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FORMULATION AND EVALUATION OF ACECLOFENAC SOLID DISPERSION WITH SUITABLE CARRIERS

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ABSTRACT

Aceclofenac is a long acting potent NSAID with inflammatory potency and good analgesic-antipyretic action. Thus it can inhibit inflammation in diverse ways. Solid dispersion were by preliminary solubility analysis was carried out for the selection of carriers and solid dispersion was prepared with PEG 4000, PEG 6000 and mannitol. To increase the solubility of drug solid dispersion was prepared. These solid dispersions were analysed for the solubility and *In vitro* dissolution profile, solid dispersion of drug with PEG 6000 had shown enhanced solubility with improved dissolution rate. The FTIR and DSC studies revealed that there is no interaction between drug and carriers. Solid dispersion prepared with PEG 4000 shows the presence of amorphous form confirmed by the characterization study like SEM studies. The study also shows that dissolution rate of Aceclofenac can be enhanced to considerable extent by solid dispersion technique with PEG.

INTRODUCTION

Chiou and Riegelman 1971 defined the term solid dispersion as "A dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by the melting (fusion), solvent or melting-solvent method." Dispersions obtained through the fusion process are often called melts, and those obtained by the solvent method are frequently referred to as co-precipitates or co-evaporates[1].

The different ways of increasing the rate of absorption or total bioavailability of drugs are: -

1 Micronization
2 Use of soluble salt
3 Use of minuscular form of drug adsorbed on insoluble adsorbents
4 Use of surfactants
5 Use of polymorphs

By micronization, reduction in the therapeutic dose of griseofulvin to the extent of 50% and it also produced a constant blood-level.

OBJECTIVE

The basic aim of the present investigation is to *Formulation and Evaluation of Aceclofenac Solid dispersion with various carriers*[4]. The objectives of the research work under taken in detail are as follows: To prepare using different polymers like PEG 6000, PEG 4000, Mannitol & drug is Aceclofenac, To characterize the formulation with respect to drug – excipients interaction (using FTIR and DSC), To evaluate the formulation with respect to various physical parameters like Priliminary Solubility, To study *invitro* dissolution studies of Acelcofenac Solid dispersion was obtained was fitted, The complicating the delivery of these new drugs also affect the delivery of many existing drugs. The extended duration of time hence not only reduces the systemic side effects but also improve the therapeutic efficacy patient compliance.

METHODOLOGY

Preparation of Solid dispersion:

The preparation of Aceclofenac solid dispersions using different concentration of PEG 6000, PEG 4000 & Mannitol by using the Physical Mixture & Fusion methods.

Preparation by physical mixture method

The ratio of drug: mixed excipient system was kept constant (1:1 w/w) in all formulations. Physical mixtures of aceclofenac with mixed excipient system including PEG 6000, PEG 4000

& Mannitol were prepared by mixing accurately the weighed amount of drug and carrier with the help of a spatula in a glass mortar[5].

Fusion method:

The melting or fusion method involves the preparation of physical mixture of a drug and a water-soluble carrier and heating it directly until it method mixture is then solidified rapidly in an ice – bath under vigorous stirring[6]. The final solid mass is crushed, pulverized and sieved. appropriately this has undergone many modifications in pouring the homogenous melt in the form of a thin layer onto a ferrite plate or a stainless steel plate and cooled by flowing air or water on the opposite side of the plate in addition, a super-saturation of a solute or drug in a system can often be obtained by quenching the melt rapidly from a high temperature. Under conditions, the solute molecule is arrested in the solvent mixture by the instantaneous solidification process. The quenching technique gives a much final dispersion of crystals when used for simple eutetic mixtures.

Table:1 Formulation of Aceclofenac Solid dispersion

SI.No	Formulation Codes	Carrier	Drug: Carrier	Method
1.	SDA 1	PEG 4000	1:1	Physical Method
			1:2	Fusion method
2.	SDA 2	PEG 6000	1:1	Physical Method
			1:2	Fusion method
3	SDA 3	Manniitol	1:1	Physical Method
			1:2	Fusion method

Preliminary solubility studies of Aceclofenac

Solubility measurements of Atorvastatin were performed according to a published method (Higuchi and Connors, 1965). An excess amount of Aceclofenac was added to 25ml of aqueous solution of water soluble carriers like PEG 4000, PEG 6000 & Mannitol in the various ratios such as 1:1, 1:2 (Physical & Fusion method) in screw capped bottles. Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no 1. Filtered solution diluted properly with methanol. The diluted solution analyzed for the Atorvastatin in UV 275nm.

