Available online at www.icjpir.com ISSN: 2349-5448

INTERCONTINENTAL JOURNAL OF PHARMACEUTICAL INVESTIGATIONS AND RESEARCH

ICJPIR |Volume 3 | Issue 4 | Oct – Dec- 2016 **Research Article**

Effect of hydrophilic polymers on solubility of some antihypertentives drugs by enhancement of solubility using solid dispersion technique

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ABSTRACT

The main aim of the present study is to carried out to enhance solubility of Felodipine. Felodipine.was selected as model drug and different carriers like Vitamin-E, Polyethylene Glycol 8000, Polyvinyl pyrrolidone K-30 were used in drug to carrier ratio 1:1, 1:2, 1:4 by weight respectively. Solid dispersions were prepared by physical mixing method and solvent evaporation method. Solid dispersions were evaluated by drug content, *in-vitro* release, FT-IR, DSC and XRD. The obtained data of solid dispersion prepared by solvent evaporation method were compared with physical mixing method. The result showed decrease in melting point change from crystalline to amorphous form and improved dissolution rate as compared to physical mixing as well as pure Felodipine. The finding of present study proposes that solid dispersion approach is beneficial in enhancing solubility of drug and bioavailability as well.

Keywords: Felodipine, solid dispersion, Vitamin-E, PVP K-30, PEG 8000.

INTRODUCTION

Enhancement of bioavailability of poorly water soluble drug is a big challenge for formulation scientist. Solid dispersion technique is useful in improving bioavailability by increasing solubility. Solid dispersion is defined as dispersion of drug in matrix of hydrophilic carrier. Solid dispersion technique is basically used for BCS class II drugs. Drugs which come under BCS class II have low water solubility and high permeability and these drugs have solubility as rate limiting step. Thus if we increase solubility of drug, then bioavailability of drug will also increases [1, 2]. Felodipine is atypical antipsychotic drug. This has low bioavailability (9-19 %) and high protein binding (98 %). It acts by antagonizing D2 and 5-HT2A receptor which improve negative of symptoms of psychoses and reduce extrapyramidal side effects which are associated with typical antipsychotics. It is used in treatment of schizophrenia [3]. There are various methods which are used for making solid dispersion like solvent evaporation method, melting method, spray drying method and other also. In present investigation physical mixing method and

solvent evaporation method was employed for preparation of Felodipine solid dispersion. The carriers used were vitamin-E, polyethylene glycol 8000 and polyvinylene pyrrolidone K-30. The samples were formulated in different drug: carrier ratios.

MATERIAL AND METHOD

Drug and chemicals

Felodipine obtained as gift sample from Merck lab, Vitamin-E, Polyethylene Glycol, Polyvinylene K-30 were procured from Merck chemical Ltd. All carriers and solvents used were of analytical grade.

Preparation of solid dispersion by physical mixing method

Physical mixtures were prepared by trituration of drug and carrier in mortar pestle then proper blending in poly bags. Then mixtures were sieved and stored in desiccator at room temperature for further evaluation [5].

Preparation of solid dispersion by solvent evaporation method

Solid dispersions of Felodipine were prepared with drug and carrier (Vitamin-E, PVP K-30, PEG 8000) ratio 1:1, 1:2, 1:4 by weight, using solvent evaporation method. The drug was dissolved in ethanol then further carriers were dissolved in ethanol. Then solvent was removed by evaporation keeping at 40^{o}C under proper stirring for 24 hours. Then solid dispersions were collected and dried at room temperature for 48 hours. Then solid mass was pulverized in porcelain mortar and pestle and then passed through sieve no. 80 and store at room temperature in desiccator for further use [6].

Drug content

Samples equivalent to 40 mg Felodipine was placed in 100 ml volumetric flask containing some quantity of 0.1 N HCl pH 3.8 and then finally volume was made up to mark. Then it was shaken for some time to dissolve the sample, and then filtered through Whatman filter paper number 42 and suitably diluted and analyzed with double beam UV-VIS spectrophotometer at 314 nm[5].

In vitro dissolution study of Felodipine and its formulations

It was performed in USP type II apparatus (Paddle type). Accurately weighed solid dispersion containing 40 mg Felodipine was used for dissolution study. 0.1 N HCl pH 3.8 solution was used as dissolution medium at 37 ± 0.5°C and paddle speed was 100 rpm. Dissolution study was carried out for 60 minutes. 10 ml sample was withdrawn at predetermined time interval of 5, 10, 15, 30, 45, 60 min. Sink condition was maintained by adding 10 ml fresh medium. Samples were filtered by Whatman filter paper no. 42 and analyzed by UV- visible spectrophotometer at 314 nm[1].

