From the Research Laboratories
В изследователските лаборатории

SOLUBILITY AND DISSOLUTION ENHANCEMENT OF IBUPROFEN BY SOLID DISPERSION TECHNIQUE USING PEG 6000-PVP K 30 COMBINATION CARRIER

M. Saquib Hasnain, Amit Kumar Nayak
Seemanta Institute of Pharmaceutical Sciences, INDIA

Abstract. Ibuprofen solid dispersions were prepared with the objective of solubility and dissolution improvement using PEG 6000-PVP K 30 combination carrier by solvent evaporation technique. The saturation solubility and *in vitro* dissolution studies showed remarkable improvement in solubility and drug dissolution of these new ibuprofen solid dispersions over pure ibuprofen, ibuprofen solid dispersions using PEG 6000 and PVP K 30, individually and physical mixtures. The *in vitro* drug dissolution from these new ibuprofen solid dispersions was followed Hixson-Crowell model. The XRD and DSC studies indicated the transformation of crystalline ibuprofen (in pure drug) to amorphous ibuprofen (in solid dispersions using PEG 6000-PVP K 30 combination) by the solid dispersion technology. Stability studies of these solid dispersions does not show any significant changes ($p < 0.05$) in drug content and drug dissolved in 60 minutes ($Q_{60\ min,}$ %) within 6 months study periods (at 25 ± 2°C and 60 ± 5 % RH). This study concluded that the improved solubility as well as drug dissolution of these new ibuprofen solid dispersions using PEG 6000-PVP K 30 combination may be attributed to improved wettability, and reduction in drug crystallinity, which can be modulated by appropriate level of hydrophilic carriers.

Keywords: solid dispersion, ibuprofen, solubility, dissolution, polyethylene glycol, polyvinyl pyrrolidone

Introduction

Oral bioavailability of a drug depends on its solubility and/or dissolution rate, and dissolution may be the rate-determining step for the onset of therapeutic activity. Therefore, poorly aqueous soluble drugs are usually characterized by a low bioavailability due to less absorption, which is a major concern of pharmaceutical industries worldwide. Various approaches available to improve drug solubility as well as drug dissolution of poorly aqueous soluble drugs include micronization (Gupta et al., 2003), formation of inclusion complexes with cyclodextrins (Cavallari et al., 2002), formation of amorphous drugs (Corrigan, 1995), and formation solid dispersions of drugs using various hydrophilic carriers (Ambike et al., 2004; Paradkar et al., 2004; Das et al., 2011). Among them, solid dispersion technique has attracted substantial interest as an efficient means of improving the dissolution rate as well as the bioavailability of a wide range of poorly aqueous soluble drugs (Chiou & Rielman, 1971; Leuner & Dressman, 2000; Dhirendra et al., 2009). Fast and immediate drug dissolution from solid dispersions has been observed due to increased wettability and dispersibility of drug particles, existence of the drug in amorphous form with improved solubility, and absence of aggregation of drug particles using various hydrophilic carriers (Zerrouk et al., 2001; Tashtoush, et al., 2004; Van der Mooter, 2006; Kalaiselvan et al., 2006; Vijaya Kumar & Mishra, 2006; Shah et al., 2007; Batra et al., 2008; Mehta et al., 2009; Das et al, 2011).

Ibuprofen, a phenyl propionic acid derivative, is widely used as first line non-steroidal anti-inflammatory, analgesic, and antipyretic agents with a half-life of 1.8-2 hours (Eichie et al., 2009). It is poorly aqueous soluble and its oral absorption is dissolution rate limited, which leads to a potential bioineqivalence problem (Chowdary & Srinivas, 2000; Hu et al., 2007). Thus, the improvement of ibuprofen dissolution for its immediate release is desirable for rapid ibuprofen absorption, which is prerequisite for quick onset of its pharmacological actions. In the previous literature, various solid dispersions of ibuprofen are reported for improving its dissolution using various carriers (Xu et al., 2007; Ali & Sharma, 1991; Khan & Jiabi, 1998; Esnaashari et al., 2005; Loganathan et al., 2000; Newa et al., 2007; Newa et al., 2008a; Newa et al., 2008b; Newa et al., 2008c; Islam et al., 2010; Park et al., 2009; Dabbagh & Taghipour, 2007). Polyethylene glycol (PEG) and polyvinyl pyrrolidone (PVP) are amongst the most frequently investigated hydrophilic polymeric carriers (Kalaiselvan et al., 2006; Wade & Paul, 1994; Kaur et al., 1980; Broman et al., 2001; Trantishaiyakul et al., 1991). Previous literature also revealed that the combination of two hydrophilic polymeric carriers like PEG and PVP could improve the solubility as well as dissolution profiles of various poorly aqueous soluble drugs (Suhagia et al., 2006; Shah et al., 2009; Patel & Patel, 2008). However, the ibuprofen solid dispersion using PEG and PVP combination carrier was not reported. In the present investigation, we attempted to investigate the enhancement of the aqueous solubility and dissolution of ibuprofen using the combination of these two different carriers. Therefore, the objec-

tives of this investigation are: (i) preparation of ibuprofen solid dispersions using PEG 6000 and PVP K 30 in combination and individually, as carriers by solvent evaporation technique, (ii) characterization of newly prepared ibuprofen solid dispersions by X-ray diffraction (XRD) and Differential scanning calorimetry (DSC), (iii) estimation of drug solubility and evaluation of drug dissolution of prepared ibuprofen solid dispersions and comparison of these data with pure drug and respective physical mixtures of drug-carriers, and (iv) stability studies of these new ibuprofen solid dispersions.