Evaluation of solid dispersion

Solid dispersions obtained in above methods were screened for their solubility. Solid dispersion showing good solubility further studied for drug content,*in vitro* release studies,FTIR,DSC study.

Drug content

The amount of drug present in a 10 mg equivalent amount of solid dispersion was determined by, dissolving the powder mixture in 10 ml of methanol and suitably diluted with methanol and UV absorbance was measured at 275 nm. Drug concentration was determined from standard graph.

Characterization of solid dispersions of Aceclofenac:

Differential Scanning Calorimetry (DSC) Analysis

DSC scans of the powdered samples Aceclofenac, PEG 6000, PEG 4000 & Mannitol were recorded using DSC- Shimadzu 60 with TDA trend line software. All samples were weighed (8-10 mg) and heated at a scanning rate of 20°C/min under dry air flow (100 ml/min) between 50 and 300°C. Aluminum pans and lids were used for all samples[7].

Infrared (IR) Spectroscopic Analysis

Fourier–transform infrared (FTIR) spectra of moisture free powdered samples were obtained using a spectrophotometer (FTIR-8300, Shimadzu Co., Kyoto, Japan) by potassium bromide (KBr) pellet method (2 mg sample in 200 mg KBr). The scanning range was 750–4000 cm^{-1} and the resolution was 1 cm^{-1}

RESULTS AND DISCUSSION

Preparation of Solid dispersion:

The preparation of Aceclofenac solid dispersions using different concentration of PEG 6000, PEG 4000 & Mannitol by using the Physical Mixture & Fusion methods. Batches of solid dispersions of aceclofenac were prepared using factorial design as described in methodology

- Preparation by physical mixture method & Fusion method:

Table: 2 Physical Appearance of Aceclofenac Solid Dispersions

Method	Physical properties of solid dispersions	
	Colour	Appearance
Physical mixture	White	Fine powder
Fusion method	White	Fine powder

Preliminary solubility studies of Aceclofenac

The preliminary solubility of Aceclofenac From this physical mixtures & Fusion method of PEG 4000, PEG 6000 & Mannitol, containg different ratio of 1:1, 1:2 for the preparation of the solid dispersion. After preparation of solid dispersion solubility analysis were carried out this is compared with physical mixtures & Fusion method. Drug content of the formulation found to be are in case of PEG 4000 (1:1) carries 0.21mg/ml, (1:2) 0.24 mg/ml, PEG 6000 (1:1) 0.23 mg/ml (1:2) 0.26, Mannitol (1:1) 0.25 mg/ml (1:2) 0.27 mg/ml.

Table: 3 Preliminary Solubility (µg/ml) of Aceclofenac

SI.No.	Carrier (Drug: Carrier)	Solubility mg/ml
1	Aceclofenac + PEG 4000 (1:1)	0.21
	Aceclofenac + PEG 4000 (1:2)	0.24
2	**Aceclofenac + PEG 6000 (1:1)**	**0.23**
	Aceclofenac + PEG 6000 (1:2)	**0.26**
3	Aceclofenac + Mannitol (1:1)	0.25
	Aceclofenac + Mannitol (1:2)	0.27

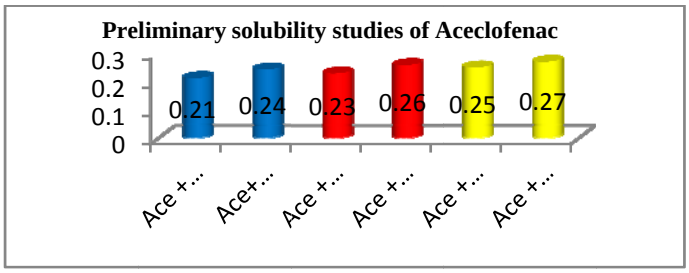

Figure 4. Preliminary solubility studies of Aceclofenac

***In vitro* drug dissolution studies**

For understanding the mechanism of drug release rate kinetics of the drug from dosage forms, the *in vitro* drug dissolution data.

