

# Development of Aceclofenac Mouth Dissolving Tablets using Solid Dispersion Technique: *In-vitro* Evaluation

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## ABSTRACT

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Formulating mouth dissolving tablet using solid dispersion of drug shall not only improve solubility and consequent bioavailability but also improved patient compliance and convenience. The aim of the present study was to improve the solubility of Aceclofenac (ACE) by solid dispersion (SD) technique and formulate it as mouth dissolving tablets using some superdisintegrants. Solid dispersion (SD) of ACE was prepared by solvent evaporation method using PEG 6000 as carrier. Different weight ratios of drug and carrier i.e. 1:1, 1:2, 1:3, 1:4, and 1:5 were taken. Solubility of drug was determined in physical mixture and SD formulations.

The prepared SD formulations were characterized by Fourier Transform Infra-Red (FTIR) spectroscopy, differential scanning calorimetry (DSC), and *in vitro* drug release. Mouth dissolving tablets of ACE were formulated using optimized SD formulation of drug and carrier along with super-disintegrants such as croscarmellose sodium, crospovidone, and sodium starch glycolate. From IR and DSC studies, it was concluded that there is change in crystalline form of drug into amorphous state during formation of SD.

Mouth dissolving tablets containing crospovidone (20%) as super-disintegrants showed the fastest disintegration (39s) and *in vitro* drug release (92.2%). It can be concluded that combination of solid dispersion and super-disintegrants is a promising approach to prepare efficient mouth dissolving tablets of Aceclofenac.

**Keywords:** Mouth dissolving tablets; solid dispersion; aceclofenac; polyethylene glycol 6000

## INTRODUCTION

The solubility of certain drugs presents a challenge to the formulator for developing a suitable oral formulation. The bioavailability of poorly water-soluble drug is often limited by its dissolution rate, which in turn is controlled by the surface area available for dissolution. For such drugs, solid dispersion is a vital approach to achieve reduction in size and increase in solubility and hence, dissolution characteristics.<sup>1</sup> Formulating mouth dissolving tablet using solid dispersion of drug shall not only improve solubility and consequent bioavailability but also improved patient compliance and convenience. The combination of solid dispersion and mouth dissolve tablet (MDT) technology are required to address the problem of low bioavailability.

Mouth dissolving tablets of oxazepam<sup>2</sup>, glyburide<sup>3</sup>, tenoxicam<sup>4</sup>, valdecoxib<sup>5,6</sup>, rofecoxib<sup>7</sup>, itraconazole<sup>8</sup>, furosemide<sup>9</sup>, diazepam<sup>10</sup>, artemether<sup>11</sup>, clonazepam<sup>12</sup>, celecoxib<sup>13</sup>, meloxicam<sup>14</sup> and oxcabazepine<sup>15</sup> were developed

using SD technique. Recently, our research group developed mouth dissolving tablets of ibuprofen using solid dispersion technique.<sup>16</sup>

Aceclofenac (BCS Class II drug) is a non-steroidal anti-inflammatory drug that acts via multifactor mechanisms and is used to treat pain and inflammation.<sup>17</sup> It is practically insoluble in water. The solubility of aceclofenac in double-distilled water was found to be 3.8 µg/ml.<sup>18</sup> There are certain short comings of using aceclofenac as conventional oral tablets which includes, (i) bioavailability of aceclofenac is highly variable due to its low aqueous solubility, and first pass metabolism, and (ii) common adverse effects such as dyspepsia, nausea, diarrhea, constipation, gastritis, and vomiting. Thus in order to improve the solubility of drug and reduce side effects, it was attempted to prepare solid dispersion of Aceclofenac (ACE) and further develop mouth dissolving tablets using some super-disintegrants.

## MATERIALS AND METHODS

### Materials

Aceclofenac, croscarmellose sodium, crospovidone, sodium starch glycolate, microcrystalline cellulose and aspartame were received as gift sample from M/s Ranbaxy Labs. Pvt.

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Ltd. India. Polyethylene glycol (PEG) 6000, Talc, magnesium stearate, and strawberry flavor were purchased from SD Fine Ltd., India. All other chemicals and reagents used were of analytical reagent grade.

### Preparation of Solid Dispersion

The SD of ACE was prepared by conventional solvent evaporation method<sup>19</sup> using PEG 6000 as carrier. The ACE and carrier were weighed accurately in different ratios and triturated in a mortar and pestle for 5 min. This physical mixture was then dissolved in acetone with constant stirring. The solvent was evaporated on a heating mantle (Rolex, Mumbai, India) maintained at  $45 \pm 2^\circ\text{C}$ . The samples were dried in a desiccator for 24 h over anhydrous calcium chloride. Dried mass was scrapped, crushed, pulverized and passed through sieve (#60). Solid dispersion formulations were prepared using different ratios of drug and carrier i.e. 1:1, 1:2, 1:3, 1:4, and 1:5. The ratio and assigned batch code are given in Table 1.

