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Development of a new technology for the production of microcapsules based in atomization processes

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Abstract

A new microencapsulation technology of polyelectrolyte complex beads which produce very small particles (1–50 μm) with particle size control has been developed. The polymers used were sodium alginate as polyanion and barium chloride as polycation. To do that, an air-blast atomizer that uses compressed air was used. This works by spraying a solution of sodium alginate in a solution of barium chloride, which induces the gelation. The air flow rate, alginate flow rate and viscosity of the alginate solution effects were studied. The behaviour curves of the system were built with the microparticles size data obtained at different operation conditions. These curves will allow knowing the operation conditions for a suitable microparticle size.

Keywords: Microencapsulation; Polyelectrolite complexes; Atomization; Control size

1. Introduction

Over the past few decades, the rise of modern pharmaceutical technology and the amazing growth of the biotechnology industry have revolutionized the approach to drug discovery and development.

The most common method of administration of drugs is in the form of pills or injections. These methods of administration meet the requirements of efficacy for several drugs. However, these methods are inadequate for many new drugs. To overcome these difficulties, new technologies, like the microencapsulation, have been developed [1–5].

These technologies are based on the use of polymers. Polysaccharides, such as alginate, have been widely used in the microencapsulation technology.

Alginate is a water soluble linear polysaccharide extracted from brown seaweed, and is composed of alternating blocks of 1–4 linked α-L-guluronic and β-D-mannuronic acid residues. Depending on the source of the alginate, the molecules can be composed of three types of blocks: polymannuronic acid blocks (MM), polyguluronic acid blocks (GG) and mixed blocks (MG). Also, the amount of each component (M and G) varies with the source of the alginate. Alginate has an excellent biocompability and biodegradability.

Probably, the most important property of alginates is their ability to form gels by reaction with divalent cations such as calcium or barium by binding between guluronic acid blocks in alginate and the divalent cations. These gels are similar to solids because they retain their shape and resist stress. This process of gelation is an almost instantaneous and irreversible process, which is governed by the relative rate of diffusion of barium ions and polymer molecules into the gelling zone.

Most methods of microencapsulation involve one of two harsh conditions (contact with an organic solvent and/or heating during processing) which usually is a problem, especially for biomaterials handling [2,3]. The previous work done on microencapsulation without harsh conditions produce capsules with diameters ranged between 300 and 1000 μm [4,5–13].

Several attends have been done in order to produce very small particles based in polyelectrolyte complexes, but there is not a technology able to produce these microparticles below 300 μm, with control size and narrow distribution [7–13].

Microcapsules prepared by spinning disk atomization, in which the fluid breakup is induced by a rotating disk, have sizes ranging from 300 to 600 μm [6,7]. Other sample is the alginate beads produced by a vibrating nozzle device. In this, a suspension of active material to be encapsuled, in an immobilization media solution, is forced through a small orifice; the subsequent

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liquid jet is put into vibration and breaks up into drops that are then solidified to form particles. However, a big limitation in this technology is the viscosity of the solution to be used. It is not possible to break up jet with higher viscosities of 50 cP. This type of device produce capsules with diameters within the range 300–600 μm [4,8,9].

Other technology used to encapsulation is the coaxial air-flow dropping that produces microcapsules within the range 400–800 μm [4,9–11].

Other example of encapsulation technology is the JetCutter technology, which is essentially based on rotating wires that cut falling jets of the hydrogel precursor solution into small pieces. These are cut at regular intervals, forming identically sized drops that are gelled in a crosslinking bath as they fall. The JetCutter can be operated either in the "normal mode" or in the "soft-landing mode". Normal mode means that the JetCutter is places somewhere at a definite height and the beads are collected in a $CaCl_2$ bath placed on the floor. Soft-landing mode means that the JetCutter is placed on the floor and the beads are collected at a height of about 2 m, this reduces the velocity of the bead when entering the gelation bath. Both modes of this technology produces capsules within the range 320–800 μm [4,9].