Experimental

Materials

Ibuprofen was obtained as a gift sample from Techno Remedies, Kolkata, India. PEG 6000 and PVP K 30 were purchased from Loba Chemie, India. Ethanol (Bengal Chemicals and Pharmaceuticals Ltd, India) was used. All reagents were of A.R. graded. Double distilled water was used throughout the experiment.

Preparation of ibuprofen physical mixtures

Physical mixtures of ibuprofen were prepared by mixing ibuprofen with PEG 6000 and PVP K 30 in combination and individually in a glass mortar by trituration for 15 minutes.

Preparation of ibuprofen solid dispersions by solvent evaporation technique

Solid dispersions of ibuprofen were prepared by solvent evaporation technique using PEG 600 and PVP K 30, as carriers in combination and individually, in various ratios. Ibuprofen was dissolved in ethanol to get clear solution. PEG 6000 and PVP K 30 were dispersed as fine particles and the solvent was removed by evaporation on a water bath at 60°C. The dried mass was stored in desiccators until constant mass was obtained, pulverized and passed through sieve no. 22.

Determination of percent yield

The percent yield of ibuprofen solid dispersions can be determined by using the following expression:

$$\text{Percent yield} = (\text{weight of prepared solid dispersion} / \text{weight of drug + carriers}) \times 100 \quad (1)$$

Determination of percent drug content

Weight amount of physical mixtures and solid dispersions, each sample equivalent to 25 mg of ibuprofen were separately taken and added to 50 ml of ethanol in stoppered conical flasks. The sealed flasks were agitated on a rotary shaker for 1 hour. The solution was diluted with ethanol and was assayed by a UV-VIS spectrophotometer (SHIMADZU Corporation, Japan) for drug content at 220 nm using the following expression:

Percent drug content = (practical drug content in solid dispersions / theoretical drug content in solid dispersions) x 100 (2)

Determination of saturation solubility

Saturation solubility of ibuprofen were determined and compared these data with that of pure ibuprofen and physical mixtures of respective ratios. The known excess samples (ibuprofen solid dispersions, physical mixtures and pure ibuprofen), 0.5 gm equivalent weight of ibuprofen was added to 5 ml of phosphate buffer, pH=7.2 and these samples were rotated at 20 rpm in a water bath (37 ± 0.5°C) for 48 hours. The samples were then filtered through 0.45 µm membrane filter, suitably diluted, and analyzed by UV-VIS spectrophotomer (SHIMADZU Corporation, Japan) at 222 nm wavelength.

X-ray diffraction (XRD) studies

Powder X-ray diffraction patterns were recorded on an X-diffractometer (Phillip PW 1130/00 diffractometer, The Natherlands), employing CuK∞ radiation source operating at 30 mA and 40 kV. Samples were scanned from 6 to 40° 2θ at a scanning rate of 0.02° 2θ s^{-1}.

Differential scanning calorimetry (DSC) analysis

The samples were analyzed by differential scanning calorimeter (Model DT-60, Shimadzu) at a constant scanning speed of 10°C min^{-1} from 0-300°C. The 5-7 mg samples were accurately weighed into solid aluminum pans without seals.

Dissolution studies

Dissolution studies were performed in phosphate buffer (pH 7.2, 900 ml) at 37 ± 0.5 °C, using USP XXIII apparatus (Electrolab, India) with a paddle rotating at 50 rpm. The samples equivalent to 100 mg ibuprofen, were subjected to dissolution. At fixed time intervals, samples (5 ml) were withdrawn and equal amount of fresh dissolution medium was added. Withdrawn samples were filtered through 0.45 µm membrane filter, and spectrophotometrically assayed for drug content at 222 nm wavelengths using a UV-VIS spectrophotometer (SHIMADZU Corporation, Japan).

Stability studies

Stability studies were carried out by keeping the samples in screw cap vials in stability chambers (Analytical technology, Bangalore, India) at 25 ± 2°C and 60 ± 5 % relative humidity (RH). Samples were drawn regularly and analysed for drug content and dissolution studies until 6 months. All the data obtained from the stability study were analyzed for significant differences by one-way analysis of variance (ANOVA) using a Student-Newman-Keuls test for all pair wise comparisons in this study. The statistical analysis was conducted using MedCalc software version 9.6.4.0.

Results and discussion

Various ibuprofen solid dispersions were prepared using PEG 6000 and PVP K 30 in combination and individually, as carriers by solvent evaporation technique to increase the solubility as well as dissolution of poorly aqueous soluble drug ibuprofen.

The percent yield of various ibuprofen solid dispersions was within the range of 88.76 ± 2.04 % to 94.88 ± 3.32 % (Table 1). The percentage drug content in various ibuprofen solid dispersions ranged from 96.33 ± 3.05 % and 98.61 ± 2.92 %, as reported in Table 1. This indicated that ibuprofen was uniformly distributed in all these prepared solid dispersions, even in also ibuprofen solid dispersions using PEG 6000 and PVP K 30 in combination (SD-5, and SD-6).

