

ORIGINAL RESEARCH PAPER

Preparation and Evaluation of Solid Dispersions of Aceclofenac for the Improvement of Dissolution Rate

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Abstract

Aceclofenac is an anti-inflammatory drug and is helpful in the treatment of inflammation. Low dissolution rate of this drug is one of the major problems with this drug, which results into low bioavailability on oral administration. The present work aims to prepare the solid dispersions of aceclofenac by solvent wetting method by using potato starch as carrier in the ratios of 1:1 and 1:2. Formulated solid dispersions were characterized for % practical yield, Carr's Index, angle of repose, Hausner's ratio, drug content and in vitro drug dissolution. The solvent wetting method was found to be efficient method to produce solid dispersions with good flow properties and to get good yield. The drug content was found in the ranges of 98.02 to 99.10 %. In vitro release study has shown that there is an enhancement in the release rate of aceclofenac from all prepared batches in comparison to pure aceclofenac. Experimental results showed that formulation F2 (1:2 ratio of drug: potato starch, prepared by solvent wetting method) showed more release in comparison to other batches.

INTRODUCTION

Oral bioavailability of drugs depends on its dissolution rate. Thus, for poorly water soluble compounds the major problem is with their poor water solubility. This results in poor oral bioavailability. There are numerous techniques (such as formation of salt, size reduction, use of co-solvents or surfactants, solid dispersions, lipid based formulations, etc) to enhance dissolution rate of poorly water soluble drugs.¹⁻⁴ But the most simple technique for this is the solid dispersions.^{5,6} Many water soluble carriers such as citric acid, mannitol, β -cyclodextrin, lactose, di-calcium phosphate, lactose, corn starch, polyvinyl pyrrolidone, polyethylene glycols, etc has been used as carriers in solid dispersions for the improvement of the dissolution rate of drug.⁷⁻¹⁰ Aceclofenac is an anti-inflammatory agent that decreases inflammation and pain.¹¹ It inhibits cyclooxygenase and the synthesis of prostaglandins.⁵ Poor aqueous solubility and low dissolution rate of aceclofenac prompted us to investigate the possibility of improving the dissolution rate of drug by preparing solid dispersion. The method used was solvent wetting method and potato starch as carrier.

MATERIALS AND METHODS

Materials

Aceclofenac was obtained as gift sample from Cipla Ltd., Mumbai, India. Potato starch of CDH Laboratories, New Delhi was purchased. All chemicals and solvents were of analytical grade and there was no need of further purification.

Preparation of Solid Dispersion by Solvent Wetting Method

Solid dispersions were prepared using aceclofenac as drug and potato starch as carrier in the ratios of 1:1 and 1:2 (F1 and F2). Weighed quantity of drug was taken in a mortar and dissolved completely in required volume of isopropyl alcohol. Accurately weighed quantity of carrier (potato starch) was then added to drug solution. The solvent was removed by evaporation at room temperature. The dried solid mass was then passed through sieve number 40 and stored in a desiccator for further use.⁶

Preparation of Physical Mixture

Physical mixtures were prepared in drug: potato starch ratios of 1:1 and 1:2 (F3 and F4). The physical mixtures were prepared by mixing weighed quantity of drug and carrier simply in polythene bag. The physical mixtures were passed through sieve number 40 and stored in desiccators.

Characterization of Solid Dispersions

Percentage Yield

The % yield was helpful to observe the efficiency of preparation method and it was evaluated by weighing the obtained solid dispersion formulation divided by total weight of drug and carrier incorporated in solid dispersion multiplied by 100.

Flow Properties

Solid dispersions were evaluated for bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio. Fixed funnel method was used to evaluate the angle of repose. Bulk density was calculated by dividing the mass of solid dispersion with the bulk volume. Tapped density was estimated by employing Tap Density Tester (Electro lab Ltd- 1020) by giving 100 taps to cylinder. Carr's index was determined from values of tapped density and bulk density. Hausner's ratio was determined by dividing tapped density by bulk density.¹²

Drug Content

Solid dispersion of each formulation equivalent to 100 mg of drug was accurately weighed and it was dissolved in methanol. The solution was filtered through Whatman filter paper. Then, the amount of drug present in solution was analyzed by using UV-Visible spectrophotometer at 273 nm.⁶

In vitro Dissolution Rate Study

The release profile of drug describes its *in vivo* release behavior. *In vitro* release profile for each solid dispersions as well as pure drug was performed using USP type 2 dissolution apparatus (Electrolab Ltd-

8L, Mumbai, India). Sample equivalent to 100 mg of aceclofenac was added to 900 mL 0.1N HCl (pH 1.2) at $37\pm 0.5^\circ\text{C}$ and stirring rate 50 rpm. An aliquot sample (5 ml) was withdrawn at an interval of 10 min with replacement of fresh medium to maintain the sink condition. Each sample was analyzed for aceclofenac content by UV-Visible spectrophotometer at 273 nm.⁶

RESULTS AND DISCUSSION

Solvent wetting method was found to be efficient methods to obtained good yield solid dispersions. The practical yields of all the formulations of solid dispersion were satisfactory as shown in Table 1. The yields varied from 98.00 to 99.02 %, suggesting that the processing parameters did not affect the yield.

