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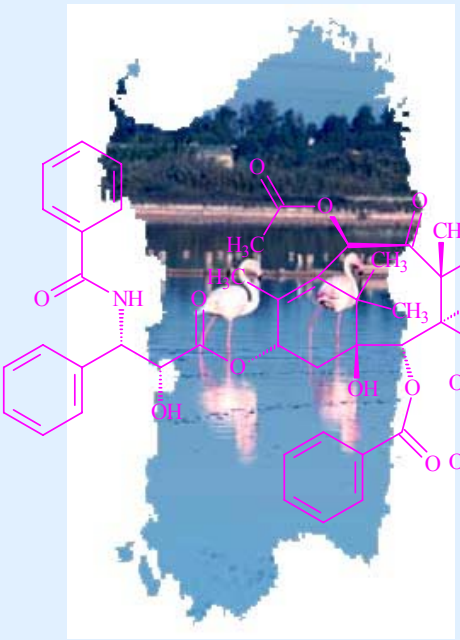

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DESIGN AND EVALUATION OF DRY-COATED TABLETS FOR COLONIC DELIVERY OF DICLOFENAC SODIUM

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A colonic drug delivery system is required to protect a drug during its transit through the upper gastro-intestinal tract and allow its release in the colon (1).
The aim of this study was the preparation of dry-coated tablets designed for colonic release of the model drug Diclofenac sodium (DS). The system consists of a drug-pectine (PC) mixture as the core and hydroxypropylmethylcellulose (HPMC) alone or mixed in different ratios with poly(ε-caprolactone) (CL) as the coat layer.

In vitro tests were carried out to determine the drug release in conditions mimicking mouth to colon transit in absence and presence of pectinolytic enzymes.

The core tablet (containing 25 mg of DS and 275 mg of PC) was compressed using a single punch-tableting machine equipped with a 8 mm diameter flat-faced punch. The core tablets were transferred into the die manually, covered with the components of coat layer and compressed by using a hydraulic press equipped with 13-mm flat punches.
In order to select the optimal thickness of coating material, tablets were coated using four different amounts of HPMC (200, 300, 400 and 500 mg). The composition of coat layer was then modify using 300 mg of HPMC and CL mixture in different ratios (50:50%, 70:30% and 30:70% w/w).
For all formulations, the *in vitro* release tests were performed using USP basket method. The test was carried out for 2 h at pH 1.2 and continued for another 22 h at pH 6.8 dissolution medium, simulating a gastric and intestinal environment respectively. The dissolution tests with pectinolytic enzymes were carried out in the same conditions by adding 3 ml of a commercial pectinase preparation (Pectinex-3XL®) to medium after 6 h to simulate the colon arrival time under normal conditions.
The results of the *in vitro* release tests in conditions mimicking mouth to colon transit, in absence of pectinolytic enzymes, are reported in Fig. 1a–b.

Fig. 1a shows the percentage of DS released as a function of time from tablets prepared with different quantity of HPMC as coat layer. No drug is released in the acidic medium; at pH 6.8 all formulations display a very slow release of the drug depending on the matrix composition. After 10 h less than 30% of drug is released from tablets containing 200-400 mg of HPMC. Formulation containing 500 mg of HPMC exhibits the highest drug release rate (in 10 h 100% of the drug was released).

The release profiles of systems containing a mixture of HPMC:CL as coat layer are compared in Fig. 1b. Larger amounts of PC produced faster release, while 50:50 HPMC:CL and 70:30 HPMC:CL systems result able to sustain the drug release.

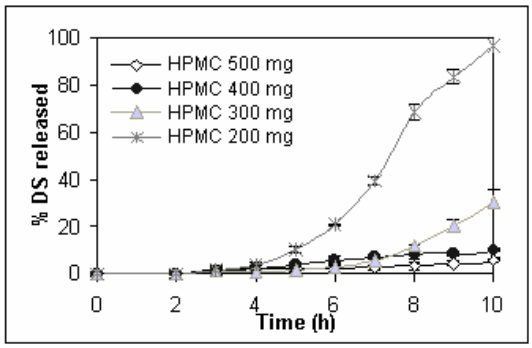

figure 1a

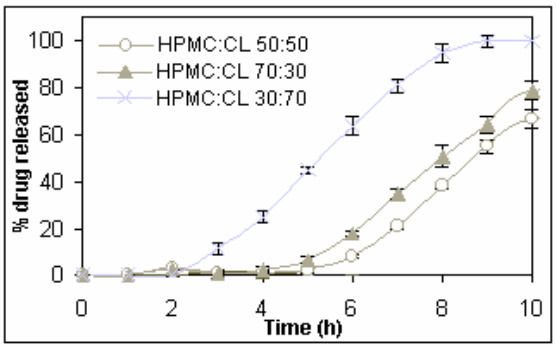

figure 1b

On the basis of the *in vitro* release results, the formulations containing HPMC (300 mg) and 50:50 HPMC:CL were selected for the test in the presence of pectinolytic enzymes. The addition of enzymes leads to a significant improvement of the release rate. In the case of HPMC (300 mg) formulation the percentage of drug released increased from 60 to 100% after 10 h.

During the same period 50:50 HPMC:CL system releases 70% of drug with respect to 30% found without enzyme.

In conclusion, the HPMC (300 mg) and 50:50 HPMC:CL tablets were found to be promising systems for the targeting delivery of DS to the colon.

References

[1] Ashford M, Fell J, Attwood D, Sharma H, Woodhead P. Studies on pectin formulations for colonic drug delivery. J Controlled Release. 1994;30:225-232.