

## Development and *in Vitro* Evaluation of Ibuprofen Mouth Dissolving Tablets Using Solid Dispersion Technique

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The aim of present study was to prepare and evaluate mouth dissolving tablets of ibuprofen (IBU). Ternary solid dispersion (SD) of IBU was prepared using PEG 4000 as carrier and Tween 80 as surfactant. The SD formulations were prepared by solvent evaporation and melt solvent method by varying ratio of PEG 4000. Different weight ratio of carrier, drug and surfactant 5 : 5 : 1, 10 : 5 : 1, 25 : 5 : 1, 35 : 5 : 1 and 45 : 5 : 1 was taken. The prepared SD formulations were characterized by Fourier Transform Infra-Red (FT-IR) spectroscopy, differential scanning calorimetry (DSC), X-ray diffraction (XRD) and *in vitro* drug release. Mouth dissolving tablets of IBU were formulated using optimized SD formulation of carrier : drug : surfactant ratio, 10 : 5 : 1 along with super-disintegrants. The best developed formulation was compared with marketed tablet product of IBU. From IR and XRD studies, it may be concluded that there is change in crystalline form of drug into amorphous during formation of SD. From DSC studies, it was predicted that drug was completely dissolved in the carrier. Mouth dissolving tablets containing Ac-Di-Sol (12%) as super-disintegrant showed the fastest disintegration (202s) and *in vitro* drug release (84.57%). The release pattern of all developed formulations followed Peppas–Korsmeyer model as the plot between log cumulative % drug released versus log time showed good linearity ( $r > 0.99$ ) with a comparatively high slope ( $n$ ) value within the range of 0.44–0.67. The tablets containing SD exhibited better dissolution profile than commercial tablets.

**Key words** mouth dissolving tablet; solid dispersion; ibuprofen; hydrophilic carrier; dissolution

Since the introduction of mouth dissolving tablet (MDT) in 1980s, it has become one of the fastest growing segments of oral drug delivery. About one-third of the world's population mainly the geriatric and pediatric patient have swallowing difficulties and for such a group, MDT is emerged as an attractive alternative. Mouth dissolving tablets are characterized by hydrophilic matrix which allows rapid disintegration of the tablets when comes in contact with saliva and disintegrates/dissolves/disperses in saliva within few seconds, without the need of water, so, alleviating the problem of swallowing or chewing. Techniques that have commonly been used to improve dissolution and bioavailability of poorly water-soluble drugs, in general, include micronization, the use of surfactant and the formation of solid dispersion (SD).<sup>1</sup> The SD approach has been widely and successfully applied to improve the solubility, dissolution rates, and consequently, the bioavailability of poorly water soluble drugs. A number of drugs have been shown to improve their dissolution character, which converted to SDs. To date, some reports on the formulation of these systems have appeared.<sup>2–5</sup> An obstacle of SD technology in pharmaceutical product development is that a large amount of carrier, *i.e.*, more than 50 to 80% wt/wt, was required to achieve the desired dissolution. This high percentage of carrier causes consistency of product performance at the time of manufacturing. This is a major consideration in that the number of market products arising from this approach has been less than expected.<sup>6–9</sup> With regard to carriers for SD formulations, many carriers such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), hydroxypropylmethylcellulose (HPMC), hydroxypropylcellulose, hydroxypropyl methylcellulose phthalate (HPMCP), Gelucires<sup>®</sup>, Eudragits<sup>®</sup> and chitosans have been reported to improve the solubility and bioavailability of poorly water soluble drugs.<sup>10–12</sup> Among the various carriers used in the for-

mation of SD, PEG is most commonly used. PEGs are semi-crystalline polymers that have been used extensively in the SDs preparation for their wetting, solubilizing and surface active properties.<sup>13</sup> Newa *et al.*<sup>14</sup> reported enhancement of solubility, dissolution and bioavailability of ibuprofen (IBU) in SD systems using PEG 8000 as a meltable hydrophilic polymer carrier. The non-ionic surfactant Tween 80 was used as the third component in the ternary SD system.<sup>15</sup>