Formulation	Cumulative % release of drug at 60 minutes
Drug	23.92
F-1	22.18
F-2	25.22
F-3	28.87
F-4	32.66
F-5	36.31
F-6	39.47
F-7	44.23
F-8	48.92
F-9	54.85
F-10	59.06
F-11	61.77
F-12	64.82
F-13	68.65
F-14	71.58
F-15	74.30

F-16	77.31
F-17	82.53
F-18	92.41

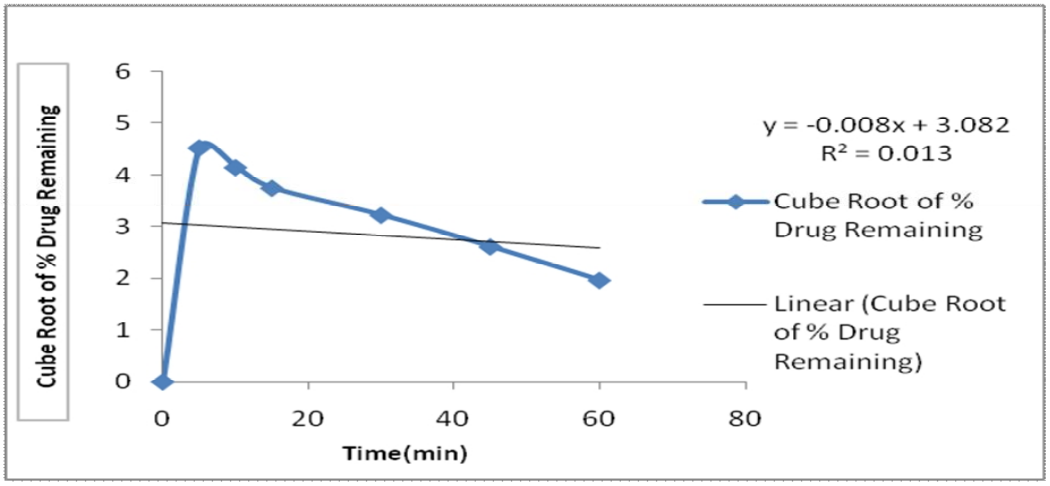

Figure 1: Dissolution profile Hixson Crowell Cube root Curve of F18

Infrared spectroscopy

Infrared spectroscopy was performed to determine interaction between drug and carrier. Sample (fine pure drug or prepared solid dispersion) was mixed with potassium bromide and then compressed into pellet. Spectra were recorded on shimadzu FTIR 8700 at 8000 to 400 $cm^{1.7}$.

Differential scanning calorimetric studies

It was performed on scanning calorimetry. The instrument was calibrated with standard indium. Sample (2-5) were placed in sealed aluminium pans and heated from 40°C to 390°C at rate of 10°C/in. in nitrogen atmosphere with reference to empty pan [8].

X-Ray Diffraction Studies

The powder x-ray diffraction (XRD) was performed by X'pert Pro with Spinner PW3064 using Ni-filtered, CuKa radiation, a voltage of 45 kV, and a current of 40 mA with a scintillation counter. The instrument was operated in the continuous scanning speed of 4°/min over a range of 5°C to 40°C[9].

Drug Release Kinetics

For understanding kinetics of drug release, the results of *in-vitro* dissolution study were fitted in various linear kinetic equations like zero order, first order, Hixson- Crowell's cube root model and Higuchi model. Dissolution data of best formulation were fitted and the value of regression coefficient was determined and compared to each other. The model which gave highest value of Regression Co-efficient (r^2), the release of drug follows that kinetics [10].

Stability Study

Accelerated stability studies were carried out on the F-18 formulation as per ICH Guidelines Q1C. The most satisfactory formulation was stored and sealed in aluminum foil. The samples were stored 40 ± 2^0C (75 ± 5 % RH) for 3 months. Solid dispersion formulation was evaluated for physical characteristics, and *in-vitro* drug release study, drug content study, solubility [11].

RESULT AND DISCUSSION

Calibration curve

Estimation of Felodipine was carried out in 0.1 N HCl buffer pH 3.8 ranging from 5-50 ug/ml at 314 nm absorbance. The standard curve was linear with regression coefficient 0.9967. Felodipine is very slightly soluble in water and having poor bioavailability and comes under BCS class II. To improve its bioavailability, solid dispersions of drug were prepared. (Table 1)

Stability Study

Formulation was found to be stable with insignificant change in physical appearance, *In-vitro* release study, drug content and solubility.

Table: List of formulations containing different carriers in different ratios

Formulation	Method of Formulation	Drug (Felodipine)	Carrier used		
			Vitamin-E	PVP K-30	PEG 8000
F-1	PM method	400 mg	400 mg	-	-
F-2	PM method	400 mg	800 mg	-	-
F-3	PM method	400 mg	1600 mg	-	-
F-4	PM method	400 mg	-	400 mg	-
F-5	PM method	400 mg	-	800 mg	-
F-6	PM method	400 mg	-	1600 mg	-
F-7	PM method	400 mg	-	-	400 mg
F-8	PM method	400 mg	-	-	800 mg
F-9	PM method	400 mg	-	-	1600 mg
F-10	SE method	400 mg	400 mg	-	-
F-11	SE method	400 mg	800 mg	-	-
F-12	SE method	400 mg	1600 mg	-	-
F-13	SE method	400 mg	-	400 mg	-
F-14	SE method	400 mg	-	800 mg	-
F-15	SE method	400 mg	-	1600 mg	-
F-16	SE method	400 mg	-	-	400 mg
F-17	SE method	400 mg	-	-	800 mg
F-18	SE method	400 mg	-	-	1600 mg

CONCLUSION

Among all formulations F-18 showed highest release rate F-18 was selected as optimized formulation. I.R. spectroscopy of F-18 shows that there is no incompatibility between drug and different polymers. D.S.C. study of F-18 shows that melting point of F-18 formulation has decreased, thus after formulation drug is converted in amorphous form from crystalline form. Release kinetics of F-18 was determined by different models like zero order, First order, Higuchi, Korsmeyer and Hixson-Crowell Mode. Formulation F-18 follow Higuchi model curve. Solubility of Felodipine was increased thus solid dispersion formulation of Felodipine was found to be significant.

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