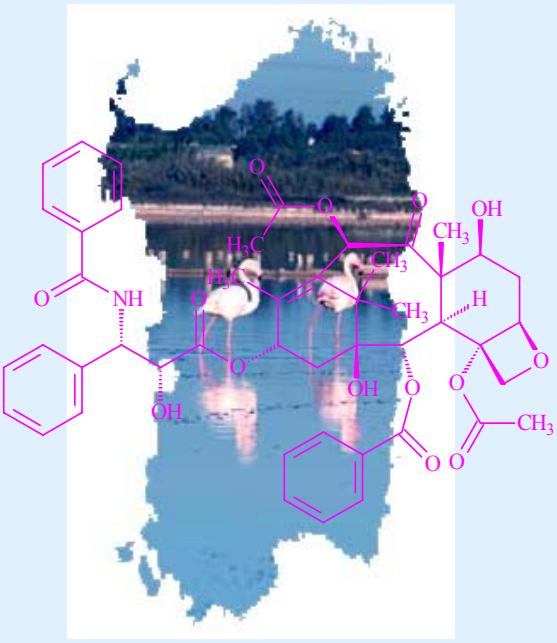
SardiniaChem 2006

GIORNATA DI STUDIO DEDICATA ALLA CHIMICA ORGANICA DELLE MOLECOLE BIOLOGICAMENTE ATTIVE

5 Giugno 2006, Complesso Universitario di Monserrato, Cagliari



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SPRAY-DRIED MICROSPHERES BASED ON METHYLPYRROLIDINONE CHITOSAN: IN-VITRO AND EX-VIVO STUDIES

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Methylpyrrolidinone chitosan (MPC) is a derivatized chitosan polymer obtained by chemical modification of natural chitosan; it is characterised by pyrrolidinone groups covalently attached to the polysaccharide backbone. This chitosan derivative combines the biocompatibility of chitosan and the hydrophilic characteristics of the pyrrolidinone moiety, being particularly susceptible to the hydrolytic action of lysozyme [Giunchedi, et al. 1998; Muzzarelli, 1992).

The purpose of this work was the preparation and the study of methypyrrolidinone chitosan spray-dried microspheres for the intranasal release of metoclopramide hydrochloride (Met). Chitosan (CH) microparticles were prepared as comparison.

Microspheres were obtained by the spray-drying technique; a solution containing 1.0% (w/v) of total solid (drug and polymer) in acidic media was sprayed. Two different polymers to drug ratios, 1:1 and 1:2 were chosen. The microparticles obtained were characterised by a series of pharmaceutical properties including encapsulation efficiency, microspheres morphology, size distribution and drug release behaviour at pH 7.0. Swelling tests and ex-vivo mucoadhesion and permeation studies using sheep nasal mucosa were carried out.

The results obtained show drug content values close to the theoretical amounts and the incorporation efficiencies of the model drug, Met, within the range 95-100%.

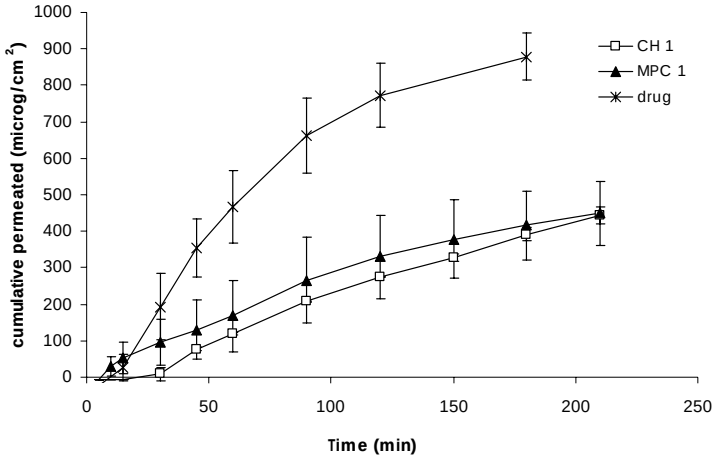
Particle size analyses indicate that the preparations are characterised by narrow size distributions regardless polymeric composition and drug loaded: microparticles have dvs values of about 6-8 μm.

In vitro Met release test shows that the total amount of drug is released within 1 h regardless polymer used and drug to polymer ratio. The microspheres control the drug release compared to the dissolution rate of the Met.

Microparticles based on chitosan derivatised interact with the mucin showing good ex-vivo mucoadhesive properties and also good ex-vivo drug permeation profiles (Figure 1).

In conclusion these preliminary results show that MPC microspheres could be suitable for nasal administration of metoclopramide.

Figure 1



This work is supported by a grant from Ministero dell' Istruzione, dell' Università e della Ricerca..

References

1) Giunchedi P., Genta I., Conti B., Muzzarelli R.A.A., Conte U., *Preparation and characterization of ampicillin loaded methylpyrrolidinone chitosan and chitosan microspheres,* Biomaterials 19 (1998) 157-161.

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