Mouth dissolving tablets of itraconazole,<sup>16</sup> valdecoxib,<sup>17</sup> diazepam,<sup>18</sup> glyburide,<sup>19</sup> clonazepam,<sup>20</sup> and rofecoxib<sup>15</sup> were prepared using SD technique. Ibuprofen (IBU) is a propionic acid derivative, non steroidal anti inflammatory drug (NSAIDs). It is available as an “Over the Counter” (OTC) drug. It is used for relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and relief of mild to moderate pain and is used in chronic and acute conditions of pain and inflammation. Rate of bioavailability of IBU is highly variable due to their low aqueous solubility. One of the major problems with drug is its very low solubility in biological fluids and its short biological half-life of 2 h.<sup>21</sup> Thus these two factors act as the rate determining step or the barrier to rapid onset of action upon oral ingestion of IBU. The aim of the present study was to prepare and evaluate the SD formulation of IBU. Moreover, it was also attempted for the incorporation of optimized SD formulation for the development of mouth dissolving tablets of IBU.

### Experimental

**Materials** Ibuprofen (IBU) was kindly received as gift sample from M/s Kentreck Laboratories Pvt. Ltd. Ahmedabad, India. Ac-Di-sol<sup>®</sup> (cross-carmellose sodium, FMC Co.) and Avicel PH-102<sup>®</sup> (microcrystalline cellulose, FMC Co.) were obtained as gift sample from M/s Reliance cellulose, Secunderabad, India. Primojel<sup>®</sup> (sodium starch glycolate, DMV-Fonterra Excipients) was supplied as gift sample from Prachim Chemicals, Ahmedabad, India. Polyethylene Glycol (PEG) 4000 and Tween 80 were procured from Central Drug House (CDH) New Delhi, India. Color (Tartrazine) and Flavor

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(Pineapple) were purchased from Garden flavor Co. Pvt. Ltd., Mumbai, India. All other chemicals and reagents used were of analytical reagent grade.

**Preparation of Solid Dispersion Formulations** Two methods were used to prepare SD of IBU with PEG 4000, which are as follows:

The SD of IBU was prepared by conventional solvent evaporation method<sup>22)</sup> using PEG 4000 as a carrier and Tween 80 as surfactant. IBU and PEG 4000 were weighed accurately in the different ratios and triturated in a mortar and pestle for 5 min. This physical mixture was then dissolved in ethanol with constant stirring. To this solution, Tween 80 was added and stirred. 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 12 h over anhydrous calcium chloride. Dried masses were powdered and passed through sieve (#60). The ratio and assigned batch code are given in Table 1.

SDs containing IBU and carrier in different proportions were prepared by melt solvent method.<sup>23)</sup> The carrier, PEG 4000 was first melted at a temperature of  $58^\circ\text{C}$  in a heating mantle (Rolex, Mumbai, India). The IBU dissolved in ethanol was incorporated to the melt of PEG 4000 and then Tween 80 was added to it and kept in an ice bath for sudden cooling. The solidified mass was scrapped, crushed, pulverized and passed through sieve (#80). The ratio and assigned batch code are given in Table 1.

**Fourier Transform Infrared Spectroscopy (FT-IR)** FT-IR spectra were obtained on a Shimadzu 8400S FT-IR 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)** DSC examination was conducted for the optimized formulation, pure drug, and carrier using a DSC instrument (Mettler 305, Switzerland). Samples of 2–6 mg were placed in aluminum pans (Al-Crucibles, 40 Al) and sealed. The probes were heated from 30 to  $100^\circ\text{C}$  at a rate of  $5^\circ\text{C}/\text{min}$  under nitrogen atmosphere. The temperature was calibrated using pure indium with a melting point of  $156.60^\circ\text{C}$ . An empty pan was used as a reference.

