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ENHANCEMENT OF DISSOLUTION RATE OF ACECLOFENAC BY SOLID DISPERSION TECHNIQUE

T. V. RAO* and S. VIDHYADHARA[a]

Bapatla College of Pharmacy, BAPATLA (A. P.) INDIA
[a]Chebrolu Hanumaiah College of Pharmaceutical Sciences, GUNTUR (A. P.) INDIA

ABSTRACT

Aceclofenac, a selective cyclooxygenage inhibitor is used in the treatment of rheumatoid arthritis and ankylosing spondylitis. One of the major problems with the drug is that, it is practically insoluble in water, which results in poor bioavailability after oral administration. In the present study, solid dispersions of aceclofenac were prepared by solvent evaporation method with two hydrophilic carriers such as poly vinyl pyrrolidine (PVPk-30), and PEG-6000 were used in the ratio of (drug : carrier) 1 : 1, 2 : 1, and 3 : 1, respectively. Prepared solid dispersions were subjected to IR study for determining any interaction between drug and carriers. Study showed no interaction between drug and carriers. Solid dispersions were subjected for determination of percentage drug content, particle size analysis and in vitro dissolution study. The dissolution rate studies were performed in phosphate buffer pH 6.8 using USP XXII type-2 apparatus. Solid dispersion in the ratio of 2 : 1 (Drug : PVPk-30) gave faster dissolution rate than other SDs, corresponding physical mixtures and pure drug.

Key words: Solid dispersions, PVP k-30, PEG 6000, Dissolution rate, Aceclofenac.

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are considered to be the first-line drugs in the symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Aceclofenac[1] is one of the emerging NSAID molecules for arthritis treatment. It is practically insoluble in water[2]. It shows erratic dissolution profile in gastric and intestinal fluid due to its poor water solubility, rate of absorption and extent of bioavailability for such insoluble hydrophobic drug is controlled by rate of dissolution in gastric-intestinal fluids. The peak-plasma concentration and the time taken to reach Cmax depend upon extent and rate of dissolution of drug, respectively. Hence, the present work was aimed to increase rate of dissolution of aceclofenac and to minimize the enteric dissolution profile of drug. Dissolution of drug can be increased by variety of

* Author for correspondence

contemporary approaches like solid dispersions[3], complexation etc. The present investigation was carried out with a view to evaluate the feasibility of using PVPK-30 and PEG 6000 as hydrophilic carriers. Solid dispersions of aceclofenac were prepared by solvent evaporation technique. The prepared SDs with carriers were subjected to drug carrier interaction study by IR spectrometry. *in vitro* studies were carried out and the results were reported.

EXPERIMENTAL

Materials

Aceclofenac, PEG-6000 and PVPk-30 was procured from M/S Seeko Biotech, Vijayawada. Ethanol and all other materials used were of IP grades.

Methods

Preparation of solid dispersions (SDs) by solvent evaporation

Solid dispersions of aceclofenac with PVPk-30 and PEG 6000 were prepared by dissolving the drug and carriers in the ratios of 1 : 1, 2 : 1 and 3 : 1 in a solvent like ethanol to get a clear solution. The solvent was then evaporated at 40 to 45^{O}C with continued mixing to get dry mass. The obtained dry masses were kept in a desiccator until solid dispersions attains constant weight. The solidified masses were passed through sieve No. 80.

The physical mixtures were prepared by manually mixing pre-weighed amounts of sieve No 80 sieve fractions of aceclofenac and carriers (PVP K-30 and PEG-6000) in the ratios of 1 : 1, 2 : 1and 3 : 1. Two batches of Aceclofenac : carriers in different ratios as stated above were prepared under similar set of conditions.

Characterization

Drug content

SDs equivalent to 100 mg of aceclofenac was accurately weighed and dissolved in 100 mL of phosphate buffer pH 6.8. From that, 1 mL of solutions were made and assayed for drug content using UV- Visible spectrophotometer at 275 nm.

Particle size analysis[4]

The prepared SDs were evaluated for its particle size distribution and average particle diameter was determined by microscopic method.

Compatibility study

Compatibility of the drug and carriers were confirmed by comparing the IR spectra.

Dissolution study

In vitro dissolution studies[5] were performed by using USP XXII paddle type dissolution test apparatus in 900 mL of pH 6.8 buffer solution as dissolution medium for 30 min at 75 rpm. Aceclofenac (pure drug), solid dispersions equivalent to 200 mg of Aceclofenac and its physical mixtures were transferred into a dissolution test apparatus, maintained at a temperature of 37 ± 0.5ºC were used in each test. Samples of dissolution medium (5 mL) were withdrawn at fixed time intervals. The samples were sufficiently diluted and the released drug was analyzed by UV spectrophotometrically at 275 nm.

