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Article

Solubility and dissolution enhancement of flurbiprofen by solid dispersion using hydrophilic carriers

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The intent of the current work is to study the effect of polyethylene glycol 8000 and polyethylene glycol 10000 as hydrophilic carriers on dissolution behaviour of flurbiprofen. In the present study, solvent evaporation method was used to prepare flurbiprofen solid dispersions and evaluated for physico-chemical properties, drug-carrier compatibility studies and dissolution behaviour of drug. Solubility studies showed more solubility in higher pH values and formulations SD4 and SD8 were selected to prepare the fast dissolving tablets. FTIR and DSC study showed no interaction and drug was dispersed molecularly in hydrophilic carrier. XRD studies revealed that there was change in the crystallinity of the drug. The results of *In vitro* studies showed SD8 formulation confer significant improvement ($p<0.05$) in drug release, Q_{20} was 99.08±1.35% compared to conventional and marketed tablets (47.31±0.74% and 56.86±1.91%). The mean dissolution time (MDT) was reduced to 8.79 min compared to conventional and marketed tablets (25.76 and 22.22 min.) indicating faster drug release. The DE (% dissolution efficiency) was increased by 2.5 folds (61.63%) compared to conventional tablets (23.71%). From the results, it is evident that polyethylene glycol solid dispersions in less carrier ratio may enhance the solubility and there by improve the dissolution rate of flurbiprofen.

Keywords: Polyethylene glycol/effects. Flurbiprofen/solubility. Flurbiprofen/dissolution rate. Drug-carrier compatibility/study. Dissolution efficiency.

INTRODUCTION

In the pharmaceutical industries, formulation scientists has a major challenge in the formulation of orally administered solid dosage forms is solubility enhancement and improvement of dissolution of poor water soluble drugs (Horter, Dressman, 2001).Solid dispersion technologies enhance the solubility and dissolution of drugs and thereby improve the oral bioavailability of poorly water soluble drugs (Patil, Gaikwad, 2009). Thus, drug's acceptability and bioavailability will depends on enhancement of solubility and dissolution that reduces dose required for showing fast onset of action (Chauhan, Shimpi, Paradkar, 2005).

Solid dispersions (SDs) are molecular dispersions of drug in the carriers and they were formulated by different methods, important are solvent evaporation and fusion (melt) method (Vippagunta, Maul, Tallavajhala, 2002). SD is a technique, in which drug is obtained as fine particles by dissolving the carriers in an aqueous fluids. It is a simple and flexible formulation process of obtaining solid dispersions without using toxic substances and enhances solubility and dissolution rate of drug (Bikiaris, 2011).

Flurbiprofen (FPN) is non-steroidal anti-inflammatory drug that belongs to BCS class II because of its poor water solubility (Veerareddy, Vemula, 2012). Different molecular weights of polyethylene glycols (PEG8000 and PEG10000) were used for the preparation of SDs. In this work, solvent evaporation method was employed for formulating FPN solid dispersions utilizing PEGs as carrier.

The reported literatures for solid dispersions arenisoldipine (El-Maghraby, Elsergany, 2014), simvastatin

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(Bolourchian, Mahboobian, Dadashzadeh, 2013), lycopene (Faisal *et al*., 2013), diclofenac sodium (Cwiertnia, 2013), gliclazide (Biswal, Sahoo, Murthy, 2009) and ritonavir (Sinha, Ali, Baboota, 2010). The need of present study is to develop the solid dispersions in less carrier ratio with improved results (Ozkan*et al.,* 2000). In the current work, we prepared FPNSDs to increase solubility and dissolution of the drug using PEGs as carrier.

MATERIAL AND METHODS

Material

Flurbiprofen was kindly gifted FDC Ltd., (Mumbai, India). PEG 8000 and PEG 10000 were gift samples from Central Drug House Pvt. Ltd., (Delhi, India). Crospovidone and Spray-dried lactose were obtained from Matrix laboratories Ltd., (Hyderabad, India). All other chemicals and reagents were purchased from S.D. Fine Chemicals, (Mumbai, India).

