Research Article

Dissolution Rate Enhancement of Aceclofenac By Solid Dispersion Technique

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Abstract: The aim of this study was to prepare and characterize solid dispersions of aceclofenac, employing a different excipient system composed of PEG6000, Glycine, and PVPk30 and to study the effect of a mixed excipient system on rate of dissolution of drug. The solid dispersions were prepared by physical mixture method and solvent wetting method using 1:1 ratios of drug to mixed excipients system. The formulations were evaluated for % practical yield, drug content, and in vitro drug release. In this study it was concluded that there was considerable increase in invitro drug release for solid dispersion as compared to the pure drug taken alone. Based on the drug release pattern, the solvent wetting method showed more in vitro drug release as compared to physical mixture method. Finally it could be concluded that solid dispersion of Aceclofenac using hydrophilic polymers would improved the aqueous solubility, dissolution rate and thereby enhancing its systemic availability.

Keywords: Dissolution, solid dispersion, physical mixture, solvent wetting, aceclofenac

INTRODUCTION

Oral drug delivery is the easiest and simplest way of administering solid dosage form. Oral bioavailability of a drug depends on its solubility and/or dissolution rate. If these drugs are not completely released in the gastrointestinal tract, they will have a low bioavailability [1-4]. Drug release is a critical and rate limiting step for oral drug bioavailability, particularly for drugs possessing low gastrointestinal solubility and high permeability. Thus, attempts to increase the rate of dissolution of drugs having limited water solubility are frequently required [5]. Enhancement in the dissolution rate of such drugs is one of the most important concerning aspects of the pharmaceutical industries [5-8]. Various techniques are available to improve this characteristic such as solid dispersions, micronization, and salt formation of drug and addition of surfactants. Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) and is poorly water-soluble. It is widely used to treat swelling and pain in rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Solid dispersion technique is used to enhance the dissolution of a poorly water-soluble drug. Solid dispersions are one of the most successful techniques to improve dissolution rate of poorly water-soluble drugs [9,10]. Solid dispersions are molecular mixtures of poorly aqueous soluble solid drug with an inert hydrophilic carrier. Drug release profile from such mixtures is driven by the carrier properties [11]. Various hydrophilic carriers employed in preparation of solid dispersions include polyethylene glycols, carbohydrates (lactose), poloxamers, polyvinyl pyrollidone K-25, polyols (such as sorbitol and mannitol), organic acid (citric acid) and hydrotopes (urea) [12-15]. Among these, lactose is the most widely used in pharmaceutical industries because of its inertness and cost. There are various methods for preparing solid dispersion which includes solvent wetting method, physical mixture, solvent evaporation method, melting method, solvent wetting method, fusion method, kneading method and super critical fluid method, etc [16- 18].

MATERIALS AND METHODS
Materials

Aceclofenac was of pharmaceutical grade sample gifted from Dr.Reddy's laboratory, India.PEG6000, PVPk30 from Yarrow chemicals, Mumbai. All solvents were of analytical grade and were used without further purification.

Method
Preparation of solid dispersions by solvent wetting method

The required amount of aceclofenac was dissolved in an appropriate amount of Acetone. This solution was dropped onto mixed excipient system placed in mortar and was constantly stirred. Finally the solvent was removed by evaporation at room temperature. The powder so obtained was ground in a mortar and stored in desiccators.

Various ratios of PEG6000, Glycine and PVPk30 used for preparation of solid dispersion
Aceclofenac (F1)
Aceclofenac +PVP k30 (F2)
Aceclofenac + PEG6000 (F3)
Aceclofenac + Glycine (F4)
Aceclofenac + PEG6000+ Glycine (F5)
Aceclofenac + Glycine + PVP k30 (F6)
Aceclofenac + PEG6000+PVP k30 (F7)
The complete profile of seven formulations, along with their quantities are mentioned in the table:1

Table 1 - Formulations

S.NO	Ingredients	Quantity (mg)						
		F1	F2	F3	F4	F5	F6	F7
1	Aceclofenac	50	50	50	50	50	50	50
2	PEG 6000	-	-	50	-	25	-	25
3	Glycine	-	-	-	50	25	25	-
4	PVP k30	-	50	-	-	-	25	25

