with an extra virgin olive oil (EVO), kindly supplied by Gabro (Italy), as the solvent, policosanol from rice bran wax (P) as the first organogelator [21,22], glyceryl stearate (GS), as the second organogelator/emulsifier and tocopherol as an antioxidant. All the ingredients were supplied by A.C.E.F. (Italy).

Firstly, organogels were produced by adding tocopherol in the extra virgin olive oil to prevent oxidation (the ratio tocopherol/olive oil was kept constant and equal to $6.15 \cdot 10^{-4}$ (w/w) according to a preliminary optimisation, data not shown), and then heating the oil in a water bath thermostated by a plate heater (VELP Scientific, Italy) up to 85 °C. Afterwards, the gelators (i.e. P and GS in ratio 1:1) in the proper amount were added to the hot oil, and the system was continuously stirred with a laboratory stirrer (RW 20, IKA-Werke, Germany) at approximately 200 rpm. On complete melting of organogelator, mixing was continued for 5 min. Finally, it was slowly cooled from 85 to 25 °C in a thermostatic water bath (F25, Julabo, USA) and maintained at 25 °C for the time necessary to reach thermal equilibrium. Organogels were prepared by using 25% (w/w) (sample OM1) and 50% (w/w) (sample OM2) of organogelator mixture.

The hydrogel was prepared by using a LM pectin (Degree of Methoxylation 30.5%, Galacturonic Acid content 89.9% & Molecular Weight 60.2 kDa) kindly supplied by Silva Extracts S.r.l. (Italy), glycerine (Sigma Aldrich, Italy), citrate buffer solution with pH equal to 4.2 ± 0.1 [23] (constituted of distilled water, citric acid, and tribasic sodium citrate, Carlo Erba, Italy), sodium chloride and calcium chloride dihydrate (Carlo Erba, Italy).

The buffer solution was prepared by mixing 0.85 g tribasic sodium citrate and 0.715 g citric acid into 500 ml of distilled water (magnetic stirrer, Velp Scientific, Italy). Then, 2.9 g NaCl (corresponding to a final 0.1 M concentration) were added to the buffer (for the electrical conductivity tests) and finally 0.0176 g calcium chloride dihydrate were dissolved in the system to give gelation of LM pectin via calcium bridges between carboxyl groups of the biopolymer, according to the well-known egg box model [23,24].

The hydrogel was prepared by mixing pectin within buffer solution. In order to achieve the best dissolution of pectin powder, preventing aggregate formation, pectin was initially mixed with glycerine and then the buffer solution was slowly added into the mixture at room temperature (25 °C) , while stirring at 500 rpm for 2 min with an Ultra Turrax homogeniser (UT T50, IKA-Werke, Germany). The composition of hydrogel used for all the prepared bigels was fixed: in particular, it was made of 95% (w/w) of aqueous solution, 1.25% (w/w) of pectin, the rest being glycerine.

2.2. Bigels

All bigels (batches of 200 g) were prepared by slowly incorporating the organogel into the hydrogel at room temperature (approximately 25 °C) while stirring at 1200 rpm for 8–12 min with an Ultra Turrax homogeniser (T50, IKA-Werke, Germany). Mixing time was progressively increased, according to the increasing consistency of the systems with higher amounts of organogel during the first part of the