Report

Physicochemical and permeation of NSAIDs and H_2-antagonist binary system

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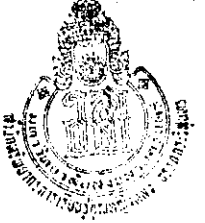

Abstract

The coadministration of cimetidine (C) and piroxicam (P) has advantages that it results in decrease of side effects and increase in the plasma concentration of piroxicam. In addition, the binary mixtures of these drugs may result in an improvement in low dissolution of piroxicam. The coprecipitates and physical mixtures of cimetidine and piroxicam were thus prepared at mole ratios of C:P = 1:10, 1:5, 1:4, 1:2, 1:1, 10:1, 20:1, 30:1, 40:1 and 52:1. The physicochemical properties of these coprecipitates and physical mixtures were investigated using powder X-ray diffraction (XRD), Fourier Transform infrared Spectroscopy (FTIR) and solid state ^{13}C-NMR spectroscopic. Additionally, dissolution of piroxicam in these binary mixtures was examined. The XRD and FTIR analyses indicate that intermolecular interactions between cimetidine and piroxicam in the coprecipitates cause transformation of the crystalline states of both the original starting materials (cimetidine form A and the piroxicam form II). In coprecipitates where the proportions of C:P were 1:1, 10:1, 20:1, 30:1 and 40:1, the starting crystalline drugs in all the mixtures were transformed to amorphous states. A mixture of amorphous state and cimetidine crystalline form A was observed for the coprecipitate with C:P mole ratio of 52.5:1. The dissolution studies suggest that this coprecipitate (52.5:1, C:P) may contain amorphous piroxicam. Moreover, in copricipitates where the proportion of C:P were 1:2, 1:4, 1:5 and 1:10, cimetidine form A was transformed to form C, whereas piroxicam form II was modified to piroxicam form I. The dissolution of pure piroxicam is higher at pH 1.2 compared to that at pH 4. Both binary mixtures of coprecipitates or simple physical mixtures with C:P mole ratios of 10:1, 20:1, 30:1, 40:1 demonstrate higher dissolution of piroxicam compared to that of drug alone, which clearly indicates that cimetidine can enhance the dissolution of piroxicam at both pH values. The highest piroxicam dissolution was obtained at a C:P ratio of 52.5:1 for both coprecipitates and simple physical mixtures. Furthermore, the permeability study is correlated with the dissolution profile of prioxicam. The value of logPa obtained at pH 4 is -5.09.