The saturation solubility of pure ibuprofen, various prepared ibuprofen solid dispersions using PEG 6000 and PVP K 30 in combination as well as individually, as carriers and their respective physical mixtures in phosphate buffer, pH 7.2 was measured. Ghosh et al. (1998) reported that the solubility of this drug is pH dependent. Therefore, the change in pH may hamper the results during solubility measurement from ibuprofen solid dispersion. So, to maintain pH constant, phosphate buffer, pH 7.2 was used. Pure ibuprofen showed 2.56 ± 0.22 mg/ml of saturation solubility. All of samples, both physical mixture and solid dispersions of ibuprofen showed an increase in drug solubility (Table 2). All physical mixtures showed higher saturation solubility as compared with pure ibuprofen. Again, ibuprofen solid dispersions showed higher saturation solubility than their respective physical mixtures of drug and carrier. This might be attributable to an improvement of wetting of drug particles and localized solubilization by the hydrophilic polymeric carriers. Among various ibuprofen solid dispersions, solid dispersions using PEG 6000 and PVP K 30 combination showed higher saturation solubility than solid dispersions using PEG 6000 and PVP K 30, separately.

Table 1. Yield and drug content of ibuprofen solid dispersions

Solid dispersion type content (%)*	Code	Ratio	Yield (%)*	Drug
Ibuprofen : PEG 6000	SD-1	1:1	88.79 ± 3.58	98.61 ± 2.92
	SD-2	1:2	92.12 ± 3.37	98.39 ± 2.42
Ibuprofen : PVP K 30	SD-3	1:1	89.44 ± 3.43	98.54 ± 2.56
	SD-4	1:2	90.54 ± 3.82	98.27 ± 2.83
Ibuprofen : PEG 6000 : PVP K 30	SD-5	1:1:1	94.88 ± 3.32	96.78 ± 2.88
	SD-6	1:2:2	88.76 ± 2.04	96.33 ± 3.05

(*Mean ± S.D.; n = 3)

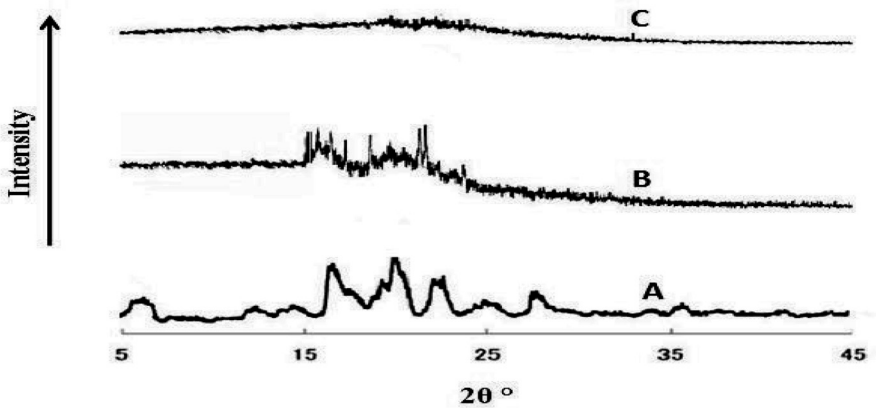

Fig. 1. The X-ray diffraction patterns of pure ibuprofen (A), ibuprofen physical mixture (PM-6) (B), and ibuprofen solid dispersion (C) using PEG 6000-PVP K 30 combination carrier (SD-6)

Table 2. Saturation solubility of different ibuprofen solid dispersions along with pure ibuprofen and physical mixtures using same carriers

Type	Ratio	Saturation solubility (mg/ml)	
		Solid dispersions	Solid dispersions
Ibuprofen : PEG 6000	1:1	4.53 ± 0.24	5.00 ± 0.32
	1:2	4.70 ± 0.27	5.24 ± 0.36
Ibuprofen : PVP K 30	1:1	4.61 ± 0.30	5.16 ± 0.28
	1:2	4.78 ± 0.25	5.35 ± 0.32
Ibuprofen : PEG 6000 : PVP K 30	1:1:1	5.12 ± 0.33	6.20 ± 0.35
	1:2:2	5.93 ± 0.32	6.62 ± 0.36
		Saturation solubility (mg/ml)	
Pure Ibuprofen	-	2.56 ± 0.22	

(*Mean ± S.D.; n = 3)

The XRD patterns of pure ibuprofen and ibuprofen solid dispersion using PEG 6000 and PVP K 30 combination (SD-6) are presented in Fig. 1. Pure ibuprofen showed

numerous characteristic sharp and intense peaks, suggesting that the drug was present as a crystalline state. The XRD pattern of ibuprofen solid dispersion using PEG 6000 and PVP K 30 combination showed that some characteristics peaks shown by pure ibuprofen were absent and others were appeared with the markedly reduced intensity. Meanwhile, in physical mixture (PM-6) of the same combination and ratio, diffraction peaks were observed clearly and a few peaks were appeared very small reduction of intensity than that of pure ibuprofen. The complete disappearance of diffraction peaks in ibuprofen solid dispersion demonstrated that solid dispersion with ibuprofen using PEG 6000 and PVP K 30 combination has changed to an amorphous state.