RESULTS AND DISCUSSION

All the SDs were found to be free flowing under dry conditions. Percentage drug contents in different batches of SDs were found to be in confirmation with the theoretically calculated values, which indicated the reliability of the analytical method used.

Particle size of the SDs with PVPk-30 and PEG 6000 ranged from 5-150 µm and the average diameter was found to be in the range of 50-70 µm The spectra showed the characteristic peaks for aceclofenac, C-Cl group (1094.4 cm^{-1}), N-H group (3315.03 cm^{-1}), C-N group (1344.14 cm^{-1}) and C=O group (1711.51 cm^{-1}), respectively. For physical mixture, peaks appeared at the same region. Stabilities of SDs and absence of interaction between the drug and carrier was confirmed from IR study (Fig. 2).

Comparison of results obtained from dissolution studies for aceclofenac, physical mixtures of aceclofenac with carriers and SDs of aceclofenac with same carriers were shown in Table 1 (Fig 1). The dissolution rates were found in the following order : SDs > physical mixtures > Pure drug. The increased solubility of SDs was due to the reduction in particle size or the presence of drug in the form of solid solution in a water soluble carrier in molecular form. Greater solubility of physical mixture than the pure drug could be attributed to the wetting of hydrophobic surface of aceclofenac due to solublization of hydrophilic carriers. In the above studies, SDs with 2 : 1 Aceclofenac : PVPk-30 was found to gave higher dissolution rate than the other prepared SDs and physical mixtures. The enhancement of the dissolution rate may be due to increase in the effective surface area made available to the dissolution media. Further, it may be attributed that the use of

hydrophilic carriers improves the wettability of the drug particles and enhance the dissolution rate.

Table 1. Results of dissolution studies of SDs in phosphate buffer, pH 6.8

Sample	Drug : Carrier	% Drug release at 30 min	
Pure drug	1 : 0	79.94	
		Physical mixture	Solid dispersion
SDs with PVPk30	1 : 1	70.55	93.85
	2 : 1	72.32	94.36
	3 : 1	84.38	90.72
SDs with PEG 6000	1 : 1	75.42	84.24
	2 : 1	78.05	85.95
	3 : 1	80.74	82.90

