EUROPEAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Official Journal of the European Federation
for Pharmaceutical Sciences

Volume 11/Supplement 1 (2000)

Elsevier
Amsterdam — Lausanne — New York — Oxford — Shannon — Tokyo

PO-23 INVESTIGATION OF ETACRYNIC ACID-CYCLODEXTRIN COMPLEXES

Z. Aigner, M. Kata, E. Szepesi, Cs. Novak
Depanment of Pharmaceutical Technology, University of Szeged, Hungary; Institute of General and Analytical Chemistry, Technological University of Budapest, Hungary

Etacrynic acid (E) is a very effective diuretic drug, whose solubility is very low. It is official in several pharmacopoeias, in different oral and parenteral dosage forms. Drug release from lipophilic suppository bases has been shown to be very poor, and our research therefore focused on the preparation of a cyclodextrin (CD) complex form. The products were prepared in four different mole ratios (E:CD mole ratio =2:1, 1:1, 1:2 and 1:3), by using two methods. Dissolution studies were performed, using different acceptor phases; and in vitro membrane diffusion (MD) experiments were also carried out. Thermoanalytical investigations confirmed the interaction between the components of the products. Those compositions were selected (on the basis of the dissolution and MD studies) which were found to be appropriate for incorporation into suppositories.

Results and discussion:

● The CD derivatives increased the solubility of the drug; random-methyl-β3-CD was used for the preparation of the products.

● The drug is characterized by poor solubility in an acidic medium, which increases in a basic environment. The CDs displayed better efficiency in the acidic artificial gastric juice: a 6-fold solubility increase was measured for the physical mixtures (PM), while a 6.5-fold increase was achieved with the kneaded products (KP). The solubility of the drug itself and of the CD-containing products proved to be the same in artificial intestinal juice. The CD concentration did not significantly affect the dissolution rate. The dissolution rate depended on the preparation method.

● The diffusion characteristics of the drug were shown to be improved by in vitro MD measurements. A 2-fold increase in the drug amount diffused and in the diffusion rate was experienced in artificial gastric juice for the physical mixtures; a 2.5-fold was attained for the KPs. The diffusion process was only slightly affected by the CD concentration.

● The melting point of the drug decreased by 20°C in the case of PMs, independently of the CD content, which may be a result of a eutectic interaction. The DSC results on the KPs revealed that the maximum shifted to higher temperatures with increasing CD concentration. The shift between the 2:1 and 1:3 preparations was more than 40°C. This study points to an interaction between the components.

Conclusion: The 1:1 KP is proposed for incorporation into lipophilic suppository bases.

PO-24 5-FU LOADED PLGA MICROSPHERES BLENDED WITH CHITOSAN GEL FOR LOCAL APPLICATION IN BREAST CANCER: FORMULATION AND IN VITRO RELEASE PROFILES

B. Arıca[1], S. Çalış[1], İ. Vural[1], S. Kaş[1], F. Kumbaradzi[2].
A.A. Hıncal[1]
[1]Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical, Technology, Ankara, Turkey: [2]University Sv.Kiril and Metodij, Faculty of Pharmacy, Institute of Pharmaceutical Technology, Skopje, Macedonia

Poly(D,L-lactide-co-glycolide) PLGA (50:50) is an amorphous, water insoluble and aliphatic polyester polymer which is very useful for many applications in drug delivery. A wide range of drugs, peptides, hormones, enzymes and antineoplastic agents has been encapsulated using this polymer as it is non-toxic, biocompatible and biodegradable. 5-FU is one of the antineoplastic agents which is commonly used for the treatment of several malignant neoplasms. It is also used topically in the treatment of some tumours on the skin, but the absorption from the skin is very low for 5-FU.

The purpose of this work is to prepare and analyze release characteristics of 5-FU loaded PLGA microspheres blended with chitosan gel base for topical delivery of 5-FU.

In the present study, 5-FU loaded PLGA microspheres were prepared according to the solvent evaporation method. Solution of polymers in dichioromethane was dispersed in 100 ml of sodium carboxymethylcellulose:sodium oleate (4:1) solution whilst vigorously stirring. After removing the organic solvent, the microspheres were centrifuged three times at 2000 rev./min, washed with distilled water, filtered and dried. A weighed amount of 5-FU loaded microspheres was dispersed in 2% chitosan gel. This mixture was poured into glass cells. Glass cells were incubated at 37°C and 1 ml of solution was removed at various time points. Released 5-FU was determined spectrophotometrically at 266 nm.

The release of 5-FU from chitosan gel was about 80% in 24 h whereas from PLGA microsphere blended chitosan gel it was about 22% within the same period.

PO-25 TESTING AND COATING OF DIMENHYDRINATE CRYSTALS

J. Bajdik, K. Pintye-Hódi, P. Szabó-Révész, P. Kása Jr., I. Erós
Departemnt of Pharmaceutical Technology, University of Szeged, Eötvös u. 6, H-6720 Szeged, Hungary

The surface treatment of particles usually involves a coating process in the case of solid dosage forms. The aim of the coating may be the protection of an active agent, the masking of the drug taste or smell, the separation of incompatible ingredients or prolongation of the effect. The coated crystals can be compressed or filled into capsules. Dimenhydrinate, ethanolamine-derivative antihistamine, was used as a model