Alginate microparticles produced by atomization system: Biomedical applications

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INTRODUCTION

Alginate is a biomaterial of great interest to use for biomedical purposes. It has also shown to be an attractive vector for the controlled release of drugs or cells [1], due to its low immunogenicity level, biocompatibility, low toxicity and low cost [2]. Alginate has the ability to form hydrogels under mild aqueous conditions of divalent cations such as Ca^{2+} or Ba^{2+} [3]. Alginate microparticles have inert aqueous environment inside the matrix and high degree of porosity in their surface that allows a high speed of diffusion of drug encapsulated inside [2].

In **atomization system** [4] there are two important parameters, liquid and air pressures. Due to the effect of liquid pressure, polymer solution flows from the container through a nozzle. On the other part of the nozzle, air is introduced from an air cylinder and breaks the jet of polymer in small droplets. These droplets are sprayed into a divalent solution under magnetic stirring.

The main objective of this study was to compare between two types of alginate gels formed with two divalent ions, barium chloride and calcium chloride. Secondly, production of alginate microparticles by atomization system.

ATOMIZATION TECHNIQUE

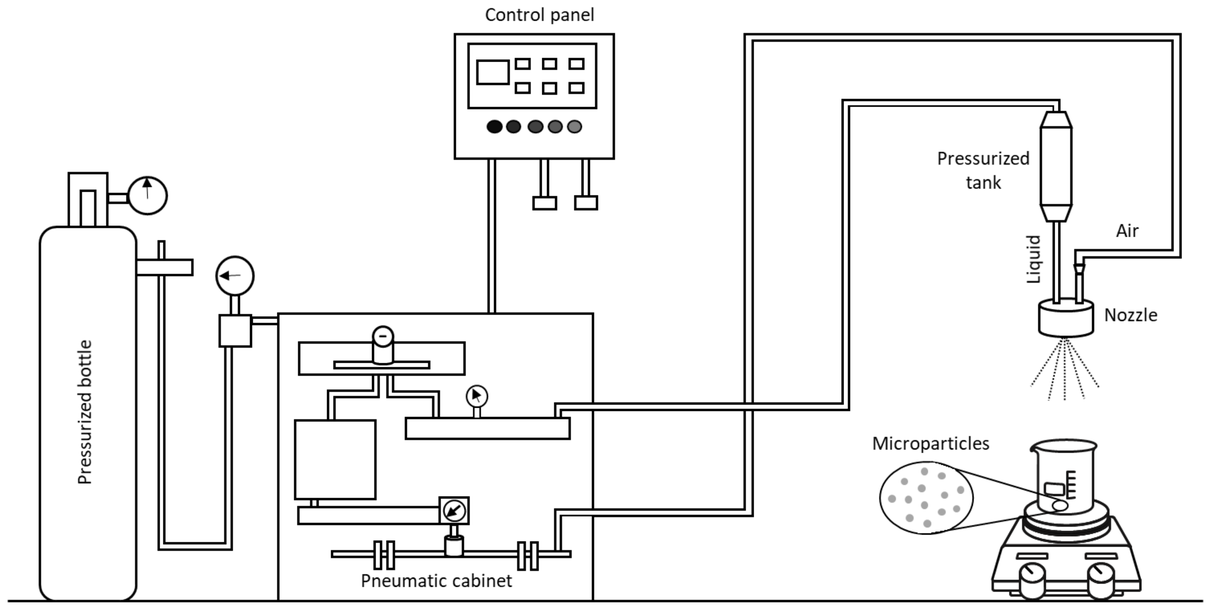

***Figure 1. -* Atomization system:** *Pressurized bottle* contains synthetic air; *Pneumatic cabinet* allows to control and supply air flows with two different valves; *Control panel,* has a software that allow to modify the pressure values; *Pressurized tank,* polymer is keep inside and it is submit to high pressure (50 mL maximum volume); *Nozzle*, inner diameter 250 µm and outer diameter 350 µm;