Table 1. Assignment of Product Code to Different Formulations Prepared by Solvent Evaporation and Melt Solvent Method

S. No.	Carrier : drug : surfactant ratio (PEG 4000 : IBU : Tween 80)	Product code assigned to SDs prepared by	
		Solvent evaporation method	Melt solvent method
1	5 : 5 : 1	SEA1	MSA1
2	10 : 5 : 1	SEA2	MSA2
3	25 : 5 : 1	SEA3	MSA3
4	35 : 5 : 1	SEA4	MSA4
5	45 : 5 : 1	SEA5	MSA5

IBU, ibuprofen; PEG 4000, polyethylene glycol 4000; SEA1–5, solid dispersion formulations of ibuprofen prepared by solvent evaporation method; MSA1–5, solid dispersion formulations of ibuprofen prepared by melt solvent method.

Table 2. Composition of Ibuprofen Mouth Dissolving Tablet

S. No.	Ingredients	Formulation code					
		MDT1	MDT2	MDT3	MDT4	MDT5	MDT6
1	MSA2 (solid dispersion formulation of ibuprofen)	40	40	40	40	40	40
2	Superdisintegrants						
	Primojel	4	8	12	—	—	—
	Ac-Di-Sol	—	—	—	8	10	12
3	Talc	2	2	2	2	2	2
4	Magnesium stearate	1	1	1	1	1	1
5	Flavor (pineapple)	0.5	0.5	0.5	0.5	0.5	0.5
6	Color (tartrazine)	0.5	0.5	0.5	0.5	0.5	0.5
7	Sodium saccharine	0.5	0.5	0.5	0.5	0.5	0.5
8	Avicel PH-102	51.5	47.5	43.5	47.5	45.5	43.5
	Total	100%	100%	100%	100%	100%	100%

MDT1–6, mouth dissolving tablets.

**X-Ray Diffraction (XRD)** X-Ray patterns were obtained using XPERT-PRO diffractometer (PANalytical, Amelo, Netherlands) with Ni-filtered  $\text{CuK}\alpha$  radiation. Diffractograms were run at scan type continuous, a voltage of 30 kV, a current of 40 mA, scan speed  $4^\circ\text{ min}^{-1}$  over the  $0\text{--}90^\circ$  diffraction angle ( $2\theta$ ) and the count range 2000 cps.

**In Vitro Dissolution Study** The quantity of SD equivalent to 50 mg of IBU was filled in hard gelatin capsule by hand filling method. Dissolution study of capsules was conducted using USP dissolution apparatus II (Dissolution rate test apparatus, USP/IP/BP/STP, Electrolab, Mumbai, 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 concentration of IBU was estimated by using UV spectroscopy at  $264\text{ nm}$ .<sup>24)</sup>

**Preparation of IBU Tablets** Different batches of IBU containing mouth dissolving tablet were prepared according to the proportions given in Table 2. The raw materials were passed through a sieve (#40) prior to mixing. Powdered SD, containing amount equivalent to 200 mg of IBU, 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 500 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 weight individually. The average weight and standard deviation were calculated. Five tablets from each batch were crushed and tablet powder equivalent to 50 mg of IBU was weighed and estimated for drug content.

The procedure for determination of wetting time was followed as reported by Ghoel *et al.*<sup>25)</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. A 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. For determination of disintegration time, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted.

**In Vitro Drug Release Study** The *in vitro* drug release of conventional marketed tablets of IBU (Brufen; IBU 200 mg, Abbott Laboratories, 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  $37 \pm 0.5^\circ\text{C}$ . At appropriate time intervals, 5 ml of the mixture was withdrawn, filtered through a Whatman filter paper (#40) and equal volumes of fresh dissolution medium were replaced. Samples were analyzed for IBU content by using UV spectrophotometer 2101 (Systronics, India) at  $264\text{ nm}$ .

