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Cold Iodide Encapsulation in Alginate Matrix for Future Radioiodine Precise Dosage in Thyroid Disorders

K. V. A. S. Loureiro[1], R. C. Nunes[2], F. J. O. Ferreira[2], J. C. Pinto[3], M. G. Martins[3] and L. Carvalheira[2]

[1] *kethele@eq.ufrj.br,*
Escola de Química
Universidade Federal do Rio de Janeiro
Av. Athos da Silveira Ramos, 149, Centro de Tecnologia, Bloco E, Cidade Universitária, 21941-909, Rio de Janeiro, RJ, Brazil

[2] *chaffin@ien.gov.br,*
fferrreira@ien.gov.br,
luciana@ien.gov.br,
Instituto de Engenharia Nuclear
Comissão Nacional de Energia Nuclear
Rua Hélio de Almeida, 75, Ilha do Fundão, 21941-614, Rio de Janeiro, RJ, Brazil

[3] *pinto@peq.coppe.ufrj.br,*
martins@peq.coppe.ufrj.br,
Programa de Engenharia Química,
Universidade Federal do Rio de Janeiro,
Centro de Tecnologia, Bloco G, sala 115, Cidade Universitária, 2194-972, Rio de Janeiro, RJ, Brazil

1. Introduction

Alginate is a natural polymer extracted from brown seaweed. Due to its biocompatibility, biodegradability, low toxicity and gelling ability, alginate has been used for the formulation of controlled release systems in the pharmaceutical and biomedical area [1]. Through the ionotropic gelation process, the interaction of alginate with divalent cations, such as Ca^{+2}, forms cross-links and the material transforms into gelatinous structures, usually spherical [2]. This mechanism enables the encapsulation of biomolecules in alginate matrices, which allows drugs to be administered orally in a minimally invasive manner with well-defined dosage [1,2].

The diagnosis and treatment of thyroid diseases is performed by oral administration of radioiodine doses in the form of solutions. This method can present problems, such as the lack of precision in dosage and the possibility of contamination of the patients and the professionals involved [3]. The objective of this project is to supply the patients' need for a safer procedure and more precise radioiodine dosage. For this purpose, in this paper, the efficiency of cold iodide encapsulation in an alginate polymeric matrix was evaluated, the study of iodide release from this matrix was performed, and the particles exudation was evaluated.

2. Methodology

First, cold iodide was used in this study stage to avoid unnecessary exposure to ionizing radiation besides providing sufficient iodide mass to perform its quantification in the analytical instrument technique used herein. Previously, 150 mg of sodium iodide (NaI) was dissolved in 10 mL of deionized water. Then 200 mg of sodium alginate were dissolved in this solution with the aid of a magnetic stir plate and heating. Separately, 40 mL of 1 % (w/v) calcium chloride ($CaCl_2$) solution was prepared with deionized water. Using a Pasteur pipette, the alginate solution was dropped into this $CaCl_2$ solution. The obtained microspheres were filtered through a sieve. The microparticles were obtained in triplicate.

To evaluate the encapsulation efficiency, the microparticles were degraded using 5 mL of an EDTA (ethylenediaminetetraacetic acid) solution (0.01 $mol \cdot L^{-1}$) and the iodide was quantified using spectrophotometry at 225 nm (equipment Thermo Scientific Multiskan GO). The calibration curve ($r^2 = 0.9974$) used for this quantification was prepared with NaI solutions in the range of 0.03 to 0.15 $mg \cdot mL^{-1}$. The release study was performed by contacting, approximately, 400 mg of the obtained microparticles with 5 mL of chloridric acid (HCl) 0.1 $mol \cdot L^{-1}$ and sodium chloride (NaCl) 0.9 % (w/v). Aliquots of 5 µL were taken from each medium after the defined time intervals (5, 10, 15, 30, 60, 120 min) for posterior iodide quantification by spectrophotometry. For the exudation evaluation, approximately 4 g of the obtained microparticles was stored in olive oil and another equal quantity, without medium. The visual inspection was performed twice for one week.

3. Results and Discussion

As can be seen in Fig. 1, the iodinated microparticles presented a gelatinous aspect and spherical shape, as expected. Besides, their average diameter equals approximately 3 mm. Microspheres loading with iodide and its encapsulation efficiency occurred with good reproducibility (Table I).

Figure 1: Microparticles loaded with iodide.

Table I: Results for the batches of iodide encapsulation and their efficiency.

