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ENHANCEMENT OF DISSOLUTION RATE OF ATENOLOL BY SOLID DISPERSION TECHNOLOGY

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ABSTRACT

In the present investigation the enhancement of dissolution profile of Atenolol using solid dispersion (SD) technique with Poly ethylene Glycol 4000 (PEG 4000), Poly ethylene Glycol 6000 (PEG 6000) and Polyvinyl pyrrolidone (PVP) as carriers. Solid dispersions were prepared by the solvent evaporation method at different drug: polymer ratios using each carrier. The physical state and drug carrier interactions were analyzed by X-ray diffraction, infrared spectroscopy and scanning electron microscopy. Dissolution studies using the USP type II paddle method were performed for all solid dispersions. All solid dispersions showed increased dissolution rate as compared to pure Atenolol and PVP was found to be better than PEG 4000 and PEG 6000. The tablets were formulated using solid dispersion of Atenolol containing PVP as carrier. The tablets containing solid dispersion exhibited better dissolution profile than commercial tablets. Thus solid dispersion technique can be effectively used for improvement of solubility and dissolution character of the drug Atenolol.

KEY WORDS: Atenolol, PVP, PEG 4000, PEG 6000, Solid dispersion.

1. INTRODUCTION

Atenolol is a member of a class of drugs selective Beta adrenergic antagonist's derivative belonging to the category of Anti Hypertensive drugs (Satoskar RS and Bhandarkar SJ, 1994). It acts to inhibit the action of adrenaline on the heart and thereby slows the heart rate and lowers the blood pressure. Atenolol, the drug is sparingly soluble in water and therefore shows poor solubility or poor wettability which leads to decrease in bio-availability. Solid dispersion is one of the unique approaches, to increase the solubility, dissolution and absorption of poorly soluble drugs. In SD technique dissolution rate can be improved by increasing the surface area and thereby reducing the particle size. The present work aims to evaluate the potential of the solid dispersion technique for the development of Solid dispersion of Atenolol using PVP, PEG 4000 and PEG 6000 as hydrophilic carriers (Martindale, 1999).

2. MATERIALS AND METHODS

2.1. Materials: Atenolol was procured as gift sample from Micro Labs, Hosur. Polyethylene glycol 4000 and Polyethylene glycol 6000 were obtained from Sisco Research Laboratories Private Limited. All reagents and solvents used were of analytical grade.

2.2. Methods:

Preparation of solid dispersion by solvent evaporation method: Solid dispersions of Atenolol with carriers at 90:10, 75:25, 50:50, 25:75, and 10:90, weight ratios were prepared by the solvent evaporation method using various carriers such as PVP, PEG 4000 and PEG 6000 (Craig DQM, 2002). Firstly respective amount of carrier was dissolved in required amount of solvent methanol which is taken in a conical flask to get a clear completely soluble polymer solution with the help of magnetic stirrer. Then the weighed amount of Atenolol was added to this solution carefully with constant stirring. Stirring was continued until the drug is completely incorporated in solvent. Then the solvent was removed by evaporation at 40º C under vacuum (Serajuddin A, 1999). The mass obtained was dried, crushed, pulverized, and shifted through mesh no 80 (Chiou WL and Riegelman S 1971).

2.3. SOLID STATE STUDIES

2.3.1. Estimation of drug content: The uniform distribution of Atenolol SD system was confirmed by estimating the drug content by using Shimadzu UV, 1700 visible spectrophotometer at 274nm.

2.3.2. Drug Carrier interaction studies: The drug carrier interactions were studied by TLC method and IR spectral analysis (Van den Mooter G, 1998).

2.3.3. TLC: A silica gel- G coated thin glass plates were used for the determination of RF values of Atenolol pure sample and SD systems. The toluene, acetic acid and methanol mixture were used as mobile phase and it is detected by Iodine vapor method.

2.3.4. Fourier transform infrared (FTIR) spectroscopy: IR spectra of pure drug and their solid dispersions and physical mixtures were carried out by using FT-IR 8201 PC spectrometer. The IR spectra obtained were studied and confirmed the absence of chemical interaction between the drug and carriers.

2.3.5. X-ray powder diffractometry: The crystalline nature of Atenolol was studied for pure drug and for solid dispersions by using Siemens Kristallofex D- 5000 diffractometer.

2.3.6. Scanning electron microscopy: The particle size of the prepared solid dispersions were analyzed and samples were coated with gold to a thickness of 100 A using Hitachi scanning vacuum evaporator model HUS 5 GB. The coated samples were analyzed by using Hitachi scanning electron microscope model S – 540 operated at 15 V and photographed (Ali A and Sharma SN, 1991)(Patil C.C, 2001).