Phase solubility studies of FPN

An excess amount of FPN was taken into a flask containing aqueous solution (0, 5, 10, 15, 20, 25 and 30% w/v)of PEG 8000 and PEG 10000 separately (Suresh *et al.,* 2013).The samples were continuously stirred on a stirrer for 48 h at room temperature. The samples were filtered by using 0.45 µm filter. Then clear filtrates were appropriately diluted and drug concentration was analysed byUV spectrophotometer at 247nm.

The solubilisation of drug in an aqueous solution was explained by Gibbs free energy of transfer (ΔG^{o}_{tr}) and determined by equation given below.

$$(\Delta G^{o}_{tr}) = -2.303\ RT \log S_o/S_s$$

where, S_o/S_s was FPN molar solubility ratio in PEGs solutions to that of water.

Preparation of FPN solid dispersions

Solvent evaporation method was employed to prepare FPNSD susing PEG8000 and PEG10000 as continuous phase in different weight ratios (Table I). PEGs and drug were dissolved in a round bottom flask containing 10 mLof ethanol. At a temperature not exceeding 45 °C, the solvent was evaporated in a vacuum oven. The resultant solid dispersions were grounded in a mortar with the help of pestle, kept in a vial and were stored in desiccators till further use (Christian, Jennifer, 2000).

Solubility studies

Solubility studies were performed for prepared SDs in various solvent systems (0.1 N hydrochloric acid, distilled water and pH 7.2 phosphate buffer). Excessive quantities of SDs were placed into a flask containing10 ml of each solvent. The flask was sonicated at 25 ˚C for 1 h, stirred and agitated for 2 days at 25 ˚C. The suspension was filtered using a 0.45 µm filter, diluted suitably and spectrophotometrically (UV-3200, LabIndia, Mumbai, India) analyzed at 247 nm.

Flow properties of powder

Angle of repose and Carr's compressibility index were used to determine the powder flow properties. Angle of repose (θ) was measured by fixed funnel method and it was determined by given formula:

$$\text{Tan}\ \theta = \frac{h}{r} \qquad (1)$$

TABLE I - Formulation of FPN solid dispersions using PEGs

Formulation Code	Excipients (mg)			
	Flurbiprofen	PEG 8000	PEG 10000	FPN:PEG ratio
SD1	50	25	-	1:0.5
SD2	50	50	-	1:1
SD3	50	100	-	1:2
SD4	50	200	-	1:4
SD5	50	-	25	1:0.5
SD6	50	-	50	1:1
SD7	50	-	100	1:2
SD8	50	-	200	1:4

where'θ' was angle of repose, 'h' and 'r' were height and radius of the cone of powder.

The tendency of a powder to be compressed can measured by Carr's index and determined using given below formula:

$$\text{Carr's Index} = \frac{\left[\left(\rho_P - \rho_b\right)\right]}{\rho_P} \times 100 \qquad (2)$$

where 'ρ_b'and 'ρ_p' were bulk density and tapped density respectively.

Preparation of tablets

From the results of above studies, SD4 and SD8 formulations were prepared in oro dispersible tablets (ODTs) form (Table II). SDs equivalent to 50 mg of FPN and all other ingredients were sieved (# 60). Except lubricant and glidant, powder blend was mixed for 5 min. The powder blend was then lubricated for 2-5 min and compressed directly using rotary compression machine (CMD-3, Cadmach, Ahmedabad, India). In this way, conventional tablets were also prepared using 50 mg of pure FPN.

Characterization of tablets

The ODTs were characterized by different evaluation tests like weight variation, friability, hardness, disintegration, wetting time and drug content. All the tests were performed as per the procedure described in our previous work (Bhaskar, Rama, Sateesh, 2015).

In-vitro dissolution studies

The *in-vitro* dissolution studies of various FPN formulation (SD4, SD8, marketed and conventional formulations) was performed in USP Type II dissolution apparatus (TDL – 08L, Electrolab, Mumbai, India) using 900 mL of phosphate buffer (pH 7.2) rotated at 50 rpm and maintained at 37.0±0.5 °C. Aliquots of 5 ml were withdrawn at pre-determined time intervals and the same amount of fresh dissolution media was replaced. The samples were analyzed by UV spectrophotometer at 247 nm after filtration through 0.45 µm filter and appropriate dilution.

