Dissolution Rate Enhancement of Felodipine by Solid Dispersions using Novel Amphiphilic Polymer Soluplus®

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ABSTRACT SUMMARY

The purpose of this study was to enhance the dissolution rate of felodipine, a poorly water soluble drug via solid dispersion (SD) using a novel amphiphilic polymer, Soluplus®. SDs of ratios 1:2, 1:4, 1:6 and 1:10 were prepared by solvent evaporation method. In vitro dissolution profile of the pure felodipine, physical mixtures (PMs) and SDs proved the superiority of the SDs in terms of the rate and extent of dissolution of the drug. In order to unfold the process of the dissolution enhancement, solid state characterization of all the samples were done. These studies indicate the amorphous nature of the drug to be one of the reasons for improvement of the dissolution rate.

INTRODUCTION

A significant increase in the number of active pharmaceutical ingredients with poor aqueous solubility has been observed in the past decade. The rate of oral absorption and hence bioavailability of the poorly soluble drugs are often controlled by their rate of dissolution. Solid dispersion has been emerged as an attractive technique to address this problem. Felodipine, a BCS class II drug, is a calcium channel blocker that selectively reduces smooth muscle contractile activity in resistant vessels and is widely used in the treatment of hypertension, heart failure and angina pectoris. In this study, an effort was made to increase the dissolution rate of felodipine by preparing solid dispersions using a novel amphiphilic polymer, Soluplus®. Soluplus® is a polyvinyl caprolactum- polyvinyl acetate-polyethylene glycol graft copolymer with an amphiphilic chemical structure.

EXPERIMENTAL METHODS

Felodipine and Soluplus® were dissolved in the varying ratios (1:2, 1:4, 1:6 and 1:10) in adequate quantity of ethanol to prepare SDs. The solutions were poured in petriplates, dried and sieved (#60) to obtain SDs. PMs of the same ratios were also prepared, powdered and sieved (#60). Content uniformity of both SDs and PMs was assessed. In vitro dissolution study of pure drug (#60), SDs and PMs was carried out using an in-house modified USP Type I apparatus in pH 6.8 phosphate buffer with 1% SLS maintained at 37±1°C. The dissolution study was carried out using 100 ml of media agitated at 25 rpm. Samples were withdrawn (over a period of 1 hour), filtered through 0.22 µm membrane and analyzed. All analysis were done at 363 nm using previously validated UV-Visible spectrophotometric method.

Solid state characterization of SDs and PMs was done using differential scanning calorimetry (DSC), powder X-ray diffraction (XRD) and fourier transform-infrared spectroscopy (FTIR) in order to assess crystalline/amorphous nature of SDs.

RESULTS AND DISCUSSION

Good content uniformity of SDs indicated suitability of method used. In vitro release studies suggested that SDs and PMs significantly increased dissolution rate when compared with pure drug as indicated by amount dissolved within 1 hour and the rate of drug release (Fig. 1). Further, it was observed that SDs increased the rate and extent of dissolution to a significantly greater level than PMs. Pure felodipine showed very poor dissolution where less than 19% was dissolved in 1 hour. Solid dispersion of ratio 1:10 showed almost 100% cumulative release in a time of 30 minutes.
DSC study of pure drug, PMs and SDs were performed. The thermal analysis of pure drug revealed an endothermic peak at 146.7°C corresponding to its melting point, indicating crystalline nature of the drug. The melting peak of the drug was observable in the thermogram of all PMs. In case of the solid dispersions, the drug peak was completely disappeared which indicates the conversion of crystalline drug into amorphous form.

Fig. 1. In vitro dissolution profile of PMs, SDs and pure felodipine

The FTIR spectrum study of pure felodipine showed sharp characteristics peaks at 3369.64 cm\(^{-1}\) and 1689.64 cm\(^{-1}\) corresponding to N-H and C=O stretching. In all physical mixtures these characteristic peak were invariably present suggesting no interaction occurred between drug and soluplus®. Whereas, FTIR spectra of solid dispersions showed a considerable broadening of N-H and C=O stretching. These results give indication of the possibility of some sort of interaction in between the drug and the polymer. X-ray diffraction patterns revealed that pure felodipine was in crystalline state (Fig 2), as it showed sharp distinct peaks notably at 20 diffraction angles of 10.32°, 11°, 16.32°, 16.64°, 20.6°, 23.38°, 24.6°, 25.5° and 26.6°. X-ray patterns of solid dispersions showed no sharp peaks attributable to the drug in all the ratios indicating that the felodipine crystals were transformed to complete amorphous forms. Whereas, the characteristic peaks of the drug were present in all the physical mixtures but with lower intensity.

The results of DSC, FTIR and XRD study were found to be consistent with each other and indicated the crystalline state of drug in PMs and pure drug. However, the crystallinity of the drug was completely disrupted in all SDs which connotes the significant increase in the dissolution of the drug via SDs.

CONCLUSION

Amorphous SDs of felodipine can be easily prepared with Soluplus® which shows a substantial enhancement in the rate and extent of dissolution of the drug. These SDs could be used to prepare formulations with increased bioavailability. However, the prepared SDs need to be further tested in vivo for confirmation of hypothesis.

REFERENCES


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