**Release Kinetics** Five kinetic models including the zero order (Eq. 1),

first order (Eq. 2), Higuchi matrix (Eq. 3), Peppas–Korsmeyer (Eq. 4) and Hixon–Crowell (Eq. 5) release equations were applied to process the *in vitro* release data of tablets to find the equation with the best fit.<sup>26,27)</sup>

$$R = k_1 t \quad (1)$$

$$\log UR = \frac{k_2 t}{2.303} \quad (2)$$

$$R = k_3 t^{0.5} \quad (3)$$

$$R = k_4 t^n \quad (4)$$

or

$$\log R = \log k_4 + n \log t$$

$$(UR)^{1/3} = k_5 t \quad (5)$$

where  $R$  and  $UR$  are the released and unreleased percentages, respectively, at time ( $t$ );  $k_1$ ,  $k_2$ ,  $k_3$ ,  $k_4$ , and  $k_5$  are the rate constants of zero order, first order, Higuchi matrix, Peppas–Korsmeyer and Hixon–Crowell model, respectively.

## Results and Discussion

All of the ingredients used for the preparation of the ternary systems were dissolvable in ethanol. The solvent was evaporated from the system until the weight of the remaining solid mass was constant. Consequently, the solvent was expected to be completely removed from the system.

**Fourier Transform Infrared Spectroscopy** In order to get evidence on the possible interaction of the drug with carrier, FT-IR was used. Figure 1 shows the FT-IR spectra of original IBU, PEG 4000, physical mixture of IBU/PEG 4000, and IBU SDs prepared by solvent evaporation method and melt solvent method. Pure IBU displays a peak characteristic of C=O stretching vibration at  $1720 \text{ cm}^{-1}$  and a broad peak at  $3450 \text{ cm}^{-1}$  indicative of O–H stretching of acidic group

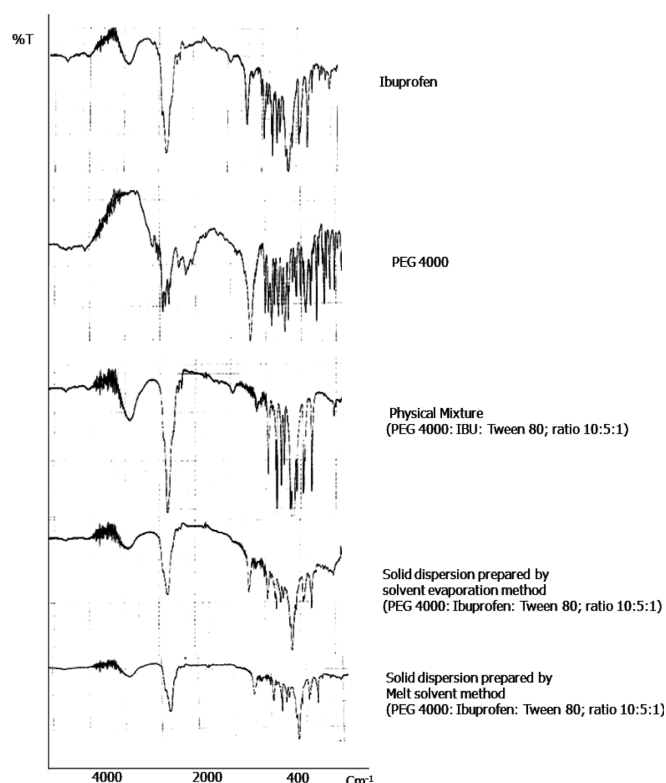


Fig. 1. FT-IR Spectra of Ibuprofen, PEG 4000, Physical Mixture of Ibuprofen and PEG 4000, SD Prepared by Solvent Evaporation Method and Melt Solvent Method

and a medium peak at  $800 \text{ cm}^{-1}$  for benzene ring. The spectrum of PEG 4000 showed important peaks at  $2955 \text{ cm}^{-1}$  of C–H stretching vibration and C=C at  $1507 \text{ cm}^{-1}$ . The FT-IR spectra of physical mixture and SDs still showed peak of C=O stretching vibration, O–H vibration of the acidic group, and the important peaks of PEG 4000 with decrease in the peak height. Consequently, the FT-IR spectra of physical mixture and SDs seemed to be of drug and PEG 4000 spectra with changes in peak height. It may be due to the change in the physical form of the drug *i.e.*, from crystalline form to amorphous form.

