Original article

Studies on formulation development of a poorly water-soluble drug through solid dispersion technique

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Abstract:

An attempt has been made to enhance dissolution of aceclofenac (AC) by solid dispersion technique using water soluble carriers PEG 6000 and β-cyclodextrin (β-CD). Solid dispersions of AC with PEG 6000 were prepared by melting solvent method and with β-CD were prepared by co-grinding, kneading and co-evaporation methods. Solid dispersions with both carriers were prepared in drug: carrier (1:1 and 1:2) ratios along with the corresponding physical mixtures. The prepared dispersions were evaluated by differential scanning calorimetry (DSC), scanning electron microscopy (SEM), *in vitro* dissolution studies. The results from DSC and SEM analysis showed that AC might exist in an amorphous state in the solid dispersion. Considerably improved dissolution profile was obtained by higher PEG ratios (1:2), whereas there was no significant improvement in dissolution of AC along with β-CD at higher carrier ratios. The solid dispersion prepared as AC: PEG 6000 (1:2), exhibited the fastest dissolution among all solid dispersions, was formulated into tablets using direct compression method and further compared with three popular immediate release marketed brands of AC. Model independent parameters were used for comparing tablets dissolution profiles viz. percentage of drug dissolved in 50 minutes (DP_{50}), dissolution efficiency at 50 minutes (DE_{50}), time for 50% drug release ($t_{50\%}$), similarity factor (f_2) and difference factor (f_1). The results indicated that formulated tablets displayed better dissolution profiles as compared to existing commercial tablets.

Keywords: Aceclofenac; BCS class II; Dissolution enhancement; Poorly water soluble drug; Solid dispersion; Water soluble carriers

Introduction

Aceclofenac (AC), a phenylacetic acid derivative, [(2-{2,6-dichlorophenyl)amino} phenylacetooxyacetic acid] is a non-steroidal anti-inflammatory drug (NSAID) indicated for the symptomatic treatment of pain and inflammation with a reduced side effect profile, especially gastro-intestinal events that are frequently experienced with NSAID therapy [1]. Aceclofenac is practically insoluble in water with good permeability (calculated log P = 2.170) and belongs to biopharmaceutics classification system (BCS) class II (low solubility, high permeability). Therefore, AC shows dissolution rate limited absorption that gives rise to difficulties in pharmaceutical formulations for oral delivery, which may lead to variable bioavailability. This fact motivated the development of drug delivery technologies to overcome the obstacle to its solubilization. Besides enhancement of solubility or micronization of drug substances in order to increase the surface area and replacement of crystalline drugs by amorphous material, the solid dispersions with water soluble carriers is the promising and widely used approach to enhance the dissolution properties of water insoluble drugs [2-5]. The present work reports potential of water soluble carriers β-cyclodextrin (β-CD) and PEG 6000 in enhancing the dissolution properties of the aceclofenac. The selected solid binary systems were further subjected to direct compression in order to determine their suitability in developing better oral dosage form with improved dissolution and bioavailability.

Materials and Methods

Aceclofenac was obtained as a generous gift from Kairav Chemicals (Ahmedabad, India). β-cyclodextrin was purchased from SD fine chemicals (India), PEG 6000, spray-dried lactose, sodium starch glycolate were from Merck (India) Ltd. Double distilled water was used throughout the studies.

Preparation of AC-βCD binary systems

The solid binary systems of AC and β-CD in 1:1 and 1:2 molar ratios were prepared using 0.3542 gm AC with 1.135 gm and 2.7 gm β-CD respectively. The coground dispersions (CG) were prepared by geometric mixing and triturating AC and β-CD powders (sieved through 85-mesh) for 20 min in the glass mortar pestle. To obtain kneaded product (KN), AC and β-CD were triturated in mortar with 0.5 mL of water: ethanol (1:1 v/v) solution to obtain dough like mass. This was kneaded for 45 min and dried under vacuum at room temperature to constant weight. The dried mass was pulverized and screened through 85-mesh sieve. To obtain coevaporated product (CE), an aqueous solution of β-CD was added to alcoholic solution of AC. The resulting mixtures were dried on magnetic stirrer (maintained at 45-50°C) by continuous stirring for 4 h. The nearly dried mass was pulverized and sieved through 85-mesh [6]. The solid systems were coded as CG-1 and CG-2 (coground dispersion of AC: β-CD in 1:1 and 1:2 ratio), KN-1 and KN-2 (kneaded product of AC: β-CD in 1:1 and 1:2 ratio), CE-1 and CE-2 (coevaporated product of AC: β-CD in 1:1 ratio and 1:2).