**Table 1: Composition of solid dispersion and their assigned batch codes**

S. No	Ratio (Aceclofenac: PEG 6000)	Batch code
1	1:1	SPE-1
2	1:2	SPE-2
3	1:3	SPE-3
4	1:4	SPE-4
5	1:5	SPE-5
SPE <sub>1-5</sub> - Solid dispersion of aceclofenac prepared using PEG 6000 as carrier		

### Solubility Determination

The samples (physical mixtures and solid dispersions) equivalent to 10 mg of ACE was added to 10 ml each of distilled water and PBS (pH 6.8). The dispersions were shaken well and kept for 24 h. The solution was filtered and analyzed spectrophotometrically at 273 nm using UV-1800 spectrophotometer (Shimadzu, Japan) after suitable dilutions.

### Characterization of Solid Dispersion

#### *Fourier Transform Infrared Spectroscopy (FTIR)*

FTIR spectra of ACE, PEG 6000, & their solid dispersion formulation were obtained on a Shimadzu 8400S FTIR spectrometer (Japan). The KBr discs (2 mg sample in 200 mg KBr) of different samples were prepared. The scanning range and resolution was  $400\text{--}4000\text{ cm}^{-1}$  and  $4\text{ cm}^{-1}$ , respectively.

#### *Differential Scanning Calorimetry (DSC)*

Differential scanning calorimetry (DSC) measurements were performed on ACE, PEG 6000 and its solid dispersion

formulations using Differential scanning calorimeter (JADE DSC-6, PYRIS, USA) equipped with a liquid nitrogen sub-ambient accessory. The temperature was calibrated using pure indium with a melting point of  $156.60^\circ\text{C}$ .<sup>20</sup> The instrument operated under nitrogen purge gas at a rate of 20 ml/min. Samples (3–6 mg) were weighed in open aluminum pans (Al-Crucibles, 40 Al) and sealed. The probes were heated from 30 to  $300^\circ\text{C}$  at a rate of  $10^\circ\text{C}/\text{min}$  under nitrogen atmosphere. An empty pan was used as a reference.

#### *Drug content analysis*

Accurately weighed quantity of solid dispersion (theoretically equivalent to 10 mg of ACE) was dissolved in small amount of methanol and volume was made up to 10 ml with PBS (pH 6.8). The solution was sonicated for 5 min. Then solution was filtered through Whatman filter paper (#41). The sample was assayed by UV-spectrophotometer (UV-1800 double beam spectrophotometer Shimadzu, Japan) at 273 nm.

#### *In vitro Dissolution Studies of Solid Dispersion*

The quantity of SD equivalent to 50 mg of ACE was filled in hard gelatin capsule by hand filling method. Dissolution study of capsules was conducted using USP dissolution apparatus 2 (Dissolution rate test apparatus, USP/IP/BP/STP, Electrolab, India) in 900 ml of phosphate buffer (pH 6.8) maintained at  $37 \pm 0.5^\circ\text{C}$  at a speed of 50 rpm. Aliquots were withdrawn at appropriate time intervals and equal volumes of fresh dissolution medium were replaced. The samples were filtered and analyzed spectrophotometrically at 273 nm<sup>21</sup> using UV-1800 spectrophotometer (Shimadzu, Japan) after suitable dilutions. In dissolution study, the initial % drug dissolved in 2 h was examined by plotting % drug dissolved in the PBS (pH 6.8) against a function of time. The experiment was performed in triplicate.

### Formulation of Tablets Using Solid Dispersion of Aceclofenac

Different batches of ACE containing mouth dissolving tablets were prepared by direct compression method and various formulae used in the compositions of prepared mouth dissolving tablets are given in Table 2. Microcrystalline cellulose was utilized as diluents in MDT. Magnesium stearate was utilized as lubricant. All ingredients were properly mixed and the blends were passed through a sieve (#40). Powdered SD, containing amount equivalent to 50 mg of ACE, was mixed with the other excipients and compressed on a single punch tablet machine (Square Pharma Machineries, Mumbai, India) equipped with flat-faced 10-mm punches. The tablet weight was adjusted to 400 mg.

Table 2: Different formula for tablets formulation

S.No.	Ingredients	Formulation code*								
		A-I	A-II	A-III	A-IV	A-V	A-VI	A-VII	A-VIII	A-IX
1	SPE-4 (Solid dispersion of ACE)	250	250	250	250	250	250	250	250	250
<b>2</b>	<b>Superdisintegrants</b>									
2.1	Crospovidone	5	10	20	-	-	-	-	-	-
2.2	Croscarmellose sodium	-	-	-	5	10	20	-	-	-
2.3	Sodium starch glycolate	-	-	-	-	-	-	5	10	20
3	Talc	4	4	4	4	4	4	4	4	4
4	Aspartame	5	5	5	5	5	5	5	5	5
5	Strawberry flavor	5	5	5	5	5	5	5	5	5
6	Mannitol	25	25	25	25	25	25	25	25	25
7	Magnesium stearate	2	2	2	2	2	2	2	2	2
8	Avicel PH-102	104	99	94	104	99	94	104	99	94
	<b>Total</b>	<b>400</b>	<b>400</b>	<b>400</b>	<b>400</b>	<b>400</b>	<b>400</b>	<b>400</b>	<b>400</b>	<b>400</b>

\* Quantity of ingredients in mg

### Evaluation of Prepared Tablets

The crushing strength (hardness) was determined using a Monsanto hardness tester (Sheetal Scientific Industries, Mumbai, India). The tablet friability of a sample of 10 tablets was measured using a Roche friabilator (Shreeji Pharmaceutical Scientific and Instruments, Mumbai, India). The tablet geometry was determined by a means of a micrometer (Baty Co., Ltd, England). Twenty tablets were randomly taken from each batch and weighed individually. The average weight and standard deviation were calculated.

