Jordan University of Science and Technology

Development and Evaluation of a Novel Dosage Form of Diltiazem HCl Using Ethylene Vinyl Acetate Copolymer and Sodium Starch Glycolate (in Vitro/ in Vivo Study)

Authors: Suhair S Alnimri, Khouloud A Alkhamis, Hussein G Ibrahim, Mutaz S Salem

Abstract: The work aims at developing a CR formulation, with high encapsulation efficiency of diltiazem HCl, suitable for twice daily administration. Microparticles, using EVA copolymer, were prepared by coacervation-phase separation technique, subjected to controlled extraction and vacuum freeze drying processes to generate and immobilize a non uniform initial drug concentration distribution, and evaluated in vitro and in animals. Effects of increasing initial drug concentration, varying polymer system, increasing porosity, and decreasing tortuosity, varying the size of the microparticles and the pH of the dissolution medium on the release rate were evaluated. The results indicated that the release rate from microparticles was constant (zero order) for an appreciable period of time but it was low for twice-daily administration. It increased with increasing initial drug concentration, varying polymer system, increasing porosity and decreasing tortuosity, and decreasing the size of the microparticles but the duration of constant release was shorter except for formulations containing 2.00 and 2.25% sodium starch glycolate. 10-h duration of constant release was achieved and the zero-order release rate was within the required rate to achieve the desired therapeutic level. The pH of the dissolution medium did not have any effect on the release rate. The results of the in vivo study indicated that in vitro dissolution correlated well with in vivo AUC 0-10 and Cmax between the new CR formulation and Cardizem CD. According, a new CR formulation that delivers diltiazem HCl at a constant rate, suitable for twice daily administration was developed.