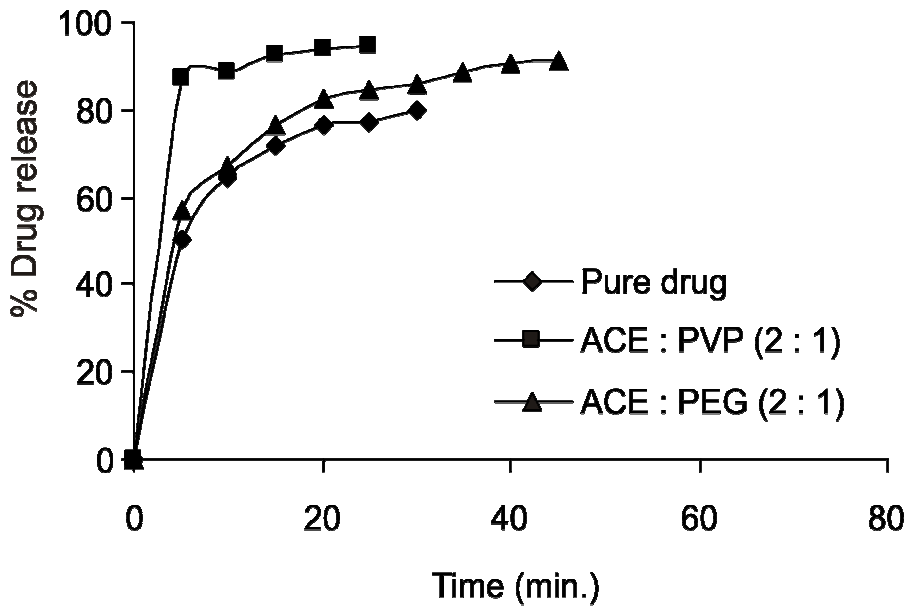

Fig 1: Comparison of release profile between polymers vs pure drug

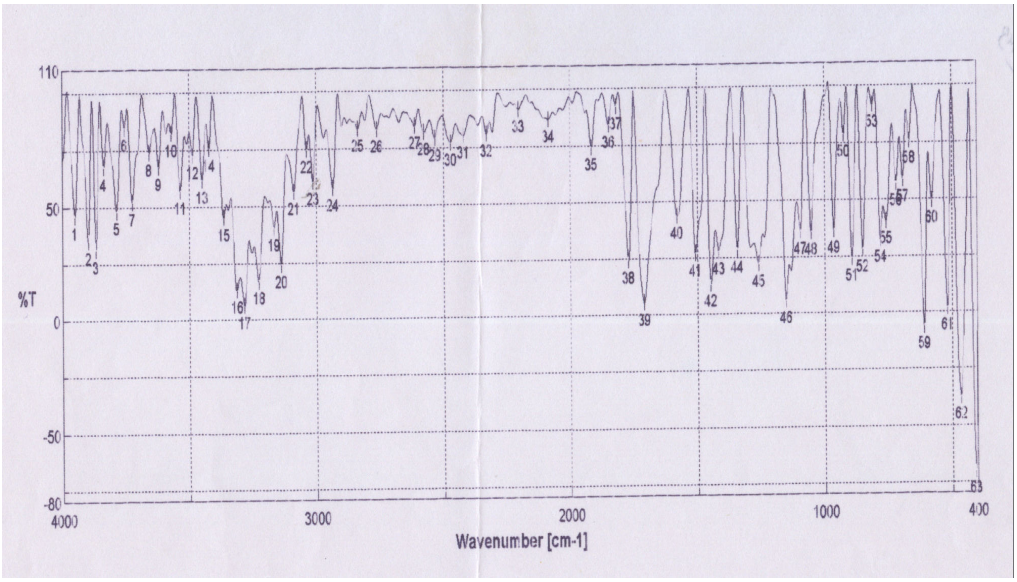

Fig. 2(a): IR Spectra of aceclofenac

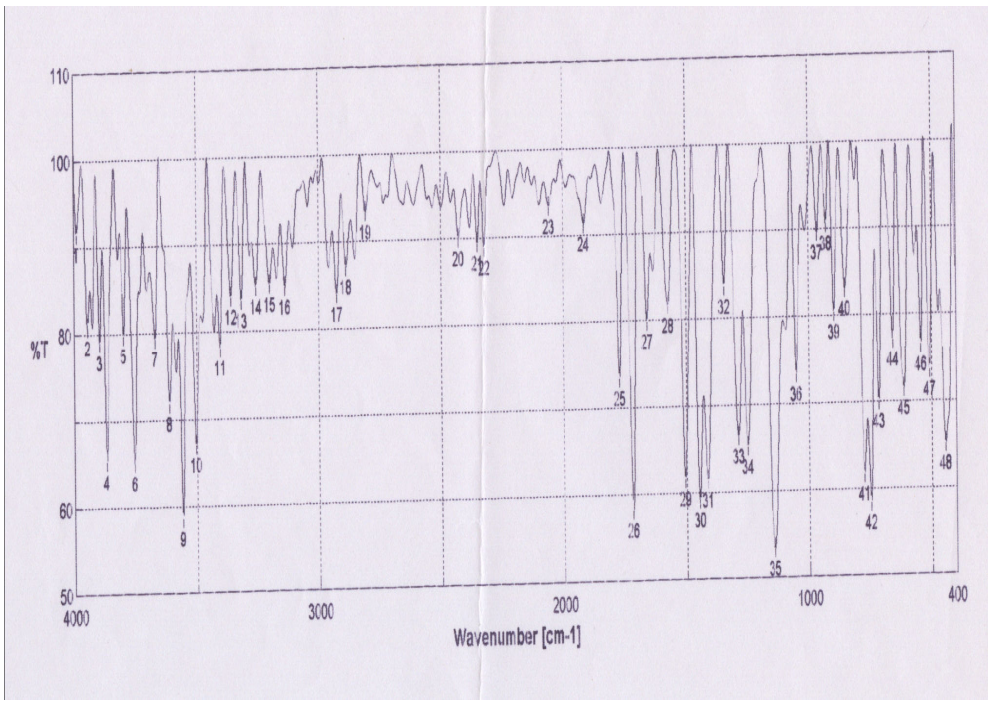

Fig. 2(b): IR Spectra of physical mixture of aceclofenac with PVP

CONCLUSION

SDs of aceclofenac with two hydrophilic carriers PVPk-30 and PEG 6000 showed high dissolution rate than pure drug and its corresponding physical mixture. This may due to the solubilizing effect of carriers and reduction in the particle size or retarding the crystallization of the drug, entrapping the drug in the molecular state by the carrier.

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