Electrostatic droplet generation produces microcapsules by an electrostatic pulse generator within the range 300–800 μm [11,12,4]. A new method based on a microfluidics device, that use a silicon micro-nozzle array, have achieved reduce the diameter of the capsules to 162 μm. Alginate is extruded through the micro-nozzle and is sheared by the viscous drag force of oil flow to form calcium alginate gel beads [13].

For that reason, based in atomization processes, a new microencapsulation technology of polyelectrolyte complex beads (alginate–barium) which produced very small particles (1–50 μm) has been developed. The system alginate–barium was used because a wide knowledge was already obtained from previous work done [14,15].

Atomization is a process in which the disruptive action of externally applied aerodynamic forces is opposed by the consolidating influences of the liquid viscosity and surface tension forces. Disintegration of liquid jets injected into quiescent and high-velocity gas streams has been studied by many researchers [16].

From the different atomization techniques air-blast or twin-fluid atomization has been widely used suspension spray drying [11–13].

In air-blast atomization, low-speed liquid jets are accelerated by the surrounding high-speed gas flow, usually in the spray flow direction. The liquid is subjected to both tensile and shearing stresses. The magnitude of the extension has been shown to be significant for applications involving polymer solutions. Twin-fluid atomizers have a number of advantages over pressure atomizers including lower requirements for the liquid injection pressure and finer sprays. Unfortunately, the process of air-blast atomization is very complex and its physical mechanisms are not fully understood [16].

Therefore, in order to have a better understanding of the atomization process for microencapsulation applications the disintegration of polymer liquid jets (sodium alginate) injected into high-velocity gas streams were studied. The air flow rate effect, alginate flow rate effect and viscosity of the alginate solution were studies. The behaviour curves of the system were built with the size data obtained for the microparticles at different operation conditions. These curves will allow knowing the operation conditions for a suitable microparticle size and a better understanding of the use of this technology for microencapsulation proposes.

2. Materials and methods

2.1. Material

Sodium alginate from macrocystis pyrifera (medium viscosity) was purchased from Sigma Chemicals, barium chloride dehydrate, reagent grade was purchased from Scharlau.

2.2. Production of microcapsules

The microencapsulation procedure, optimized to produce microcapsules in the size range 1–50 μm, can be described as follow. Sodium alginate (0.7 wt.%) was fed from a beaker to an atomization nozzle of 1.8 mm by air intake. After that, sodium alginate is sprayed into a crystallizer containing 1000 ml of hardening solution, 2 wt.% calcium chloride solution, which induces the gelation. The device to the atomization works with pressurized air that mixes with the liquid, forcing liquid droplets out through the orifice of the nozzle. The divalent barium ions crosslink the droplets of sodium alginate on contact to form the microcapsules. The microbeads were kept 5 min under crosslinked conditions to form a semi-permeable membrane. The resultant microbeads were collected by filtration and washed with 30 ml of 0.9% of barium chloride and kept in distilled water. The scheme of the microencapsulation device is shown in Fig. 1.

2.3. Particle size analysis

We have obtained the particle size distribution of the microcapsules produced with laser diffractometry. To do that we have used a Leeds and Northrup Microtac Particle Size Analyzer. This device utilizes the phenomenon of scattered light from a laser beam projected through a stream of particles.

3. Results

3.1. Behaviour curves of the system

In order to obtain the behaviour curves of the atomization system, experiments at different alginate flow rate, different air flow rate and three different alginate solution viscosities were carried out.

3.1.1. Sodium alginate flow rate effect

In order to study the effect of the alginate flow rate in the average diameter, atomization experiments were conducted at

