Ca-, Ba- and Al-alginate matrices as the carriers for the phosphatidylcholine liposomes

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Introduction

In this work the possibility of Ca-, Ba- and Al-alginate matrices using as the carriers for phosphatidylcholine liposomes delivery on different areas of human gastrointestinal tract have been examined. It is important while protein delivery systems creation (Ramadas M. et al. (2000), Xing L. et al. (2003), Dai C. et al. (2006)). The using for this aim of Ba-alginate matrix is promising (Dhoot N.O. et al. (2003), Dai C. et al. (2005)).

Material and methods

Alginic acid Sodium salt from brown algae was obtained from Fluka (loss on drying ≤ 15 %; ash ≤ 30 %; pH (10 mg/ml H_2O) 6.0 – 8.0). Phosphatidylcholine liposomes were obtained from Institute of biomedical chemistry (Moscow, Russia). All other reagents used were of analytical grade.

300 mg of phosphatidylcholine liposomes were dissolved in 30 ml of distilled water by stirring on the magnetic stirrer. For 2.0 % (w/v) sodium alginate solution obtaining to received solution of phosphatidylcholine 0.6 g of alginate powder were added. 3.0 % $CaCl_2$, $AlCl_3$, $BaCl_2$ solutions were prepared on distilled water.

Results and Discussion

Makeup alginate beads with phosphatidylcholine were placed in mediums with the temperature of 37 ^{0}C. As mediums used sequentially:

- 0.1 M hydrochloric acid (90 min);
- phosphatic buffer (pH = 6.0, 30 min);
- phosphatic buffer (pH = 7.4, for complete solution of beads).

In table 1 the changes, happened with beads in mediums, simulated stomach, duodenum and intestine conditions are shown.

On a Fig. 1 the graph of phosphatidylcholine release from Ca-alginate beads is presented. During 90 minutes of beads staying in 0.1 M hydrochloric acid, the yield formed 16.8 %. Herewith the beads weren't subjected to any changes.

After the first stage of experiment, the beads were extracted from hydrochloric acid and immersed in phosphatic buffer with pH 6.0, where they remained by stirring for 30 minutes. During this time interval the rate phosphatidylcholine release increased. Close to thirtieth minute the yield was 60.0 % from initial amount. The release rate growth caused by beads swelling.

At the third stage of experiment the beads were extracted from phosphatic buffer with pH 6.0 and immersed in phosphatic buffer with pH 7.4. It was shown that the dissolving of Ca-alginate matrix happened by buffer ions influence. Beads solution complete occurred in 20 minutes. So, at the third

stage of experiment the rate of phosphatidylcholine release in liquid phase was limited by Ca-alginate beads dissolving rate.

Preparing of Al-alginate beads with phosphatidylcholine, experiment conditions were identical to described above ones. In table 1 the external of beads obtained are shown. In consequence of physicochemical peculiarities of coordination of Al^{3+} iones with alginate polymer chain oxygen atoms, the beads form wasn't homogeneous and changed from spherical to concavo-concave.