CHARACTERIZATION OF SAMPLES
Fourier transform infrared spectroscopy

All the prepared solid dispersions were subjected to FTIR spectroscopic studies, to determine drug-carrier interaction. The FTIR spectra were recorded on samples prepared in potassium bromide (KBr) discs, using a fourier transform IR spectrophotometer.All the spectras of individual polymers and formulations are inserted in the below figures-
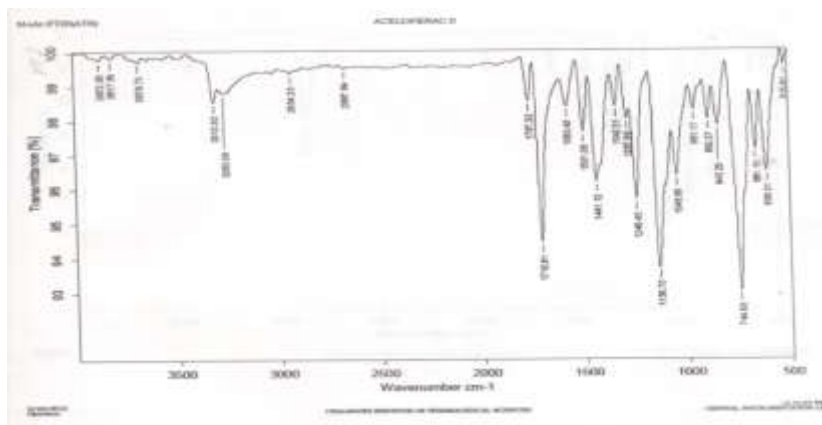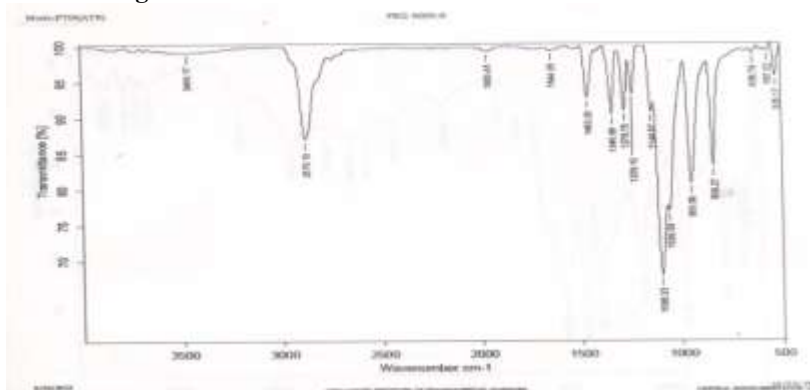

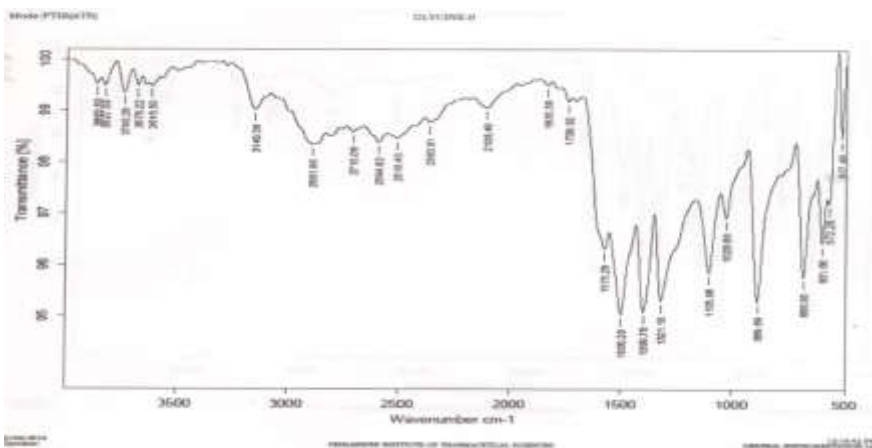**Figure No:1- FTIR SPECTRA OF ACECLOFENAC**