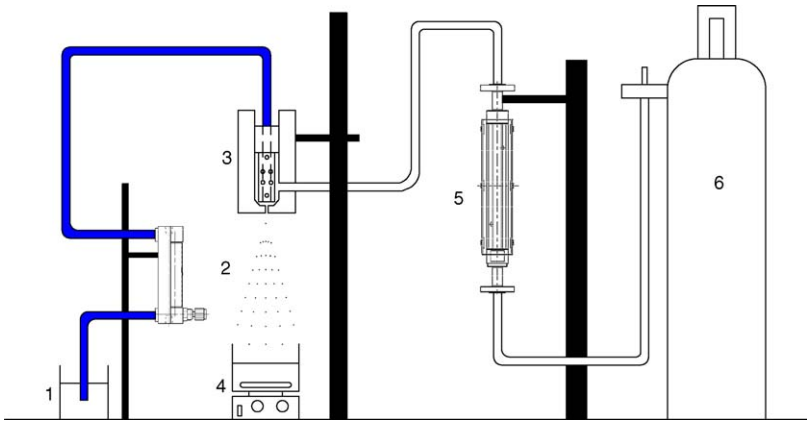

Fig. 1. A scheme of the microencapsulation device: (1) beaker with sodium alginate (0.7 wt.%); (2) rotameter of sodium alginate; (3) nozzle; (4) crystallizer with calcium chloride (2 wt.%) and a magnetic stirrer; (5) rotameter of air; (6) gas cylinder of pure pressurized air.

constant flow of pressurized air of 138.000 L/min, sodium alginate viscosity of 64.50 cP and sodium alginate flow rate ranged from 0.003 to 0.037 L/min. Flow rate of sodium alginate lower than 0.003 L/min requires long time of atomization. Flow rate higher than 0.037 L/min produces agglomerates.

Under these conditions the microcapsules were produced. After that, the particle size distribution was obtained. It has been measured the distribution in number. We have considered the 50% percentile of the particle size distribution as the average diameter of the microcapsules. With these data the behaviour curve was plot (Fig. 2).

3.1.2. Air flow rate effect

In order to study the air flow rate effect atomization experiments were conducted at constant alginate flow rate (0.003, 0.006, 0.009 L/min), a constant viscosity of alginate solution of 64.50 cP, and an air flow rate ranged from 78.40 to 138.00 L/min. Air flow rate lower than 78.40 L/min did not produce atomization. Air flow rate higher than 138.00 L/min generated the deformation of the surface of the barium chloride solution when atomization is performed.

Under these conditions the microcapsules were produced. After that, the particle size distribution was obtained. It has been measured the distribution in number. We have considered the 50% percentile of the particle size distribution as the average diameter of the microcapsules. With these data the behaviour curve was plot (Fig. 3).

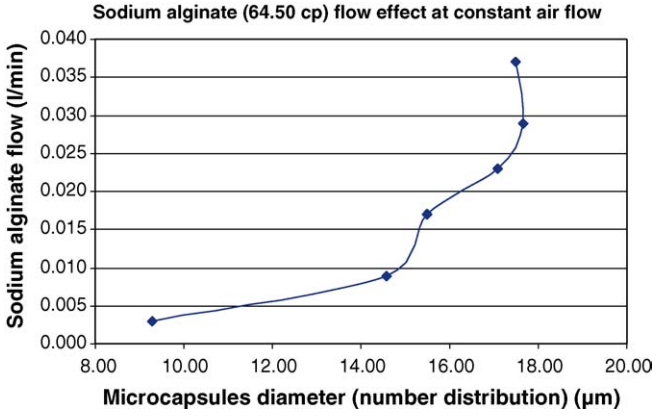

Fig. 2. Variation of the microcapsules size at different sodium alginate flow rate.

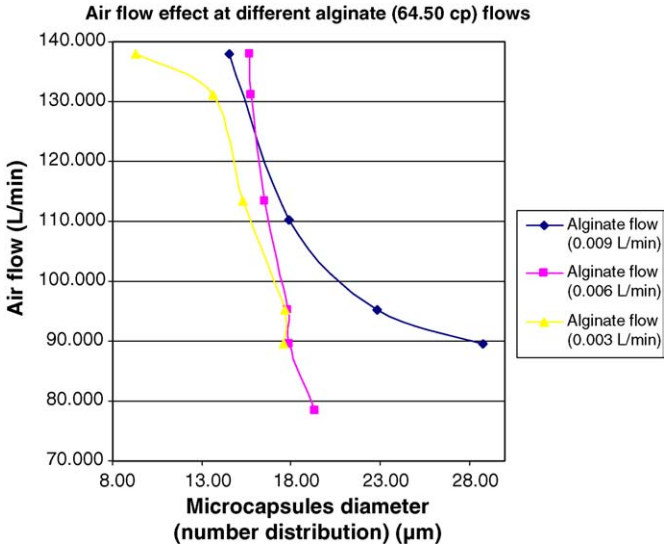

Fig. 3. Variation of the microcapsules size at different air flow rate.

