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RESEARCH ARTICLE

EFFECT OF SUSTAINED RELEASE SOLID DISPERSIONS ON DISSOLUTION OF POORLY SOLUBLE DRUG

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Abstract

There are various techniques to control the release rate of the drugs, among which, controlling dissolution rate is most popular due to its success and low cost. Fenofibrate is a lipid lowering drug used in the treatment of hyperlipidemia, there are some reports on solid dispersions of Fenofibrate to enhance bioavailability but sustained released solid dispersion still untouched. The present study deals with preparation and evaluation of sustained release solid dispersions of Fenofibrate using retarding polymers. Solid dispersions were prepared by solvent evaporation techniques using EVA, EU (RL) – 100 and EC. Drug polymer interactions were studied by I.R. and *in–vitro* drug release was performed at 37 ± 0.5^{0}C. The IR studies confirmed absence of any possible interaction. Incorporation of PEG 6000 in solid dispersions increases the release of Fenofibrate. However, the release of Fenofibrate was retarded with an increasing the concentration of EC, EU RL 100 and EVA & sustained the release of drug.

Keywords: *Fenofibrate*, Sustained release, Solid dispersions, hyperlipidemia.

Introduction

More recently, the concept of solid dispersion has been explored using insoluble carrier materials. These sustained release solid dispersion system may be useful for enhancing bioavailability and suitable for sustained release formulations[1]. The sustained solid dispersion offer various potential advantages for drugs having poor bioavailability and can be delivered efficiently there by maximizing their bioavailability and sustained action[2]. Fenofibrate has been used for many years to lower cholesterol levels and its pharmacokinetic profile is well understood[3, 4]. Originally launched in 1975, it is poorly insoluble in water[5, 6] and has high lipophilicity (log P = 5.24). Thus the dissolution rate of Fenofibrate is expected to limit its absorption from the gastrointestinal tract. The dissolution rate improved by incorporating the drug in insoluble carriers which are considered as matrix system, help in prolonging the duration of time over which the drug is released and are considered suitable for formulations as sustained release dosage forms.

MATERIALS AND METHODS

Fenofibrate (99% purity) was obtained from Cadila Pharmaceuticals Ltd, India. Solvents were purchased from; S.D. Fine Chemicals India. EU RL-100 obtained from All the solid dispersions prepared were tested for drug content uniformity. Accurately weighed amount of solid dispersion was dissolved in Methanol (100ml) in volumetric flask and the volume was made up to the mark. The solution was then suitably diluted with methanol and assayed for drug content by measuring the Fenofibrate content at an absorbance of 286 nm. Results were tabulated in table no 2.

Degussa India Pvt Ltd. India. All other reagents and chemicals used were of analytical reagent grade.

Preparation of Sustained Release Solid Dispersions by[7]

The sustained solid dispersions of Fenofibrate were prepared by the solvent method. The weighed amount of drug was dispersed in a given volume of polymer Ethyl vinyl acetate (EVA), Eudragit RL-100 (EU RL) and Ethyl acetate (EC) acetone solution of required concentration. These were stirred for 15 minutes to ensure homogenous mixing. The dispersion was then evaporated to dryness in a desiccator under vacuum the mass was then pulverized. The particles were subjected for *in-vitro* dissolution performance. In each case different ratios (1:1.5, 1:2.5, 1:3.5, and 1:4.5) of the drug and carrier were used for the preparation of sustained solid dispersions.

Preparation of sustained release solid dispersions containing PEG [8-10]

The weighed amount of PEG 6000 was dissolved in the polymer-acetone solution. Drug was then dispersed in this solution, which was then evaporated, to dryness. The dried mass was then pulverized.

EVALUATION PARAMETERS: Drug Content Uniformity

All the solid dispersions prepared were tested for drug content uniformity. Accurately weighed amount of solid dispersion was dissolved in Methanol (100ml) in volumetric flask and the volume was made up to the

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Dissolution Rate Studies[11-14]:

Dissolution of Fenofibrate from various solid dispersions was studied by using Acetate buffer. 900 ml of dissolution fluid and a sample of solid dispersions equivalent to 120 mg of Fenofibrate was tied in a mucilin cloth were used in each test. A temperature of $37^0 \pm 0.5^0$C was maintained throughout the experiment. 10 ml of sample of dissolution medium were withdrawn at known time intervals and analyzed for Fenofibrate content by measuring the absorbance at 286 nm. The volume withdrawn at time interval was replaced with fresh quantity of dissolution medium. Percent of Fenofibrate dissolved at various times was calculated and plotted against time.

I.R. Studies:

IR spectra of prepared lyophilized solid dispersion were recorded on Shimadzu IR – 8400 Spectrophotometer (Shimadzu Corporation, Kyoto, Japan). Potassium bromide pellet method was employed and background spectrum was collected under identical situation. Each spectrum was derived from single average scans collected in the region 400 – 4000 cm^{-1}.

