Two different approaches for the prediction of in vivo plasma concentration-time profile from in vitro release data of once daily formulations of diltiazem hydrochloride

Ehab Rasmy

Professor

Abstract

The aim of this study was to employ two different mathematical approaches: first, a convolution approach using computer software; second, a mathematical calculation exploiting Wagner-Nelson calculation to predict in vivo plasma concentration — time profile from the in vitro release study for the once daily formulations of a model drug diltiazem hydrochloride. The once daily extended release tablets (120 mg) were prepared by the wet granulation technique. Ethanol or ethanolic solutions of ethylcellulose (N22), were used as granulating agents along with hydrophilic matrix polymers like hydroxypropyl methylcellulose (HPMC) (K 15M). The granules showed satisfactory flow properties, compressibility, moisture content and drug content. All the tablet formulations showed acceptable properties and complied with pharmacopeial limits. The in vitro drug release study revealed that formula F7-T which contains drug: HPMC ratio 1:1 and 20 mg of ethylcellulose was able to sustain the drug release for 24 h and satisfied the USP dissolution limits. Fitting the in vitro drug release data to Korsmeyer-Peppas equation indicated that the mechanism of drug release could be zero-order. The capsule formulation F14-C which consists of drug: HPMC ratio 1:2, 12 mg of ethylcellulose and 20 mg of polyox 100 showed in vitro drug release similar to the tablet F7-T using the similarity factor (f2). The mechanism of drug release could be coupled diffusion, and polymer matrix relaxation. The percent dissolved data from the two formulations were used as input function to predict the in vivo plasma data by the two approaches (Convolution by Kinetica® software and Wagner-Nelson calculation). The two methods were validated by prediction of plasma data from in vitro release data of FDA approved 300 mg extended release capsule. Prediction errors were estimated for Cmax and area under the curve (AUC) to determine the validity of the methods. The percent prediction error for each parameter is not exceeding 15%.

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