The procedure for determination of wetting time was followed as reported by Ghoeil et al.<sup>22</sup> Five circular tissue papers of 10 cm diameter were placed in a Petri dish with 10 cm diameter. Ten milliliters of water containing methylene blue, a water-soluble dye, was added to the petridish. One tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet was noted as a wetting time.<sup>23</sup> For determination of disintegration time, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully placed in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted.<sup>24</sup>

For determination of moisture uptake, ten tablets from each formulation were kept in a desiccator over calcium chloride at 37°C for 24 h. The tablets were then weighed and exposed to 75% relative humidity, at room temperature for two weeks. Tablets were weighed and the percentage increase in weight was recorded.

### Drug content of tablet formulations

The amount of active ingredient was determined by taking 5 tablets randomly. Tablets were then weighed accurately, and

then powdered in mortar and pestle. An amount equivalent to 10 mg of drug powder was dissolved in PBS (pH 6.8) and sonicated for 30 min. The solution was then filtered, diluted properly and analyzed spectrophotometrically at 273 nm.

### *In vitro* Drug Release Study of Mouth Dissolving Tablets

The *in vitro* drug release of conventional marketed tablets of ACE (Aceclo; ACE 100 mg, Aristo Pharma. Ltd., Mumbai, India) and tablets of different formulation batches were studied by using six rotating paddle apparatus (USP Dissolution apparatus II, Electrolabs, Mumbai). Each tablet was placed in the paddle dissolution assembly containing 900 ml of phosphate buffer (pH 6.8). The paddle was rotated at 100 rpm and temperature of dissolution medium was thermostatically controlled at 37± 0.5°C. At appropriate time intervals, 5 ml of the medium was withdrawn, filtered through a Whatman filter paper (# 40) and equal volumes of fresh dissolution medium were replaced. Samples were analyzed for ACE content by using UV-1800 spectrophotometer (Shimadzu, Japan) after suitable dilutions at 273 nm. The experiment was performed in triplicate.

## RESULTS AND DISCUSSION

### Preparation of Solid Dispersion

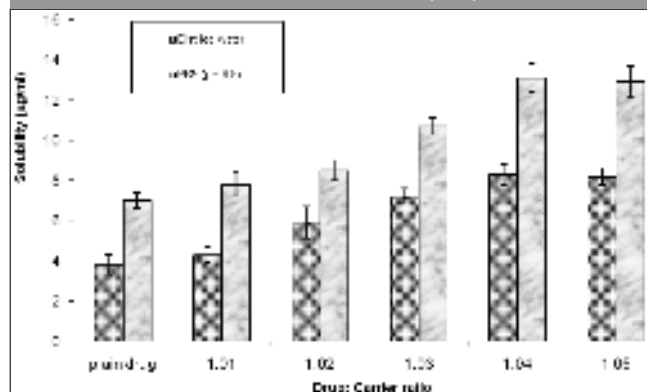
It was attempted to improve the aqueous solubility of ACE by solid dispersion technique. PEG 6000 was used as carrier for preparation of solid dispersion with aceclofenac due to their characteristics i.e. easily soluble in water, physiologically inert, non-toxic, lack of absorption, thermally stable at melting temperature, and improved compound wettability. Binary solid dispersions using drug and carrier were prepared by varying ratios of PEG 6000. The drug and carrier ratio of

1:1, 1:2, 1:3, 1:4 and 1:5 were used for preparation of solid dispersions by solvent evaporation method to enhance the solubility of ACE.