The values of bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose of the prepared solid dispersion are represented in Table 1. The bulk density was found in the ranges of 0.85 to 0.90 gm/ml. The solid dispersion of all formulations had Hausner's ratio of 1.06 or less indicating good flowability. The Carr's index was found between 2.24 to 5.55 indicating good flowability. The good flowability of the solid dispersion was also evidenced by angle of repose within range of 22.01 to 23.48°, which is below 25°. Drug content was found in the ranges of 98.02 to 99.10 %. The maximum drug content was obtained with formulation F2.

The release profile of aceclofenac from solid dispersions is shown in Fig 1. Cumulative % drug released after 90 min was 91.03 ± 0.02 , 92.21 ± 0.21 , 45.22 ± 0.04 and 53.06 ± 0.45 % for F1, F2, F3 and F4 respectively, whereas, pure drug aceclofenac was releasing only $22.02\pm 0.02\%$ in 90 min. *In vitro* release studies revealed that there was marked enhancement in the dissolution rate of drug from all the solid dispersions when compared to pure aceclofenac.

From drug release profile data, it can be seen that formulation F2 (1:2 ratio of drug: potato starch) exhibited higher release in comparison to other formulations. The reason may be increase in drug wettability because of hydrophilic carrier.⁶ Cumulative per cent drug release data was found to be statistically significant at 5% level of significance ($F_{\text{tabulated value}} < F_{\text{calculated value}}$) by testing through one way ANOVA.

Table 1: Yield and physicochemical properties of different batches of developed aceclofenac solid dispersions

Evaluation Parameters	F1	F2	F3	F4
Practical yield (%)	98.00	98.54	98.20	99.02
Bulk density (gm/ml)	0.90	0.85	0.87	0.88
Tapped density (gm/ml)	0.93	0.90	0.89	0.91
Carr's index (%)	3.22	5.55	2.24	3.29
Hausner's ratio	1.04	1.06	1.03	1.04
Angle of repose (Degree)	22.01	23.48	23.05	22.12
Flow	Good	Good	Good	Good
Drug content (%)	99.05	99.10	98.02	99.00
Cumulative % drug release	91.03 ± 0.02	92.21 ± 0.21	45.22 ± 0.04	53.06 ± 0.45

CONCLUSION

The study concluded that the solid dispersion prepared by solvent wetting method (F2, 1:2 ratio of drug: potato starch) shows higher dissolution rate compared to other formulations. The study shows that the dissolution rate of aceclofenac can be enhanced by solid wetting method. The experimental results concluded that the solvent wetting method is suitable for formulation of solid dispersions of aceclofenac.

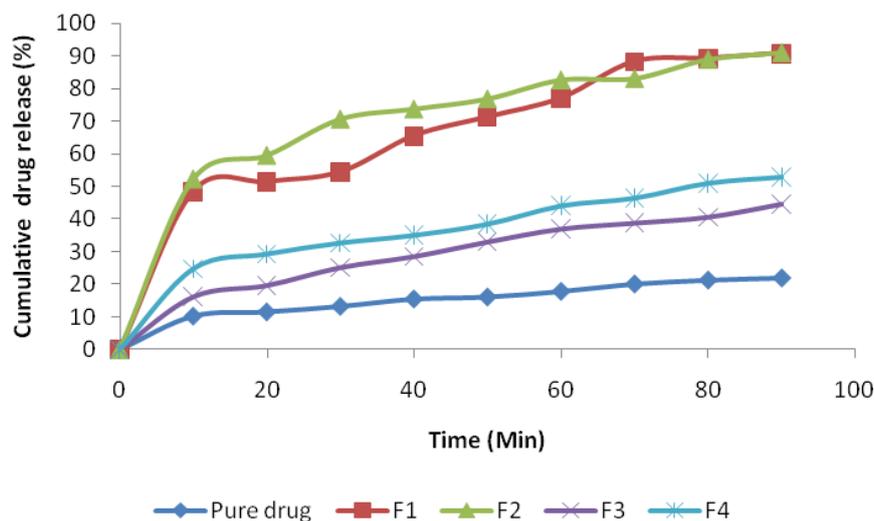


Fig 1. *In vitro* release profiles of different batches of aceclofenac solid dispersions

DECLARATION OF INTEREST

It is hereby declared that this paper does not have any conflict of interest.

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