P-061	**Polysaccharide hydrogel particles for drug delivery**	

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INTRODUCTION AND OBJECTIVES

Many biomolecules are very sensitive compounds and have their administration limited by physicochemical and biopharmaceutical features (George 2007).

Microencapsulation has been presented as a promising strategy both to protect the drugs from aggressive conditions related to specific routes of administration and to provide controllable kinetics (Deshmukh 2009). Designing adequate drug delivery systems had, thus, become a very important task and it is known that materials selection plays a major role in the efficacy of the final system. Natural polymers are frequently preferred for carriers production because they easily comply with the mandatory requisites of biocompatibility, biodegradability and low toxicity (George 2007).

Locust bean gum (LBG) is a polysaccharide obtained from seeds of *Ceratonia siliqua*, belongs to the group of galactomannan hydrocolloids and is currently applied in food industry as thickener, providing high viscosity solutions even at low concentrations (Pollard 2008). LBG was reported to provide good encapsulation efficiency and controlled drug release when included in a alginate matrix (Deshmukh 2009).

Alginate (ALG) is also a natural polymer that has been used for many years in drug delivery because of its gelling properties, with demonstrated stability of the produced hydrogels in physiological conditions and delay of erosion (Chiellini 2008).

The aim of this work was to produce LBG-containing beads, by incorporation of LBG in an alginate matrix. Furthermore, LBG solubility in water was evaluated.

MATERIALS AND METHODS

Locust bean gum purification

5 g of LBG were dispersed in 1000 mL of deionized water, heated at 80-85 ºC with stirring for 1 h, cooled down, and then centrifuged (22.000 g, 1 h , 20 ºC).The supernatant was precipitated in ethanol and LBG was then filtered and dried overnight at 30 ºC under reduced pressure.

Solubility Study

The equilibrium aqueous solubility of purified LBG was investigated by determining the percentage of soluble components as a function of dissolution at 25 ºC and 80 ºC in different stirring periods (from 5 min to 24 h). Final LBG amount was adjusted to obtain a final concentration of 0.1% (w/v). After solubilisation procedure, the solutions were centrifuged (18.000 g, 30 min, 20 ºC) and the supernatant recovered. The percentage of solubility was then calculated by comparing the amount of LBG determined in the dried supernatant with the initial amount of LBG added.

Preparation of ALG/LBG beads

ALG/LBG beads were prepared according to a method based on the ionotropic gelation of alginate with Ca^{2+} ions. LBG was dissolved in purified milliQ water at 80 ºC during 1 h with stirring. After cooling, alginate powder was added and solubilised under stirring. Beads were produced with ALG concentrations between 2 and 2.5% (w/v) and LBG concentrations from 0 to 1.25% (w/v). When insulin was associated (2% respective to total solids), it was dissolved in NaOH 0.01 M and was previously mixed with alginate and LBG.

ALG/LBG or ALG/LBG/Insulin solutions were extruded dropwise through a needle into a $CaCl_2$ solution, under magnetic stirring. Formed beads were maintained under stirring for an additional period of 2 h to stabilize and, afterwards, were washed with deionized water.

Particles were then stored in a desiccator under vacuum and dried until constant weight.

Characterization of ALG/LBG beads

Beads shape, morphology and mean diameter were determined using a magnifier (Lumar V12-Zeiss). The determination of mean diameter was based on the assessment of a minimum of 100 dried particles.

Swelling behaviour

The water-sorption behaviour was determined by swelling in purified milliQ water approximately 300 mg of beads at room temperature. The wet weight of the swollen beads was determined after 4 h and 24 h of contact with water, by removing all the water by filtration and weighing the swollen beads immediately.

The percentage of swelling (S) was then calculated using the following equation:

$$S(\%) = \frac{S_e - S_0}{S_e} \times 100$$

where S_e represents the weight of beads at swelling equilibrium and S_o the initial weight of the beads.

RESULTS AND DISCUSSION

Solubility study

The effect of temperature on LBG solubility didn't show significant differences, given that solubilisation at 25 ºC and 80 ºC yielded approximately the same result. The same was observed for different periods of stirring. In general, the solubility achieved values above 90%.

Beads characterisation

Freshly prepared beads display a round shape and hydrogel appearance (data not shown). As expected, particles spherical shape was lost after drying, as revealed in the observation of dried beads (Figure 1). Instead, an irregular shape with tendency for sphericity and a slightly wrinkled surface was observed.

Produced formulations resulted in mean particle sizes between 1200-2000µm.

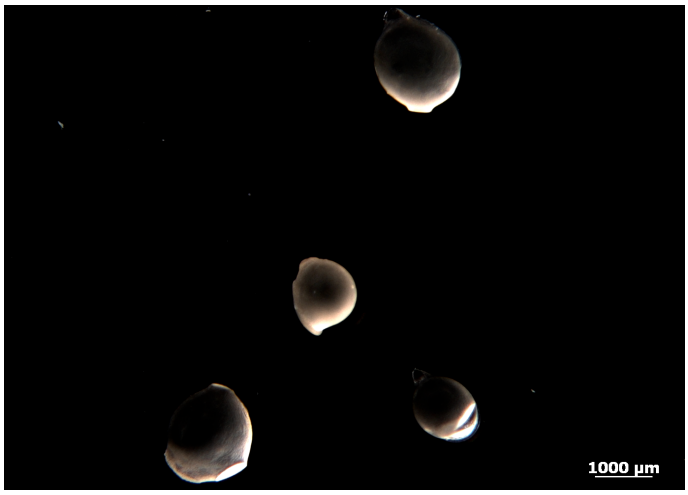

Figure 2: Microphotograph of representative ALG/LBG beads

Swelling study

Table 1 shows the alterations in beads weight as a result of water uptake upon 4 h and 24 h incubation. The developed beads showed a maximum swelling rate of 72% after 4 h incubation, which increased to 126% at 24 h, corresponding to the formulation with the highest polymer concentration (ALG + LBG). As compared to beads without LBG, it is observed that the addition of this polymer increases the swelling capacity of the particles. It is further observed that increased amounts of LBG lead to a corresponding increase in particles swelling rate.

Table 1: Swelling behaviour of the developed ALG/LBG beads at 4 h and 24 h (n = 3; mean ± SD)

Formulation	ALG/LBG (%)	4 h swelling (%)	24 h swelling (%)
Control	2.5/ 0	27.3 ± 13.1	34.3 ± 7.3
A	2.5/ 1.25	71.5 ± 17.1	126.0 ± 17.9
B	2.5/ 1.0	56.9 ± 2.0	66.1 ± 12.4
C	2.0/ 1.0	50.1 ± 9.1	57.5 ± 10.3
D	2.0/ 0.5	43.2 ± 12.5	71.1 ± 28.0

CONCLUSIONS

The produced particles display adequate sizes for drug delivery. The presence of LBG in the final formulations is demonstrated by the different swelling behaviour as compared to the control.

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