EXPERIMENTAL RESULTS

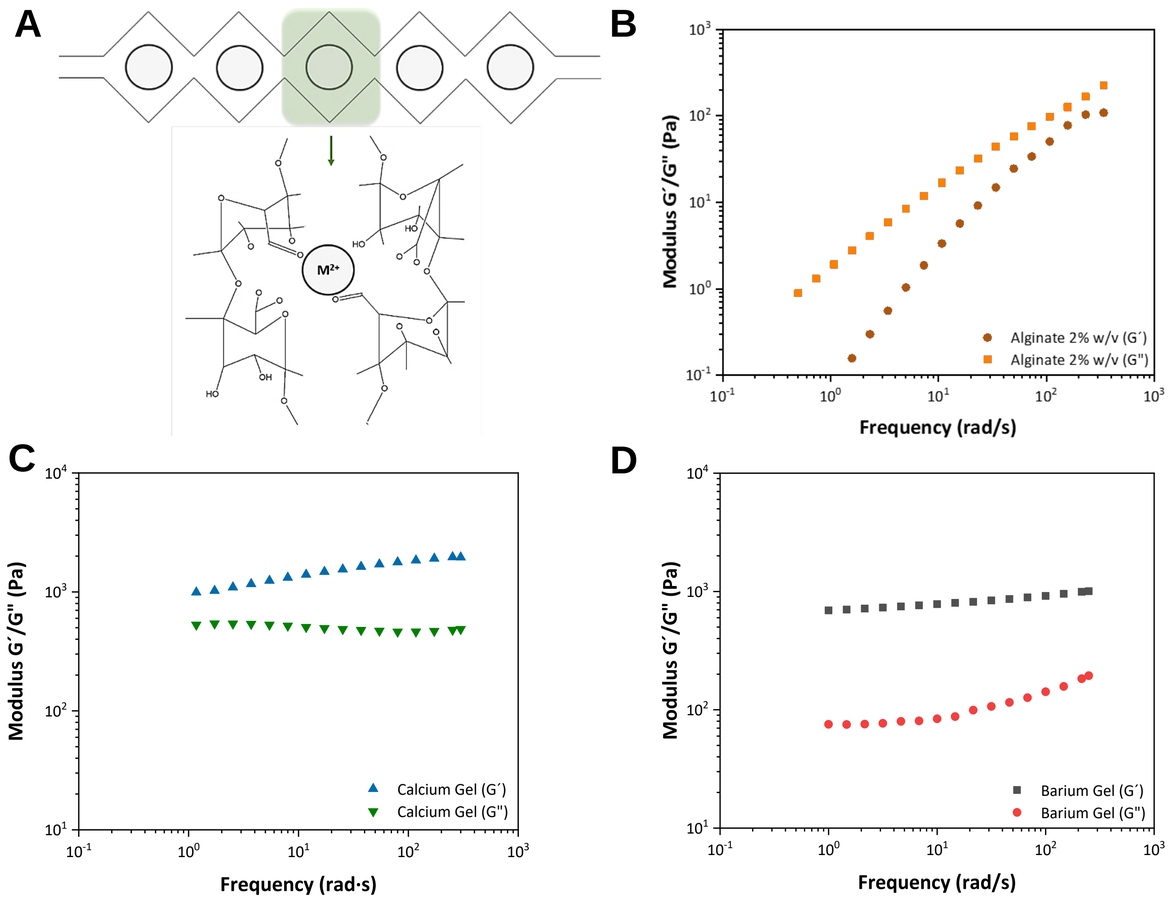

***Figure 2. -* Alginate hydrogels:** A) Schematic representation of the interaction between alginate and divalent ions; B) G´and G" modulus of alginate solution; C) G´and G" modulus of alg – $CaCl_2$ gel; D) G´and G" modulus of alg – $BaCl_2$ gel.

A

P liq (bar)	P air (bar)	Span	Surface Weighted Mean (µm) (3,2)	d 0.1 (µm)	d 0.5 (µm)	d 0.9 (µm)
1	**0.9**	**1,407**	**41,046**	**26,481**	**60,810**	**112,028**
0.9	0.9	2,747	47,379	23,267	149,610	434,288
0.9	0.8	2,168	40,458	24,707	64,751	165,092
0.8	0.8	4,580	60,947	27,608	84,737	415,727
0.8	0.7	2,020	37,562	23,550	58,736	141,622
0.7	0.7	1,892	62,590	27,719	211,893	428,673
0.7	0.6	3,154	50,991	32,940	74,870	269,062
0.6	0.6	2,334	30,752	20,277	43,990	122,945