3.1.3. Alginate solution viscosity effect

In order to study the effect of alginate viscosity in the average diameter, atomization experiments were carried out, varying alginate flow rate and air flow rate like Sections 3.1.1 and 3.1.2, at sodium alginate viscosities of 64.50, 138.00, and 190.00 cP. Alginate viscosities were obtained varying alginate concentration (Table 1). To measure the alginate viscosity it was used a

Table 1
Alginate viscosity with the alginate concentration variation

Alginate concentration (wt.%)	Alginate viscosity (cP)
0.7	64.50
0.8	138.00
1.0	190.00

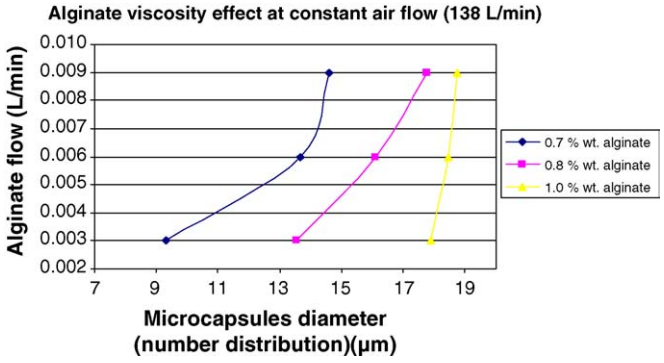

Fig. 4. Alginate viscosity effect on the microparticle size at constant air flow rate of 138 L/min.

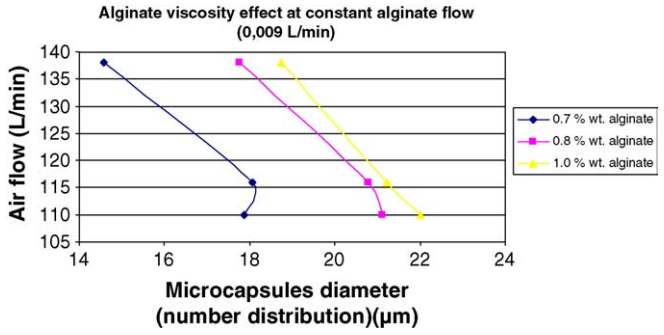

Fig. 5. Alginate viscosity effect on the microparticle size at constant alginate flow rate of 0.009 L/min.

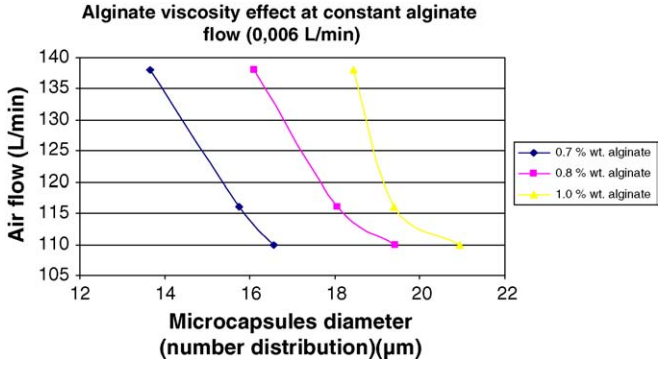

Fig. 6. Alginate viscosity effect on the microparticle size at constant alginate flow rate of 0.006 L/min.

rotational viscometer VISCO ELITE, purchased to FUNGILAB S.A.

Under these conditions the microcapsules were produced. After that, the particle size distribution was obtained. It has been measured the distribution in number. We have considered the 50% percentile of the particle size distribution as the average diameter of the microcapsules. With these data the behaviour curves were plot (Figs. 4–7).