Fourier transforms Infrared (FTIR) Spectroscopic Analysis

The IR spectrum of the pure Aceclofenac sample recorded by FTIR spectrometer is shown in Figure 6. This was compared with standard functional group frequencies of Aceclofenac as shown in Table 4. From FTIR study, the characteristic peaks of drug such as of Dichloro phenyl stretch Aceclofenac (3340cm^{-1}), PEG 6000(3000cm^{-1}),PEG 4000(3180CM^{-1}),Mannitol (3000cm^{-1}). N-H Stretch for the pure drug Aceclofenac(3260 cm^{-1}), PEG 6000(1860cm^{-1}),PEG 4000(2600cm^{-1}),Mannitol(2000cm^{-1}). Oxa acetic acid Stretch the pure drug Aceclofenac (1665 cm^{-1}),PEG 6000 (1250 cm^{-1}), PEG 4000(1760cm^{-}1),Mannitol(1760cm^{-1}). Acetyl group the pure drug aceclofenac (1318cm^{-1}),PEG 6000(1000 cm^{-1}),PEG 4000 (1250 cm^{-1}),Mannitol(1760 cm^{-1}). For Solid dispersion all peaks which have been obtained for the pure drug were available at same wave length for Remaining peaks also either shifted or replaced in the IR spectrum of formulation.

Table. 4 IR Interpretations for Pure drug Aceclofenac, PEG 6000, PEG 4000 and Mannitol

Functional groups	Pure drug Aceclofenac	PEG 6000	PEG 4000	Mannitol
Dichloro phenyl stretch	3340cm^{-1}	3000 cm^{-1}	3180cm^{-1}	3000 cm^{-1}
N-H Stretch	3260 cm^{-1}	1860 cm^{-1}	2600 cm^{-1}	2000 cm^{-1}
Oxa acetic acid Stretch	1665 cm^{-1}	1250 cm^{-1}	1760 cm^{-1}	1760 cm^{-1}
Acetyl group	1318 cm^{-1}	1000 cm^{-1}	1250 cm^{-1}	1270 cm^{-1}

