Carbohydrate Polymers 84 (2011) 1011–1018

Contents lists available at ScienceDirect

Carbohydrate Polymers

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

Preparation of biodegradable nanoporous microspherical aerogel based on alginate

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ARTICLE INFO

Article history:
Received 4 November 2010
Received in revised form
16 December 2010
Accepted 19 December 2010
Available online 25 December 2010

Keywords:
Spherical aerogel microparticles
Biodegradable nanoporous materials
Supercritical CO_2 extraction
Polysaccharides
Alginate aerogels

ABSTRACT

Supercritical extraction of the solvent from organic gels, like polysaccharides, enables the production of highly porous biodegradable aerogel with a high surface area. The structural properties of the produced aerogel depend mainly on the preparation methods and the composition of the gel phase. This work presents a new method to produce biodegradable microspherical alginate aerogels particles using an emulsion technique. Water in oil (W/O) emulsion was produced by mixing a Na–alginate solution (dispersed phase) with oil (continuous phase) followed by cross-linking the dispersed phase to form the gel particles. The gelation parameters as well as the emulsion process parameters were investigated in order to control the form and the structural properties of the produced alginate aerogel. Alginate aerogel microspherical particles with a high surface area up to 680 m^2/g and relatively large pore volume up to 4.0 cm^3/g and different mean particle diameters ranging from 25 μm to few hundred microns were produced using the presented method.

1. Introduction

Silica aerogels are regarded as promising drug delivery systems (Patel, Purohit, & Suthar, 2009; Smirnova, Mamic, & Arlt, 2003; Smirnova, Suttiruengwong, Seiler, & Arlt, 2004; Smirnova, Turk, Wischumerski, & Wahl, 2005). Due to their large specific surface area, high drug loadings can be reached. The drug release kinetics show remarkable characteristics that can be tailored by adjusting the functional groups on the aerogel surface, based on the affinity of each specific drug (Alnaief & Smirnova, 2010; Gorle, Smirnova, & Arlt, 2009). However, for some applications in the pharmaceutical industry biodegradability is a limiting factor. For those applications silica aerogels cannot be used since they are biocompatible, but not biodegradable. This demand can be met using matrices made out of organic materials or biodegradable polymers like polysaccharides (Dumitriu, 2005; Walter, 1998). Polysaccharides are one of the most abundant renewable resources on the earth. Due to their physiological compatibility, polysaccharides are quite common additives in food and drug formulations (Qiu, 2009). The combination of the outstanding structural properties of aerogels with the biocompatibility and biodegradability of polysaccharides would result in high potential drug delivery systems (Mehling, Smirnova, Guenther, & Neubert, 2009; Robitzer, David, Rochas, Di Renzo, & Quignard, 2008).

Alginate is a natural polysaccharide polymer, found in great abundance in brown seaweeds. Because of non-toxicity, biodegradability and accessibility, alginate has been used in food industry, pharmaceutics and medicine (Domb & Kost, 1997; Dumitriu, 2005; Phillips & Williams, 2000; Walter, 1998). Alginate consists of a linear copolymer composed of 1,4-linked-β-D-mannuronic acid (M) and α-L-guluronic acid (G) residues of varying composition and sequence (Fig. 1). The presence of the carboxylate group within G blocks rings bears a global negative charge at pH 7 usually compensated by sodium cations. Adding divalent ions like Ca^{2+} induces the cross-linking of the polymer and thus the formation of a gel (Rehm, 2009). This property was explained by the so-called "egg-box" model, Fig. 1, suggesting a possible binding site for Ca^{2+} in a single alginate chain (Phillips & Williams, 2000; Rehm, 2009). Gelling of alginate depends mainly on the strength, number and length of cross-linking; hence, the composition and the sequence of G and M residues are the main properties of alginate, which influence the mechanical properties of the produced gel (Draget, Østgaard, & Smidsrød, 1989; Dumitriu, 2005; Rehm, 2009). Generally, two fundamental methods are used to induce gelation of the alginate solution: (1) the diffusion method; (2) the internal setting method. In case of the diffusion method the cross-linking ion diffuses from a large reservoir into an alginate solution (Trens, Valentin, & Quignard, 2007; Valentin, Molvinger, Quignard, & Di Renzo, 2005; Valentin et al., 2006). Internal setting method differs from the former one by control release of the cross-linking

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doi:10.1016/j.carbpol.2010.12.060

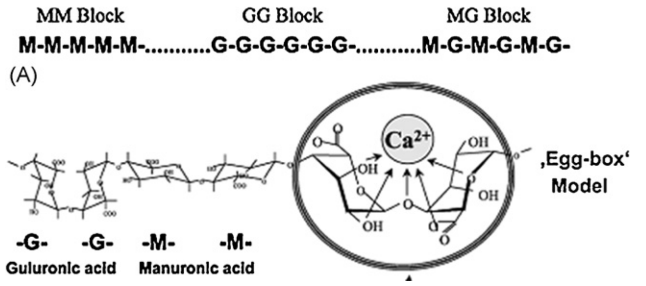

Fig. 1. General alginate, (A) block structure; (B) the formation of the "egg-box" model (Dumitriu, 2005).