The DSC thermograms of pure ibuprofen and ibuprofen solid dispersion using PEG 6000 and PVP K 30 combination (SD-6) are shown in Fig. 2. The DSC thermogram of pure ibuprofen showed an apparent sharp endothermic peak at 75.03°C corresponding to ibuprofen with enthalpy (ΔH) of 129.0 J/g. On the other hand, the DSC thermograms of pure ibuprofen and ibuprofen solid dispersion using PEG 6000 and PVP K 30 combination showed an endothermic peaks, a small peak at 55.91°C corresponding to PEG with enthalpy (ΔH) of 174.4 J/g. But, the sharp melting peak of ibuprofen was absent in the DSC curve of the ibuprofen solid dispersion, indicating absence of crystalline drug and presence of amorphous drug in the solid dispersion sample. Again, this could be attributed more uniform distribution of the drug in crust of polymer.

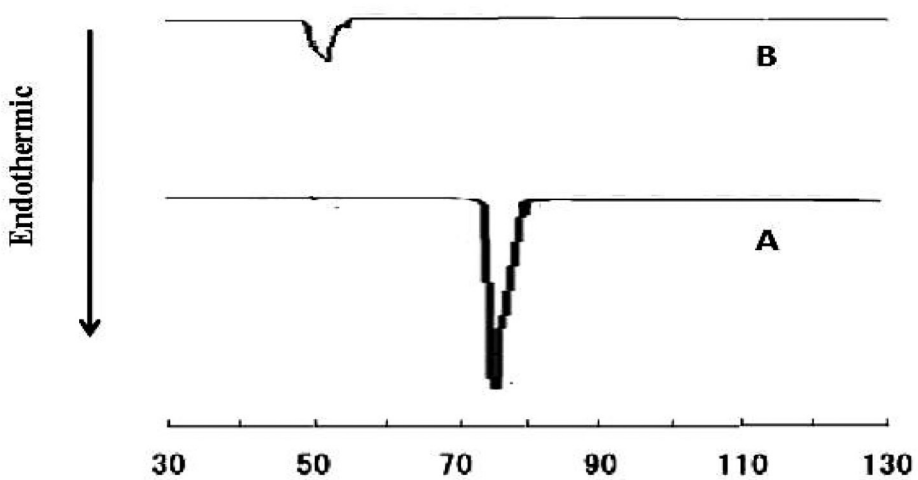

Fig. 2. The DSC thermogram of pure ibuprofen (A), and ibuprofen solid dispersion (B) using PEG 6000-PVP K 30 combination carrier (SD-6)

The *in vitro* dissolution profiles of the drug (ibuprofen), various solid dispersions using PEG 6000 and PVP K 30 in combination and individually with their respective physical mixtures in phosphate buffer (pH=7.2) for 60 minutes are shown in Figs. 3-5. All of the physical mixture and solid dispersion samples showed improved dissolution of ibuprofen over that of pure ibuprofen. The improved dissolution of ibuprofen is mainly attributed to increased wettability and accordingly solubility due to the higher level of hydrophilicity by the use of polymeric carriers. Again, all of the solid dispersion samples revealed more improved ibuprofen dissolution than their respective physical mixture samples. This observation indicated that the increased dissolution of ibuprofen from ibuprofen solid dispersion due to presence of drug in amorphous state as compared the physical mixtures and pure drug, where drug is present in crystalline state (Ghosh et al., 1998). In case of various ibuprofen solid dispersions, the dissolution of ibuprofen solid dispersions using PEG 6000 and PVP K 30 combination (SD-5, and SD-6) was better than that of prepared ibuprofen solid dispersions using these polymers as carriers individually and this was increased with the increase of polymer ratio in the solid dispersion. It was also noticed that more than 80 % of drug released from ibuprofen solid dispersion using PEG 6000-PVP K 30 combination (SD-6, Drug:PEG 6000:PVP K 30 = 1:2:2) in 60 minutes. These observations are well correlated with the results of saturation solubility.

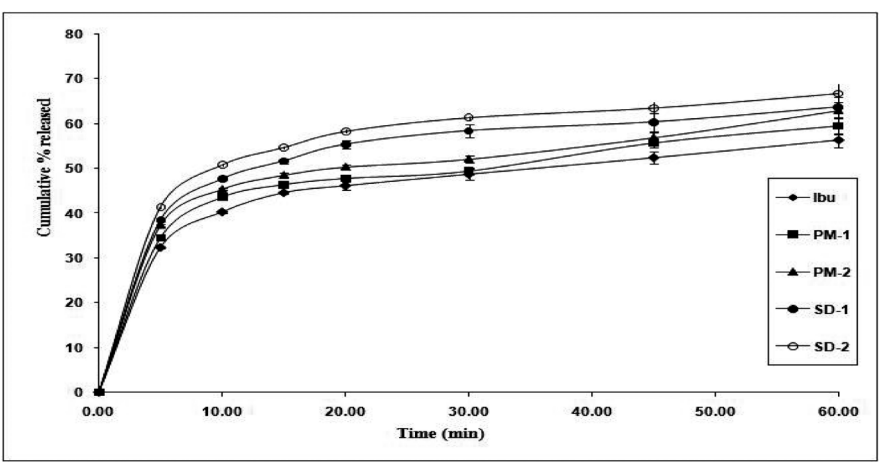

Fig. 3. Comparative *in vitro* dissolution profiles of pure ibuprofen (Ibu), ibuprofen solid dispersions using PEG 6000 [SD-1 (1:1), SD-2 (1:2)], and their corresponding physical mixtures [PM-1 (1:1), PM-2 (1:2)] (Mean ± S.D., n = 3)