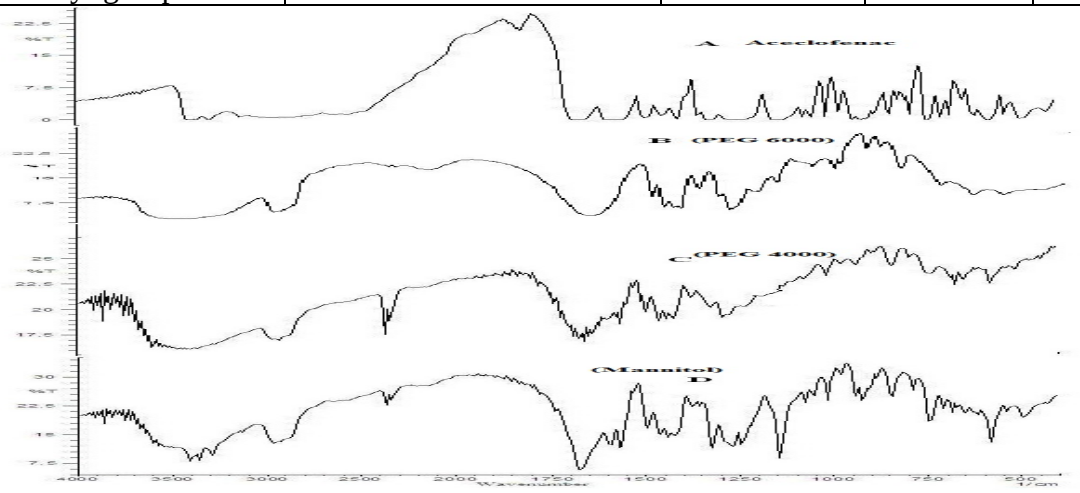

Figure: 6 FTIR Spectra of a) Aceclofenac b) PEG 4000 c) PEG 6000 d) Mannitol

Differential Scanning Calorimetry (DSC) Analysis

The pure drug Gatifloxacin shown as an endothermic peak at 240 ^{o}C. The peak neither is nor shifted in the case of DSC of the Solid disersion formulation containing PEG 6000, PEG 4000 & Mannitol. The DSC of physical mixture of the PEG 6000 as showed an endothermic peak at 110 ^{o}C & Exothermic peak it shows linear position. The DSC of PEG 4000 showed an endothermic peak 110^{o}C. The DSC of Mannitol shows 100^{o}C which shown endothermic there is no incompatibility exist in the formulation. The IR spectra as shown in Figure 7.

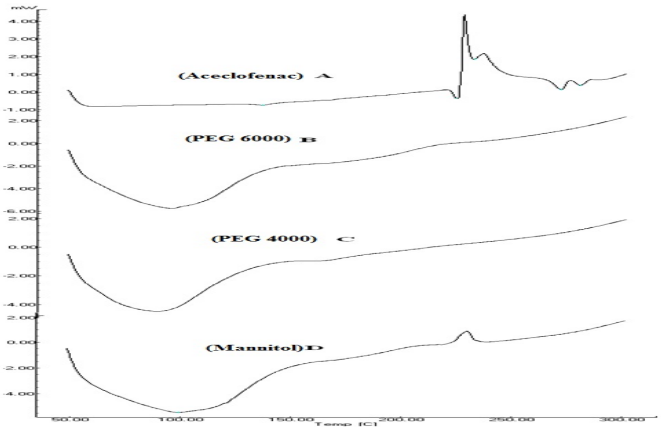

Figure: 7 DSC Spectra of a) Aceclofenac b) PEG 4000 c) PEG 6000 d) Mannitol

CONCLUSION

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. In present study solid dispersion prepared with PEG 6000 shows the presence of amorphous form confirmed by the characterization study. Solid dispersion preliminary solubility analysis was carried out for the selection of carriers and solid dispersion was prepared with PEG-6000, PEG 4000 and Mannitol, The best formulation for is PEG 6000 1:1, 1:2 (Physical & Fusion method). These solid dispersions were analysed for the solubility and Invitro dissolution profile, solid dispersion of drug with PEG 6000 had shown enhanced solubility with improved dissolution rate. From IR & DSC spectroscopy concluded that the there is no compatability studies interaction between aceclofenac and carriers.

REFERENCES

1. Beten, D.B. Amighi, K. Moes, A.J. Preparation of controlled-release co evaporates of dipyridamole by loading neutral pellets in a fluidized-bed coating system. Pharmaceutical Research. 1995, 12, 1269-1272.
2. Chiou, W. Riegelman, S. Increased dissolution rates of water-insoluble cardiac glycosides and steroids via solid dispersions in polyethylene glycol 6000. Journal of Pharmaceutical science. 2006, 60, 10, 1569 – 1571.
3. Chiou, W.L. Riegalman, S. Pharmaceutical applications of solid dispersion systems. Journal of Pharmaceutical Science. 1971, 60, 1281–1302.
4. Christian, L. Jennifer, D. Improving drug solubility for oral delivery using solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2000, 50, 47-60.
5. Craig, D.Q.M. The mechanism of drug release from solid dispersion in water-soluble polymers. International Journal of Pharmaceutics. 2002, 231, 131-144.
6. Goldberg, A.H. Gibaldi, M. Kanig, J.L. Increasing dissolution rates and gastrointestinal absorption of drugs via solid solutions and eutectic mixtures. III. Experimental evaluation of griseofulvin-succinic acid solution. Journal of Pharmaceutical science. 1966, 55, 487-492.
7. Goldberg, A.H. Gibaldi, M.; Kanig, J.L. Increasing dissolution rates and gastrointestinal absorption of drugs via solid solutions and eutectic mixtures. II. Experimental evaluation of eutectic mixture: urea-acetaminophen system. Journal of Pharmaceutical science. 1966, 55, 482-487.