ion which is already dispersed as an inert source within the alginate solution. Usually control release of the ion can be performed by pH control or by limiting solubility of the ion salt (Mehling et al., 2009; Phillips & Williams, 2000; Silva, Ribeiro, Figueiredo, Goncalves, &, Veiga, 2006). The feasibility of producing highly porous structures, based on alginate, by supercritical drying with CO_2 has been reported (Horga, Di Renzo, & Quignard, 2007; Mehling et al., 2009; Quignard, Valentin, & Di Renzo, 2008; Robitzer, David, Rochas, Di Renzo, & Quignard, 2008; Valentin et al., 2005, 2006). It is possible to differentiate two different forms of alginate aerogels produced so far: (1) monolithic alginate aerogel following the internal setting method (Mehling et al., 2009); (2) spherical alginate aerogel beads following the diffusion method (Quignard et al., 2008; Robitzer et al., 2008a; Valentin et al., 2005). The general procedure of the internal setting method is to mix the alginate solution with the divalent cation (usually Ca^{2+} ions) source and a gelation inducer agent. After that the alginate solution can be poured in to a mould of the desired shape and size. Finally a gel is formed after certain time depending on the gelation mechanism. In the diffusion method, the alginate solution is dropped into a divalent cation, generally a Ca^{2+}, bath. The art of generating these droplets can vary from using simple syringe to pressing the alginate solution through a micro opening mesh (Chuah, Kuroiwa, Kobayashi, Zhang, & Nakajima, 2009; Escudero, Robitzer, Di Renzo, & Quignard, 2009). As soon as the droplets come into contact with the divalent cation bath an instantaneous gelation is induced. The size of the gel beads depend mainly on the size of the opening of the feeding device.

In the previous work of our group, it has been shown that it is possible to produce microspherical silica aerogel particles by combining the sol–gel process with the emulsion formation followed by supercritical extraction of the oil-particles dispersion (Alnaief & Smirnova, 2011). The aim of this work is to adopt the described process to produce microspherical alginate particles and to study different gelling mechanisms for their suitability to be coupled with the emulsion process.

The adopted process was modified to meet the needs of alginate aerogel production. The modified process consist of 5 main steps (Fig. 2): (1) preparation of the dispersed aqueous phase; (2) emulsification of the aqueous phase in a continuous phase (immiscible with the first one); (3) cross-linking of the dispersed phase (liquid micro-droplets) to form stable gel microspheres; (4) multistep solvent exchange of the hydrogel with ethanol to obtain an alcogel; (5) CO_2 supercritical extraction of the microspherical alcogel particles to obtain the final microspherical aerogel particles.

2. Experimental methods

2.1. Reagents

Carbon dioxide with a purity of >99.9% was supplied by AGA Gas GmbH (Hamburg, Germany). Na–alginate was purchased from Sigma life science. Ethanol 99.8%, glacial acetic acid and $CaCl_2$ where purchased from Merck GmbH, Germany. $CaCO_3$ was kindly provided by Magnesia GmbH Germany. Glucono-δ-lactone (GDL) was purchased from Alfa Aesar. Vegetable oil was purchased from domestic shops. Paraffin oil was purchased from Carl Roth GmbH

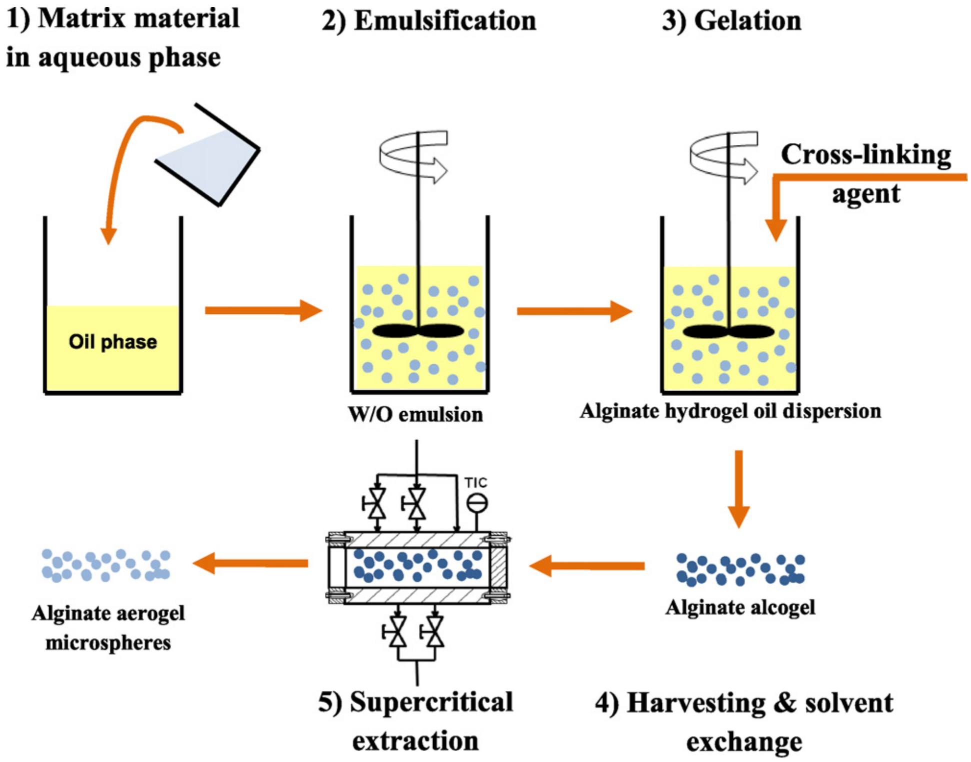

Fig. 2. Schematic overview over the five main steps in alginate aerogel microsphere preparation by emulsion method combined with supercritical extraction.

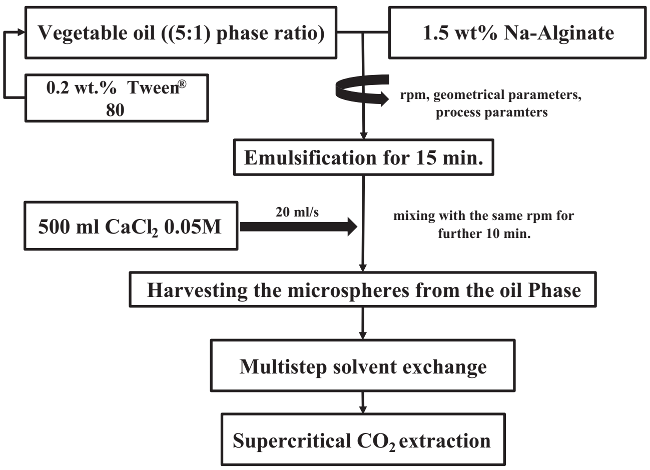

Fig. 3. Preparation of alginate aerogel miceoparticles following the diffusion method combined with the emulsion (procedure 1).