### Solubility Studies

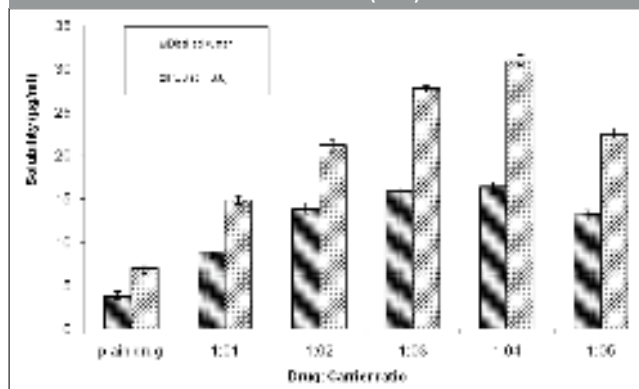
The solubility of ACE in water was reported as 3.8 µg/ml, therefore, ACE can be considered as a practically insoluble drug. The drug is also available in crystalline form. According to observations obtained from the solubility analysis of physical mixture of drug and carrier, there were significant changes in the solubility of drug as compared to that of pure drug in distilled water and PBS (pH 6.8). The solubility values of physical mixtures for drug, carrier ratio 1:1, 1:2, 1:3, 1:4, and 1:5 were found to be 4.3, 5.9, 7.2, 8.3 and 8.2 µg/ml, respectively in distilled water. Similarly, the solubility values of physical mixtures for drug, carrier ratio 1:1, 1:2, 1:3, 1:4, and 1:5 were found to be 7.8, 8.5, 10.7, 13.1 and 12.9 µg/ml, respectively in PBS (Fig. 1). Solubility of physical mixture in distilled water and PBS was found to be increased with increase in carrier ratio up to 1:4. At drug, carrier ratio 1:5, the solubility was found to be decreased slightly. Enhanced solubility of aceclofenac from physical mixtures could be related to the surface activity, wetting effect which may lead to reduced agglomeration and hence increased surface area, and solubilizing effect of PEG 6000.<sup>25</sup>

Fig. 1. Solubility profile of aceclofenac in physical mixture containing different drug and carrier ratio  
Values are mean ± s.d. (n=3)



The solubility of ACE (3.8 µg/ml) in distilled water was increased to the value 16.4 µg/ml of 1:4 drug, carrier solid dispersion formulation. Similarly, the solubility of ACE (7 µg/ml) in distilled water was increased to the value 30.9 µg/ml of 1:4 drug, carrier solid dispersion formulation (Fig. 2). The increase in solubility of ACE by PEG 6000 may be due to the increased wettability of ACE and formation of soluble complex between water-soluble polymeric carrier and poorly soluble drug. On the basis of solubility, it was found that solid

Fig. 2. Solubility profile of aceclofenac in solid dispersion prepared by different drug and carrier ratio Values are mean ± s.d. (n=3)

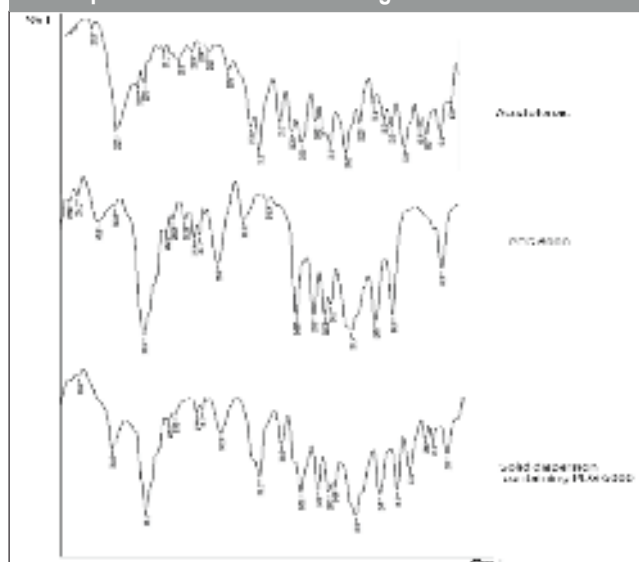


dispersion (1:4) had sufficient solubility among all other prepared solid dispersion formulations and physical mixtures.

### Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR studies were carried out to investigate the possible interactions between the ACE and carrier (PEG 6000) in the solid dispersion formulations. Fig. 3 shows the FTIR spectra of ACE, PEG 6000, and their solid dispersion formulation. The FTIR spectrum of ACE shows characteristic bands at 1718.58 & 1770.55  $\text{cm}^{-1}$  of C=O (carbonyl group of ester) stretching vibration, O-H (carboxyl group) stretching of acidic group at 3313.71  $\text{cm}^{-1}$ , C-Cl stretching at 761.88 and 800.67  $\text{cm}^{-1}$ , and N-H (secondary amines) stretching at 1581.63  $\text{cm}^{-1}$ . The spectrum of PEG 6000 shows important bands at 2883.58  $\text{cm}^{-1}$  of C-H (aromatic ring) stretching, C=C (aromatic ring) stretching at 842.89 & 954.76  $\text{cm}^{-1}$ , and C-O (ether) stretching at 1107.14  $\text{cm}^{-1}$ .

Fig. 3: FTIR spectra of aceclofenac, PEG 6000, and solid dispersion of aceclofenac using PEG 6000 as carrier





The peak of C=O (carbonyl) band at  $1770.55\text{ cm}^{-1}$  is disappeared in solid dispersion of ACE. The reason might be interaction of O-H of ACE and oxygen atom in PEG 6000. The interaction is also possible between the acidic group of drug and carbonyl group of carrier in hydrogen bonding. The absorption bands which can be assigned to the free O-H and involved in intra-molecular hydrogen bonding of N-H at  $1581.63\text{ cm}^{-1}$  is disappeared.