Preparation of AC-PEG 6000 binary systems

The binary systems of AC with PEG 6000 were prepared using melting solvent method in 1:1 and 1:2 weight ratios. PEG 6000 was melted at 50-60 °C in preheated china dish on water bath. The ethanolic solution of AC was added into melted PEG 6000 with stirring. The mass obtained was cooled to room temperature and dried under vacuum to constant weight [7]. The prepared solid systems were pulverized using glass mortar pestle and sieved through 85-mesh. The solid systems were coded as AP-1 and AP-2 (dispersion of AC: PEG 6000 in 1:1 and 1:2 ratio).

Preparation of physical mixtures

To obtain physical mixtures (PMs), the required amounts of drug and carriers were geometrically mixed (previously screened through 85-mesh) for 20 min in the glass mortar with the help of stainless steel spatula. PMs were prepared for each drug: carrier ratios for characterization and coded as PM-1 and PM-2 (physical mixture of AC: β-CD in 1:1 and 1:2 ratio), PMAP-1 and PMAP-2 (physical mixture of AC: PEG 6000 in 1:1 and 1:2 ratio).

Drug content analysis

Ten mg of each of binary system was diluted to 10 ml with methanol. This solution was shaken for one min using vortex shaker (Hicon, Grover Enterprises, New Delhi). All the samples were filtered using Whatman® no. 1 filter paper. From this, 0.5 mL solution was withdrawn and again diluted to 10 mL with methanol. The concentration of AC in the filtrates was determined spectrophotometrically at 275 nm (Shimadzu-1700, Japan) with reference to suitably constructed calibration curve of AC in methanol. Drug content estimations were performed in triplicate.

In vitro dissolution studies

In vitro dissolution tests for pure AC or its binary systems equivalent to 100 mg of AC were carried out with the USP 23 dissolution test apparatus (Type II paddle) at 37˚C and 100 rpm using 900 mL of simulated intestinal fluid (SIF) pH 7.5 without enzyme as dissolution medium (n=3) [8]. Five ml of test samples were withdrawn at predetermined time intervals and replaced with an equal volume of fresh dissolution medium. The samples were filtered, suitably diluted and assayed spectrophotometrically for AC content at 275 nm and the amount of AC in each sample was calculated with reference to regression equation generated from suitably constructed calibration curve of AC.

Differential scanning calorimetry studies

Thermograms were recorded on Perkin Elmer (Pyris Diamond) model differential scanning calorimeter. About 10 mg of samples were sealed in quartz pans and heated at a rate of 10˚C/min at 50˚C to 350˚C in nitrogen atmosphere of flow rate 400 ml/min.

Scanning electron microscopy studies

The surface morphology was examined by scanning electron microscope (Joel, JSM-840 A, Tokyo, Japan). The samples were fixed on a brass stub using double sided tape and then gold coated in vacuum by a sputter coater. The pictures were then taken at an excitation voltage of 15 KV.

Preparation of tablets

Tablets were prepared from the selected binary systems by direct compression method using 10 mm punches on a hand operated single punch tablet machine (Hicon, India). Each tablet consisted of solid dispersion amount ≅ 100 mg of AC. The formulated tablets prepared incorporating pure AC, KN-1 and AP-2 (coded as TAC, TKN-1 and TAP-2 respectively) and their PMs (TPM-1 and TPMAP-2).

Evaluation of tablets

Thickness and diameter

Both diameter and thickness of the tablet were determined using the average of three measurements in each case using vernier calipers in millimeters.

Hardness test

Hardness was measured using Monsanto hardness tester in terms of kg/sq.cm. Average hardness of three tablets was taken to study the reproducibility.

Friability test

Ten tablets from each batch were exposed to friability test apparatus for 100 rotations and percentage loss in weight was measured against initial weight.

Uniformity of weight

Twenty tablets were selected at random from each formulated batch to check the uniformity of weight using electronic balance. Average weight and maximum percent deviation (positive and negative) were determined.

Disintegration test

The disintegration test was carried out using disintegration test apparatus USP (Hicon, India) using distilled water as disintegration medium. One tablet was introduced into each tube and a disc was added to each tube. Assembly was suspended in the beaker containing 900 mL distilled water. Time for disintegration of all six tablets was noted down.

Assay

Twenty tablets were selected at random from each batch of formulated tablets and powdered. Ten mg powder from each tablet batch was diluted to 10 ml using methanol and the resultant solution was shaken

for one min using vortex mixer. All the samples were filtered using Whatman® No. 1 filter paper. From this, 0.5 mL solution was withdrawn and diluted to 10 mL with methanol. The concentration of AC in the filtrates was determined spectrophotometrically at 275 nm with reference to suitably constructed calibration curve of AC in methanol.