Figure.No:2 -FTIR SPECTRA OF PEG6000

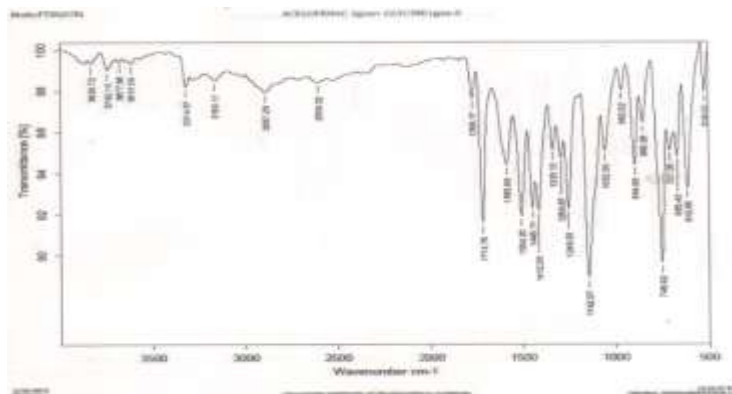**Figure.No:3-FTIR SPECTRA OF GLYCINE**

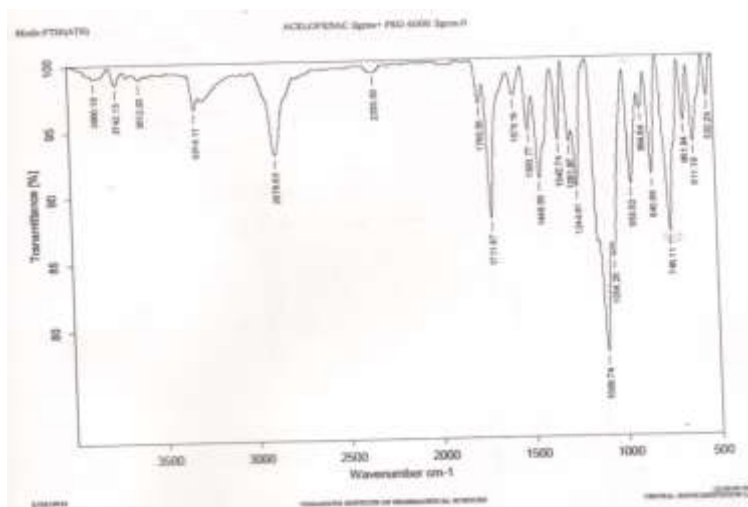**Figure.No:4 -FTIR SPECTRA OF ACECLOFENAC + GLYCINE**

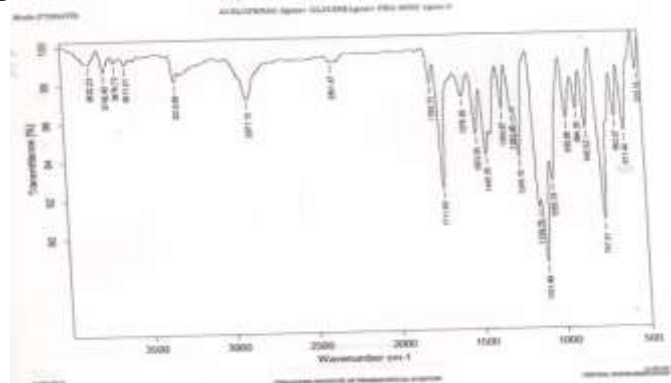**Figure.No:5- FTIR SPECTRA OF ACECLOFENAC + PEG6000**

Figure.No:6-FTIR SPECTRA OF ACECLOFENAC + GLYCINE + PEG6000

PHYSICAL CHARACTERIZATION OF SOLID DISPERSIONS

Determination of apparent bulk density:
The powder blend was weighed first and then placed in a graduated cylinder and measure the volume of it. This gives the relationship to find out the apparent bulk density (g/ml).

Apparent bulk density =   Weight of powder blend
                          Volume of powder blend

Determination of tapped density:
Tapped density was measured for each batch using Tap Density Tester (USP) (Electro lab Etd-1020). The pre-weighed amount of powder blend was placed in a Graduated cylinder and tapped for fixed number of taps (around 100) on mechanical tapping apparatus. From this the tapped volume was noted. Finally the tapped density was computed using the formula:

Tapped density =   Weight of powder blend
                     Tapped volume of powder blend

Determination of Carr's index:

It was used to determine the % compressibility of powder blends. It was calculated by using the value of tapped density and bulk density.

Carr's index = (Tapped density - Apparent bulk density)
Tapped density

Determination of angle of repose:

It was determined by using funnel method. A funnel with its tip at a given height (H), above a piece of graph paper was fixed on a plane surface. Powder blend was poured through the funnel such that the apex of the conical pile touched the tip of the funnel. The angle of repose (θ) was then calculated as follows:

$$\tan \theta = \frac{H}{R}$$

Where, R is the radius of the conical pile.