Germany. All chemicals were used as provided without any further purification.

2.2. Methods

2.2.1. Preparation of alginate gel microspheres

Different procedures were studied to produce alginate gel microparticles. These procedures follow the main two principles of cross-linking the alginate solution, namely, the internal setting method and the diffusion method. In the following sub-sections a detailed description is provided.

2.2.1.1. Preparation of alginate stock solutions. In order to compare the results from different batches, the same stock solution of alginate was used for all experiments. Stock solutions with different alginate concentrations were prepared (1.5 wt.%, 2 wt.% and 3 wt.%). A certain amount of sodium alginate salt was mixed with distilled water using a magnetic stirrer to obtain the desired concentration. Mixing was left overnight to ensure complete dehydration. The stock solutions were then stored at 5 °C. The stock solution was allowed to reach room temperature before starting any preparation.

2.2.1.2. Preparation of alginate gel microspheres.

2.2.1.2.1. Procedure 1: diffusion method. The main criterion of this procedure is to obtain the gel microspheres out of alginate droplets using the principle of diffusion gelation method (Phillips & Williams, 2000). Fig. 3 shows schematically the main steps used in preparing alginate aerogel microparticles following this procedure. A detailed description can be found elsewhere (Sheu, Marshall, & Heymann, 1993). For a typical experiment, sodium alginate solution was added to an oil phase, vegetable oil, which contains 0.2 wt.% Tween® 80, to obtain 1:5 W/O phase ratio. The mixture was emulsified in a beaker (diameter: 11 cm) using a marine propeller (diameter: 5 cm) with a certain stirring speed for 15 min. After that, 500 ml of 0.05 M $CaCl_2$ was introduced into the previous W/O emulsion very fast but gently with constant rate at about 20 ml/s. Finally the gel–oil dispersion was centrifuged (25 °C, 350× g, 10 min). The collected gels were washed with distilled water, and multistep solvent exchange was carried out to prepare the microparticles for CO_2 supercritical extraction.

2.2.1.2.2. Procedure 2a: internal setting method. This procedure differed from the former one mainly in the cross-linking method mechanism, which follows the internal setting method (Silva, Ribeiro, Figueiredo, & 2006). The main steps used in this procedure are schematically shown in Fig. 4. 50 g of alginate solution with the desired concentration was mixed vigorously with 5 wt.% $CaCO_3$ solution to attain a certain molar ration (Ca^{2+}/Na–alginate = 7.3 wt.%) using an ultra-turrax mixer for 5 min. Paraffin oil (continuous phase) was placed in a 500 ml vessel (diameter: 11 cm) and mixed using a marine propeller with a certain stirring rate. 1 vol.% (V surfactant/V oil) of the surfactant (Span® 80) was added to the oil phase. The dispersion (alginate solution + $CaCO_3$) was then poured at once into the oil phase to obtain 1:2 phase ratio (dispersion/oil). Subsequently, microsphere droplets were formed. After 15 min, 20 ml of paraffin oil + glacial acetic acid (acid/Ca^{2+} molar ratio = 3.5) was added to the system to induce the cross-linking of the alginate solution. After 15 min the propeller was stopped and the oil–gel dispersion was filtered to harvest the gel particles. Finally, multistep solvent exchanges were carried out to prepare the microparticles for CO_2 supercritical extraction.

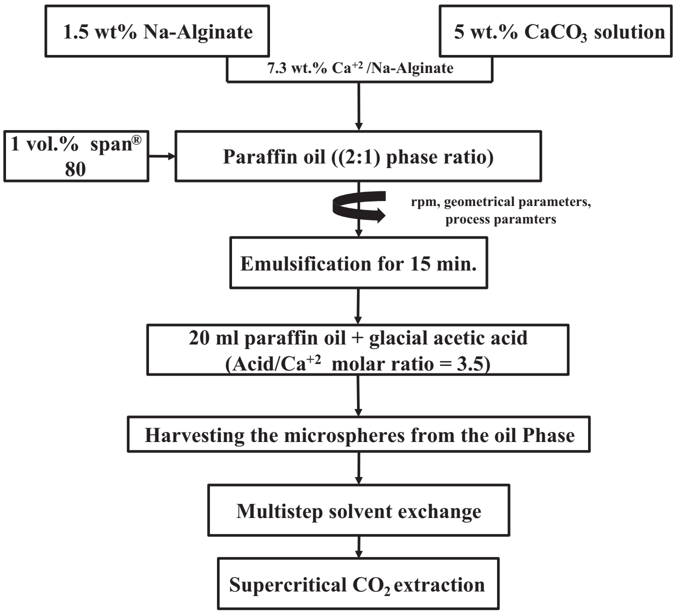

Fig. 4. Preparation of alginate aerogel microspheres following the internal setting method combined with the emulsion (procedure 2a).