Batch	Mass of iodinated microparticles (g)	Encapsulation Efficiency (%)
A	9.3	22.8
B	9.5	35.4

C	9.7	40.7
Mean ± SD	9.5 ± 0.1	33.0 ± 6.8

The encapsulation efficiency of iodide in the produced alginate microparticles was only 33.0 ± 6.8 %, that is, more than half of the iodide mass used in the preparation of the microparticles remained in the supernatant. In alginate encapsulation, small molecules are easily lost without promoting changes in the polymer matrix due to the porosity of this matrix. The diffusibility of larger molecules, on the other hand, depends on their molar masses [4,5].

Another important factor that interferes with diffusion is the charge of the encapsulated active compounds. Positively charged molecules interact with alginate, which promotes a diffusion inhibitory effect. In this case, the release occurs in a slower and more controlled way [4]. As a negatively charged hydrophilic compound, iodide has a repulsive effect in relation to alginate, which is also an anionic material. Thus, the interaction between species is relatively low and therefore, the iodide is rapidly released to the external aqueous phase [5].

Fig. 2 displays the kinetic profile of iodide release from the studied media. In this study, NaCl solution represents a general medium used to store many pharmaceuticals while HCl emulates the stomach pH. As seen in Fig. 2, the iodide release completely occurred for both media studied at about 15-30 min.

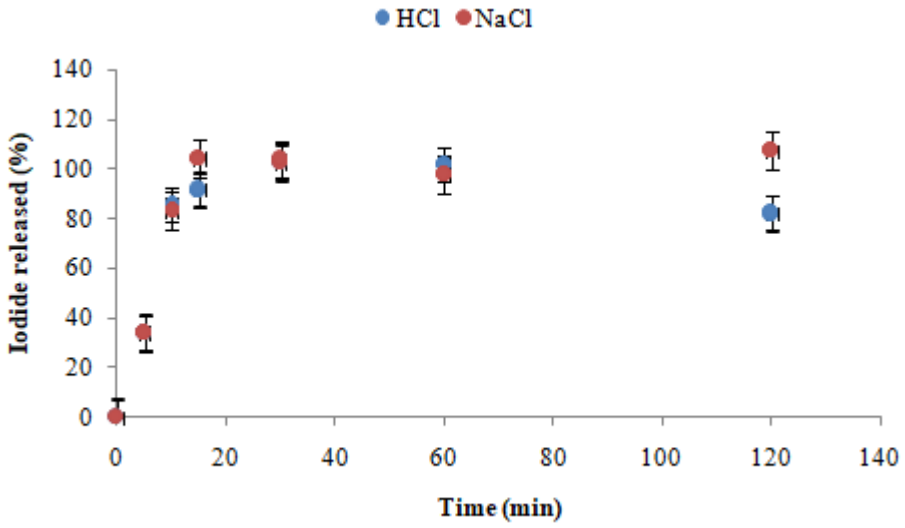

Figure 2: Cumulative iodide release profile of alginate microparticles, with standard deviation bars.

In the exudation study (Fig. 3), after 48 hours, the microparticles not exposed to any medium suffered greater loss of turve solution (Fig. 3A). Differently, on immersion in olive oil, there was greater resistance to the solution loss. After 7 days, a greater release of solution, microparticles deformation, and mold presence were observed in tube 1 (Fig. 3B). In tube 2, the volume of solution also increased in the same period. However, the sphericity of the microparticles was preserved and mold did not appear. Therefore, storage in olive oil is more suitable to reduce exudation.

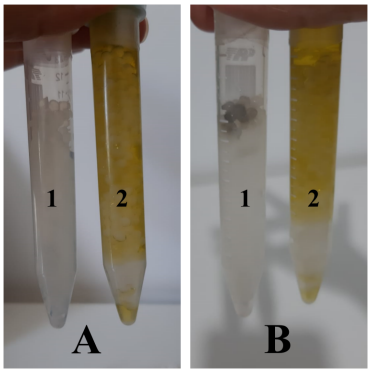

Figure 3: Exudation study results. Tube 1 without medium, tube 2 with olive oil.

4. Conclusions

The ionotropic gelation proved to be a viable method for the encapsulation of iodide in the alginate matrix. However, it is necessary to modify the methodology to improve the encapsulation efficiency. The release assay revealed that the alginate matrix briefly delayed the release of iodide in the studied media and the exudation study showed that storage in olive oil was the most appropriate for the obtained microparticles.

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