**Differential Scanning Calorimetry** DSC thermograms of the (a) IBU, (b) PEG 4000, (c) physical mixture of IBU with the PEG 4000 and SD formulation prepared by (d) solvent evaporation and (e) melt solvent method are shown in Fig. 2. IBU exhibited an endothermic peak at around  $80^\circ\text{C}$ , which corresponds to the melting of IBU. The carrier, PEG 4000 showed an endothermic peak at around  $60^\circ\text{C}$ , which corresponds to the melting point of PEG 4000. The physical mixture of IBU and PEG 4000 showed two endothermic peaks one at about  $75.45^\circ\text{C}$  and another at  $56.45^\circ\text{C}$  which corresponds for IBU and PEG 4000, respectively. While in case of SD prepared by solvent evaporation and melt solvent method, only one endothermic peak was observed at around  $51^\circ\text{C}$  and  $57^\circ\text{C}$ , respectively. The disappearance of characteristic endothermic peak of IBU in SD gives an idea that IBU might be in dissolved state in melted PEG 4000. Only one endothermic peak for SDs prepared by solvent evaporation and melt solvent method was observed, which corresponds to a near value of melting point of PEG 4000.<sup>28)</sup> Tween 80 was liquid at room temperature, therefore it was not possible to record a DSC trace under the experimental conditions used.

**X-Ray Diffraction** In general, it is well known that a drug in SD formulation often exists in an amorphous form. The amorphous form of a drug has a higher thermodynamic activity than its crystalline form. The higher thermodynamic energy level of the drug leads to the rapid dissolution property.<sup>29,30)</sup> The XRD investigation was carried out to investi-

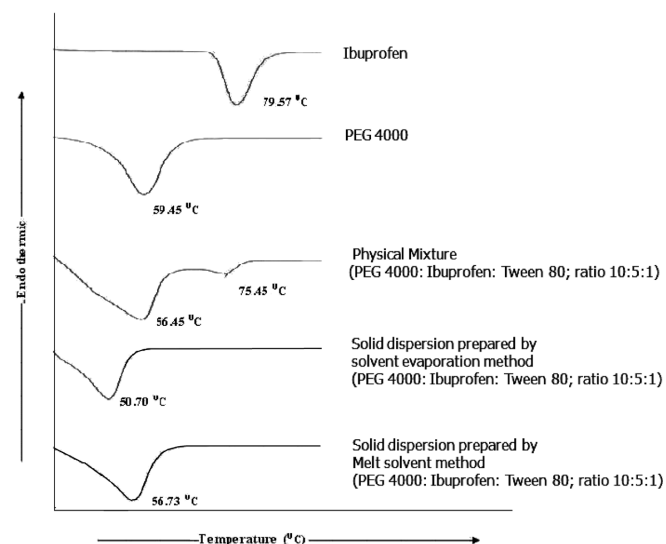


Fig. 2. DSC Thermograms of Ibuprofen, PEG 4000, Physical Mixture of Ibuprofen and PEG 4000, and SD Prepared by Solvent Evaporation Method and Melt Solvent Method

gate the crystallinity of IBU in SD formulation with PEG 4000, prepared by the solvent evaporation and melt solvent method. The XRD pattern of IBU, PEG 4000, the physical mixture of IBU with PEG 4000 and SD formulations of IBU prepared by solvent evaporation method and melt solvent method are shown in Fig. 3. The XRD pattern of the physical mixture of IBU with PEG 4000 was similar to the XRD pattern of IBU crystalline powder alone. It was confirmed that the crystallinity of IBU does not change in the physical mixture with the PEG 4000 *i.e.* XRD patterns of pure drug and physical mixture showed intense peaks indicating the crystalline nature of IBU. The peaks are broadened in the SD formulations indicating the amorphous nature of IBU, which might be also the reason for enhanced dissolution.<sup>31)</sup>