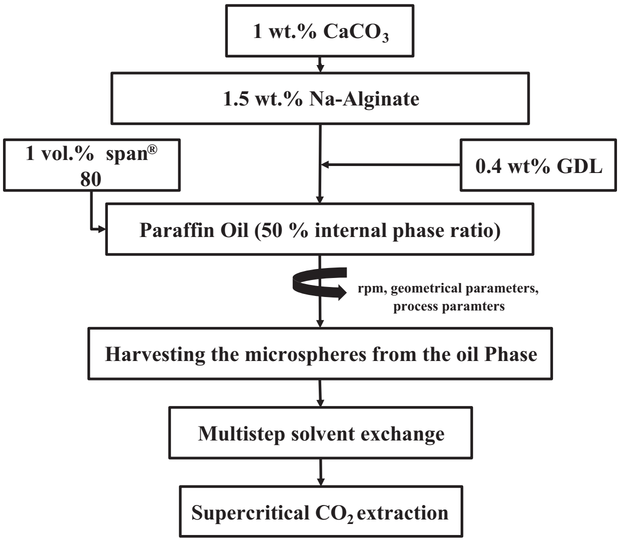

Fig. 5. Preparation of alginate aerogel microspheres following the internal setting method combined with the emulsion (procedure 2b).

2.2.1.2.3. Procedure 2b: internal setting method. The last used procedure follows the same principle as that of the previous one (procedure 2a). However, different mechanism was used to reduce the pH of the solution: addition of GDL was used (Mehling et al., 2009). 50 g of alginate solution was mixed vigorously with 1 wt.% $CaCO_3$ ($CaCO_3$/alginate solution) using ultra-turrax mixer for 5 min. After that, 0.4 wt.% GDL (GDL/alginate solution) was added to the dispersion and mixed for further 2 min. The next step is the addition of the dispersion (alginate solution + GDL + $CaCO_3$) to the oil phase (paraffin oil), which contain 1 vol.% Span® 80, to reach 1:2 W/O phase ratio. The emulsion was then stirred using a marine propeller for 30 min with constant stirring rate. Alginate droplet were converted to alginate gel microspheres due to the gradually reduction of the dispersion pH (upon hydrolyses of GDL). Then, the microspherical particles were harvested using filter paper. Finally, multistep solvent exchanges were carried out to prepare the microparticles for CO_2 supercritical extraction (Fig. 5).

2.2.2. Solvent exchange

In order to convert the gel to an aerogel using supercritical CO_2 extraction, it is obligatory to exchange the solvent of the gel (water) with one that can be extracted with sc CO_2. In this work hydrogel was converted to an alcogel using multistep solvent exchange with ethanol. In typical solvent exchange process steps of 30:70, 50:50, 70:30, 100:0 and 100:0 (ethanol/water) were used. Exchange time of 3 h was used, except for the last step, which lasts for overnight.

It should be mentioned that the solvent exchange plays an important role in production of organic aerogels. Till now, no sufficient studies of this process are present in the literature. The solvent exchange process and its effect on the final properties of different organic aerogels with different forms are under investigation.

2.2.3. Supercritical extraction of the alginate gel particles

A process flow diagram of the supercritical drying is shown in Fig. 6. In a typical experiment, the produced gel were wrapped separately in a filter paper and placed into the 4 l cylindrical stainless steel vessel. Supercritical CO_2 was delivered using a high pressure diaphragm pump and was introduced from the top of the vessel at constant flow rate (100–200 g/min). Temperature was maintained constant (40 °C) using an oil heating jacket. At the outlet of the vessel, supercritical CO_2 loaded with solvent was directed to another 2 l cylindrical stainless steel vessel (separator), where the solvent was separated. The pressure and temperature of the separator were maintained constant at 40 °C and 60 bar respectively. Solvent-lean CO_2 was then recycled for the process. After 8 h the extraction was completed and the aerogel microspheres was removed from the 4 l autoclave and the solvent from the bottom of the separator. Typically the recycled CO_2 was exchanged with a fresh CO_2 at least four times during the extraction process to ensure complete extraction of the aerogel.

2.3. Characterization

The produced microspheres were characterized using different methods to evaluate the production process and the effect of process parameters. Surface area, pore size and pore size distribution were analyzed using nitrogen adsorption/desorption (surface analyzer Nova 3000e). Gel particle size distribution (PSD) was measured using laser diffraction spectrometer in wet state (Beckman Coulter LS13320 equipped with the universal liquid module). Particle shape and form were analyzed using scanning electron microscopy (SEM) (Leo Zeiss 1530).