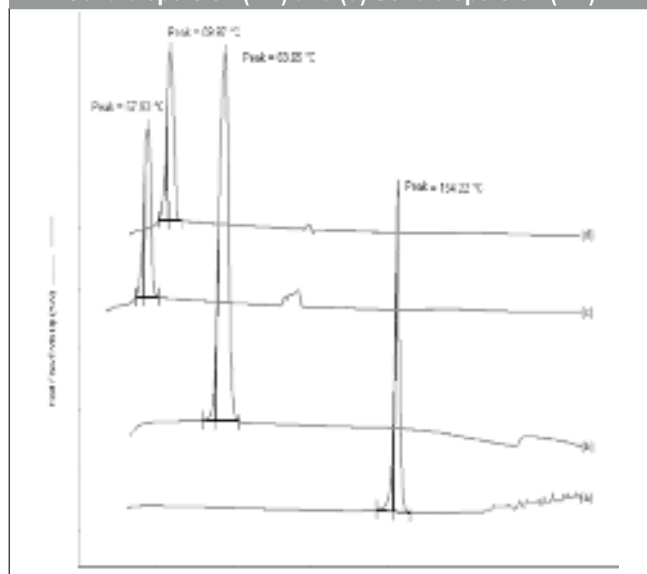
### Differential Scanning Calorimetry

The DSC thermogram of ACE exhibited an endothermic peak at  $154.22^\circ\text{C}$ , which corresponds to the melting point of ACE. The carrier PEG 6000 showed an endothermic peak at  $63.65^\circ\text{C}$  which corresponds to the melting point of PEG 6000.<sup>20</sup> There was only one endothermic peak observed for solid dispersions prepared using drug: carrier ratio, 1:1 & 1:4 at  $59.97^\circ\text{C}$  and  $57.93^\circ\text{C}$ , respectively which corresponds to the melting of PEG 6000 (Fig. 4). The disappearance of endothermic peak of drug (ACE) in solid dispersion gives an idea that ACE might be in dissolve state in melted PEG 6000. This could be attributed to higher PEG 6000 concentration and uniform distribution of drug in the crust of PEG 6000 resulting in complete miscibility of molten drug in PEG 6000. The disappearance of endothermic peak in solid dispersion formulations confirms the amorphous state of drug in prepared solid dispersion formulations.

### Drug content of solid dispersions

Percent drug content of various solid dispersion formulations i.e. SPE1, SPE2, SPE3, SPE4, and SPE5 were found to be 95.5%, 95.1%, 92.7%, 98.5%, and 97.2%, respectively. The percent drug content was found to be  $95\pm 5\%$  for all the solid dispersion formulations.

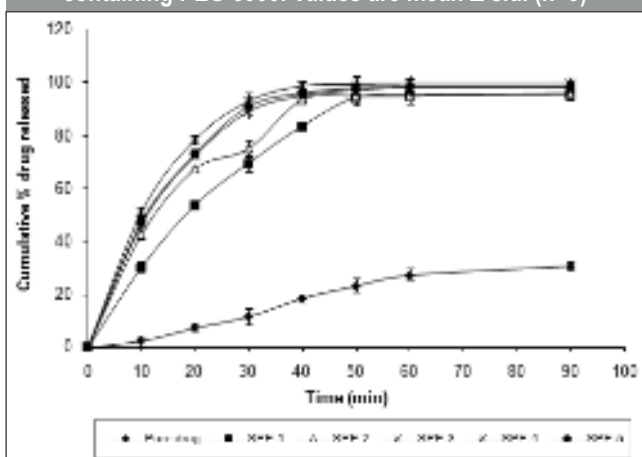
Fig. 4: DSC Thermogram of (a) Aceclofenac (b) PEG 6000 (c) Solid dispersion (1:1) and (d) Solid dispersion (1:4)



### *In vitro* Drug Release Studies of Solid Dispersions

The dissolution behavior of ACE from various SD formulations and pure drug in PBS (pH 6.8) was examined in comparison with the intact drug by plotting the percentage of drug released against time as shown in Fig. 5. The drug release from different SD formulations prepared by solvent evaporation method followed the order: SPE4 > SPE5 > SPE3 > SPE2 > SPE1. It is evident that the rate of dissolution of pure drug is very low, only 37.10 % of the drug being dissolved within 2 h. Dispersion of the drug in the hydrophilic carrier's considerably enhanced dissolution compared to the pure drug.<sup>26</sup> This was supposed to be due to the effect of molecular dispersion of drug in PEG, and the decreased crystallinity of ACE existing in SDs.<sup>27</sup> The dissolution rate of the solid dispersion formulations was higher compared to pure ACE. From the *in vitro* drug release profile for different SD formulation, it is evident that amongst the SD formulated, there was increase in dissolution up to the ratio 1:4, but after this there is no significant increase in the dissolution of the drug. This might be due to complete dispersion of drug with PEG 6000 at 1:4 ratio. Further, increase in carrier concentration, a decrease in dissolution rate was observed. This might be due to formation of viscous boundary layer around the drug particles, leading to decrease in the dissolution rate. So, formulation SPE 4 was selected for further studies and tablets were formulated. Possible mechanisms of increased dissolution rates of drug in solid dispersions<sup>26,28</sup> could be improved wettability and dispersibility of drug from the dispersion, solubilization effect of the carrier, absence of the aggregation of drug, reduction of drug crystallinity, dissolution of the drug in the hydrophilic carrier and conversion of the drug to the amorphous state.