In vitro dissolution test

In vitro dissolutions for the formulated tablets of AC equivalent to 100 mg were analyzed for drug release profiles using USP 23 type II paddle dissolution apparatus at a temperature of 37°C and a stirring rate of 100 rpm, using 900 ml simulated intestinal fluid (SIF) pH 7.5 without enzyme as dissolution medium (n=3). Samples were withdrawn at predetermined time intervals and replaced with fresh dissolution medium, suitably diluted and analyzed at 275 nm.

Analysis of dissolution data

The dissolution data was analyzed by model independent parameters calculated at different time intervals, such as dissolution percent (DP), dissolution efficiency (DE) and time to release 50% of the drug ($t_{50\%}$). DP at different time interval and $t_{50\%}$ can be obtained from percent dissolution vs time profile/data. DE is defined as the area under the dissolution curve up to the time t, expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time. The DE can have a range of values depending on the time interval chosen. In any case, constant time interval should be chosen for the comparison of profiles. In the present investigation, DE_{10} and DE_{50} values were calculated from the dissolution data of each product and used for comparison.

The best formulated tablet was selected based on its evaluation parameters and compared with three commercial brands using similarity factor f_2 and difference factor f_1 [9].

$$f_1 = 100\left[\frac{\sum_{i=1}^{n}|R_i - T_i|}{\sum_{i=1}^{n}R_i}\right] \quad (1)$$

$$f_2 = 50\log\left[100\left(1\Big/\sqrt{1+\frac{1}{n}\sum_{i=1}^{n}(R_i - T_i)^2}\right)\right] \quad (2)$$

where R_i and T_i are the percentage dissolved of the reference and test profile respectively, at i^{th} time point.

Results and Discussion

The theoretical drug content in formulations containing PEG 6000 were calculated based on weight ratio of drug and carrier whereas for binary systems containing β-CD, the drug content was calculated based on molar ratio of drug and carrier. According to this, the theoretical drug content in AC: PEG 6000 in 1:1 and 1:2 binary system was 50% and 33.33% whereas for AC: β-CD 1:1 and 1:2 binary system was found to be 23.78% and 11.59% respectively. Hence, the range of theoretical drug content were between 11.59% to 50%. The actual drug content of binary systems ranged between 10.728 to 50.970% and exhibited good agreement with theoretical drug content (Table 1). The results of dissolution studies revealed that about 64% of AC was released from its pure powder form in 2 h which is due to its poor aqueous solubility. All the PMs showed marginal improvement in dissolution which may be attributed to hydrophilic nature of the carriers. However, both the type and amount of carrier influenced the release behavior as evidenced by comparison of dissolution performance of binary systems prepared in 1:1 ratio with that of 1:2 ratio (Fig. 1 and Fig. 2). When 1:1 molar ratio was used with β-CD, 86.75% drug was released at 30 min in kneaded product as compared to only 67.27% drug release when PEG 6000 was used in 1:1 weight ratio by using melt-solvent method. However, when 1:2 molar ratio was used with β-CD, 78.69% drug was released at 30 min by kneading method as compared to 90.44% drug release when PEG 6000 was used in 1:2 weight ratio by melt-solvent method. This fact suggested that the systems prepared with β-CD showed marked improvement in dissolution even in equimolar ratio but increment of molar ratio from 1:1 to 1:2 did not result in proportionate enhancement of AC release. The cogrinding and coevaporation was found to be less effective as compared to kneading method as kneading allowed better interaction of drug and carrier. Percent drug dissolved at 10 min (DP_{10}), dissolution efficiency

at 10 min (DE_{10}), and time for 50% drug release ($t_{50\%}$) were found to be 67.28%, 40.41%, 5.6 min for AC: PEG 6000 (1:2) prepared by melt-solvent method (AP-2) and 64.25%, 35.79%, 6.4 min for AC: β-CD (1:1) prepared by kneading method (KN-1) (Table 2). However, the AP-2 and KN-1 formulations showed 90.44% and 86.75% drug released at the end of 30 min compared to that of 21.93% by pure AC. This fact revealed that both the solid systems fulfilled the criteria of at least 85% drug release within 30 min which is set by FDA for immediate release dosage forms of class I drugs [10]. Hence, selected binary systems were further characterized by DSC and SEM and subjected to tablet preparation by direct compression.