EVALUATION PARAMETERS
Determination of % practical yield

Determination of practical yield is useful to determine the efficiency of a preparation technique. The practical yield is calculated by using following equation:

$$PY (\%) = \frac{\text{Practical mass (solid dispersion)}}{\text{Theoretical mass (Drug + Carrier)}} \times 100$$

Estimation of drug content

Dissolve solid dispersions (equivalent to 100 mg of drug) in 100 ml of methanol. The solution was filtered, diluted suitably and analyzed at 275 nm by employing UV spectrophotometer. The drug content is calculated by following formula:

$$\% \text{ Drug content} = \frac{\text{Actual amount of drug in solid dispersion}}{\text{Theoritical amount of drug in solid dispersion}} \times 100$$

Dissolution studies

An *in vitro* release profile for each batch *was* performed using USP dissolution apparatus (Electro lab TDL- 8L, Mumbai, India). Pure drug and solid dispersions of drug were kept in the baskets of dissolution apparatus. The dissolution testing was carried out at a temperature $37 \pm 0.5°$ C and a stirring rate of 50 rpm in 900 ml of 6.8 pH of Phosphate buffer solution. Aliquot of 5 ml were withdrawn every five minutes. The same amount of withdrawn volume was replaced with the dissolution medium in order to maintain the sink condition. Aceclofenac concentration was determined spectrophotometrically at 274 nm. All the details of the evaluation parameters are mentioned in table.no:2.

RESULTS:

Percent practical yield for all the formulations of aceclofenac solid dispersions are found to be between 92-98%. The drug content of the prepared solid dispersions are found to be in the range of 69-92%. Maximum % drug content is found in the formulation 1. Percent drug content decreased as the polymer mixture addition varied added to each formulation increased. All the obtained results are tabulated in table: 2.The dissolution of aceclofenac which is in the form of solid is shown in figure: 1 and table: 3 shows the cumulative percent drug released as a function of time for all formulations. Cumulative percent drug released after 60 min was 33.44%,86.26%, 42.74%,67.8%, 60.2%, 65.28% and 53.82% for F1-F7 respectively and was 33.44% in 60 min for the pure drug.

Table: 2 Evaluation Parameters

Evaluation parameters	F1	F2	F3	F4	F5	F6	F7
% practical yield	93 ± 0.04	98 ± 0.08	92 ± 0.06	97 ± 0.04	95 ± 0.03	96 ± 0.05	94 ± 0.07
Bulk density (gm/cm)	0.75	0.73	0.75	0.73	0.70	0.69	0.70
Tapped density (gm/cm)	0.81	0.80	0.82	0.80	0.82	0.77	0.77
Carr's index (%)	7.40	8.75	8.53	8.75	14.6	10.38	9.09
Hausner' ratio	1.08	1.09	1.09	1.09	1.17	1.12	1.10
Drug content (%)	92 ± 0.05	88 ± 0.02	69± 0.01	84± 0.03	74 ± 0.05	78± 0.02	77± 0.04
Angle of repose (Degree)	24.07	23.22	22.76	15.32	12.05	11.89	14.45

In vitro release studies reveal that there is marked increase in the dissolution rate of aceclofenac from all the solid dispersions when compared to pure aceclofenac itself. From the invitro drug release profile, it can be seen that formulation F2 containing PVPk30

shows higher dissolution rate compared with other formulations.

DISCUSSION:

Findings of study reveal the fact that granules prepared by both method posses better flow behavior. Granules were having bulk density and tapped density within good range; hence their Compression is easily done. This factor is thus of greatest importance while studying the physical parameters. The comparision of the dissolution profiles of all formulations were represented in figure no: 7. The increase in the dissolution rate is in the order of pvpk30: glycine (1:1) > pvpk30 > Glycine > Glycine: PEG6000 (1:1) > PVPk30: PEG6000 (1:1) >PEG6000. In tne case of solid dispersions of aceclofenac with the mixture of PVPk30 and Glycine ratio of 1:1, the dissolution rate of drug increased. While in case of those prepared in the ratio 1:1with other polymers individually and in the mixture the dissolution rate of drug was decreased. This might be due to formation of viscous layer around the drug particles leading to decrease in the dissolution rate.