2.3.7 *In-vitro* release studies of pure drug and solid dispersion: *In-vitro* dissolution of pure drug, physical mixture and SD of drug with PEG 4000, PEG 6000, PVP were carried out on USP XXII type II dissolution test apparatus using 900 ml of 7.4 pH Phosphate buffer as a medium at 37 ± 1º C temperature with stirring rate of 50 rpm. The samples were analyzed for the drug content at 274 nm using Shimadzu UV, 1700 visible spectrophotometer (Chowdary KPR and Hymavathi R, 2001) (Sethia S and Squillante E, 2004).

Table no 1 Formulation Table of Atenolol Solid dispersion

S. NO	Ingredients	Formulations (mg)		
		FI	F II	F III
1	Atenolol	-	-	-
2	Atenolol : PEG 6000 SD (10:90)	82	-	-
3	Atenolol : PEG 4000 SD (10:90)	-	76.3	-
4	ATENOLOL:PVP SD (10:90)	-	-	99.5
5	Lactose		25	25
6	Micro crystalline cellulose		90	90
7	Talc		5	5
8	Magnesium stearate		5	5

Table no 3 *In-vitro* Dissolution of Atenolol SD from tablet formulations

Time (minutes)	Percentage Atenolol SD dissolved from			
	FI	FII	FIII	Marketed tablet
10	7.5	33.7	45.0	22.5
20	18.0	49.5	68.0	45.6
30	18.0	65.0	91.0	57.5
40	20.25	73.5	97.5	65.3
60	24.0	89.5	100	78.2
90	33.7	95.0	100	89.9

Table no 2 Percentage Release of Atenolol from various solid dispersions

Time in Min.	Percentage Release of Atenolol from														
	Atenolol : PEG 6000 SD (F I)					Atenolol:PEG4000 SD (F II)					Atenolol: PVP SD (F III)				
	9:1 (A)	7.5:2.5 (B)	1:1 (C)	2.5:7.5 (D)	1:9 (E)	9:1 (A)	75:25 (B)	50:50 (C)	25:75 (D)	10:90 (E)	90:10 (A)	75:25 (B)	50:50 (C)	25:75 (D)	10:90 (E)
10	64.8	54.1	59.2	44.1	45	70.3	44.1	64.6	45.1	37	76.1	63	57.6	59.5	41.7
20	72.1	61.2	72	61.2	52.5	84.6	64.6	69.8	54	40.6	82.6	73.4	71.1	72	55.2
30	80.1	74.3	77.4	76.3	62.2	95.9	76.3	73.6	59.2	50.2	84.7	77.4	77.7	78.6	67.6
40	86.0	83.8	87.8	84	70.3	99	82.4	79.3	76.1	54.1	91.2	83.1	84.7	88.9	79.7
60	91.4	90.1	94.3	95.4	77.7	99	93.7	86.3	80.4	66.9	95.5	90.5	92.5	96.4	89.1
90	95.7	94.3	99	99.1	82	99	96.9	99.7	92.3	76.3	99	99.3	99.3	99.5	95.5

All solid dispersions showed increased dissolution rate as compared to pure Atenolol and PVP was found better than PEG 4000 and PEG 6000.

3. RESULTS AND DISCUSSIONS

The IR spectra of pure drug, physical mixtures and solid dispersions shows no interaction between Atenolol with various carriers and X- ray diffraction studies revealed that crystalline nature of Atenolol in pure form was reduced to amorphous form in the dispersions. In this study solid dispersions prepared using various hydrophilic carriers which enhanced the solubility of the Atenolol to varying degree. Results of dissolution

studies showed rapid and fast dissolution of Atenolol from all solid dispersions when compared with pure drug and physical mixture. Among these formulations of Atenolol solid dispersions with different carriers, the formulation of Atenolol with PVP in the ratio of 90:10 (F III) showed the highest dissolution rate.