Table 1 Percentage drug content of binary systems

Binary system	% drug content*
PM-AP-1	50.970 ± 0.808
AP-1	50.565 ± 0.076
PM-AP-2	32.313 ± 1.697
AP-2	31.882 ± 1.312
PM-1	20.149 ± 0.008
CG-1	18.666 ± 0.897
KN-1	21.280 ± 3.085
CE-1	19.364 ± 0.909
PM-2	10.554 ± 0.785
CG-2	12.647 ± 2.489
KN-2	10.728 ± 0.835
CE-2	11.339 ± 0.658

*n=3

AC is aceclofenac; CG-1 and CG-2 are coground dispersions of AC: β-CD in 1:1 and 1:2 ratios, respectively; KN-1 and KN-2 are kneaded products of AC: β-CD in 1:1 and 1:2 ratios, respectively, CE-1 and CE-2 are coevaporated products of AC: β-CD in 1:1 and 1:2 ratios, respectively; AP-1 and AP-2 are solid dispersions of AC: PEG 6000 in 1:1 and 1:2 ratios, respectively; PM-1 and PM-2 are physical mixtures of AC: β-CD in 1:1 and 1:2 ratios, respectively and PMAP-1 and PMAP-2 are physical mixtures of AC: PEG 6000 in 1:1 and 1:2 ratios, respectively.

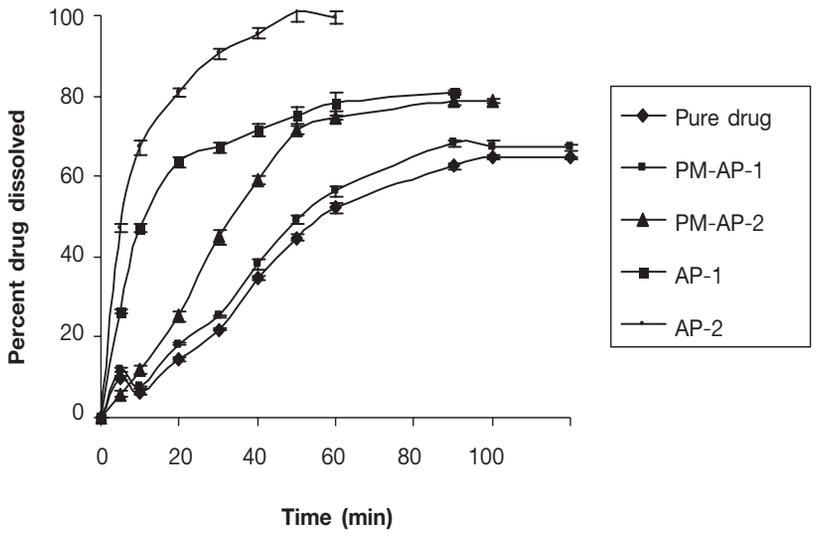

Figure 1 Comparative dissolution profiles of pure drug (aceclofenac, AC) and AC-PEG 6000 binary systems. PMAP-1 and PMAP-2 are physical mixtures of AC: PEG 6000 in 1:1 and 1:2 ratios, respectively. AP-1 and AP-2 are solid dispersions of AC: PEG 6000 in 1:1 and 1:2 ratios, respectively

Table 2 Model independent dissolution parameters of pure drug and binary systems

Binary systems	[a]DP_{10} (%)	[b]DE_{10} (%)	[a]DP_{30} (%)	[c]$t_{50\%}$ (min)
Pure drug AC	6.48	3.19	21.93	54.4
PM-AP-1	7.59	3.45	25.25	50.4
PM-AP-2	12.00	5.88	44.99	32.8
AP-1	47.12	24.95	67.27	11.2
AP-2	67.28	40.41	90.44	5.6
PM-1	11.18	5.71	44.76	36.0
CG-1	51.15	24.95	82.05	9.6
KN-1	64.25	35.79	86.75	6.4
CE-1	58.54	31.08	83.05	8.2
PM-2	9.50	4.79	42.08	38.2
CG-2	54.84	20.58	76.67	8.2
KN-2	63.57	34.11	85.74	7.0
CE-2	56.86	24.64	78.69	8.4

[a]DP = dissolution percent; [b]DE = dissolution efficiency; [c]$t_{50\%}$ = time to release 50% of the drug.

AC is aceclofenac; CG-1 and CG-2 are coground dispersions of AC: β-CD in 1:1 and 1:2 ratios, respectively; KN-1 and KN-2 are kneaded products of AC: β-CD in 1:1 and 1:2 ratios, respectively, CE-1 and CE-2 are coevaporated products of AC: β-CD in 1:1 and 1:2 ratios, respectively; AP-1 and AP-2 are solid dispersions of AC: PEG 6000 in 1:1 and 1:2 ratios, respectively; PM-1 and PM-2 are physical mixtures of AC: β-CD in 1:1 and 1:2 ratios, respectively and PM-AP-1 and PM-AP-2 are physical mixtures of AC: PEG 6000 in 1:1 and 1:2 ratios, respectively.