Fig. 5. Comparative (%) drug dissolution from different aceclofenac solid dispersion formulations of prepared using PEG 6000 as carrier SPE – Solid dispersion formulations containing PEG 6000. Values are mean  $\pm$  s.d. (n=3)



### Preparation and Evaluation of Mouth Dissolving Tablets

The super-disintegrants i.e., Croscopovidone, Croscarmellose sodium and Sodium starch glycolate were taken in various ratios to find the optimum concentration of the super-disintegrants required to yield formulation having least wetting time and disintegration time. The super-disintegrants are used from as low as 4% to as high as 66% in fast dissolving formulations or for improving dissolution of active pharmaceutical ingredients.<sup>29</sup> Super-disintegrants are generally used for developing mouth dissolving tablets or for improvement of solubility for active pharmaceutical ingredients. These super-disintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water. The absorption of water results in breaking of tablets and therefore faster disintegration. The use of super-disintegrants for preparation of mouth dissolving tablets is highly effective as well as commercially feasible.

All the prepared tablets were characterized by a uniform thickness in the range of 5.8-6.3 mm. It was observed that the variation of thickness was insignificant ( $P \leq 0.5$ ) (data not shown). The weight variation of tablets was determined according to the specifications in USP and all the tablets were found to comply with specifications. The tablet weight variation was within an acceptable range of  $\pm 5\%$ . The friability of all formulations was found to be less than 1 % (Table 3). The result shows resistance to loss of weight indicated the tablet ability to withstand abrasion in handling, packaging and shipment. A tablet requires certain amount of hardness to withstand the mechanical shocks in handling, packaging and at the time of application. The hardness of tablet ranged from 2.98-3.09 kg/cm<sup>2</sup>.

Percent drug content of various formulations i.e. A-I, A-II, A-III, A-IV, A-V, A-VI, A-VII, A-VIII and A-IX were found to be as 98.70%, 99.12%, 99.78%, 97.31%, 98.96%, 98.33%, 103.37%, 98.62% and 99.29%, respectively. The percent drug content was found to be  $100 \pm 5\%$  for all the formulations.

Since the dissolution profile of a tablet depends upon the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as confirmative test for the evaluation of mouth dissolving tablets. Wetting time of the tablets decreased with increase in the level of croscopovidone (5-20%) from 37.5 to 22.5 sec ( $P < 0.05$ ), croscarmellose sodium (5-20%) from 39.5 to 31.5 sec ( $P < 0.05$ ) and sodium starch glycolate (5-20%) from 39.5-34 sec ( $P < 0.05$ ). Lowest wetting time was observed with tablets containing croscopovidone at its highest level among all super-disintegrants. Sammour et al.<sup>7</sup> stated that wetting time decreased while increasing the level of croscopovidone. In the present study, all the tablets disintegrated in less than 75 seconds (according to European Pharmacopoeia time required less than 3 min).

It is observed that disintegration time of the tablets decreased with increase in the level of croscopovidone (53 to 39 sec), croscarmellose sodium (59 to 49 sec) and sodium starch glycolate (72 to 56 sec). It indicates that increase in the level of super-disintegrants i.e. croscopovidone, croscarmellose sodium and sodium starch glycolate had a positive effect on the disintegration of MDT formulations. Lowest disintegration time was observed with tablets containing croscopovidone at its highest level among all super-disintegrants. Disintegration time of tablets follows the pattern with various super-disintegrants: croscopovidone < croscarmellose sodium < sodium starch glycolate.

The porous structure of the tablets is responsible for faster water uptake. Moisture uptake studies for mouth dissolving tablets should be conducted to assess the stability of the formulation. The results indicated that tablets containing high concentration of super-disintegrants get softened and absorb atmospheric moisture. The tablets containing croscopovidone absorbed higher amount of moisture as compared with other two super-disintegrants. The wetting time and disintegration time of different tablet formulations are summarized in Table 3.

