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RESEARCH ARTICLE

Preparation, Characterization, and In Vitro Evaluation of Ezetimibe Binary Solid Dispersions with Poloxamer 407 and PVP K30

Komal R. Parmar · Sunny R. Shah · Navin R. Sheth

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Abstract Ezetimibe (EZE), a water insoluble drug, depicts variable bioavailability. The objective of the present investigation was to improve dissolution characteristics of EZE, which might offer improved bioavailability. The solid dispersions were prepared using poloxamer 407 (L 127) and polyvinyl pyrrolidone by melt and solvent method, respectively. Phase solubility studies indicated linear relationship between drug solubility and carrier concentration. In vitro release studies revealed improvement in the dissolution characteristics of EZE in solid dispersions. Solid dispersion with L 127 gave better rate and extent of dissolution. The best fit model indicating the probable mechanism of drug release from solid dispersions was found to be Korsemeyer–Peppas. The results of characterization of solid dispersions by Fourier transform infrared spectroscopy, differential scanning calorimetry, and powder X-ray diffraction revealed reduction in drug crystallinity which might be responsible for improved dissolution properties. The tablets of solid dispersion, containing L 127 prepared by direct compression, exhibited better drug release as compared to marketed formulation.

Keywords Ezetimibe · PVP K30 · L 127 · Dissolution · Characterization

Introduction

Recent technologies have effectively discovered new drug molecules, with good pharmacological activities [1]. However, 40% of the new drug molecules suffer from poor aqueous solubility [2]. For BCS class II drugs, dissolution is the rate limiting step for absorption from the gastrointestinal tract [3]. For such drugs, there is a need to improve solubility and dissolution characteristics for exploiting the potential therapeutic benefits. Out of numerous approaches investigated by the researchers, solid dispersions traditionally have been used effectively to improve the dissolution characteristics of poorly water-soluble drugs [4–6].

Ezetimibe (EZE; Fig. 1), (1-(4-fluorophenyl)-3(R)-[3-(4-fluorophenyl)-3(S) hydroxy-propyl]-4(S)-(4-hydroxyphenyl)-2-azetidinone), belonging to BCS class II, is first in the new class of cholesterol inhibitors used in the treatment of hypercholesterolemia as monotherapy and in combination with statins [7]. It is also recommended in sitosterolemia as monotherapy [8]. However, EZE is practically insoluble in water, thus different approaches have been worked by various investigators to improve the dissolution properties, which might lead to the decrease in variation in bioavailability demonstrated by pure EZE [9–11].

Polyvinyl pyrrolidone (PVP K30) is most commonly used as a carrier in the preparation of solid dispersion systems. Molecular size of the polymer favors the formation of interstitial solid solution [12]. PVP K30 has been extensively used to enhance the dissolution of various drugs [13–15]. Recently, poloxamers, a group of nonionic surfactants, have been reported to improve the dissolution of poorly water-soluble drugs by preparing solid dispersions. Poloxamer 407 (L 127) has been successfully utilized to enhance the dissolution rate of poorly water-soluble drugs [16–18].

The aim of the present investigation was to improve the dissolution characteristics of EZE by preparing solid dispersions with PVP K30 and L 127. Solid binary systems were prepared in different drug to polymer ratios. The

K. R. Parmar · S. R. Shah (✉) · N. R. Sheth
Department of Pharmaceutical Sciences, Saurashtra University, Rajkot 360 005, Gujarat, India
e-mail: sunnyrshah@yahoo.com