Development and in vitro evaluation of mesalamine delayed release pellets and tableted reservoir-type pellets

Ehab Rasmy, J Mark Christensen, James W Ayres

Abstract

Background: The basic objective of this study was to develop a novel technique that aids in compaction of coated pellets into tablets and obtain a release pattern from compressed pellets resembling the same pattern before compression. Method: Multi-unit dosage forms of mesalamine targeted to the colon were formulated by extrusion-spheronization, and then coated with Eudragit S (30%). These pellets were filled into gelatin capsules or further formulated and compressed into tablets. Tablets for colonic delivery of mesalamine were prepared by mixing the coated beads with cushioning agents like stearic acid and Explotab, or by applying an additional coat of gelatin (4% weight gain) onto the Eudragit S coated pellets, and then compressing into tablets (tableted reservoir-type pellets). Then additional coating of the tablets prepared by the coating technique was applied utilizing Eudragit L 100-55 (5% weight gain). Results: This technique provides additive protection for the coated beads to withstand the compression force during tableting. Excellent in vitro dissolution results were obtained, which were comparable to the results of the release of mesalamine from uncompressed beads filled in capsules. Mesalamine release from the capsules was 0.3% after 2 hours in gastric pH, 0.37% was released after an additional 1 hour in pH 6, and 89% was released after 1.5 hours in colonic pH 7.2. Conclusion: Various formulation and process parameters have to be optimized in order to obtain tableted reservoir-type pellets having the same release properties as the uncompressed pellets. The coating technique delays the release of mesalamine until the beads reach the terminal ileum and colon. Once released in the colon, mesalamine is minimally absorbed and can act locally to treat ulcerative colitis.

Drug development and industrial pharmacy - 2010, April