Dissolution data treatment

Cumulative % drug release in 20 min (Q_{20}), mean dissolution time (MDT),dissolution efficiency (%DE) and relative dissolution rate (RDR) were determined to compare the optimized SDs with marketed tablets and conventional formulation of FPN as discussed in our previous article (Chella *et al*., 2016).

Drug-carrier compatibility studies

Drug-carrier interaction studies were performed using Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC) and powder X ray diffraction (PXRD) studies. FTIR spectra of FPN, PEG and optimized SD were recorded on IR spectrophotometer (Shimadzu, Japan)in the range of 400 to 4000 cm^{-1} using pellets compacted by mixing approximately 5 mg of samples 100 mg of potassium bromide (KBr) under vacuum. The DSC thermograms of above said samples were recorded by placing approximately 5–10 mg sample in sealed aluminium pan with small openings on a differential scanning colorimetry(Shimadzu Corp., Japan), at a heating rate of 5 °C per min and a temperature from 0 to 400 °C under a flow of nitrogen gas. X-ray diffractometer (Siemens D5000, Texas, USA) was used to record the diffractograms. FPN, PEG 10000 and SD8 were exposed to Cu radiation

TABLE II - Composition of selected FPN SDs tablets

Formulation composition	Quantity in mg		
	SD4	SD8	Conventional
FPNSDs equivalent to 50 mg of FPN	250	250	-
Plain FPN	-	-	50
Crospovidone	15	15	15
Spry-dried lactose	26	26	226
Magnesium stearate	3	3	3
Talc	6	6	6
Total weight of tablet	300	300	300

of wavelength 1.540 Å, 40 KV voltage 30 mA current and analysed over the 2θ range of 2° to 50°.

Stability studies

Stability of optimized formulation (SD8) was performed as mentioned in the literature (Mathews, 1999). The optimized ODTs were packed in aluminum paper and placed in the stability chamber for 6 months at 75±5% RH and 40±2°. After completion of the storage period, *in-vitro* dissolution and assay were performed for collected samples. Paired t-test was performed to check the significant difference at p = 0.05. The similarity between before and after storage was determined by similarity index (F2) which indicates stability of optimized formulation.

RESULTS AND DISCUSSIONS

Results

Phase solubility studies

The results of phase solubility study presented in Table III indicate increase in FPN solubility linearly (R^2 = 0.970 with PEG 8000 and R^2 = 0.973 with PEG 10000) as the concentration of PEGs was increased. The phase solubility diagram is shown in Figures 1a and 1b.

Solubility studies of FPN SDs

Solubility studies of solid dispersion were performed in various solvent systems and the results are shown in Table IV. Solubility of FPN is higher in 7.2 pH phosphate buffer compared to 0.1N HCl and distilled water whereas, SDs showed more or less equal solubility in both water and phosphate buffer. The solubility of SDs increased with increase in concentration of carrier in both cases (PEG 8000 and PEG 10000). However,