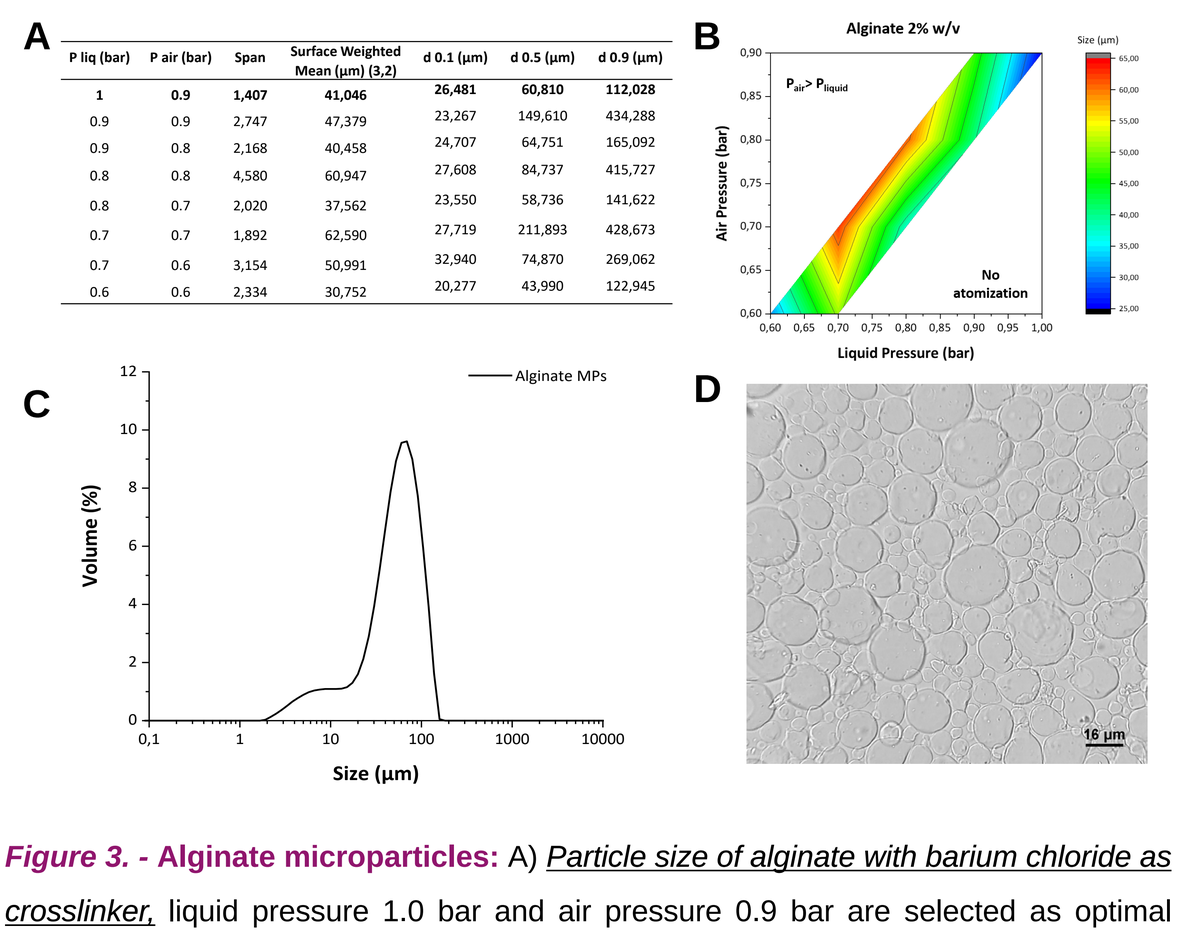

***Figure 3. -* Alginate microparticles:** A) *Particle size of alginate with barium chloride as crosslinker,* liquid pressure 1.0 bar and air pressure 0.9 bar are selected as optimal conditions; B) *Pressures map,* air and liquid pressures influence on particles size diameter for 2% w/v alginate; C) *Size distribution,* of alginate particle with optimal condition by Mastersizer2000; D) *Optical microscope image* of alginate microparticles.

CONCLUSIONS

- **The oscillatory analisis of the alginate solutions** provides the typical result for a viscous solution, where the loss modulus (G") is higher than the elastic modulus G´, the viscous nature predominates. **Alginate solution in contact with $BaCl_2$ or $CaCl_2$ form hydrogels,** in them, G´ increases and always is higher than G". The G" is higher for the alg – $CaCl_2$ gel, as consequence the **alg – $BaCl_2$ is a more permanent structure** in time due to the higher differences between viscous and elastic modulus. This fact highlights better particles in terms of mechanical propierties.
- **Alginate microparticles was produced with $BaCl_2$ as crosslinker.** The size of microparticles (d 0.5) ranges from 40 – 200 µm and Z potential was negative (- 8.60 mV). The pressures map showed that big sizes were obtained with intermediate pressures. The optimal conditions were liquid pressure 1.0 bar and air pressure 0.9 bar, where span had a lower value.

ACKNOWLEDGMENTS

University of Zaragoza: Aragon Institute of Nanoscience (INA)

University of Salamanca

B. Arauzo thanks the DGA predoctoral grant for personal researcher (2017 – 2021). The CIBER-BBN and Ibercaja for mobility aids to personal researcher (2019).

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