The influence of super-disintegrants on the dissolution of aceclofenac from tablets is shown in Fig. 6. The drug release from marketed formulation of ACE and different MDT formulations followed the order: A-III > A-VI > A-IX > A-II > A-V > A-VIII > A-I > A-IV > A-VII > Aceclo. The pattern provides an idea about the effect of super-disintegrants i.e. croscopovidone, croscarmellose sodium, and sodium starch glycolate in drug release profile of mouth dissolving tablets. The *in vitro* drug release profile of MDT formulations was found to increase with increase in super-disintegrant level. An increase in dissolution of drug from the mouth dissolving

Fig. 6. Drug release profile of conventional marketed tablet (Aceclo) and different tablet formulations in phosphate buffer (pH 6.8). Values are mean  $\pm$  s.d. (n=3).  
Aceclo- Conventional marketed tablet of aceclofenac;  
A<sub>I-IX</sub> - Mouth dissolving tablets

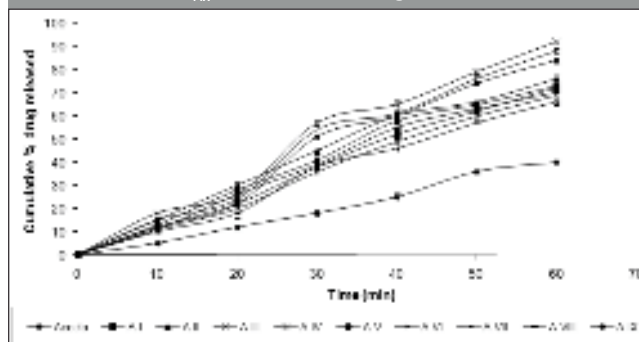


Table 3: Wetting time, disintegration time and % moisture uptake of prepared tablet batches					
S.No.	Formulations	Friability (%)	Wetting Time (Sec) *	Disintegration time (Sec) *	Moisture uptake (%) *
1.	A-I	0.632	37±1	53±2	10.71±1.0
2.	A-II	0.783	35±2	48±3	7.02±1.6
3.	A-III	0.702	22±2	39±2	11.26±2.0
4.	A-IV	0.679	39±1	59±3	7.28±1.8
5.	A-V	0.526	34±2	54±3	10.82±1.2
6.	A-VI	0.763	31±3	49±1	10.94±0.8
7.	A-VII	0.592	39±2	72±2	10.41±1.6
8.	A-VIII	0.697	37±1	60±3	10.75±2.0
9.	A-IX	0.455	34±2	56±2	10.87±1.2

A<sub>1-IX</sub> - Mouth dissolving tablets, \* Values are mean ± s.d. (n=3)

tablets containing crospovidone was observed. Crospovidone exhibits high capillary activity and pronounced hydration with a little tendency to gel formation and disintegrates the tablets rapidly but into larger masses of aggregated particles.

<sup>30,31,32</sup> The faster increase in drug release of ACE with the increase in croscarmellose sodium content may be attributed to rapid swelling and disintegration of tablet into apparently primary particles. <sup>30,31,33</sup> While, tablets prepared with sodium starch glycolate, disintegrate by rapid uptake of water, followed by rapid and enormous swelling into primary particles but more slowly due to the formation of a viscous gel layer. Mouth dissolving tablets containing crospovidone (20%) showed the fastest disintegration (39s) and drug release (92.2%).

### CONCLUSION

The fastest drug release was obtained from a solid dispersion containing ACE: PEG 6000 of 1:4 wt/wt ratio prepared by solvent evaporation method. Formulation of MDT by using solid dispersion of ACE is unique technique by which solubility of the drug can be enhanced which is most challenging aspect of drug delivery. The technique adopted was found to be economical and industrially feasible. Thus, it can be concluded that combination of solid dispersion and super-disintegrants is a promising approach to prepare efficient mouth dissolving tablet of poorly water soluble drug i.e. Aceclofenac.

### ACKNOWLEDGEMENT

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### REFERENCES

- Saha RN. Solubility enhancement of Nimesulide and ibuprofen by solid dispersion technique. *Ind J Pharm Sci* 2002; 64(6): 529-34.
- Jachowicz R, Nurnberg E. Enhanced release of oxazepam from tablets containing solid Dispersions. *Int J Pharm* 1997; 159: 149-58.
- Valleri M, Mura P, Maestrelli F, Cirri M, Ballerini R. Development and evaluation of Glyburide fast dissolving tablets using solid Dispersion Technique. *Drug Dev Ind Pharm* 2004; 30 (5): 525-34.
- Aly AM, Semreen M, Qato MK. Superdisintegrants for solid dispersion to produce rapidly disintegrating tenoxicam tablets via camphor sublimation. *Pharm Tech* 2005; 1: 68-78.
- Patel MM, Patel DM. Fast dissolving valdecoxib tablets containing solid dispersion of valdecoxib. *Ind J Pharm Sci* 2006; 68(2): 222-6.
- Modi A, Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. *AAPS PharmSciTech* 2006; 7(3): Article 68.
- Sammour OA, Hammad MA, Megrab NA, Zidan AS. Formulation and optimization of mouth dissolve tablets containing Rofecoxib solid dispersion. *AAPS PharmSciTech* 2006; 7(2): Article 55.
- Oshima T, Sonoda R, Ohkuma M, Sunada H. Preparation of rapidly disintegrating tablets containing itraconazole solid dispersions. *Chem Pharm Bull* 2007; 55(11): 1557-1562.
- Chaulang G, Patil K, Ghodke D, Khan S, Yeole P. Preparation and Characterization of Solid Dispersion Tablet of Furosemide with Crospovidone. *Res J Pharm Tech* 2008; 1(4): 386-9.