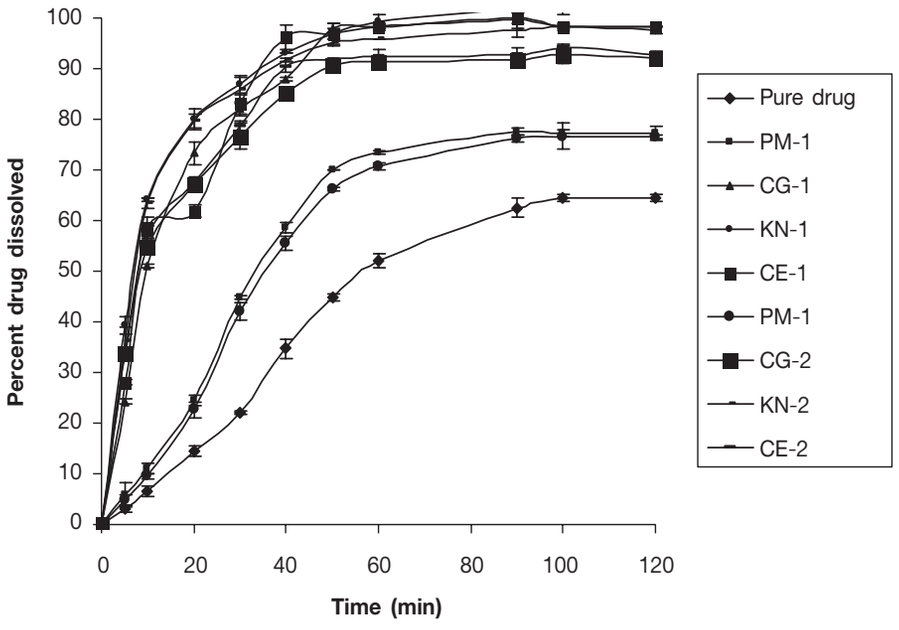

Figure 2 Comparative dissolution profiles of pure drug (aceclofenac, AC) and AC-βCD binary systems. CG-1 and CG-2 are coground dispersions of AC: β-CD in 1:1 and 1:2 ratios, respectively; KN-1 and KN-2 are kneaded products of AC: β-CD in 1:1 and 1:2 ratios, respectively, CE-1 and CE-2 are coevaporated products of AC: β-CD in 1:1 and 1:2 ratios, respectively; PM-1 and PM-2 are physical mixtures of AC: β-CD in 1:1 and 1:2 ratios, respectively

The solid state DSC studies revealed that the drug peak was almost disappeared with no significant change in carrier peak when PEG 6000 was used at higher mixing ratio using melt-solvent method (Fig. 3). Supporting evidence for possible complex formation was also obtained from DSC studies. The endothermic peak of AC observed at 150 °C corresponded to its melting point. Thermograms of PM, CG and CE showed comparatively broadened peak of β-CD with less intense peak of drug indicating decrease in the crystallinity due to mixing. The peak due to drug disappeared almost completely in thermogram of KN thereby suggesting the possibility of the formation of AC-β-CD complex.