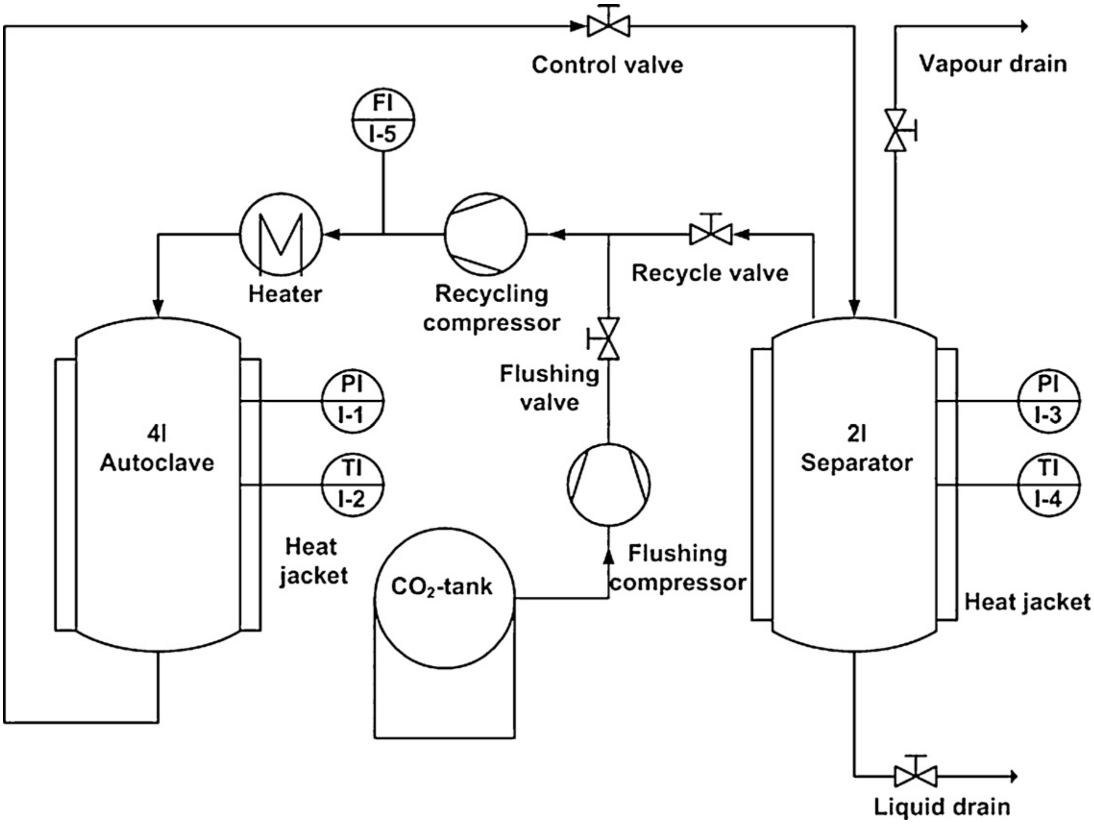

Fig. 6. Schematic diagram of the 4 l supercritical extraction unit.

3. Results and discussion:

The properties of the alginate aerogel (PSD, particle shape, structural properties, etc.) produced by the suggested processes can be influenced by many factors. These parameters can be classified into two groups: (1) sol–gel parameters; (2) emulsion process parameters. The sol–gel parameters (precursors concentration, gelling criteria, cross-linking mechanism, solvent exchange, etc.) influence mainly the textural properties of the produced gel. On the other hand, emulsion parameters (W/O ratio, stirring rate, surfactant, viscosity, etc.) affect mainly the form and PSD of the produced gel particles (Alnaief & Smirnova, 2011). However, interference between different parameters should be expected.

Because of the complexity of combining all effects together, it is beneficial to study each class of properties separately. After that it would be easier to draw some conclusions by combining the parameters from both groups.

In the first part of the following discussion the influence of gelling techniques on the final properties of the produced aerogel was studied. Based on these results procedures 2a and 2b were used to investigate the effect of some emulsion parameters on the final properties of the produced microspherical gel/aerogel particles.

3.1. *Effect of sol–gel process (gelling mechanism)*

Two main gelling mechanisms were investigated in this work. Namely: (1) the diffusion method (procedure1); which is usually used to produce alginate beads (Escudero et al., 2009); (2) the internal setting method (procedure 2); which is usually suggested to produce homogeneous gel structure (Sheu et al., 1993; Silva, Ribeiro, Ferreira, &, Veiga, 2006).

3.1.1. *Particle shape*

Fig. 7 shows four SEM images of different alginate aerogel particles produced following the three used procedures. The images are chosen to be representative for the particles results from each procedure. Fig. 7A represents the particles results from the first procedure. Irregular particle shapes were obtained. The diffusion gelation process is known to induce fast gelation (seconds); upon breaking the emulsion by addition of the $CaCl_2$ solution a distortion of alginate droplet dispersion is occurred. Because of the instantaneous gelation mechanism, the deformed alginate droplets gelled and the irregularity of the droplet is preserved. On the other hand, procedure 2, the setting method, results in microspherical aerogel particles Fig. 7B and C. Thus slow gelation mechanism is more suitable for the combination with the proposed emulsion process. Based on these results, further investigation were restricted to the setting gelation method (procedures 2a and 2b).

3.1.2. *Textural properties*

As mentioned previously it is expected that the textural properties of the alginate aerogel microparticles depend mainly on the sol–gel process parameters. Table 1 shows the textural properties of different alginate aerogel particles produced following the three used procedures; the emulsion process parameters were kept constant (rpm = 400, constant geometrical parameters, etc.). It can be seen that all procedures result in relatively large surface area, large pore volume and mesopore structure. However, it is clear that the alginate aerogel particles produced following the setting method shows larger internal specific surface area in comparison with those produced by the diffusion method. Slow gelation process offered by setting method (procedure 2) is the main reason behind this finding. Following this method, the production of homogeneous gel internal structure of the alginate microspheres is allowed, as a result better textural properties are obtained (Silva, Ribeiro, Ferreira, et al., 2006). However, the homogeneity of the cross-linking is one of the main challenges in the diffusion method (procedure 1) (Ingar Draget, Østgaard, & Smidsrød, 1990; Phillips & Williams, 2000; Qiu, 2009; Rehm, 2009; Silva, Ribeiro, Figueiredo, et al., 2006).