**In Vitro Drug Release Studies of SDs** The dissolution behavior of IBU from various SD formulations prepared by solvent evaporation method and melt solvent method was examined in comparison with the intact drug by plotting the percentage of drug released against time as shown in Figs. 4 and 5, respectively. The drug release from different SD formulations prepared by solvent evaporation method (SEA) followed the order: SEA2>SEA1>SEA3>SEA4>SEA5. Moreover, in case of solid dispersion formulations prepared by melt solvent method followed the pattern: MSA2>

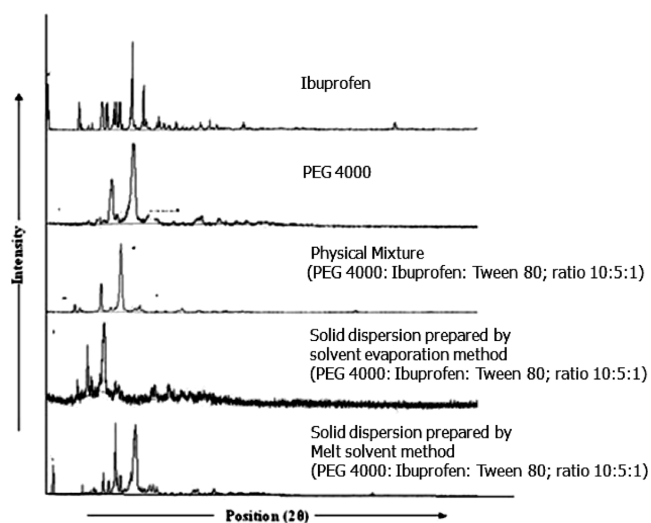


Fig. 3. XRD Patterns of Ibuprofen, PEG 4000, Physical Mixture, SD Prepared by Solvent Evaporation and Melt Solvent Method

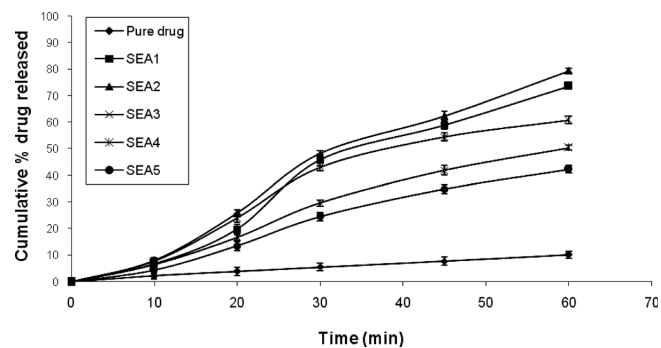


Fig. 4. Drug Release Profile of Different SD Formulations Prepared by Solvent Evaporation Method in Phosphate Buffer (pH 6.8)

Values are mean  $\pm$  S.D. ( $n=3$ ). SEA1–5, solid dispersion of ibuprofen prepared by solvent evaporation method.

MSA1>MSA3>MSA4>MSA5. In all cases, SDs exhibited faster dissolution rates than the intact drug. This was supposed to be due to the effect of molecular dispersion of drug in PEG, the decreased crystallinity of IBU existing in SDs, and the effect of Tween 80 in the ternary system.<sup>6)</sup> It was found that dissolution of all the SDs were in the range of 42 to 80% than that of the pure IBU, which was found to be 15.8% during 1h study period. 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 10:5:1, but after this there is no significant increase in the dissolution of the drug was reported. This might be due to complete dispersion of drug with PEG 4000 at 10:5:1 ratio. Further, in case of increase of carrier, 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. Slightly better drug release profile was exhibited by formulation prepared by melt solvent method, MSA2 which released 80.10% of the drug as compared with SEA2 (79.42%) in 1h study period. So, formulation MSA2 was selected for further studies and tablets were formulated from it.

