

# Preparation and Comparison of Dissolution Profiles of Aceclofenac by Solid Dispersion Approach

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**Abstract**— Approximately 40% of new chemical entities suffer from poor aqueous solubility results into poor bioavailability lead to the major challenge to modern drug delivery system. Among various approaches used to enhance aqueous solubility of BCS Class-II drugs, one of these approaches is solid dispersion which is usually used to improve the bioavailability of most hydrophobic drugs. Aceclofenac is used as an analgesic and anti-inflammatory drug in the treatment of osteo arthritis, rheumatoid arthritis and spondylitis. Three different compositions of Aceclofenac solid dispersions were prepared by solvent evaporation method using Urea as a carrier in order to enhance the solubility of BCS Class-II drugs. Based on the in-vitro drug release pattern of Aceclofenac: Urea with the ratio of 1:3 was considered as an ideal dispersion for the improvement of solubility, dissolution rate and bioavailability of poorly water soluble drug via solid dispersion.

**Key words:** Aceclofenac, Bioavailability, Carriers, Dissolution rate, Solid dispersion, Solubility

## I. INTRODUCTION

Poorly water-soluble drugs of BCS Class-II have increasingly the challenge for Pharmaceutical industries in terms of increasing solubility within the gastrointestinal tract required for good bioavailability. The challenge for existing and new drugs is not only that they should be active pharmacologically but also should have enough solubility and dissolution rate at the site of administration i.e., gastrointestinal tract [1].

Solubilization is a process by which the apparent solubility of poorly water soluble drugs is increased. Solubilization techniques include addition of a cosolvent, salt formation, complexation, particle size reduction, solid dispersion and the use of surface active agents (Micellization) [2].

Use of solvates and hydrates [3], polymorphs [4], hydrotrophy [5], use of absorbents [6], pH adjustment, solubilizing vehicles, use of conformers etc. are also the physico-chemical approaches to enhance absorption of BCS Class-II drugs given by oral route.

Solid dispersion technology is the science of dispersing one or more active ingredient/s in an inert matrix which is always in solid state in order to achieve increased dissolution rate, sustained action, prolonged action, altered solid state properties or enhanced release of drugs from ointment and suppository bases, and hence improved aqueous solubility and stability [7].

Solid dispersions are prepared by different methods like Fusion method, Solvent evaporation method, Physical mixture, Fusion Solvent process and Supercritical fluid process [8]. Thermo analytical methods like Thermal Analysis [9], DSC [10], X-ray Diffraction Methods [11], Spectroscopic Methods and Microscopic Methods [12] can

be used to provide information regarding the physical nature of the prepared solid dispersion.

Aceclofenac is aceclofenacum (O- (2, 6-dichloroaniline) phenyl] acetate glycolic acid ester, 2-(2, 6-dichloroaniline) phenyl acetoxyacetic acid. Aceclofenac is a Non-Steroidal Anti-inflammatory Drug. It is used in the management of osteoarthritis, rheumatoid arthritis and spondylitis. Aceclofenac when taken orally it causes gastrointestinal disturbances such as GI discomfort, nausea, peptic ulceration and diarrhoea. Solid dispersion technology can be used to improve the in vitro and in vivo dissolution properties of poorly water soluble drugs. PEG-4000, PEG-6000, PVP-K13 [13], Urea and surfactant like SLS [14] have been reported to be used for increasing the solubility of BCS Class-II drugs. The usual oral dose of aceclofenac is 100 mg twice daily. The initial dose should be reduced to 100 mg daily in patients with hepatic impairment. Because of its low water solubility makes it can be formulated in solid dispersion systems.

Aceclofenac is practically insoluble in water while freely soluble in organic solvents like Acetone and Alcohol. As it is a BCS Class-II drug, the aqueous solubility can be enhanced by way of solid dispersion technique in which hydrophilic polymers or carriers are used.

The mechanism behind the release of Aceclofenac drug, polymer or solubilizer used undergo physical interaction such as hydrogen bonding and there is no chemical change, thus the carrier like PVP, PEG 4000, or Urea are suitable for solid dispersion of Aceclofenac.