4. Discussion

A twin-phased gas–liquid atomizer, which utilizes the kinetic energy carried with high-velocity gas streams to disintegrate the

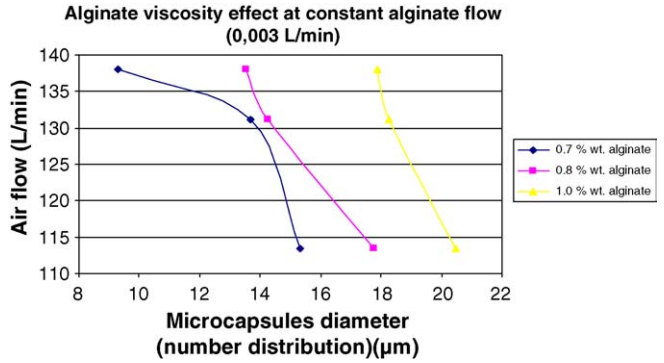

Fig. 7. Alginate viscosity effect on the microparticle size at constant alginate flow rate of 0.003 L/min.

relatively low velocity liquid sheet or jet into droplets, was used to produce the atomization. One kind of these atomizers is the air-blast atomizer, in which, an annular liquid sheet exiting from the atomizer is exposed to an inner and an outer air streams moving at high velocities.

The fundamental principle of the disintegration of a liquid consists of increasing its surface area, usually in the form of a cylindrical rod or sheet, until it becomes unstable and disintegrates into drops.

When a sheet of liquid emerges from a nozzle, its subsequent development is influenced mainly by its initial velocity and the physical properties of the liquid and the ambient gas. To expand the sheet against the contracting surface tension force, a minimum sheet velocity is required, which is provided by aerodynamic drag. Increasing the initial velocity expands and lengthens the sheet until a leading edge is formed where equilibrium exists between surface tension and inertial forces.

A number of previous studies [17,18] indicate that the curvature effect may be negligible due to the relatively small thickness of the liquid sheet compared to the radius of curvature. As a result, the liquid to be atomized may be modelled in a first approximation as a plane liquid sheet [19].

We have considerated the system of forces acting on the slightly disturbed surface of a liquid sheet moving in air, as is shown in Fig. 8. Surface tension forces try to return the protuberance back to its original position, but the air experiences a local decrease in static pressure (corresponding to the local increase in velocity) that tends to expand the protuberance farther outward. This corresponds to the normal pattern of wind-induced instability, where surface tension forces oppose any movement

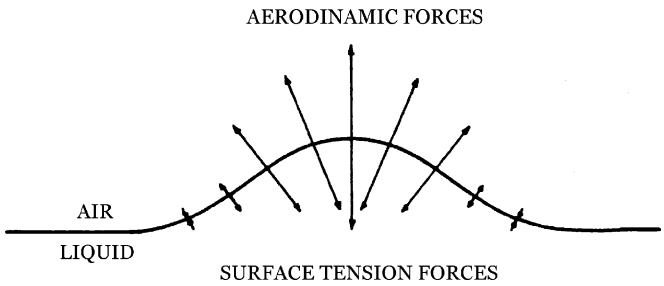

Fig. 8. System of forces acting on a liquid sheet moving in air.

of the interface from its initial plane and attempt to restore equilibrium, while the aerodynamic forces increase any deviation from the interface and thereby promote instability.

The instability of thin liquid sheets resulting from interaction with the surrounding gaseous medium gives rise to rapidly growing surface waves. Disintegration occurs when the wave amplitude reaches a critical value; fragments of the sheet are torn off and rapidly contract into unstable ligaments under the action of surface tension, and drops are produced as the ligaments break down.

The microcapsules that have been formed in this work are spherical. We have obtained a narrow particle size distribution.

4.1. Sodium alginate flow rate

An analysis of the experimental data obtained show that the microcapsules average diameter decreases when it is decreased the sodium alginate flow.

