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Chemometrics - Assisted Spectrophotometric Green Method for Correcting Interferences in Biowaiver Studies: Application to Assay and Dissolution Profiling Study of Donepezil Hydrochloride Tablets

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Abstract

A green, simple and cost effective chemometric UV-Vis spectrophotometric method has been developed and validated for correcting interferences that arise during conducting biowaiver studies. Chemometric manipulation has been done for enhancing the results of direct absorbance, resulting from very low concentrations (high incidence of background noise interference) of earlier points in the dissolution timing in case of dissolution profile using first and second derivative (D1& D2) methods and their corresponding Fourier function convoluted methods (D1/FF& D2/FF). The method applied for biowaiver study of Donepezil Hydrochloride (DH) as a representative model was done by comparing two different dosage forms containing 5 mg DH per tablet as an application of a developed chemometric method for correcting interferences as well as for the assay and dissolution testing in its tablet dosage form. The results showed that first derivative technique can be used for enhancement of the data in case of low concentration range of DH (1-8 µg ml^{-1}) in the three different pH dissolution media which were used to estimate the low drug concentrations dissolved at the early points in the biowaiver study. Furthermore, the results showed similarity in phosphate buffer pH 6.8 and dissimilarity in the other two pH media. The method was validated according to ICH guidelines and USP monograph for both assays (HCl of pH 1.2) and dissolution study in three pH media (HCl of pH 1.2, acetate buffer of pH 4.5 and phosphate buffer of pH 6.8). Finally, the assessment of the method greenness was done using two different assessment techniques: National Environmental Method Index label and Eco scale methods. Both techniques ascertained the greenness of the proposed method.

Keywords: Chemometric based UV-Vis spectrophotometry, Biowaiver study, Background noise interference, Derivative and Fourier function convolution, Donepezil Hydrochloride, Dissolution profile, Green method

Introduction

In general, biowaiver studies were applied for the purpose of post drug approval changes. Moreover, the principle of biowaiver was extended to the approval of new products of generic drugs, thus, avoiding unnecessary human experiments and lowering the costs of generic products. According to US FDA, biowaiver study could be done with no need for conducting the study of human bioequivalence if the active ingredients have certain permeability and solubility criteria in vitro and at the same time, the dosage form dissolution profile meets the conditions of immediate release [1].