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Preparation, Evaluation and Characterization of Solid Dispersion of Piroxicam

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ABSTRACT

Piroxicam is a Cycloxygenase-2 (COX-2) inhibitor used as analgesic and anti inflammatory drug. One of the major problems with the drug is that it is practically insoluble in water which results in poor oral bioavailability. In the present work solid dispersions of piroxicam were prepared by using various water soluble carriers to increase its water solubility. We used various water soluble carriers such as polyvinyl pyrrolidone (PVP), polyethylene glycol (PEG)-6000 and PEG-4000 in different ratio. Solid dispersions were subjected to Infrared spectroscopy (IR), Nuclear Magnetic Resonance (NMR), Thin Layer Chromatography (TLC), UV-visible Spectroscopy, Dissolution Studies, solubility studies and percentage drug content were performed. All solid dispersions of piroxicam show higher solubility and faster dissolution than pure drug alone. Piroxicam: PVP (1:5) ratio show highest solubility and faster dissolution than any other solid dispersion.

Keywords: *Piroxicam, PVP, solid dispersion, solubility, dissolution.*

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INTRODUCTION

The solubility behavior of a drug is a key determine of its oral bioavailability [1]. With the recent advert of high throughput screening of potential therapeutic agents the solubility of poorly soluble drugs were raised sharply and the formulation of poorly soluble compounds for oral delivery now presents one of most frequent and greatest challenges to formulation scientists in the pharmaceutical industry [2].

Piroxicam is a widely recommended in the treatment of rheumatoid arthritis and other inflammatory disorders. Piroxicam is used as an effective analgesic and anti inflammatory agent in rheumatoid arthritis, osteoarthritis and acute pain in musculoskeletal disorders. It has been shown to be an effective analgesic in fracture, dental and postoperative pain.

The major drawback of this drug is its poor water solubility which may give rise to dissolution related bioavailability problem. Drug with low aqueous solubility have low dissolution rates and hence suffer from oral bioavailability problems. So if the solubility of the drug is less, then desirable steps are to be taken to improve its solubility. Many methods have been reported for increasing bioavailability of poorly water soluble drugs.

Solid dispersion methods were also used by many researchers to enhance bioavailability of poorly water soluble drugs [3-6]. In the present study an attempt was made to increase solubility and dissolution of drug by solid dispersion technique using hydrophilic carriers such as PVP, PEG-4000 and PEG-6000 [7, 8].

MATERIALS AND METHODS

Piroxicam was obtained from Unique Laboratory Ankaleshwar. PVP, PEG-4000 and PEG-6000 were purchased from Merck, Mumbai. Solvent and chemicals used were of analytical grades and purchased from ACS Chemicals Ahmedabad, Gujarat.

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Preparation of solid dispersion of Piroxicam:

Solid dispersion of piroxicam were prepared using PVP, PEG-4000 and PEG-6000 in the ratio of 1:1, 1:3 and 1:5 individually by solvent evaporation method. Piroxicam and polymers in different ratio were accurately weighed and transferred to a beaker containing chloroform. The solvent was evaporated in vacuum evaporator and resulting solid dispersion stored in desiccators till solid dispersion attain constant weight. Solidified masses were crushed and pulverized and passed through mesh number 40.

Evaluation of solid dispersion of Piroxicam:

Drug carrier interaction study

All prepared solid dispersions were subjected to IR, TLC and NMR study to determine drug carrier interaction. IR spectra were recorded using FTIR spectro-photo-meter (8400, schimadzu, Japan), NMR was carried out at Chandigarh SAIF at 400 MHz.

TLC analysis carried out by E-Merck TLC aluminum sheets silica gel 60°F 254 (0.2 mm) using solvent system dichloro-methane: ethanol (20:1), chloroform: ethyl-alcohol (10:1) and glacial acetic acid :toluene (5:95) as mobile phase to study any drug carrier interaction between drug and carrier. The $\mathbf{R}_f$ values of pure drug and solid dispersions were calculated.

Percentage drug content study

Drug content was determined by dissolving 0.001-1% w/v solution of solid dispersion of drug in 0.01M methanolic hydrochloric acid kept in ultra sonicator for 20 min. The solution then filtered with whatman filter paper no. 41. The absorbance was measured at 242 nm using double beam UV spectrophotometer (2450, schimadzu, Japan).

Solubility study

Solubility study was performed according to method reported by *Higuchi and Connors* [9]. Excess of solid dispersion were added to 25 ml distilled water and taken in stoppered conical flask. Mixture was shaken for 24 hours in rotary flask shaker. Shaking is performed till equilibrium achieved and 2 ml aliquots were withdrawn at 1 hour interval and filtered through Whatman filter paper no. 41. Filtrate obtained was analyzed by UV spectrophotometer at 242 nm.

Dissolution study:

Solid dispersion equivalent to 15 mg of piroxicam was filled in hard gelatin capsules by hand filling method. Dissolution study was carried out using USP XXI six dissolution test apparatus (Lab India) employing USP type I apparatus. Dissolution study was carried out using 900 ml of 0.1N HCl and rotating basket at 100 revolutions per minute. Withdraw a 10 ml sample of medium at time interval of 5, 10, 15, 20, 25, 30, 45 and 60 minutes. The volume of dissolution medium adjusted to 900 ml by replacing each 10 ml aliquot with 10 ml fresh 0.1 N HCl. Concentration of piroxicam samples were determined by measuring absorbance at 242 nm.