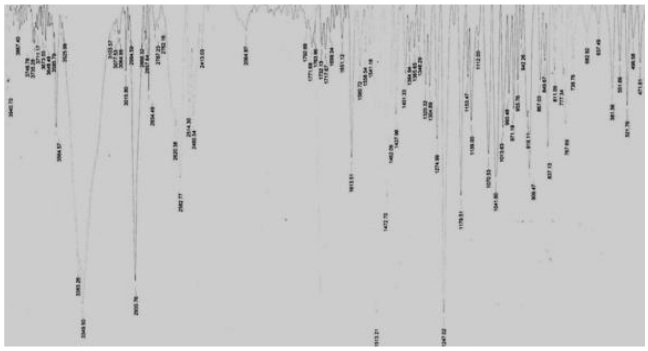

Figure no 1 FTIR of the pure drug, Atenolol

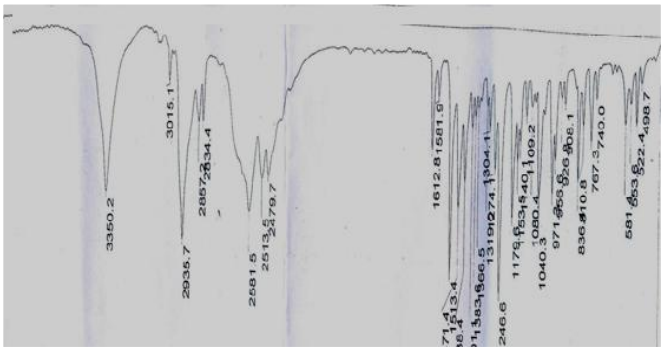

Figure no 2 FTIR of the Atenolol solid dispersion

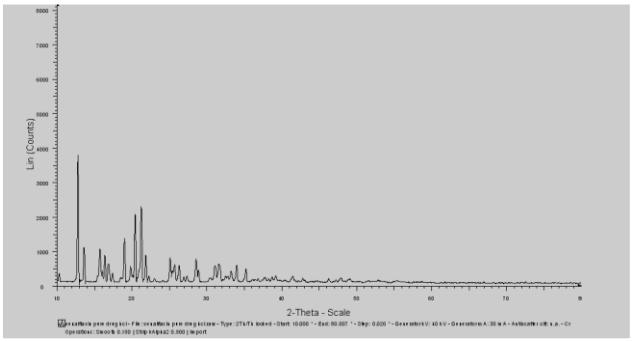

Figure no 3 XRD of the atenolol pure drug

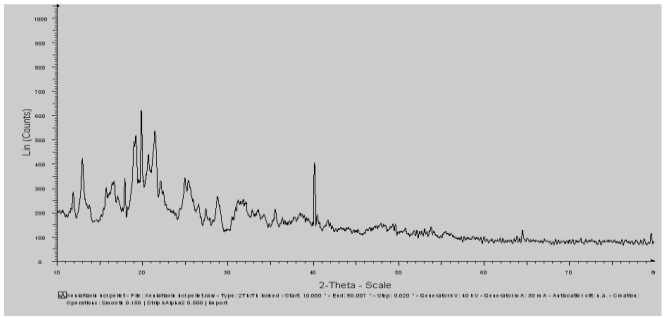

Figure no 4 XRD of the atenolol solid dispersion

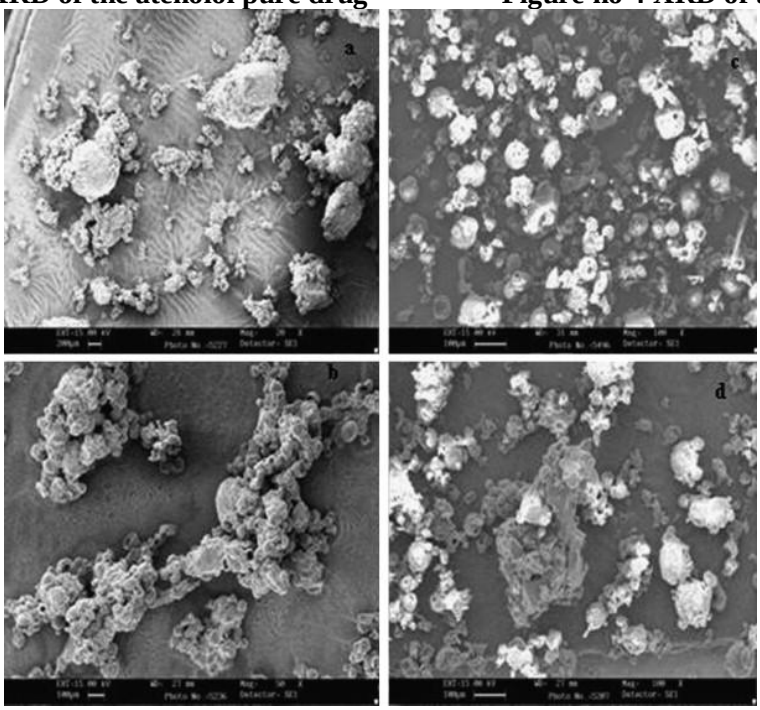

Figure no 5 SEM images of atenolol solid dispersion

4. CONCLUSIONS

SDs of Atenolol prepared with PVP by the solvent evaporation method resulted in greater increases in drug dissolution. As demonstrated by both X-ray diffraction and SEM, a decreased crystallinity of atenolol and the surface morphology of the polymeric particles explained this improved dissolution rate. Tablets containing those SD particles had drug dissolution profiles that were better than those of conventional tablets without PVP. Moreover, flow properties of the granules as well as the disintegration analysis technological parameters of the tablets indicated that PVP is a suitable excipient for the development of Atenolol fast release tablets.

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