Dissolution rate of Aceclofenac can be increased by solid dispersion technique which may be due to increased hydrophilic nature of the carrier and also possibly due to reduction in drug crystallinity.

## II. MATERIALS AND METHODOLOGY

### A. Materials

Aceclofenac was gifted by Mepro Pharmaceuticals Pvt. Ltd., Surendranagar, Gujarat, India. Polyvinyl pyrrolidone K30 (PVP K30), Polyethylene Glycol 4000 and Urea were purchased from Sisco Research Lab., Mumbai, India. All other solvents and chemicals used were of analytical grade.

### B. Methodology

#### 1) Scan and Standard plot of Aceclofenac

Find out the absorption maxima  $\lambda_{max}$  of Aceclofenac solution by scanning in UV spectrophotometer.

Dissolve 50 mg Aceclofenac in 50 ml of Phosphate buffer 6.8 pH. Pipette out 2 ml from this solution and dilute it upto 100 ml with Phosphate buffer 6.8 pH. Pipette out the solution in such a way that 8 to 10 different concentrated solutions in  $\mu\text{g/ml}$  are obtained which shows the absorbance in between 0.2 to 0.8 in UV spectrophotometer.

Note down the Absorbance with respective concentrated solutions and plot the Standard Curve i.e., Absorbance  $\rightarrow$  Concentration ( $\mu\text{g/ml}$ )

2) Preparation of Aceclofenac Solid Dispersion System by Solvent Evaporation Method

The calculated quantity of aceclofenac and the carrier viz. 1:1, 1:2 and 1:3 (drug:urea) were dissolved in sufficient volume of methanol with continuous stirring. The solvent was then completely evaporated at 45°C with continuous stirring to obtain a dry mass. The dried mass was pulverized, passed through 44 mesh sieve and stored in dessicator until used for further studies.

C. Characterization of Aceclofenac Solid Dispersion System

1) Physical Appearance

Different ratios of Aceclofenac solid dispersions were evaluated for color and appearance.

2) Determination of Aceclofenac Content

An accurately weighed amount of each preparation containing 50 mg equivalent dose of Aceclofenac was dissolved in small volume of methanol and further diluted with Phosphate buffer 6.8 pH. The content of aceclofenac was determined spectrophotometrically at 273.5 nm using Shimadzu UV-visible spectrophotometer.

3) In Vitro Dissolution

The dissolution study was carried out using USP XXIII apparatus type-II (Electrolab TDT-OCT). The dissolution medium was 900 ml, 6.8 pH phosphate buffer kept at 37±1°C. The drug or physical mixture or solid dispersions (equivalent weight containing 50 mg Aceclofenac) was taken in a muslin cloth/filter paper in the basket of dissolution apparatus, the basket was rotated at 50 rpm. Samples of 5 ml were withdrawn at specified time intervals and analyzed spectrophotometrically at 273.5 nm [15] using Shimadzu 1800 UV- visible spectrophotometer; the samples withdrawn were replaced by fresh buffer solutions.

D. Results and discussion

The in vitro dissolution behaviour of the prepared solid dispersion by different methods was compared with those of pure drug.

1) Physical Appearance

The aceclofenac solid dispersion was prepared by Solvent evaporation method. Solid dispersion was prepared by using different concentration of Urea as a carrier and Solid dispersions obtained were white fine powders.

2) Standard plot of Aceclofenac drug

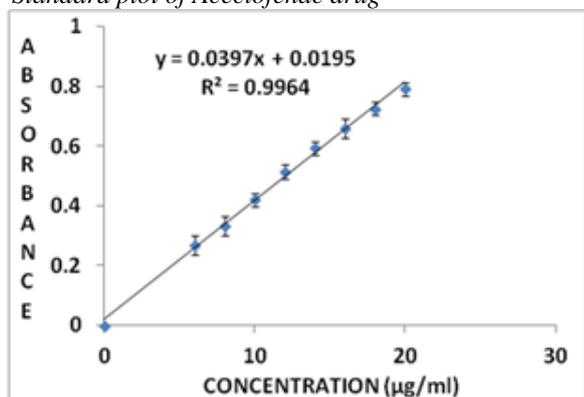


Fig. 1: Standard plot of Aceclofenac drug in Phosphate buffer pH 6.8 at  $\lambda_{max} = 273.5nm$ .