**Evaluation of Mouth Dissolving Tablets of IBU** The uniformity of thickness and diameter values acceptable and was found to be in the range of 4 to 4.20 mm and 10 to 10.05 mm, respectively. The weight uniformity met the United States Pharmacopoeia (USP) requirements, with less than  $\pm 5\%$  variation in all cases. All the tested formulations showed acceptable drug content values, with less than  $\pm 5\%$  deviation. Super-disintegrants are generally used for developing mouth dissolving tablets or for improvement of solubility for active pharmaceutical ingredients. These super-disinte-

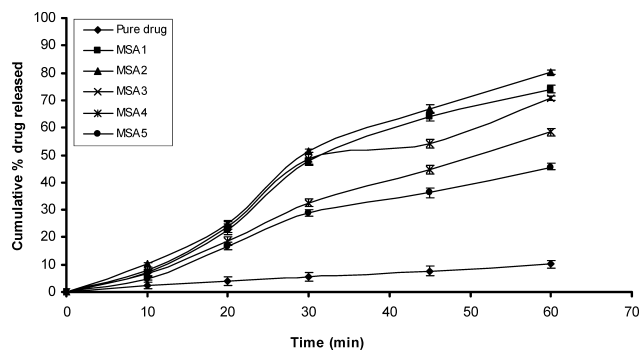


Fig. 5. Drug Release Profile of Different SD Formulations Prepared by Melt Solvent Method in Phosphate Buffer (pH 6.8)

Values are mean  $\pm$  S.D. ( $n=3$ ). MSA1–5, solid dispersion of ibuprofen prepared by melt solvent method.

Table 3. Wetting and Disintegration Time of Tablet Formulations

S. No.	Batches	Wetting time (s)	Disintegration time (s)
1	MDT1	299.50 $\pm$ 3.12	456 $\pm$ 4
2	MDT2	244.75 $\pm$ 3.25	365 $\pm$ 6
3	MDT3	190.75 $\pm$ 2.87	302 $\pm$ 4
4	MDT4	226.25 $\pm$ 2.63	293 $\pm$ 5
5	MDT5	177.25 $\pm$ 3.14	254 $\pm$ 3
6	MDT6	146.50 $\pm$ 3.42	202 $\pm$ 8

MDT1–6, mouth dissolving tablets. Values are mean  $\pm$  S.D. ( $n=6$ ).



Table 4. Release Kinetics of Mouth Dissolving Tablet of Ibuprofen

S. No	Batch	Release kinetics										
		Zero order		First order		HM model		P-K model			H-C model	
		$k_1$	$r$	$k_2$	$R$	$k_3$	$r$	$k_4$	$r$	$n$	$K_5$	$r$
1	MDT1	0.0150	0.986	0.0036	0.819	7.20	0.974	0.656	0.9955	0.44	2.925	0.706
2	MDT2	0.0145	0.974	0.0033	0.812	7.44	0.976	0.550	0.9952	0.66	2.915	0.686
3	MDT3	0.0134	0.950	0.0025	0.792	8.02	0.970	0.582	0.9910	0.58	2.875	0.616
4	MDT4	0.0141	0.975	0.0031	0.816	7.61	0.974	0.547	0.9957	0.67	2.931	0.688
5	MDT5	0.0140	0.970	0.0029	0.815	7.73	0.971	0.556	0.9942	0.65	2.929	0.674
6	MDT6	0.0124	0.957	0.0017	0.790	8.68	0.974	0.618	0.9917	0.54	2.987	0.561

MDT1–6, mouth dissolving tablets;  $r$ , correlation coefficient;  $n$ , slope value for P–K model;  $k_1$ ,  $k_2$ ,  $k_3$ ,  $k_4$ , and  $k_5$ , rate constants of zero order, first order, Higuchi matrix (HM), Peppas–Korsmeyer (P–K) and Hixon–Crowell (H–C) model, respectively.