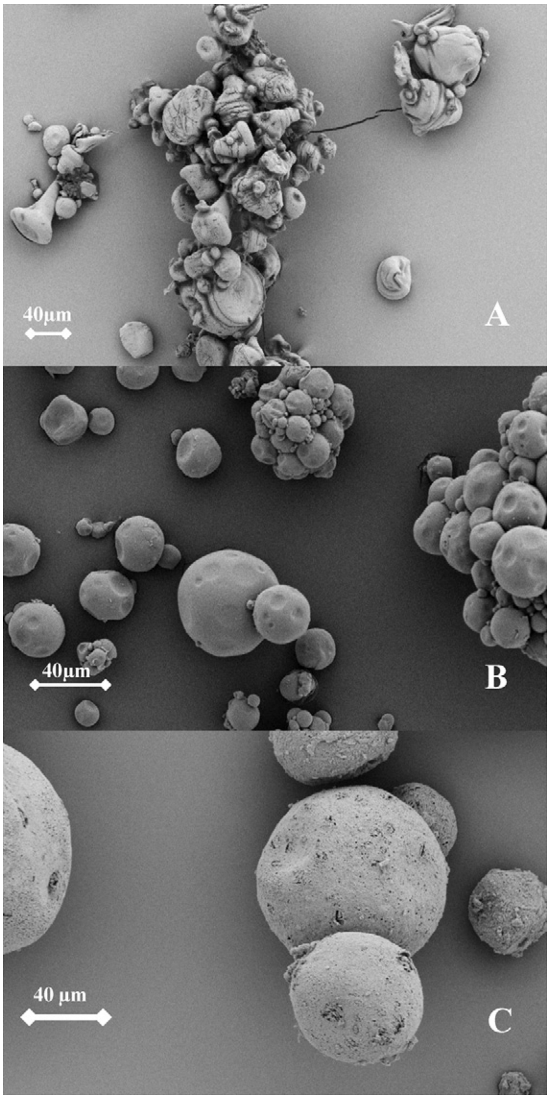

Fig. 7. Influence of gelling process on the final shape of alginate aerogel particles: (A) procedure 1; diffusion gelation method, (B and C) procedures 2a and 2b respectively; setting gelation method.

Table 1
Textural properties of alginate aerogel particles produced using different procedures.

Structural properties	Procedure 1	Procedure 2a	Procedure 2b
Surface area (BET) (m^2/g)	394 ± 71	590 ± 80	469 ± 54
Pore radius (BJH) (nm)	10 ± 2	15 ± 2	13 ± 3
Pore volume (BJH) (cm^3/g)	2.70 ± 0.95	4.10 ± 0.78	2.89 ± 1.6

3.2. *Effect of emulsion process on alginate aerogel particles*

Emulsion process parameters, including surfactant concentration, stirring rate, dispersed phase viscosity (alginate concentration), were investigated using procedure 2. In all preparations a marine propeller was used to emulsify 150 ml of emulsion in a beaker (diameter = 9 cm) at room temperature.

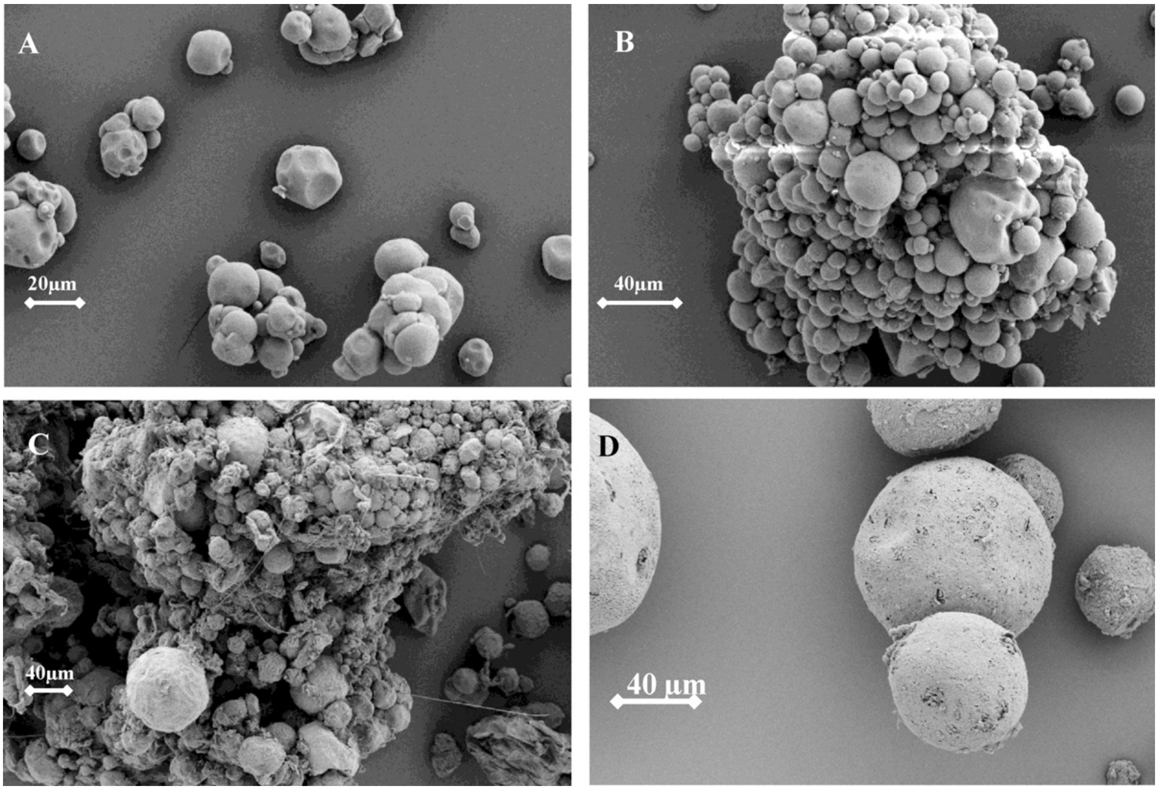

Fig. 8. Influence of surfactant concentration of the emulsion on the PSD of alginate aerogel particles: (A) procedure 2a 1 vol.% Span® 80; (B) procedure 2a 5 vol.% Span® 80; (C) procedure 2b 1 vol.% Span® 80; (D) procedure 2b 5 vol.% Span® 80.