RESULTS AND DISCUSSION

Sustained release solid dispersions of Fenofibrate were prepared in the present investigation to prolong drug release *in-vivo* since drug shows poor aqueous solublility. Sustained release solid dispersions of Fenofibrate were prepared using hydrophobic polymers (EC, EU RL-100 and EVA). The ratio's of Drug: Polymers were 1:1.5, 1:2.5, 1:3.5 & 1:4.5. These are tabulated in Table 1. The percentage of drug content was found to be 92 - 97%, which was within acceptable limits. The results of the drug content uniformity in each of solid dispersions are presented in Table 2. IR-spectra of Fenofibrate and solid dispersion are exactly same; indicating that there is no change in chemical structure of drug after preparing its solid dispersions. Specific Fenofibrate peaks are observed at 2990, 1740, 1660, and 1600cm^{-1} and observed same in prepared solid dispersion formulation. The dissolution ratestudies were also performed; drug release profiles were shown in Figures 1, 2 and 3 respectively. Although, they release maximum percentage of drug levels at the end of 12 hours. Consistent release was observed with EVA & Eudragit RL-100 in all the cases. Further, increased consistent release behavior was observed with increasing polymer concentration in all the cases. In view of the reported results, F8 sustained release solid dispersion was found to be good.

Formulation	Drug: polymer	Drug: polymer ratio (mg)
F1	Fenofibrate: EC	00:150
F2		00:250
F3		00:350
F4		00:450
F5	Fenofibrate: EU	00:150
F6		00:250
F7		00:350
F8		00:450
F9	Fenofibrate:EVA	00:150
F10		00:250
F11		00:350
F12		00:450

Table 1: Composition of Solid dispersions of Fenofibrate

Formulation	% Drug content
F1	94.4
F2	95.3
F3	95.5
F4	97.2
F5	95.3
F6	96.6
F7	97.2
F8	97.6
F9	97.4
F10	96.4
F11	96.7
F12	96

Table 2: Drug content Uniformity

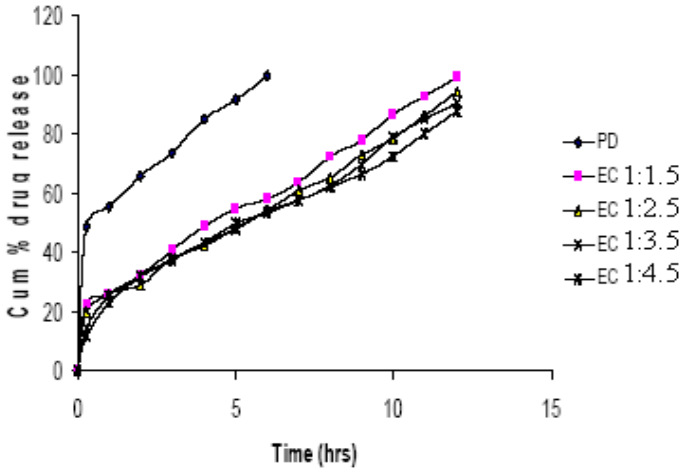

Figure 1: *In-vitro* Drug release profile for pure drug and Fenofibrate sustained solid dispersions using EC

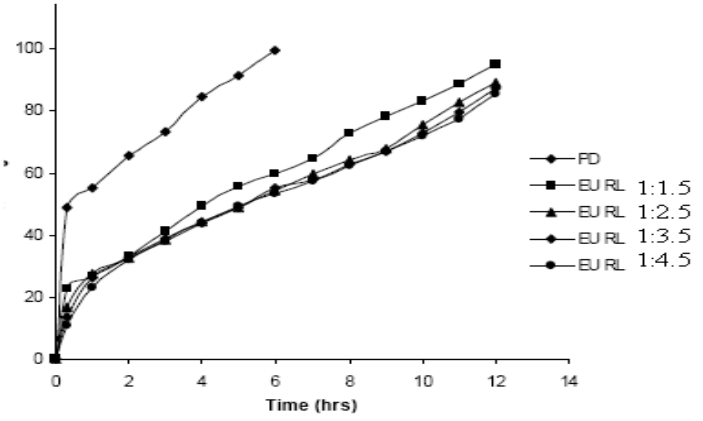

Figure 2: *In-vitro* Drug release profile for pure drug and Fenofibrate sustained solid dispersions using EU RL-100

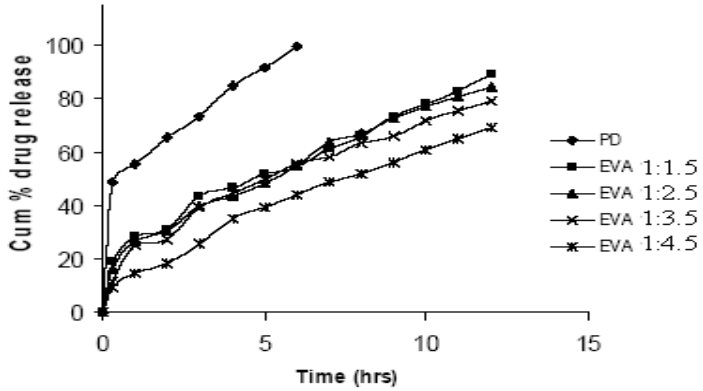

Figure 3: *In-vitro* Drug release profile for pure drug and Fenofibrate sustained solid dispersions using EVA

CONCLUSION

Drug content uniformity was made for all the prepared sustained release solid dispersions. IR studies were performed and confirmed absence of any possible solid state drug and polymer interactions. *In-vitro* release profiles studies suggested that the drug release has been extended with all the sustained release solid dispersions as compared with the pure drug. Approximately, all the sustained released solid dispersions exhibited polymer concentration dependent release retardation effect. The sustained released solid dispersion technique could be adaptable in laboratory and in industry as well since it is simple and reproducible. In conclusion, sustained release solid dispersions technique can be used to prolong drug release but further studies are needed to improve drug release within 7 – 8 hours which is the average of G.I. residence time.

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