These results are in a very good agreement with the theoretical explanation that some authors have given to justify this phenomenon.

Rizt and Lefebvre [20] studied the influence of initial liquid film thickness on spray characteristics. They found that high values of liquid flow rate result in thicker films. It was also observed that thinner liquid films break down into smaller drops. Previous workers had noted a similar relationship. For example, the analyses of York et. al. [21], Hagerty and Shea [22], and Dombrowski and Johns [23] all suggest that mean drop diameter is roughly proportional to the square root of the film thickness.

4.2. Air flow rate effect

An analysis of the experimental data obtained show that the microcapsules average diameter decreases when we increase the air flow.

These results are in accordance with the theoretic explanation that some authors have given to this phenomenon in previous studies.

Rizt and Lefebvre [20] examined the mechanism of sheet disruption and drop formation. They showed that the liquid/air interaction produces waves that become unstable and disintegrate into fragments. These fragments then contract into ligaments, which in turn break down into drops. They proved that with increase in air velocity, the liquid sheet disintegrates earlier and ligaments are formed nearer the lip. These ligaments tend to be thinner and shorter and disintegrate into smaller drops.

Arai and Hashimoto [24] studied the disintegration of liquid sheets injected into a coflowing airstream. For a constant liquid sheet thickness they showed that breakup length decrease with increase in the relative velocity between the air and the liquid.

4.3. Alginate viscosity effect

An analysis of the experimental data obtained show that the microcapsules average diameter increases when we increase the alginate viscosity.

The aqueous solutions of alginates have shear-thinning characteristics, i.e. the viscosity decreases with increasing shear rate (stirrer speed). This property is also called pseudoplasticity, or non-Newtonian fluid. The viscosity of an alginate solution depends on the concentration of alginate and the length of the alginate molecules, i.e. the number of monomer units in the chains. The longer the chains the higher the viscosity at similar concentrations [6]. Also, alginate solutions are viscoelastic liquids, that is, recover the deformation when is removed the stress. Viscoelastic fluids are much more difficult to atomize than viscoinelastic liquids. Viscoinelastic liquids showed breakup patterns similar to those of water sprays. Viscoelastic materials have remarkably different breakup patterns. The ligaments undergo a very large stretching motion before they break up, resulting in long threads of liquid attached to droplets. The normal stresses developed in viscoelastic materials are much higher than their associated shear stresses. Consequently, the development of the large normal stresses appears to be the most important rheological mechanism that inhibits breakup. The ability of viscoelastic materials to resists breakup in these contexts is caused by the molecular orientation that arises when the ligaments are extended. This extension leads to large increases in the extensional viscosity [25].

5. Conclusions

It was developed a microencapsulation technology of polyelectrolyte complex beads which produce very small particles (1–50 μm) with particle size control. The polymers used is sodium alginate as polyanion and barium chloride as polycation. To do that, it was used an air-blast atomizer.

The microcapsules that have been formed in this work are spherical. It was obtained a narrow particle size distribution. It was achieved the behaviour curves of the system.

An analysis of the curves shows that smaller microcapsules are produced at lower alginate flows because of high values of liquid flow rate result in thicker films. It was also observed that thinner liquid films break down into smaller drops.

It has been observed that higher air flow rates produce smaller microcapsules because of with an increase in air velocity, the liquid sheet disintegrates earlier and ligaments are formed nearer the lip. These ligaments tend to be thinner and shorter and disintegrate into smaller drops. Also, it is demonstrated that breakup length decrease with an increase in the relative velocity between the air and the liquid and the breakup length increases as the liquid sheet velocity increases.

The microcapsules average diameter increases when we increase the alginate viscosity because of alginate solutions are viscoelastic liquids and are much more difficult to atomize than viscoinelastic liquids. The normal stresses developed in viscoelastic materials are much higher than their associated shear stresses and this is the most important rheological mechanism that inhibits breakup.This work will be used in the future to encapsulate stem cell for therapeutical treatment of some diseases, such as multiple sclerosis, child brochopulmonary dysplasia or emphysema and pulmonary fibrosis.

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