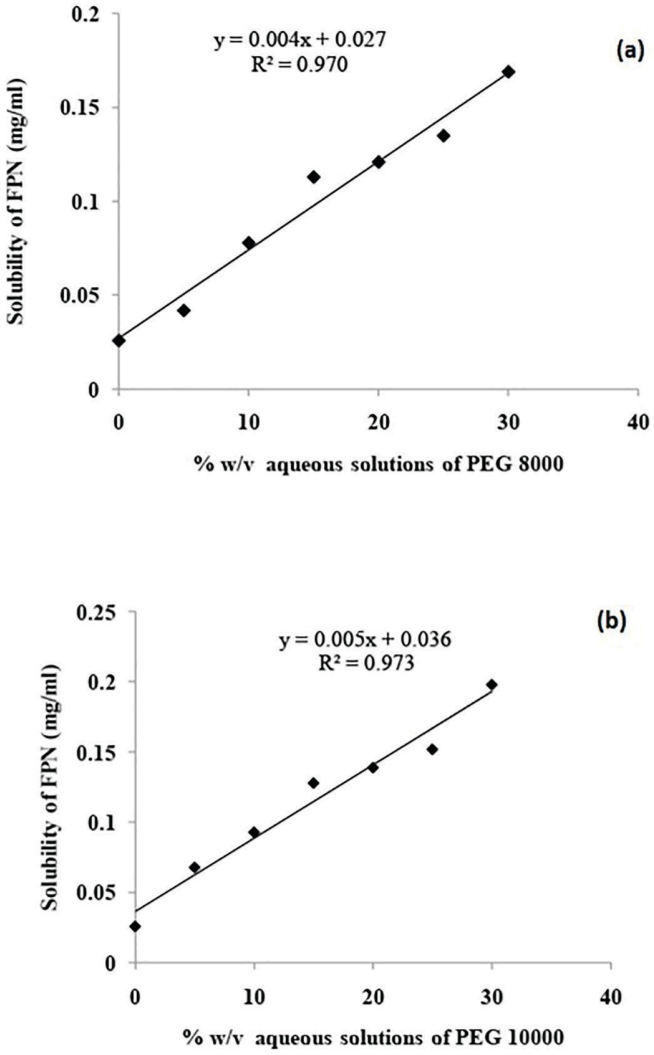

FIGURE 1 - Phase solubility curves of FPN in aqueous solution of PEGs at 25 °C (n=3) [(a) in PEG 8000, (b) in PEG 10000].

TABLE III - Phase Solubility data of FPN in different concentrations of PEG 8000 and PEG 10000 aqueous solutions (Mean ± SD, n=3)

Concentration of carrier solution (%, w/v)	PEG 8000		PEG 10000	
	Solubility of FPN (mg/ml)	ΔG°tr (Kj/mol)	Solubility of FPN (mg/ml)	ΔG°tr (Kj/mol)
0	0.026±0.0035	-	0.026±0.0052	-
5	0.068±0.0024	-1.19±0.153	0.068±0.0072	-2.38±0.134
10	0.093±0.0071	-2.72±0.182	0.093±0.0031	-3.16±0.185
15	0.098±0.0014	-3.64±0.196	0.098±0.0068	-3.95±0.191
20	0.129±0.0029	-3.81±0.175	0.129±0.0093	-4.15±0.142
25	0.142±0.0083	-4.08±0.131	0.142±0.0084	-4.38±0.167
30	0.175±0.0062	-4.64±0.173	0.175±0.0042	-5.03±0.125

TABLE IV- Solubility of FPN and its SDs (Mean± *SD;* n=6)

Formulation Code	FPN solubility (mg/ml)		
	0.1 N HCl	Distilled Water	7.2 pH Phosphate Buffer
Pure FPN	0.014±0.03	0.026±0.08	0.098±0.01
SD1	0.113±0.02	0.257±0.02	0.298±0.07
SD2	0.126±0.04	0.338±0.06	0.349±0.02
SD3	0.136±0.04	0.412±0.04	0.425±0.06
SD4	0.143±0.01	0.493±0.06	0.526±0.07
SD5	0.102±0.02	0.294±0.03	0.324±0.08
SD6	0.123±0.05	0.349±0.06	0.387±0.06
SD7	0.138±0.08	0.414±0.01	0.473±0.04
SD8	0.156±0.01	0.517±0.06	0.561±0.02

SDs prepared with PEG10000 showed higher solubility in all concentrations compared to SDs prepared with PEG8000. Among all formulations, SD8 showed highest solubility in phosphate buffer pH 7.2 i.e., 0.561±0.02 mg/mL.

Flow properties of powder

Angle of repose and Carr's compressibility index of the pure FPN and optimised formulations (SD4 and SD8) is reported in Table V. The angle of repose values lower than 30° and Carr's compressibility index less than 18 for two formulations indicates good flow properties for pure FPN and SDs.