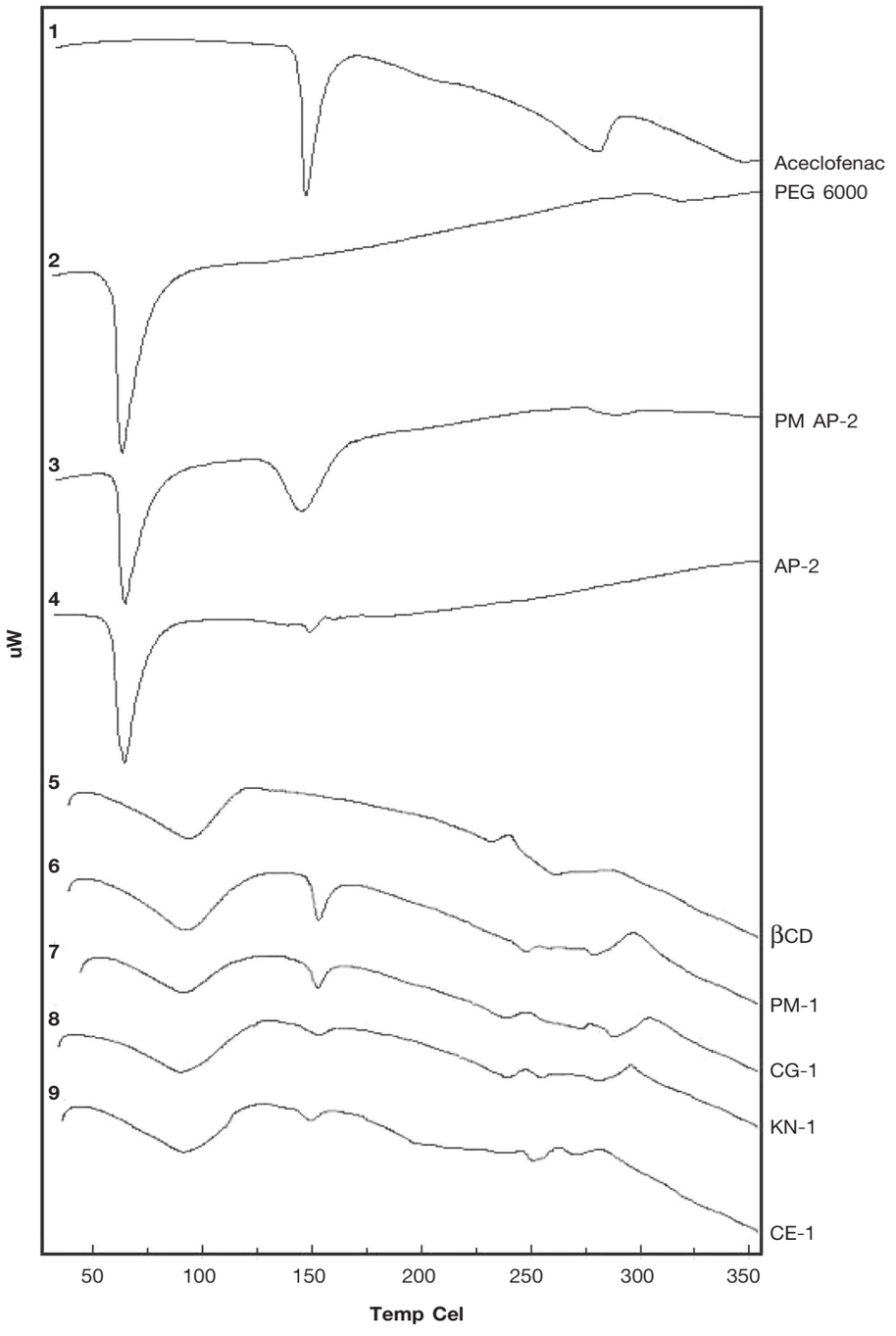

Figure 3 DSC thermograms of pure components and binary systems. CG-1 is coground dispersion of AC: β-CD in 1:1 ratio; KN-1 is kneaded product of AC: β-CD in 1:1 ratio; CE-1 is coevaporated product of AC: β-CD in 1:1 ratio; AP-2 is solid dispersion of AC: PEG 6000 in 1:2 ratio; PM-1 is physical mixtures of AC: β-CD in 1:1 ratio and PMAP-2 is physical mixture of AC: PEG 6000 in 1:2 ratio

The results of SEM studies were in agreement with DSC thermograms, as in the micrographs, it was not possible to distinguish pure components in case of binary systems prepared by melt-solvent method with PEG 6000 with uniform distribution of drug in polymer matrix. However, the corresponding physical mixture was seen merely as the combination of characteristics of pure drug and carrier (Fig. 4). The solid state characterization suggested possibility of formation of solid solution in case of AC: PEG 6000 binary systems at 1:2 mixing ratio. The possible mechanism could be that, the dispersed component that is the drug was molecularly dispersed in the carrier matrix possessing no crystal structure in the solid solution and therefore, the energy normally required to break up the crystalline structure of the drug before it can dissolve is not a limitation to the release of a drug from a solid solution [11]. However, more advanced analytical methods such as FTIR, Raman spectroscopy and solid state NMR should be employed to study and confirm the nature of the interactions between the drug and the carrier and to define the solid state structure of the solid dispersions [12].