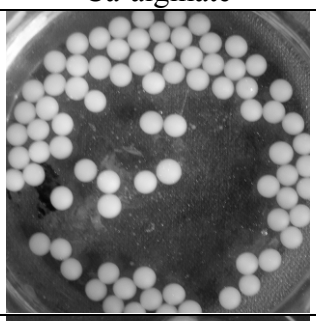
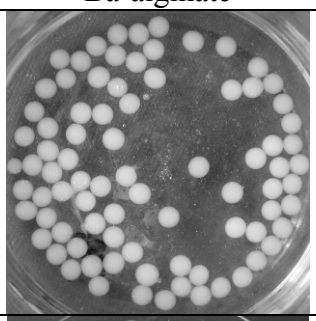
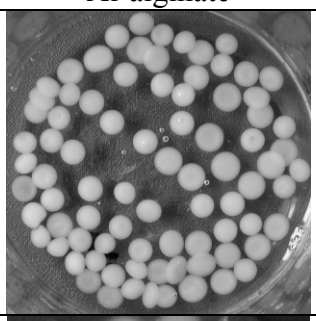
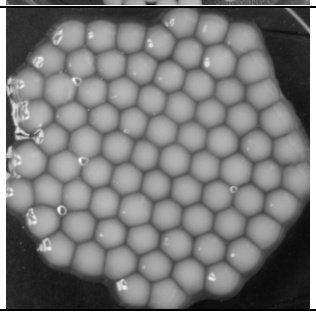
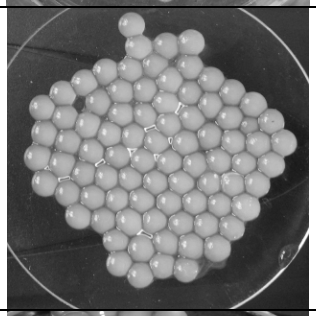
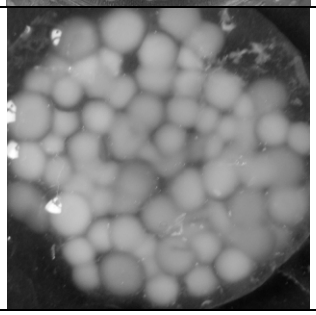
	Ca-alginate	Ba-alginate	Al-alginate
0.1 M HCl (90 min) «stomach»			
Phosphatic buffer, pH 6.0 (30 min) «duodenum»			
Phosphatic buffer, pH 7.4 «intestine»	Beads were dissolved		Beads were dissolved

Table 1 : The photos of beads located in mediums, simulated gastrointestinal tract conditions.

On fig. 2 the graph of phosphatidylcholine release from Al-alginate beads is shown. It was resulted that Al-alginate matrix holds encapsulated phosphatidylcholine considerably worse in comparison with Ca-alginate matrix. In 0.1 M HCl came out 54.4 % of its initial amount loaded into the beads. Moreover, the process of matrix dissolving started already at the second stage of experiment in the moment of beads immersion into phosphatic buffer with pH 6.0 (Table 1). In phosphatic buffer with pH 7.4 complete dissolving of beads occurred during 9 - 10 minutes. So the release rate of phosphatidylcholine at second and third stages of experiment was limited by Al-alginate matrix dissolving rate.

As a result of experiments carried out it was shown that Ba-alginate matrix possesses the best protective characteristics. In 0.1 M HCl the phosphatidylcholine release was minimal (8.7 %). At the second stage of experiment (in phosphatic buffer with pH 6.0) it was emitted from beads 26.6 %

of encapsulated phosphatidylcholine during 30 minutes. In this period occurred no external changes with beads (Table 1).

In the period of beads presence in phosphatic buffer with pH 7.4 the release of phosphatidylcholine to 280th minute of experiment increased up to 60 %. At the same time it was noticed reasonable beads volume growth due to swelling. Dissolving complete of beads didn't occure (Table 1)