Characterisation of tablets

The results of the tests performed were within the pharmacopoeial limits (Table VI). For the weight variation test, all the tablets were within 5% of average weight of tablets. The friability and hardness were found near to be 0.35% and 3.1kg/cm^{2}for optimized SD8 formulation. The disintegration and wetting time of the optimized tablet were found to be 121 sec and 26 sec respectively, indicating rapid disintegration of optimised tablets. Tablets contain 99.24% of FPN.

TABLE V- Flow properties of FPN and formulations (Mean ± SD, n=3)

Formulation Code	Angle of Repose (°)	Carr's Index (%)
SD4	28.24±0.57	15.07±0.36
SD8	27.06±0.79	15.32±0.25
Conventional	29.72±3.15	17.02±0.42

In vitro dissolution studies

The ODTs containing PEG 10000 SD showed higher release of FPN compared with to ODTs containing PEG8000 SD, marketed and conventional tablets of plain FPN. The optimized formulation (SD8) containing PEG 10000 showed significantly improved ($p<0.05$) and faster drug release (99.08±1.35% in 20 min) compared with formulation SD4 containing PEG 8000 (93.67±1.12% in 20 min), marketed tablet (56.86±1.91%) and conventional tablet (47.31±0.74% in 20 min). The release pattern of FPN from various formulations is shown in Figure 2.

Treatment of dissolution data

The %FPN release from optimized formulation

TABLE VI - Physical evaluation of FPN tablets (Mean ± SD, * n=20; † n=6; ‡ n=3)

Formulation	Weight variation* (mg)	Friability (%)	Hardness† (Kg/cm^2)	Disintegration time‡ (sec)	Wetting time‡ (sec)	Drug content‡ (%)
SD4	301.51±1.18	0.38±0.053	3.0±0.27	120±4	28±6	98.92±1.53
SD8	300.12±1.72	0.35±0.072	3.1±0.43	121±3	26±3	99.24±1.26
Conventional	301.68±1.13	0.27±0.046	3.1±0.14	248±4	45±2	97.36±1.47

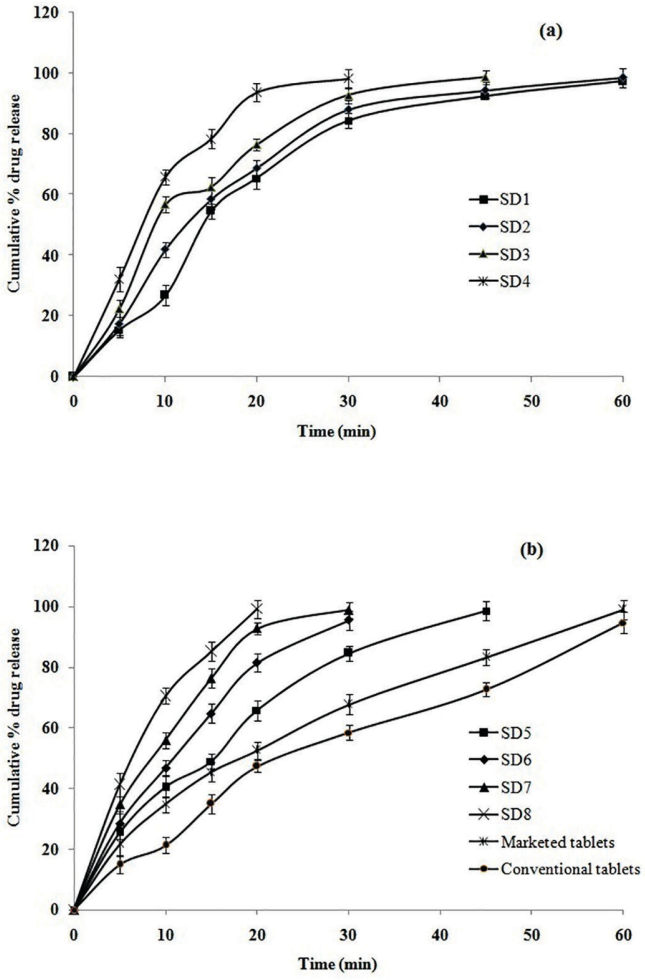

FIGURE 2 - Cumulative% drug release of FPN from various formulations.