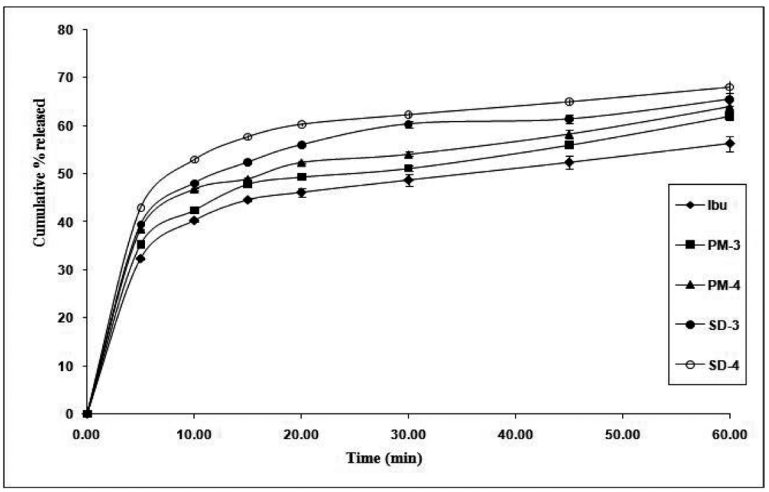

Fig. 4. Comparative *in vitro* dissolution profiles of pure ibuprofen (Ibu), ibuprofen solid dispersions using PVP K 30 [SD-3 (1:1), SD-4 (1:2)], and their corresponding physical mixtures [PM-3 (1:1), PM-4 (1:2)] (Mean ± S.D., n = 3)

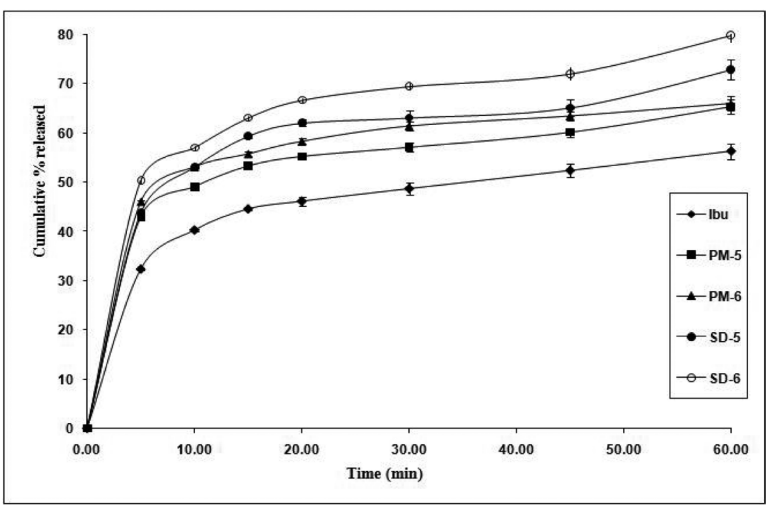

Fig. 5. Comparative *in vitro* dissolution profiles of pure ibuprofen (Ibu), ibuprofen solid dispersions using PEG 6000-PVP K 30 combination carrier [SD-5 (1:1:1), SD-6 (1:2:2)], and their corresponding physical mixtures [PM-5 (1:1:1), PM-6 (1:2:2)] (Mean ± S.D., n = 3)

In order to predict and correlate the mechanism and kinetics of ibuprofen release from ibuprofen solid dispersions using PEG 6000-PVP K 30 combination (SD-5, and SD-6); it is necessary to fit into a suitable mathematical model. The *in vitro* drug release data of these newly prepared solid dispersions (SD-5, and SD-6), were evaluated kinetically using various mathematical models like zero order, first order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas model (Dehghan et al., 2006; Jagdale et al., 2010; Appa Rao et al., 2010; Das et al., 2011).

Zero-order model: $F = K_0 t$, where F represents the fraction of drug released in time t, and K_0 is the apparent release rate constant or zero-order release constant.

First-order model: $\ln (1-F) = - K_{1st} t$, where F represents the fraction of drug released in time t, and K_1 is the first –order release constant.

Higuchi model: $F = K_H t^{½}$, where F represents the fraction of drug released in time t, and K_H is the Higuchi dissolution constant.

Hixson-Crowell model: $W_0^{1/3} - W_t^{1/3} = Kt$, where, W_0 and W_t represents initial mass, and mass remained at time t, respectively; K_{HC} is the rate constant.

Korsmeyer-Peppas model: $F = K_P t^n$, where F represents the fraction of drug released in time t, K_P is the rate constant and n is the diffusional exponent, this indicates the drug release mechanism.