Table: 3 Dissolution Profile

| TIME (min)	PERCENT DRUG RELEASE						
	F1	F2	F3	F4	F5	F6	F7
5	2.44± 0.02	5.72±0.09	6.14±0.02	4.24±0.04	3.88±0.02	6.48±0.03	2.34±0.06
10	5.06±0.05	14.16±0.01	8.03±0.04	37.4±0.04	7.30±0.05	14.3±0.04	3.87±0.03
15	8.44±0.02	23.22±0.05	13.2±0.05	48.2±0.07	8.60±0.09	29.4±0.06	21.1±0.05
20	10.72±0.08	25.18±0.09	15.3±0.06	53.3±0.07	13.5±0.08	24.4±0.02	22.1±0.07
25	16.2±0.05	25.98±0.07	17.5±0.09	54.9±0.05	17.1±0.09	47.0±0.04	22.6±0.06
30	16.46±0.03	37.22±0.06	24.8±0.08	55.8±0.08	25.3±0.04	50.8±0.05	23.5±0.07
35	23.16±0.09	40.64±0.04	25.8±0.03	57.6±0.07	35.8±0.05	51.8±0.0	24.5±0.08
40	26.64±0.06	45.24±0.05	32.4±0.05	58.7±0.08	36.9±0.09	54.4±0.07	31.1±0.05
45	30.68±0.08	59.48±0.06	33.1±0.03	60.4±0.05	44.3±0.04	57.7±0.08	34.5±0.06
50	32.6±0.09	66.52±0.05	35.1±0.07	61.8±0.02	45.1±0.04	62.5±0.06	36.0±0.03
55	32.82±0.06	79.58±0.02	36.6±0.06	67.1±0.07	55.1±0.04	63.3±0.08	44.8±0.04
60	33.44±0.08	86.26±0.02	42.7±0.05	67.8±0.04	60.2±0.02	65.3±0.04	53.8±0.03
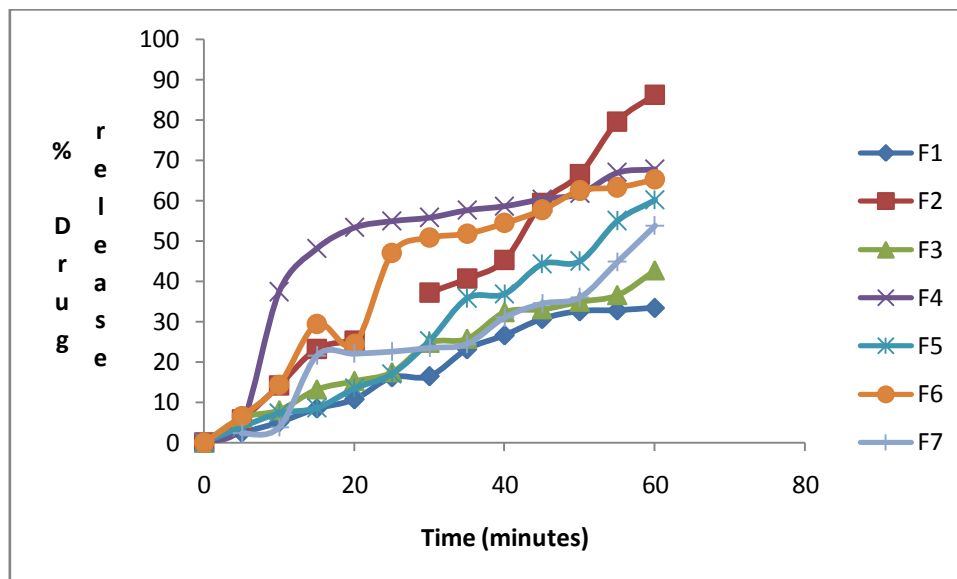
Figure:7 -Comparison of dissolution profiles of various formulations

CONCLUSION

The major problem of aceclofenac is its very poor solubility in biological fluids. From the present study it can be easily demonstrated that PVP k30 has immense potential to improve dissolution characters of any less soluble or poorly water-soluble drug. The results revealed that it is possible to enhance the dissolution rate of aceclofenac by increasing the surface area of the drug by solid dispersion method. This work also illustrates the fact that PVP k30 has more characteristic to form solid dispersions with the drug molecules, thereby increasing the dissolution rate of drug and decreasing the time of release of drug from the formulated mixture.

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