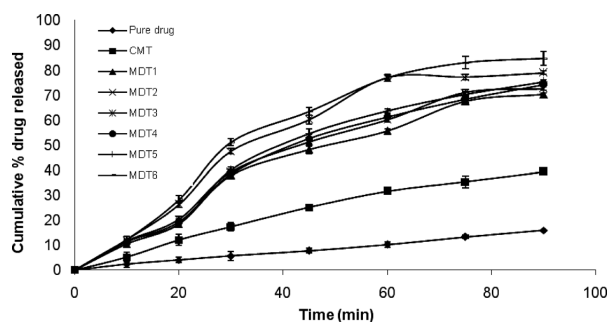


Fig. 6. Drug Release Profile of Pure Drug, Conventional Marketed Tablet and Different Tablet for Mulations in Phosphate Buffer (pH 6.8)

Values are mean  $\pm$  S.D. ( $n=3$ ). CMT, conventional marketed tablet of ibuprofen; MDT1–6, mouth dissolving tablets.

grants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. Two different super-disintegrants, primojel and Ac-Di-Sol in different concentrations were tried to achieve fast dispersion of tablets. It is observed that the disintegration time of the tablets decreased (from 299.5 to 190.75 s) with increase in the content of primojel. Also, the disintegration time decreased (from 226.25 to 146.5 s) with increase in Ac-Di-Sol content. It indicates that increase in the level of primojel and Ac-Di-Sol had a positive effect on the disintegration of MDT formulations. Wetting time of tablets decreased with increase in primojel and Ac-Di-Sol content. The wetting time and disintegration time of different tablet formulations are summarized in Table 3.

The drug release from pure drug, marketed formulation of IBU and different MDT formulations followed the order: MDT6 > MDT5 > MDT4 > MDT3 > MDT2 > MDT1 > CMT > Pure drug. The pattern also provides an idea about the effect of primojel (sodium starch glycolate) content on drug release, *i.e.*, more the primojel content, higher was the drug release in MDT1–3 formulations. The *in vitro* drug release profile of MDT formulations was found to be increased on increase of Ac-Di-Sol (croscarmellose sodium) as super-disintegrant in tablets (MDT4–6). The faster increase in drug release of IBU with the increase in Ac-Di-Sol content may be attributed to rapid swelling and disintegration of tablet into apparently primary particles. While, tablets prepared with primojel, 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. Tablets containing Ac-Di-Sol (12%) showed the fastest disintegration (202 s) and drug release (84.57%).

The correlation coefficient ( $r$ ) was used as an indicator of the best fitting for each of the models considered (Table 4). The release pattern of all developed formulations (MDT1–6) followed Peppas–Korsmeyer model as the plot between log cumulative % drug released *versus* log time showed good linearity ( $r > 0.99$ ) with a comparatively high slope ( $n$ ) value within the range of 0.44–0.67. If  $n < 0.43$ , a Fickian diffusion (case-I),  $0.43 < n < 0.85$ , a non-Fickian transport and  $n > 0.85$ , a case-II transport (zero order) drug release mechanism dominates. These  $n$  values appear to indicate a coupling of diffusion and erosion mechanism (known as anomalous non-fickian diffusion).<sup>32</sup> Hence, diffusion coupled with erosion may be the mechanism of IBU release from mouth dissolving tablets.

## Conclusion

From present study, it is concluded that solid dispersion technique can be successfully applied for preparation of mouth dissolving tablet of IBU. The fastest drug release was obtained from a ternary solid dispersion containing PEG 4000/IBU/Tween 80 of 10:5:1 wt/wt/wt prepared by melt solvent method. The reason for better dissolution may also be due to amorphization of IBU which was confirmed through XRD, IR and DSC studies.

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