10. Giri TK, Jana P, Sa B. Rapidly disintegrating fast release tablets of diazepam using solid dispersion: development and evaluation. *J Sci Ind Res* 2008; 67: 436-9.
11. Shah PP, Mashru RC. Development and Evaluation of Artemether Taste Masked Rapid Disintegrating Tablets with Improved Dissolution Using Solid Dispersion Technique. *AAPS PharmSciTech* 2008; 9 (2): 494-500.
12. Bhalerao AV, Deshkar SS, Shirolkar SV, Gharge VG, Deshpande AD. Development and evaluation of clonazepam fast disintegrating tablets using superdisintegrates and solid dispersion technique. *Res J Pharm Tech* 2009; 2(2): 375-77.
13. Pandya VM, Patel DJ, Patel JK, Patel RP. Formulation, Characterization, and Optimization of Fast-Dissolve Tablets Containing Celecoxib Solid Dispersion. *Dissolution Technologies* 2009; 16(4): 22-7.
14. Barhate SD, Shankhpal GA, Sharma AS, Nerkar PD. Formulation of fast dissolving tablets of Meloxicam. *J Pharm Res* 2009; 2(4): 646-50.
15. Kalia A, Khurana S, Bedi N. Formulation and evaluation of mouth dissolving tablets of oxcarbazepine. *Int J Pharm Pharmaceut Sci* 2009; 1 (1): 13-23.
16. Jain SK, Gupta M, Shrivastava V. Development and in vitro Evaluation of Ibuprofen Mouth Dissolving Tablets using Solid Dispersion Technique. *Chem Pharm Bull* 2010; 58(8): 1037-42.
17. Legrand E. Aceclofenac in the management of inflammatory pain. *Exp Opin Pharmacother* 2004; 5: 1347-57.
18. Soni T, Nagda C, Gandhi T, Chotai NP. Development of Discriminating Method for Dissolution of Aceclofenac Marketed Formulations. *Dissolution Technologies* 2008; 15(2): 31-35.
19. Chiou WL, Riegelman S. Pharmaceutical applications of solid dispersion systems. *J Pharm Sci* 1971; 60: 1281-302.
20. Mooter GV, Augustijns P, Bleton N, Kinget R. Physico-chemical characterization of solid dispersions of temazepam with polyethylene glycol 6000 and polyvinyl pyrrolidone K-30. *Int J Pharm* 1998; 164: 67-80.
21. Garg G, Saraf S, Saraf S. Simultaneous estimation of aceclofenac, paracetamol and chlorzoxazone in tablets. *Ind J Pharm Sci* 2007; 69(5): 692-94.
22. Ghoel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. *AAPS PharmSciTech* 2004; 5: Article 36.
23. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. *Asian J Pharm* 2008; 2: 2-11.
24. Bi Y, Sunada K, Yonezawa Y, Danjo K, Otsuka A, Iida K. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. *Chem Pharm Bull* 1996; 44: 2121-7.
25. Newa M, Bhandari KH, Kim JO, Im JS, Kim JE, Yoo BK, Woo JS, Choi HG, Yong CS. Enhancement of solubility, dissolution and bioavailability of Ibuprofen in solid dispersion systems. *Chem Pharm Bull* 2008; 56(4): 569-74.
26. Damian F, Bleton N, Kinget R, Van der Mooter G. Physical stability of solid dispersions of the antiviral agent UC-781 with PEG 6000, Gelucire 44/14 and PVP K30. *Int J Pharm* 2002; 244: 87-98.
27. Okonogi S, Puttipipatkachorn S. Dissolution improvement of high drug loaded solid dispersion. *AAPS PharmSciTech* 2006; 7(2): Article 52.
28. Ford JL. The preparation and properties of tablets containing indomethacin and polyethylene glycol 6000. *Pharm Acta Helv* 1983; 58 (4):101-08.
29. Shin SC, Oh IJ, Lee YB, Choi HK, Choi JS. Enhanced dissolution of furosemide by coprecipitating or cogrinding with crospovidone. *Int J Pharm* 1998; 175: 17-24.
30. Augsburger LL, Brzezczko AW, Shah US, Hahn HA. Ed. Superdisintegrants: Characterization and function, In Swarbrick J, Boylan JC. *Encyclopedia of pharmaceutical technology*. vol. 20, Marcel Dekker, New York, 2001. p. 269-293.
31. Zhao N, Augsburger LL. Functionality comparison of 3 classes of superdisintegrants in promoting aspirin tablet disintegration and dissolution. *AAPS PharmSciTech* 2005; 6: Article 79.
32. Gohel MC, Parikh RK, Brahmabhatt BK, Shah AR. Preparation and assessment of novel coprocessed superdisintegrant consisting of crospovidone and sodium starch glycolate: A technical note. *AAPS PharmSciTech* 2007; 8(1): Article 9.
33. Rowe RC, Sheskey PJ, Weeler PJ. *Handbook of Pharmaceutical Excipients*. 4 th Ed. Pharmaceutical Press, London; 2003.

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