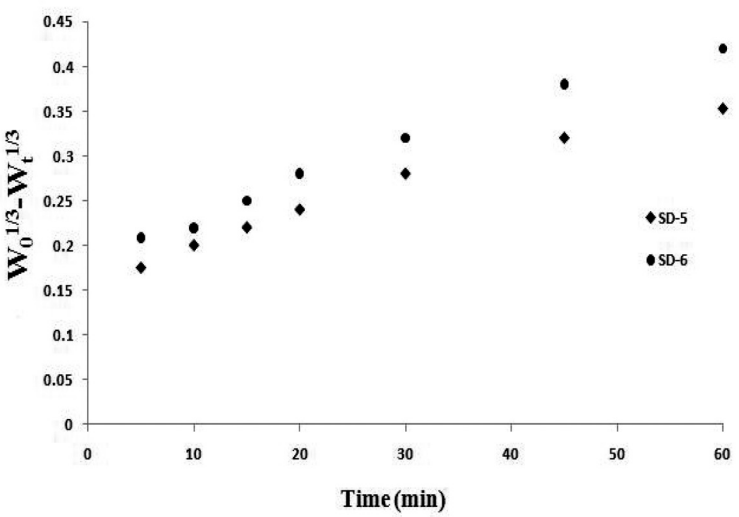

Fig. 6. Hixson-Crowell's dissolution plots of ibuprofen solid dispersions using PEG 6000-PVP K 30 combination carrier [SD-5 and SD-6]

Table 3. Correlation coefficient (R^2) values in the analysis of dissolution data of ibuprofen solid dispersions using PEG 6000-PVP K 30 combination carriers (SD-5, and SD-6)

Mathematical models	Formulation codes	
	SD-5	SD-6
Zero-order Model	0.8013	0.8879
First-order Model	0.9278	0.9314
Higuchi Model	0.8863	0.9326
Hixson-Crowell Model	0.9536	0.9717
Korsmeyer-Peppas Model	0.9047	0.9286

The results of the curve fitting into these above-mentioned mathematical models indicate the release behavior of ibuprofen from these newly prepared solid dispersions (Table 3). When the correlation coefficients of these mathematical models for ibuprofen release were compared, it was found to follow Hixson-Crowell model with the best-fit correlation coefficient value (R^2 = 0.9536 and 0.9717 for SD-5 and SD-6, respectively). Again, a plot of $W_0^{1/3} - W_t^{1/3}$ vs. time using dissolution data was drawn and it was found linear (Fig. 6) with all ibuprofen solid dispersions using PEG 6000-PVP K 30 combination (SD-5, and SD-6). This observation indicates that the dissolution of ibuprofen from these newly prepared solid dispersions occurred from discretely suspended or deposited (monodispersed) particles (Nagabhushanam et al., 2009). This might have also contributed to the enhanced dissolution rate of these ibuprofen solid dispersions using PEG 6000-PVP K 30 combinations (SD-5, and SD-6).

Table 4. Stability study results of ibuprofen solid dispersions using PEG 6000-PVP K 30 combination carrier for a period of 6 months at 25 ± 2°C and 60 ± 5 % relative humidity (RH)

Code	Drug content in solid dispersions[¥]			
	Before experiment	1 month	3 months	6 months
SD-5	96.78 ± 2.88	96.32 ± 3.03	96.28 ± 3.21	95.97 ± 2.58
SD-6	96.33 ± 3.05	96.25 ± 3.58	96.02 ± 3.32	95.83 ± 3.65
	Percent drug dissolved in 60 minutes (Q60 min) [¥]			
	Before experiment	1 month	3 months	6 months
SD-5	72.86 ± 2.06	72.22 ± 2.56	73.04 ± 3.43	71.98 ± 3.26
SD-6	80.86 ± 1.58	80.70 ± 2.33	80.56 ± 2.73	79.98 ± 2.48

The stability study for various ibuprofen solid dispersions using PEG 6000 and PVP K 30 combination (SD-5, and SD-6) was carried out for a period of 6 months at 25 ± 2°C and 60 ± 5 % relative humidity (RH). No significant differences ($p < 0.05$) in drug content and percent drug dissolved in 60 minutes ($Q_{60\ min}$) in those solid dispersions were observed throughout the study (Table 4). These observations of the stability study of various ibuprofen solid dispersions using PEG 6000 and PVP K 30 combination indicated no change in the state of solid dispersion during the study period indicating stable enough.

Conclusion

Ibuprofen solid dispersions were prepared using PEG 6000-PVP K 30 combination carrier by solvent evaporation technique. The XRD and DSC studies indicated the transformation of crystalline ibuprofen (in pure drug) to amorphous ibuprofen (in ibuprofen solid dispersions using PEG 6000-PVP K 30 combination) by the solid dispersion technology. The saturation solubility and *in vitro* dissolution studies showed a remarkable improvement in both the solubility as well as drug dissolution of these new ibuprofen solid dispersions than those of ibuprofen solid dispersions using these carriers (PEG 6000 and PVP K 30) individually. The *in vitro* dissolution of ibuprofen from these solid dispersions was found to follow Hixson-Crowell model. Stability studies revealed that these solid dispersions with PEG 6000-PVP K 30 combinations were stable enough throughout the study period. This study concluded that the improved solubility as well as drug dissolution of these newly prepared ibuprofen solid dispersions using PEG 6000-PVP K 30 combination carrier may be attributed to the improved wettability, and decreased drug crystallinity, which can be modulated by appropriate level of hydrophilic carriers.

REFERENCES

Ali, A. & Sharma, S.N. (1991). Preparation and evaluation of solid dispersions of ibuprofen. *Indian J. Pharm. Sci*., *53*, 233-236.

Ambike, A.A., Mahadik, K.K. & Paradkar, A. (2004). Stability study of amorphous valdecoxib. *Int. J. Pharm., 282,* 151-162.