3) Drug Content Estimation

The drug content estimation of formulations prepared by --- Solvent evaporation method using Aceclofenac and Urea

with the ratio of 1:1, 1:2 and 1:3 was found to be 5.84 %, 4.81 % and 3.27% respectively.

4) In vitro drug release studies

Dissolution profile of in vitro release of aceclofenac formulations as above is ---

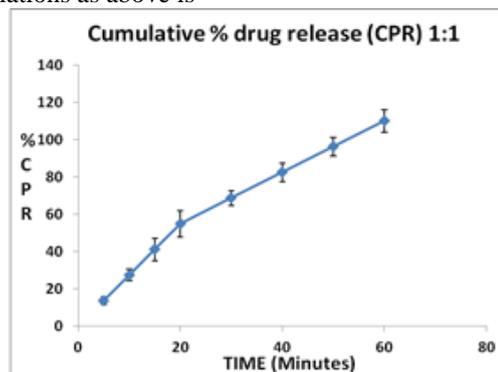


Fig. 2: Solvent evaporation method containing Aceclofenac: Urea with ratio of 1:1

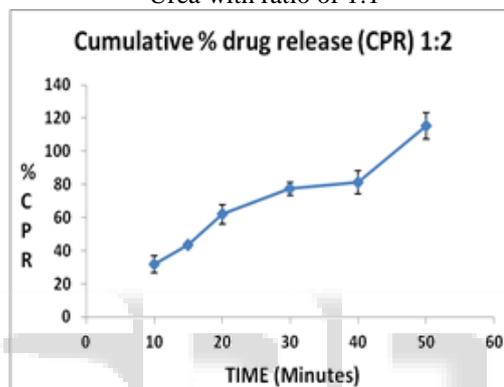


Fig. 3: Solvent evaporation method containing Aceclofenac: Urea with ratio of 1:2

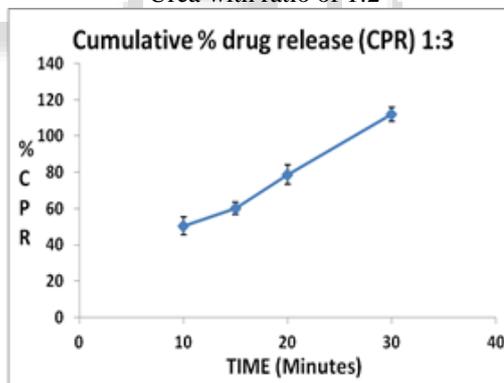


Fig. 4: Solvent evaporation method containing Aceclofenac: Urea with ratio of 1:3

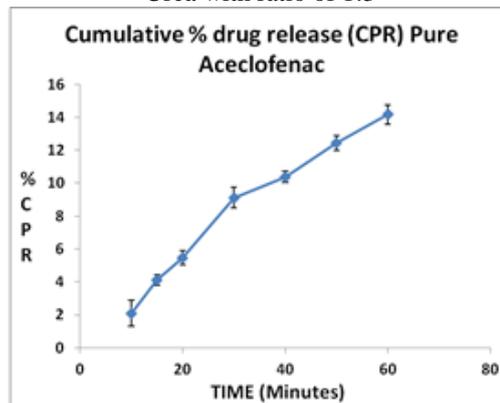


Fig. 5: Pure Aceclofenac drug

Comparison of Pure Aceclofenac drug with the different ratios of drug: carrier shown that the solubility of poorly soluble drug is enhanced by solid dispersion technique because of the formation of an effective hydrophilic matrices of carrier surrounding the hydrophobic drug which produced uniform dispersion to enhance the solubility and dissolution rate of BCS Class-II drug.

#### E. Conclusion

Solid dispersion prepared by using hydrophilic polymers by solvent evaporation method were effective in improving the solubility and dissolution rate of BCS Class-II drug. The dispersion containing Urea as a carrier shown acceptable dissolution compared to the pure drug. The study revealed that optimum levels of hydrophilic carriers and hydrophilic porous adsorbents ensure a prompt and complete dissolution of aceclofenac from solid dispersions that are used in oral route.

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