(SD8) was significantly higher compared to conventional tablets in 20 min. DE(%), MDT, and RDR were determined. DE(%) was found to be 61.63% and MDT was reduced to 8.79 min compared with conventional tablet (23.71±1.46% and 25.76 min respectively). The relative dissolution rate of optimized SD8 formulation was found to be 2.09.

Drug-carrier compatibility studies

FT IR spectra of pure FPN, PEG 10000 and optimised formulation SD8 is shown in Figure 3.FTIR spectra of FPN exhibits prominent peaks at 2998.43 cm^{-1} (C-H stretching vibration), 1463.51 cm^{-1} (C-H bending vibration), 1721.37 cm^{-1} (C=O carbonyl stretch of acid), 1576.24 cm^{-1}(C=C stretching of aromatic ring) and 1236.63 cm^{-1} (C-F stretching). Presence of all the principal peaks of FPN in SD8 formulation and absence of new peaks indicated that interaction was not present between the FPN and PEG 10000.

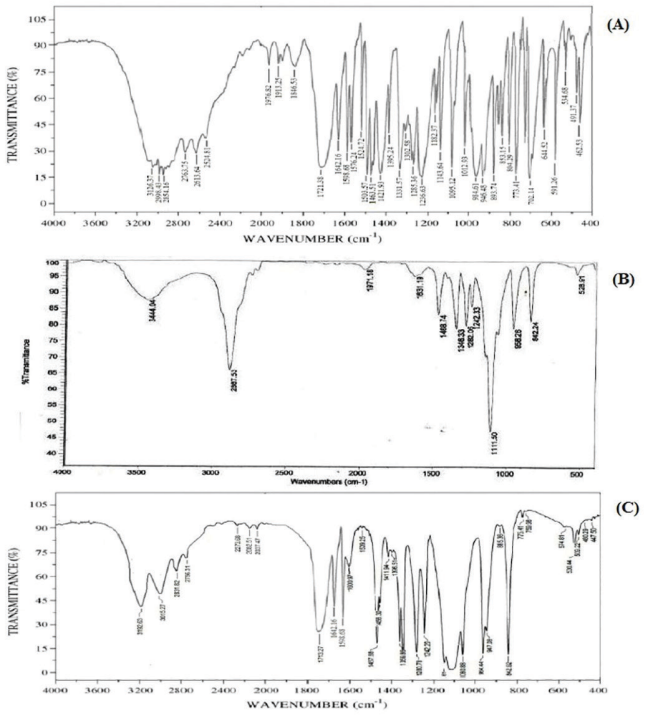

FIGURE 3 - FTIR spectra of A) FPN B) PEG 10000 C) SD8 formulation.

DSC thermograms obtained for pure FPN, PEG 10000 and SD8 solid dispersion are presented in Figure 4.The thermogram of FPN showed a sharp endothermic peak at 113.4° characteristic of its melting point, whereas thermogram of the SD8 formulation showed broad endothermic peak of drug, indicating that FPN was molecularly dispersed in carrier.

The X-ray diffractograms of pure FPN, PEG 10000

TABLE VII - Dissolution parameters of FPN from SD4, SD8, marketed and conventional tablets (Mean ± SD, n=3)

Formulation	(Q_{20})	DE (%)	MDT (min)	RDR
SD4	93.67±1.76	55.74±*1.31*	8.87±*0.32*	1.98±*0.014*
SD8	99.08±1.35	61.63±*1.62*	8.79±*0.14*	2.09±*0.032*
Marketed	56.86±1.91	31.97±*1.25*	22.22±*0.17*	1.11±*0.018*
Conventional	47.31±0.74	23.71±*1.46*	25.76±*0.26*	-