AppaRao, B., Shivalingam,, M.R., Kishore Reddy, Y.V., Rao, S., Rajesh, K. & Sunitha, N. (2010). Formulation and evaluation of aceclofenac solid dispersions for dissolution rate enhancement. *Int. J. Pharm. Sci. Drug. Res*., *2,* 146-150.

Batra, V., Shirolkar, V.S., Mahaparakale, P.R., Kasture, P.V. & Deshpande, A.D. (2008). Solubility and dissolution enhancement of glipizide by solid dispersion technique. *Indian J. Pharm. Educ. Res., 42*, 373-378.

Broman, E., Khoo, C. & Taylor, L.S. (2001). A comparison of alternative polymer excipients and processing methods for making solid dispersions of poorly water soluble drug. *Int. J. Pharm., 222,* 139-151.

Cavallari, C., Abertini, B., Gonzalez-Rodriguez, M.L & Rodriguez, L. (2002). Improved dissolution behaviour of steam granulated piroxicam. *Eur. J. Pharm. Biopharm., 54*, 65-73.

Chiou, W.L. & Rielman, S. (1971). Pharmaceutical application of solid dispersion system. *J. Pharm. Sci., 60*, 1281-1302.

Chowdari, K.P.R. & Srinivas, L. (2000). Physical stability and dissolution rate of ibuprofen suspension formulated employing solid dispersion. *Indian J. Pharm. Sci., 62,* 253-256.

Corrigan, O.I. (1995). Thermal analysis of spray died products. *Thermochim. Acta, 248,* 245-258.

Dabbagh, M.A. & Taghipour, B. (2007). Investigation of solid dispersion technique in improvement of physicochemical characteristics of ibuprofen powder. *Iranian J. Pharm. Sci., 3*, 69-76.

Das, A., Nayak, A.K., Mohanty, B. & Panda, S.B. (2011). Solubility and dissolution enhancement of etoricoxib by solid dispersion technique using sugar carriers. *ISRN Pharmaceutics*, art. no. 819765.

Dehghan, M.H.G. & Jafar, M. (2006). Improving dissolution of meloxicam using solid dispersions. *Iranian J. Pharm. Res*., *4*, 231-238.

Dhirendra, K, Lewis, S., Udupa, N. & Atin, K. (2009). Solid dispersions: a review. *Pak. J. Pharm. Sci., 22*, 234-246.

Eichie, F.E., Arhewoh, I.M. & Ezeobi, O.C. (2009). *In-vitro* evaluation of the pharmaceutical quality of some ibuprofen tablets dispensed in Nigeria. *African J. Pharm. Pharmacol., 3*, 491-495.

Esnaashari, S., Javadzadeh, Y., Batchelor, H.K. & Conway, B.R. (2005). The use of microviscometry to study polymer dissolution from solid dispersion drug delivery systems. *Int. J. Pharm., 292,* 227-230.

Ghosh, L.K., Ghosh, N.C., Chatterjee, M. & Gupta. M.K. (1998). Grinding effect on some pharmaceutical properties of drugs by adding β-cyclodextrin. *Drug Dev. Ind. Pharm., 14,* 99-118.

Gupta, M.K., Vanwert, A. & Bogner, R.H. (2003). Formation of physically stable amorphous drugs by milling with neusili. *J. Pharm. Sci*., *92*, 536-551.

Islam, M.S., Mehjabeen, K, Mustrai, I., Khan, F. & Jalil, R. (2010). Improvement of dissolution of ibuprofen and fenofibrate by poloxamer based solid dispersion. *Bangladesh Pharm. J., 13*, 54-59.

Jagdale, S.C., Kuchekar, B.S., Chabukswar, A.R., Musale, V.P. & Jadhao, M.A. (2010). Preparation and *in vitro* evaluation of allopurinol-Gelucire 50/13 solid dispersions. *Int. J. Adv. Pharm. Sci*., *1*, 60-67.

Kalaiselvan, R., Mohanta, G.P., Kannan, K., Manna, P.K. & Manavalan, R. (2006). Optimization of drug-polymer mixing ratio in albendazole-polyvinylpyrrolidone

solid dispersion by moisture absorption studies. *Acta Pharm. Sci*., *48*, 141-151.

Kaur, K., Grant, D.J.W. & Eves, T. (1980). Comparison of PEG and polyoxyethylene stearate as excipients for solid dispersion systems of griseofulvin & tolbutamide I, II: phase equillibria. *J. Pharm. Sci., 69,* 1317-1326.

Khan, G.M. & Jiabi, Z. (1998). Preparation, characterization, and dissolution studies of ibuprofen solid dispersions using polyethylene glycol (PEG), talc, and PEG-talc as dispersion carriers. *Drug Dev. Ind. Pharm*., *24,* 455-462.

Leuner, C. & Dressman, J. (2000). Improving drug solubility for oral delivery using solid dispersions. *Eur. J. Pharm. Biopharm., 50*, 47-60.

Loganathan, S., Maimaran, S., Rajasekaran, A. & Sulaiman, A. (2000). The effect of solid dispersions on (solubility) dissolution rate of ibuprofen. *Eastern Pharmacist*, *513*, 115-116.

