

INFLUENCE OF METHYL- β -CYCLODEXTRIN ON THE RELEASE KINETICS OF INULIN ENCAPSULATED IN BIOADHESIVE LIPOSOMES.

G. Piel¹, L. Boulmedarat², A. Bochot², L. Delattre¹, E. Fattal²

¹ Laboratory of Pharmaceutical Technology, Department of Pharmacy, University of Liège, Belgium
E-mail: geraldine.piel@ulg.ac.be

² UMR CNRS 8612, Faculty of Pharmacy, Paris-Sud University, Châtenay-Malabry, France

INTRODUCTION

The aim of this work is to investigate the effect of methyl- β -cyclodextrin (Rameb) on the release kinetics of inulin³H encapsulated in liposomes dispersed in a bioadhesive ge. Rameb used as an absorption enhancer has a high affinity for lipids and is known to interact with cell membrane components, especially cholesterol.

We have investigated if the dispersion of the liposomes within a bioadhesive gel containing Rameb could modify the interaction intensity between the vesicles and the cyclodextrin due to the high viscosity of the gel.

EXPERIMENTAL METHODS

PC:CHOL:SA (60/30/10) and PC:CHOL:DSPE-PEG (64/30/06) liposomes have been prepared by the film evaporation method. To calibrate the liposome diameter the suspensions were extruded through polycarbonate membranes with diameters of 0.4 μ m and 0.2 μ m. Radiolabelled inulin (³H) was encapsulated in the liposomes by freeze/thaw technique. Free inulin was removed from the vesicles by ultracentrifugation. Liposomes (total lipid concentration of 2 or 10 mM) are dispersed in a Carbopol® 974PNF gel with or without Rameb (0, 2 or 5 % w/v).

The diffusion release of inulin from the liposomes was carried out in 6 ml vials thermostated at 37°C. 500 mg of gel were placed in contact with 5 ml of HEPES buffer pH 7.5 without stirring. After 1, 2, 4, 6 and 24 hours incubation, the released inulin³H in the supernatant was measured by radioactivity.

RESULTS AND DISCUSSION

We have shown that encapsulation of inulin in liposomes decreases its release from the gel. Liposomes act as a true reservoir of inulin which delays its release. In presence of cyclodextrins, the release of inulin increases.. The reservoir effect of liposomes decreases with the cyclodextrin concentration. This shows that the interactions between cyclodextrins and liposomes depend of the cyclodextrin concentration. Cyclodextrins destroy liposomes by extraction of the cholesterol and phospholipids, which increases the diffusion of inulin.

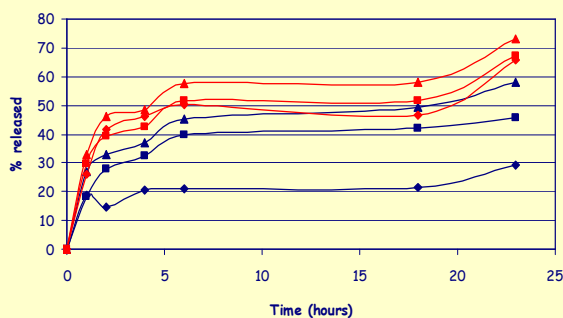


Figure 2: diffusion kinetics of inulin in function of the cyclodextrin concentration: in blue, PC:CHOL:SA liposomes; in red, PC:CHOL:PEG liposomes ◆ 0% CD, ■ 2 % CD, ▲ 5% CD

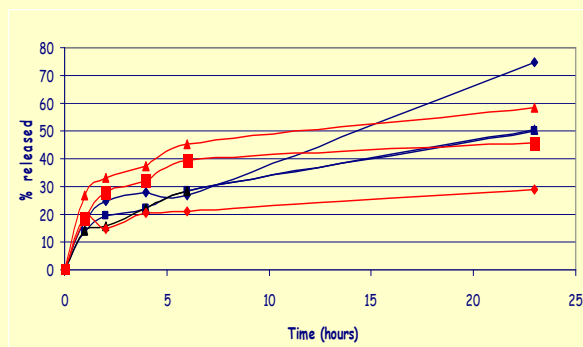


Figure 1: diffusion kinetics of inulin in function of the cyclodextrin concentration: in blue, free inulin; in red, liposome encapsulated inulin ◆ 0% CD, ■ 2 % CD, ▲ 5% CD

Contrarily to results obtained previously in less viscous systems, PC:CHOL:SA formulations dispersed in the gel show a lesser pronounced inulin release than that of PC:CHOL:DSPE-PEG formulations. This may be explained by the anionic charge of carbopol which may sterically stabilize PC:CHOL:SA liposomes, increasing the resistance to Rameb interactions (figure 2).

Analysis of the supernatant composition shows only inulin and cyclodextrin. No lipids were found in the supernatant. This shows that liposomes do not diffusate and that all liposomes-Rameb interactions occur *in situ* in the gel.

CONCLUSION

As no lipids are found in the supernatant, we can say that all the liposome-cyclodextrin interactions occur *in situ* in the gel. This interaction is probably due to an extraction of the cholesterol or the phospholipids from liposomes which destroys the bilayer structure and releases inulin. The bioadhesive gel modifies interactions probably because of the anionic charges of carbopol which stabilize PC:CHOL:SA liposomes, decreasing the release of inulin. PC:CHOL:PEG liposomes are more sensitive to Rameb in the gel.

ACKNOWLEDGEMENT

G.Piel is a post-doctoral researcher supported by the FNRS, Brussels, Belgium