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

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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 aims to tailor colon-targeted celecoxib-loaded microparticles using time-dependant and pH-dependant 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.

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