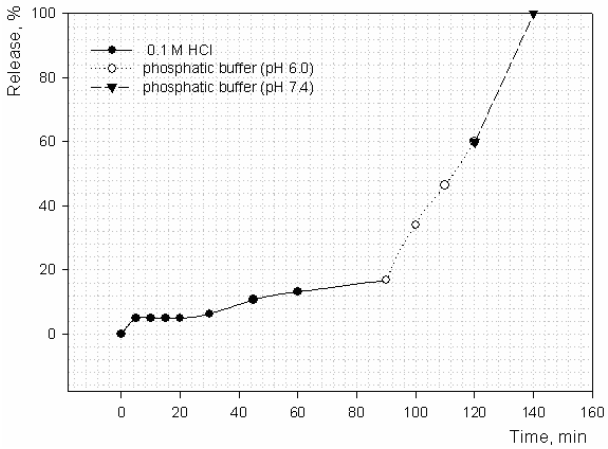


Figure 1: Phosphatidylcholine release from Ca-alginate beads

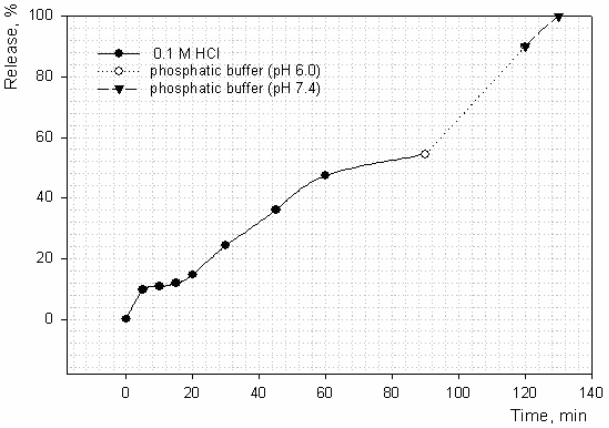


Figure 2: Phosphatidylcholine release from Al-alginate beads

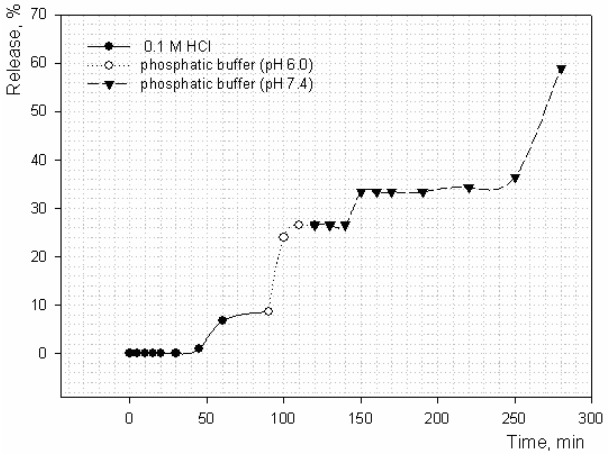


Figure 3: Phosphatidylcholine release from Ba-alginate beads

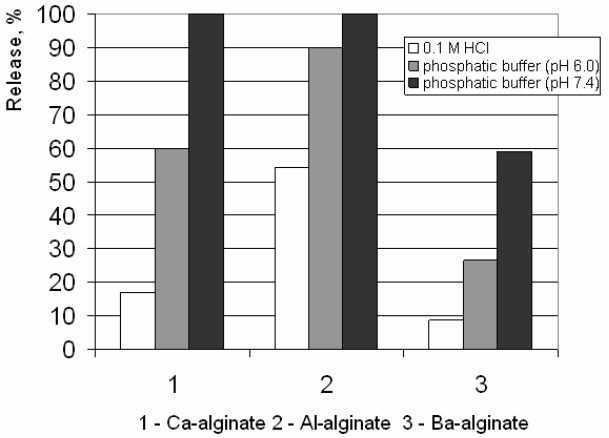


Figure 4: Phosphatidylcholine release from beads at different stages of experiment

Conclusions

As a result of experiments carried out it is possible to make following conclusions:

- out of three types of investigated matrices the ones based on Ca- and Ba-alginate meet the requirements to carriers. These two types are characterized by low release of encapsulated phosphatidylcholine in 0.1 M hydrochloric acid, thereby providing protection of encapsulated substance;

- Al-alginate matrix is characterized by extremely low retention ability of encapsulated substance. Moreover, the matrix itself is unstable in weak-acid medium at pH 6.0 where it destruction begins, and in this case encapsulated phosphatidylcholine release rate is limited by matrix dissolving rate;

- as a bioactive substances delivery means, possessing durable action, the most perspective carriers are based on Ba-alginate ones. This matrix type is characterized by the lowest phosphatidylcholine release value in acidic medium (8.7 %). Beads based on Ba-alginate appeared to be steady in alkaline medium (pH 7.4), that shows the possibility of encapsulated substances, peptides delivery in inferior intestine sections particularly;

- the type of obtained dependence of phosphatidylcholine release from Ba-alginate beads testifies the presence of physicochemical interactions between phosphatidylcholine encapsulated and matrix material.

References

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