3.2.1. *Effect of surfactant concentration*

A stabilizer (surfactant) is generally added to the continuous phase to prevent coalescence of the droplets. (Banker & Rhodes, 2002). For the first set of experiments the effect of surfactant was investigated using both procedures 2a and 2b. SEM images were used to evaluate the impact of surfactant concentration on alginate aerogel particles produced by the two procedures. It is clear that procedure 2a results in less aggregated spherical particles in comparison to procedure 2b (Fig. 8). Moreover, a higher surfactant concentration is needed for procedure 2b in order to get uniform spherical particles (Fig. 8). Although, both procedures follow the same gelation mechanism, they differ in the way of pH reduction. In procedure 2a pH reduction occurred through the addition of diluted glacial acetic acid to the emulsion during stirring. As a result a global homogeneous reduction of pH is obtained within a short time. This assists finalizing the gelation process at least on the alginate microspherical shell; no more cross-linking on the surface is possible. However, the mechanism of pH reduction following procedure 2b differs from the former one by slow release of protons by GDL hydrolysis. Consequently, the gelation starts from the very beginning of mixing, since GDL is present in the dispersion before the emulsification. Nevertheless, the degree of cross-linking increased with time, more GDL is hydrolyzed (lower pH values). At these conditions a contact between the micro-droplets during the emulsification process may result in an ionic bond (stable aggregate formation). Using higher concentration of surfactant helps to stabilize the micro-droplets until complete gelation is obtained. Based on this finding and the textural properties presented in Table 1, procedure 2a was found to be the most suitable one for coupling with emulsion process and was used to investigate further emulsion process parameters.

The spherical particles produced by procedure 2 show a kind of deformation (Fig. 8). The deformations look like a print or a position of other particles, which has detached from the surface. During harvesting of the particles from the oil dispersion, a vacuum filtration step was used. Accordingly, the particles were subject to a suction pressure, which can deform the particles.

Table 2 shows the effect of Span® 80 concentration on the final PSD of alginate gel microspheres. It can be noticed that the Sauter mean diameter was reduced from 259 μm to 115 μm by increasing the surfactant concentration from 0 to 3 vol.% at the same stirring condition (400 rpm). Increasing the surfactant concentration leads to a reduction of the interfacial surface tension between the two phases of the emulsion, this implement that less energy is needed to build the same interfacial surface area between the two phases (Chern, 2008; Freitas, Merkle, & Gander, 2005; Leal-Calderon, Schmitt, & Bibette, 2007).

3.2.2. *Effect of stirring rate*

In order to investigate the effect of the stirring, the marine propeller stirrer (diameter = 5 cm) was used to emulsify 150 ml of system (alginate solution: oil phases; volume ratio = 1:2) with different stirring rates. The particle size distributions (PSD) as a function of the stirring speed are reported in Table 3. The Sauter mean diameter (D_{32}) varies from 168 μm to 34 μm, when the stirrer revolution rate increased from 200 to 1400 rpm respectively

Table 2
PSD of alginate gel microspheres as a function of surfactant concentration on the PSD (procedure 2a, 400 rpm, 1.5 wt.% alginate solution).

	Span vol.%			
	0	1	2	3
Average (μm)	909 ± 18	534 ± 44	480 ± 44	221 ± 10
D_{32} (μm)	259 ± 8	177 ± 16	135 ± 10	115 ± 8
D_{10} (μm)	271 ± 40	80 ± 22	47 ± 4	65 ± 2
D_{50} (μm)	955 ± 34	508 ± 46	446 ± 36	186 ± 10
D_{90} (μm)	1432 ± 16	1003 ± 50	945 ± 100	405 ± 50

Table 3
PSD of alginate gel microspheres as a function of the revolution speed (procedure 2a, 1.5 wt.% alginate solution, 1 vol.% Span® 80).

	200 rpm	400 rpm	600 rpm	1400 rpm
Average (μm)	547 ± 32	534 ± 44	486 ± 100	75 ± 10
D_{32} (μm)	168 ± 16	177 ± 16	145 ± 16	34 ± 4
D_{10} (μm)	67 ± 10	80 ± 22	56 ± 6	15 ± 4
D_{50} (μm)	463 ± 46	508 ± 46	381 ± 70	60 ± 10
D_{90} (μm)	1139 ± 140	1003 ± 50	1066 ± 150	151 ± 6

(Table 3). Increasing the mixer speed results in a higher energy input to the system, this allows the building of larger interfacial surface area, thus the dispersed droplets become smaller, and consequently the gel microspheres will have a smaller mean size (Yang, Chung, Bai, & Chan, 2000). These results confirmed that the main factor in controlling the PSD is the stirrer revolution rate (Freitas et al., 2005). It can be noticed that the PSD is relatively broad in all cases. Among many other factors, viscosity of the dispersed as well as the continuous phase plays a major role in controlling PSD in the emulsion process. In our process, the viscosity of the continuous phase remains nearly constant (1000 cP) throughout the experiment; however, the viscosity of the dispersed phase (sol phase) increases continuously with time until the formation of the gel particles. This might lead to the broadening of the resulting particle size distribution (Table 3). Another possible reason is that the used geometry may need optimization in order to distribute the energy evenly throughout the complete volume of the emulsion. Moreover, comparing the results from the laser diffractometer measurement with the SEM images may help to understand the process. Fig. 9 shows a typical aggregated alginate aerogels microspheres produced at 600 rpm, 1.5 wt.% alginate concentration and 1 vol.% Span® 80 concentration. It can be noticed that almost none of the particles are larger than 50 μm, whereas the aggregate body is much larger.