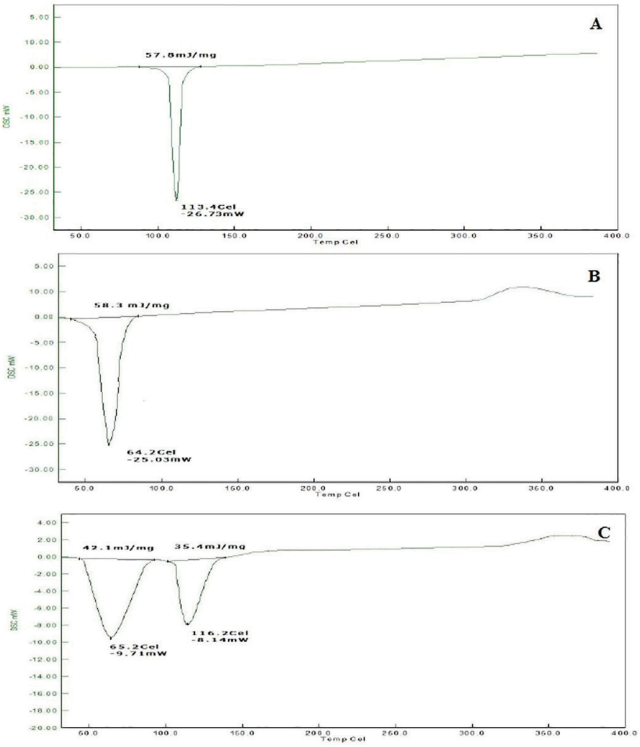

FIGURE 4 - DSC thermograms of A) FPN B) PEG 10000 C) SD8 formulation.

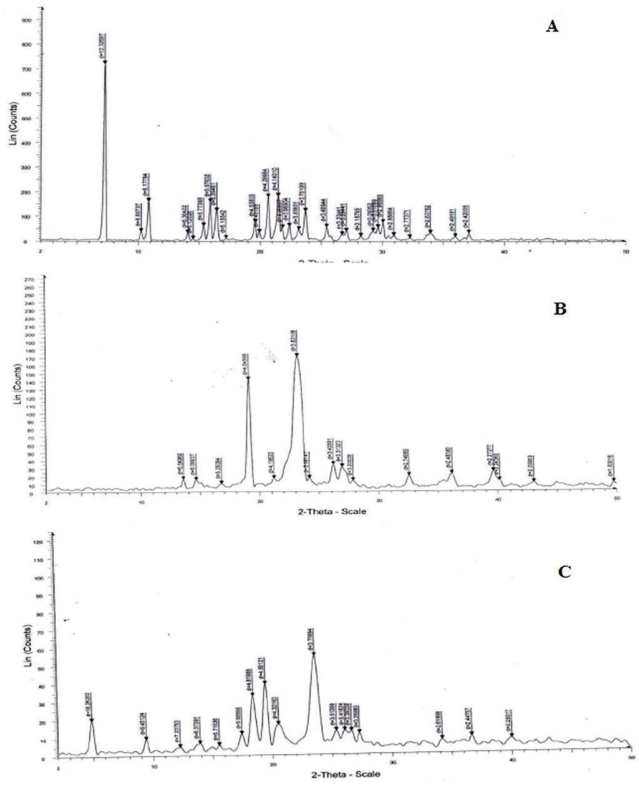

FIGURE 5 - XRD patterns of A) FPN B) PEG 10000 C) SD8 formulation.

and SD8 solid dispersion are presented in Figure 5. XRD patterns of FPN shows sharp intense peaks notably at 2θ diffraction angles of 7°, 11°, 16°, 17°, 21°, 22°, and 24° indicating FPN was in crystalline state. The decrease or disappearance of peaks intensity in SD8 formulation indicates that FPN may have undergone solid state transition to amorphous form or crystallinity was reduced.

Stability studies

Stability of the optimised formulation (SD8) was evaluated at accelerated condition. *In-vitro* dissolution studies and assay were performed after the completion of storage period. There was no significant variation i.e., $p>0.05$ in concentration of drug (Table VIII) determined by using paired t-test. Similarity index value was found to be 89.59.