Mehta, A., Vasanti, S., Tyagi, R. & Shukla, A. (2009). Formulation and evaluation of solid dispersions of an anti-diabetic drug. *Curr. Tr. Biotechnol. Pharm., 3,* 76-84.

Nagabhushanam, M.V., Beena Devi, M. & Swathi, K. (2009). Studies on enhancement of dissolution rate of mefenamic acid using solid dispersions. *Indian Pharmacist*, *8*, 67-70.

Newa, M., Bhandaria, K.H., Li, D.X., Kwon, T.H., Kim, J.-A., Yoo, B.-K., Woo, J.-S., Lyoo, W.S., Yong, C.-S. & Choi, H.-G. (2007). Preparation, characterization and *in vivo* evaluation of ibuprofen binary solid dispersions with Poloxamer 188. *Int. J. Pharm., 343,* 228-237.

Newa, M., Bhandaria, K.H., Li, D.X., Kim, J.O., Yoo, D.S., Kim, J.-A., Ypp, B.-K., Woo, J.-S., Choi, H.-G. & Yong, C.-S. (2008a). Enhanced dissolution of ibuprofen using solid dispersion with polyethylene glycol 4000. *Biol. Pharm. Bull*., *31*, 939-945.

Newa, M., Bhandaria, K.H., Li, D.X., Sung, J.H., Kim, J.O., Yoo, B.-K., Woo, J.-S., Choi, H.-G. & Yong, C.S. (2008b). Enhanced dissolution of ibuprofen using solid dispersion with polyethylene glycol 20000. *Drug Dev. Ind. Pharm., 34,* 1013–1021.

Newa, M., Bhandaria, K.H., Oh, D.H., Kim, Y.R., Sung. J.H., Kim, J.O., Woo, J.-S., Choi, H.-G. & Yong, C.S. (2008c). Enhanced dissolution of ibuprofen using solid dispersion with Poloxomer 407. *Arch. Pharm. Res., 31,* 1497-1507.

Paradkar, A., Ambike, A.A., Jadhav, B.K. & Mahadik, K.K. (2004). Characterization of curcumin-PVP solid dispersion obtained by spray drying. *Int. J. Pharm., 271*, 281-286.

Park, Y.J., Kwon, R., Quan, Q.Z., Oh, D.H., Kin, J.O., Hwong. M.R., Koo, Y.B., Woo, J.-S., Yong, C.-S. & Choi, H.-G. (2009). Development of novel ibuprofen-loaded solid dispersion with improved bioavailability using aqueous solution. *Arch. Pharm. Res., 32,* 757-772.

Patel, R. & Patel, M. (2008). Preparation, characterization and dissolution behaviour of a solid dispersion of simvastatin with polyethylene glycol 4000 and polyvinyl

pyrrolidon K 30. *J. Disp. Sci. & Technol.*, *29,* 193-204.
Shah, J., Vasanti, S., Anroop, B. & Vyas, H. (2009). Enhancement of dissolution rate of valdecoxib by solid dispersions technique with PVP K 30 & PEG 4000: preparation and *in vitro* evaluation. *J. Incl. Phenom. Macrocycl. Chem., 63,* 69-75.
Shah, T.J., Amin, A.F. & Parikh, R.H. (2007). Process optimization and characterization of poloxamer solid dispersions of a poorly water-soluble drug. *AAPS Pharm. Sci. Tech*., *8*, art. no. 29.
Suhagia, B.N., Patel, H.M., Shah, S.A., Rathod, I.S. & Parmar, V.K. (2006). Preparation and characterization of etoricoxib-polyethylene glycol 4000 plus polyvinylpyrolidone K 30 solid dispersions. *Acta Pharm*., *56,* 285-298.
Tashtoush, B.M., Al-Quashi, Z.S. & Najib, N.M. (2004). *In vitro* and *in vivo* evaluation of glibenclamide in solid dispersion systems. *Drug Dev. Ind. Pharm., 30*, 601-607.
Trantishaiyakul, V., Kaewnopparat, N. & Ingkatawornwong, S. (1991). Properties of solid dispersion of piroxicum in PVP. *Int. J. Pharm*., *181,* 143-151.
Van den Mooter, G. (2006). Evaluation of Inutec SPI as new carrier in the formulation of solid dispersion of poorly soluble drugs. *Int. J. Pharm*., *316***,** 1-6.
Vijaya Kumar, S.G. & Mishra, D.N. (2006). Preparation and evaluation of solid dispersion of meloxicum with skimmed milk. *Yakugaku Zasshi*, *126,* 93-97.
Wade, A. & Paul, J.W. (1994). *Handbook of Pharmaceutical Excipients.* Washington: Pharmaceutical Press.
Xu, L., Li, S.M. & Sunada, H. (2007). Preparation and evaluation of ibuprofen solid dispersion systems with kollidon particles using a pulse combustion dryer system. *Chem. Pharm. Bull., 55*, 1545-1550.
Zerrouk, N., Chemtob, C., Arnaud, P., Toscani, S. & Dugue, J. (2001). *In vitro* and *in vivo* evaluation of carbamazepine-PEG 6000 solid dispersions. *Int. J. Pharm., 225*, 49-62.

✉ M. Saquib Hasnain
Amit Kumar Nayak (corresponding author)
Seemanta Institute of Pharmaceutical Sciences,
Myurbhanj - 757089, Orissa, INDIA
E-Mail: amitkrnayak@yahoo.co.in