3.2.3. *Effect of alginate content*

The effect of alginate content on the final properties of the produced alginate aerogels microspheres is intricate. On one hand, this influences the sol–gel process itself, since increasing the concentration of alginate solution means more cross linking. On the other hand, increasing the alginate concentration means increasing the viscosity of the dispersed phase during the emulsification process. Table 4 shows the PSD of the alginate gel produced using different alginate solution concentration. The mean Sauter diameter decreases from 177 μm to 102 μm by increasing the alginate concentration from 1.5 wt.% to 3 wt.%. It is expected that by increasing the viscosity of the disperse phase more energy is needed to create the same interfacial surface area, as a result larger particles are expected to be formed (Freitas et al., 2005). However, here also the sol–gel process should be considered. Gelation induced following the internal setting method implies that gelation starts simultaneously in large number of locations. Accordingly, some topological strains will affect some of alginate molecules. After the primary gelation is occurred, it is expected that theses location may contains free elastic G blocks, which can form further junction points, if there is free Ca^{2+} cation and another free G block nearby (Phillips & Williams, 2000). Increasing the alginate concentration will increase the possibility of further junction points; as a result, more syneresis is expected. Table 5 shows the textural properties of alginate aerogel microspheres produced using different initial alginate concentration. As expected the textural properties were improved (in respect to: specific surface area, pore volume and pore size) by increasing the alginate concentration in the solution. As previously discussed increasing the initial concentration of alginate leads to form denser internal network with more cross-linking, which usually enhance the textural properties of the produced aerogel.

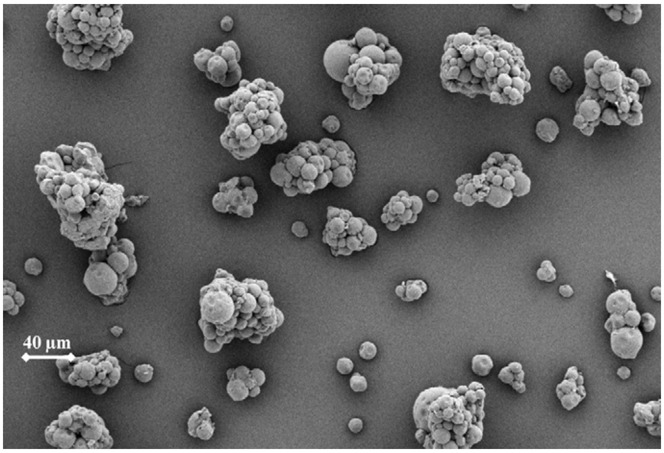

Fig. 9. Aggregated form of the resulted alginate aerogel microspheres (600 rpm, 1.5 wt.% alginate and 1 vol.% Span® 80).

Table 4
PSD of alginate gel microspheres as a function of alginate concentration on PSD (procedure 2a, 400 rpm, 1 vol.% span® 80).

	Concentration of alginate solution (wt.%)		
	1.5	2	3
Average (μm)	534 ± 44	504 ± 41	298 ± 24
D_{32} (μm)	177 ± 16	181 ± 18	102 ± 8
D_{10} (μm)	80 ± 22	163 ± 36	42 ± 5
D_{50} (μm)	508 ± 46	491 ± 41	259 ± 20
D_{90} (μm)	1003 ± 50	855 ± 50	591 ± 70

Table 5
Effect of alginate solution concentration on the textural properties of alginate aerogel particles (procedure 2a, 400 rpm, 1 vol.% Span® 80).

Structural properties	1.5 wt.%	2 wt.%	3 wt.%
Surface area (BET) (m^2/g)	318 ± 45	440 ± 27	608 ± 60
Pore radius (BJH) (nm)	9 ± 2	9 ± 2	15 ± 2
Pore volume (BJH) (cm^3/g)	2.15 ± 0.60	2.32 ± 0.38	4.05 ± 0.54

Comparing the textural properties of the aerogel produced by the proposed method with those presented in the literature shows that the proposed method results in the highest reported surface area for alginate aerogel. Reproducible high surface area 680 m^2/g (based on at least three experiments) with a large pore volume 4 cm^3/g and pore average pore radius of 15 nm were obtained. The maximum values reported in the literature following the setting gelation method were 300 m^2/g with an average pore volume of 1.9 cm^3/g (Mehling et al., 2009). However, most of other reported methods for alginate aerogels production follow the diffusion gelation method. The average reported values fall in the range of 200–400 m^2/g and average pore volume of 0.8–2 cm^3/g (Escudero et al., 2009; Horga et al., 2007; Robitzer et al., 2008b; Trens et al., 2007; Valentin et al., 2005). The best reported values fall in the range of 500–570 m^2/g, average pore volume of 1–2 cm^3/g and pore radius of 12–17 nm (Quignard et al., 2008; Trens et al., 2007). Accordingly, the presented method is suitable to produce alginate aerogel microspherical particles with superior textural properties.

Further optimizations of the emulsion process preparation are under investigation. Further optimization should allow the production of a tailor made particles with the needed textural and shape properties to meet the desired application.

4. Conclusions

The combination of the sol–gel process with supercritical extraction of the solvent from the alcogel dispersion is proposed as a versatile method for industrially relevant production of aerogel microspheres in a robust and reproducible manner. The process was demonstrated for alginate aerogel microspheres. The textural properties of alginate aerogel produced following the internal setting method shows an improvement over those produced by the diffusion method. The diffusion method is not suitable to be coupled with the emulsion process for production of microspheres particles. Among many emulsion parameters, stirrer revolution rate was found to be the main factor that controls the PSDs of the produced microspheres. Depending on the production conditions, alginate aerogel microspheres with a mean diameter of 30 μm up to several hundred microns were produced. Alginate aerogel microspheres with superior textural properties (surface area of 680 m^2/g, pore volume of 4 cm^3/g, pore radius of 15 nm) over the reported values in literature were produced following the suggested method. Principally, the process suggested in this work allows the large scale production of supercritically dried aerogel microspheres of different origin.

Acknowledgments

The first author (Mohammad Alnaief) is thankful for the German-Jordan University for supporting him with a personal scholarship. C.A. García-González acknowledges the Spanish Ministry of Education for the financial support through a postdoctoral fellowship in the frame of the National Program for Staff Mobility from the R&D&i National Plan 2008–2011.

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