Colon-targeted celecoxib-loaded Eudragit® S100-coated poly-ε-caprolactone microparticles: Preparation, characterization and in vivo evaluation in rats

Dalia M. Ghorab1, Maha Mohamed Amin1, Omneya M. Khowessah1, Mina Ibrahim Tadros1,2

1Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Cairo University, Cairo, Egypt
2Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Cairo University, Kasr El-Aini, 11562, Cairo, Egypt

Abstract

Context: Celecoxib suffers from low and variable bioavailability following oral administration of solutions or capsules. Recent studies proved that chemoprevention of colorectal cancer is possible with celecoxib.

Objective: This work aimed to tailor colon-targeted celecoxib-loaded microparticles using time-dependent and pH-dependent coats. Estimation of drug pharmacokinetics following oral administration to fasted rats was another goal.

Methods: A 23 factorial design was adopted to develop poly-ε-caprolactone (PCL) celecoxib-loaded microparticles (F1–F8). To minimize drug-percentages released before colon, another coat of Eudragit® S100 was applied. In vitro characterization of microparticles involved topography, determination of particle size and entrapment efficiency (EE %). Time for 50% drug release (t50%) and drug-percentages released after 2 hours (Q2h) and 4 hours (Q4h) were statistically compared. Estimation of drug pharmacokinetics following oral administration of double-coat microparticles (F10) was studied in rats.

Results: PCL-single-coat microparticles were spherical, discrete with a size range of 60.66 ± 4.21–277.20 ± 6.10 μm. Direct correlations were observed between surfactant concentration and EE%, Q2h and Q4h. The PCL M.wt. and drug-PCL ratio had positive influences on EE% and negative impacts on Q2h and Q4h. When compared to the best achieved PCL-single-coat microparticles (F2), the double-coat microparticles (F10) showed satisfactory drug protection; Q2h and Q4h were significantly (P < 0.01) decreased from 31.84 ± 1.98% and 54.72 ± 2.10% to 15.92 ± 1.78% and 26.93 ± 2.76%, respectively. When compared to celecoxib powder, F10 microparticles enhanced the bioavailability and extended the duration of drug-plasma concentration in rats.

Conclusion: The developed double-coat microparticles could be considered as a promising celecoxib extended-release colon-targeting system.

Published In: Drug Delivery, September-October 2011, Vol. 18, No. 7 : Pages 523-535