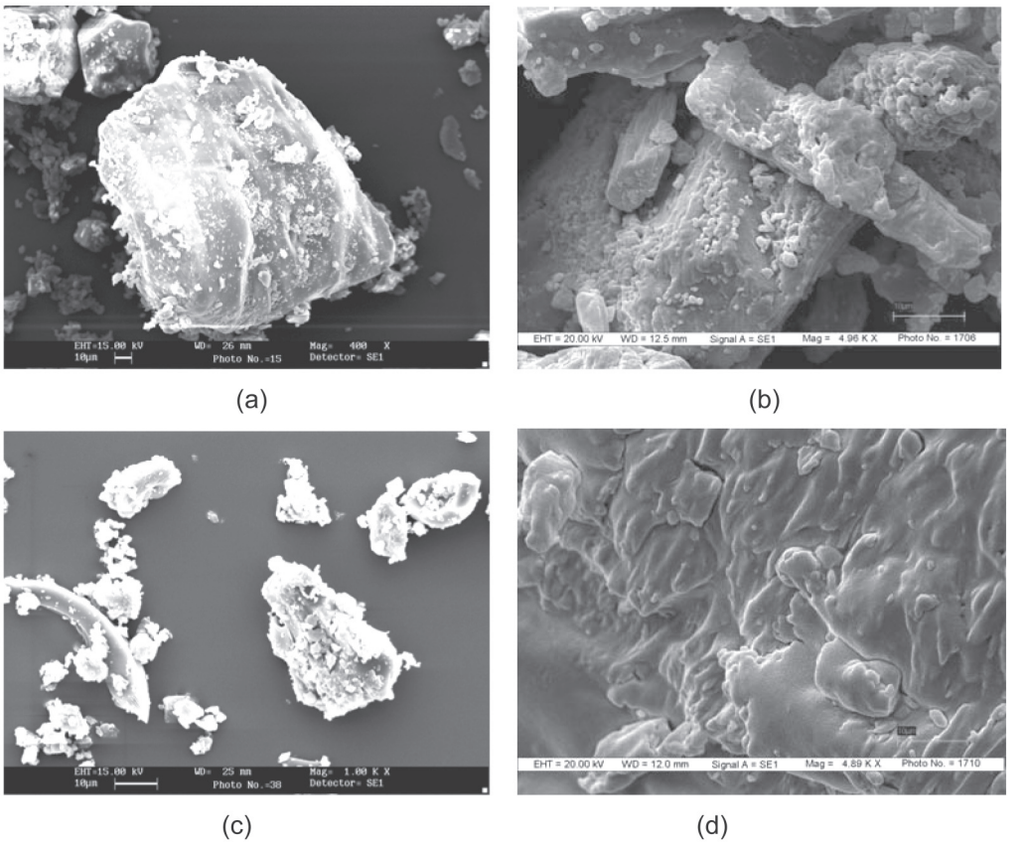

Figure 4 EM images of (a) aceclofenac (b) PEG 6000 (c) physical mixture of AC:PEG 6000 (1:2) and (d) solid dispersion of AC:PEG 6000 (1:2)

The formulated tablets prepared incorporating pure AC, KN-1 and AP-2 (coded as TAC, TKN-1 and TAP-2 respectively) and their PMs (TPM-1 and TPMAP-2) (Table 3) were satisfactory with respect to physical parameters such as thickness, diameter, hardness, friability and drug content (Table 4). The tablets also complied with test for uniformity of weight and disintegration time (Table 5). The dissolution studies from formulated tablets exhibited almost expected dissolution behavior as that previously obtained from their binary systems, with best dissolution enhancement by TAP-2. Further, it was interesting to note that none of the commercial brands provided complete drug release even at 2 h whereas TAP-2 showed 100% drug release within 50 min. The TAP-2 provided markedly improved results of DP_{30}, $t_{50\%}$, and DE_{50} as compared to three commercial brands A, B and C (Fig. 5). The similarity factor f_2 and difference factor f_1 are the important model

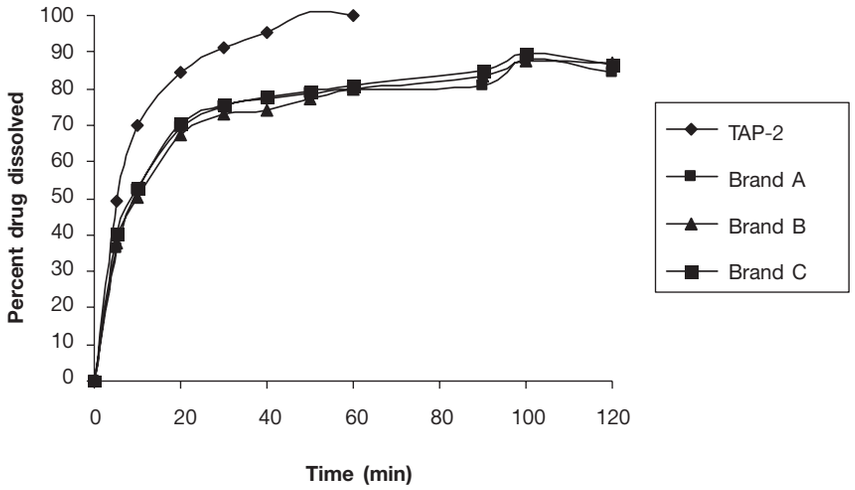

Figure 5 Comparative dissolution profiles of best formulated and marketed tablets. TAP-2 is formulated tablets incorporating AC:PEG 6000 1:2 binary system, A, B and C are marketed brands of AC tablets

Table 3 Composition for directly compressible tablets of aceclofenac incorporating selected binary systems

Ingredients (mg)	Formulations*				
	TAC	**TPM-AP-2**	**TAP-2**	**TPM-1**	**TKN-1**
Aceclofenac	100.00	326.19	313.65	496.30	469.92
Maize starch (5.0% w/w)	30.0	30.0	30.0	30.0	30.0
Sodium starch glycolate (2.0% w/w)	12.0	12.0	12.0	12.0	12.0
Magnesium stearate (0.2 % w/w)	1.20	1.20	1.20	1.20	1.20
Talc (1% w/w)	6.0	6.0	6.0	6.0	6.0
Spray-dried lactose q.s.	600	600	600	600	600

*TAC is tablet formulated with pure AC; TPM-AP-2 and TAP-2 are tablets formulated incorporating physical mixture and solid dispersion of AC:PEG 6000 1:2 binary system; TPM-1 and TKN-1 are tablets formulated incorporating AC:βCD 1:1 physical mixture and kneaded product.