Dissolution efficiency is defined as the area under dissolution curve up to the time expressed as percentage of the area of rectangle described by 100 % dissolution in the same time.

$$DE_{90} = \frac{\text{AUC of dissolution curve at 90min}}{\text{AUC of rectangle at time 90min}}$$

t_{90} – time required for 90% dissolution of drug

RESULTS AND DISCUSSION

Preparation of solid dispersion of Piroxicam:

Solid dispersion prepared using PEG-4000 and PEG-6000, were relatively easy to prepare as compared to solid dispersion prepared using PVP. Various effective formulation of solid dispersion of piroxicam is shown in table 1.

Evaluation of solid dispersion of Piroxicam

Drug: Carrier interaction study:

IR-Study:

IR spectra of solid dispersion of piroxicam show all IR peaks of drug and carrier. No other peaks were observed which indicates that there was no evidence of interactions between drug and carriers. The major

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IR peaks observed in solid dispersion are shown in table 2.

H^1 NMR Study:

NMR spectra of solid dispersion of piroxicam show all NMR peaks of drug and carrier and no other peaks were observed which indicates that there was no evidence of interactions between drug and carriers. The major IR peaks observed in solid dispersion are shown in table 3.

TLC Studies:

TLC studies shows following $\mathbf{R}_f$ values in different mobile phase

a) MDC (Dichloromethane): Ethanol (19:1)
0.50-0.56

b) Chloroform: Ethyl alcohol (9:1)
0.65-0.70

c) Toluene: acetic acid (95:5)
0.73-0.76

The results of TLC analysis are shown in table 4.

Percentage drug content study:

Percentage drug content of solid dispersion was found to be in range of (96.60±1.30) (98.50±0.95) (Table-5). It shows uniform distribution of drug in all solid dispersion.

Solubility study:

All the solid dispersion showed enhancement in solubility as compared to pure drug alone. The drug: carrier ratio (1:5) showed higher solubility as compared to 1:1 and 1:3 in all solid dispersion. Solubility enhancement is observed in following order.

PEG6000 > PEG4000>PVP

Dissolution study:

All solid dispersion prepared by solvent evaporation showed faster dissolution as compared to pure drug alone. Dissolution rate of pure drug is less because of hydrophobic nature of drug.

CONCLUSION

Piroxicam being oxicam derivatives has less solubility in water so we had prepared various solid dispersion of piroxicam with various carriers like PVP, PEG-4000, PEG-6000, in ratio 1:1, 1:3, 1:5 respectively to enhance the solubility as compared to piroxicam alone. Amongst all the solid dispersion 1:5 type of solid dispersion shows highest solubility. Various other analytical studies of solid dispersion are also performed i.e. IR studies, NMR studies, TLC studies in support of research work showing no drug carrier interaction

Table-1: Various effective formulations of solid dispersion of piroxicam

Code no.	Piroxicam	PVP	PEG-6000	PEG-4000
P1	1	-	-	-
P2	1	-	-	-
P3	1	5	-	-
P4	1	10	-	-
P5	1	-	1	-
P6	1	-	5	-
P7	1	-	10	-
P8	1	-	-	1
P9	1	-	-	5
P10	1	-	-	10

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Table-2: The major IR peaks observed in solid dispersion of Piroxicam.

S. No.	IR peaks (in cm^{-1})	Functional Groups	Piroxicam	Piroxicam	Piroxicam	Piroxicam
1.	3250	-NH,-OH Stretching	+	+	+	+
2.	1640-1680	-CONH, Amide group of drug	+	+	+	+
3.	1290-1330	-CN stretching of drug	+	+	+	+
4.	1040-1060	> S=O stretching of drug	+	+	+	+

Table-3: The major NMR Peaks of solid dispersion of Piroxicam.

S. No.	NMR band	PEG-4000	PEG-6000	PVP
1.	290ppm	+	+	+
2.	9.2ppm	+	+	+
3.	13.1ppm	+	+	+

Table-4: TLC analysis of solid dispersion of Piroxicam.

Code no.	R_f value from MDC : Ethanol	R_f value from $CHCl_3$: Ethanol	R_f value from Toluene:Acetic acid
P1	0.56	0.70	0.76
P2	0.52	0.68	0.74
P3	0.54	0.68	0.72
P4	0.55	0.69	0.75
P5	0.52	0.67	0.74
P6	0.53	0.68	0.74
P7	0.54	0.68	0.75
P8	0.50	0.65	0.73
P9	0.51	0.66	0.74
P10	0.51	0.67	0.74

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Table-5 Solubility and % drug content of solid dispersion of Piroxicam.

Code no.	System	Solubility	t_{90}	% drug content ± (S.D.)	
P1	Piroxicam		0.00285	>90	96.58±1.30
P2	Piroxicam;pvp(1:1)		0.01238	>90	97.58±1.52
P3	Piroxicam:pvp(1:3)		0.02530	>72.5	97.93±.91
P4	Piroxicam:pvp(1:5)		0.03520	>55.7	96.60±1.27
P5	Piroxicam:PEG6000 (1:1)		0.00650	>90	97.62±1.48
P6	Piroxicam:PEG6000(1:3)		0.00790	>85	98.00±.95
P7	Piroxicam:PEG6000(1:5)		0.01640	>76	
P8	Piroxicam:PEG4000(1:1)		0.00590	>90	96.62±1.33
P9	Piroxican:PEG4000(1:3)		0.00750	>90	
P10	Piroxicam:PEG4000(1:5)		0.01450	>86	97.60±1.56
					98.07±.93

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