Table 4 Physical parameters of formulated tablets

Formulation	Physical parameters			
	Diameter*	Thickness*	Hardness*	Friability**
TAC	10.412 ± 0.123	7.632 ± 0.045	5.008 ± 0.235	0.003
TPM-AP-2	10.012 ± 0.145	6.983 ± 0.062	5.162 ± 0.468	0.991
TAP-2	10.642 ± 0.188	7.062 ± 0.098	4.501 ± 0.881	0.002
TPM-1	09.998 ± 0.102	7.428 ± 0.157	4.663 ± 0.610	0.015
TKN-1	10.320 ± 0.113	7.002 ± 0.062	5.168 ± 0.957	0.443

*values are average of three determinations, **test has been performed for 10 tablets.

TAC is tablet formulated with pure AC; TPM-AP-2 and TAP-2 are tablets formulated incorporating physical mixture and solid dispersion of AC:PEG 6000 1:2 binary system; TPM-1 and TKN-1 are tablets formulated incorporating AC:βCD 1:1 physical mixture and kneaded product.

Table 5 Results for official tests of tablets

Formulation	Average weight* (g)	Disintegration time** (min)	Assay* (%)
TAC	0.5868 ± 0.0021	5.50 ± 0.25	100.258 ± 1.587
TPM-AP-2	0.5910 ± 0.0025	5.34 ± 0.25	99.326 ± 2.567
TAP-2	0.6100 ± 0.0030	3.50 ± 0.18	98.472 ± 1.679
TPM-1	0.5822 ± 0.0029	4.98 ± 0.24	100.568 ± 1.773
TKN-1	0.5510 ± 0.0030	3.32 ± 0.26	99.489 ± 3.421

*Values are average of twenty tablets **Values are average of six tablets.

TAC is tablet formulated with pure AC; TPM-AP-2 and TAP-2 are tablets formulated incorporating physical mixture and solid dispersion of AC:PEG 6000 1:2 binary system; TPM-1 and TKN-1 are tablets formulated incorporating AC:βCD 1:1 physical mixture and kneaded product.

Table 6 Results of model independent parameters of best formulated tablet and marketed brands

Formulation*	DP_{30}	DP_{50} (%)	DE_{50} (%)	$t_{50\%}$ (min)	f_1	f_2
TAP-2	91.14	100.79	80.33	33.80	27.02	54.39
Brand A	74.99	78.69	65.30	47.60	0.85	99.34
Brand B	73.31	77.35	62.39	47.70	2.54	95.05
Brand C	75.66	79.36	66.01	46.90	0.00	100.00

*TAP-2 is formulated tablets incorporating AC:PEG 6000 1:2 binary system, A, B and C are marketed brands of AC tablets.

DP = dissolution percent; DE = dissolution efficiency; $t_{50\%}$ = time to release 50% of the drug; f_2 = similarity factor; f_1 = difference factor.

independent parameters for the mathematical comparison of the dissolution data of different formulations. The values of f_2 between 50 to 100 as well as f_1 between 0 to 15 showed similarity of the dissolution profiles as per the SUPAC FDA guidance [13]. The values of f_2 and f_1 were 54.39 and 27.02 respectively for the formulated tablet, when brand C was taken as reference, indicated that dissolution profile of formulated tablet was not similar to that of the marketed brands (Table 6). Further, the amount of AC: PEG 6000 (1:2) binary system which was equivalent to 100 mg of AC was found to be 313.65 mg based on drug content analysis, which was practically feasible to be formulated as tablet dosage form for oral administration.

Conclusion

The dissolution enhancement from binary systems depended on nature of carrier, mixing ratio and method of preparation. PEG 6000 was found more effective carrier as compared to β-CD for improving the dissolution

properties of AC at higher ratio and the melt-solvent method was effective to achieve AC: PEG 6000 binary system with good flow properties and compressibility. The physicochemical characterization at solid and solution state indicated that the enhancing effect of binary systems on dissolution was mainly attributed to the transformation of AC into the amorphous state as well as improvement of solubility of binary systems in presence of water soluble carriers. The studies revealed that β-CD and PEG 6000 can be successfully used to improve the dissolution and possibly bioavailability of poorly water soluble aceclofenac by solid dispersion approach in a simple and economic manner. The studies also offered promising oral solid dosage forms after scaling up the formulation in order to be potential commercial oral dosage form of aceclofenac.

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