DISCUSSION

The intent of current work is to study the role of hydrophilic carriers (PEG 8000 and PEG 10000) in improving the solubility and dissolution rate of FPN at different concentrations. FPN SDs were prepared by solvent evaporation method using PEG 8000 and PEG 10000 at four different concentrations of FPN to PEG and optimised SD was compressed into ODTs.

TABLE VIII - Stability study data of ODTs containing SD8 (Mean ± SD, n=3)

Time (min)	Before storage	After 6 months Storage	*t*-test at 0.05 LS	Similarity Factor (F2)
0	0.00±0.00	0.00±0.00		
5	41.28±1.71	40.12±1.38		
10	70.49±1.16	69.27±1.12	Not Significant	89.59
15	85.22±1.08	83.84±1.43		
20	99.08±1.43	97.78±1.25		
% Assay	99.34±1.26	98.64±1.23	Not Significant	--

Finally, solubility and dissolution rate of FPN from ODT containing SD was compared with that of marketed formulations and conventional tablets prepared with pure FPN.

Linear increment in solubility of FPN was observed with increase in concentration of PEGs. As the calculated slopes were less than one, the phase solubility diagram follows an A_L-type of solubility diagram (Suresh *et al.,* 2013). Negative values of $\Delta G°_{tr}$ (Gibbs free energy transfer) indicated that spontaneous solubilisation of FPN and it was decreased as the concentration of PEGs increases, indicating more favourable reaction with increase in concentration of PEGs.

Solid dispersions of FPN were prepared using various concentrations of PEG 8000 and PEG 10000 separately. In presence of PEG the solubility was increased up to drug to carrier ratio 1:4. Further increase in ratio to 1:5 and 1:6 did not show any significant improvement in the solubility. Hence, the formulations up to 1:4 ratios were included in the present study. Similar types of results were reported by Chauhan et. al., (Chauhan, Shimpi, Paradkar, 2005). The solubility of FPN from SDs prepared with PEG 10000 showed higher solubility compared with PEG 8000. Among all formulations, SD8 showed higher solubility in phosphate buffer pH 7.2.

Angle of repose and Carr's compressibility index were determined to find out the flow behaviour of powder. The angle of repose (<30°) and Carr's compressibility index (<18) values indicated that the powder blend has good flow property. Then FPN solid dispersions (SD1 to SD8) were compressed into orodispersible tablets (ODTs) based on the solubility data. Prepared ODTs were evaluated for various pharmacopoeial and other general tests like weight variation, hardness, friability, disintegration time, wetting time and drug content. All the tests were within the pharmacopoeial limits.

In vitro dissolution studies showed, ODTs containing PEG 10000 SDs showed higher release of FPN compared with ODTs containing PEG8000, marketed and conventional tablets. All the formulations containing FPN in the form of SDs showed higher drug release compared to marketed tablets and conventional tablets containing plain FPN. Formulation SD5 (with FPN to drug PEG 10000 ratio 1:1) showed complete drug release in 45 min. SD6 and SD7 formulations with FPN to drug PEG 10000 ratio 1:2 and 1:3 respectively showed complete drug release in 30 min. These values were higher than the results reported by Dong *et al.* (2011), who reported only 70% drug release in 60 min (Dong *et al.,* 2011). Whereas, Formulation SD8 containing PEG 10000 of 1:4 ratio showed faster drug release (99.08±1.35% in 20 min) with significantly improved dissolution ($p<0.05$) compared with all other formulations (Figure 2).As the selected drug belongs to NSAID that needs to produce faster action we selected SD8 as final optimised formulation.

From *in vitro* dissolution studies it was evident that enhancement in dissolution rate was observed with tablets containing PEG 10000 compared with PEG 8000. It may be due to greater carrier solubilization effect, increased dispersibility and wettability of drug, increased dissolution in hydrophilic carrier, change in state of drug (may be amorphous form), decrease in crystallinity and/or a combination of the above said mechanisms (Dordunoo, Ford, Rubisteins*,* 1991).

The % flurbiprofen release (Q_{20}) from formulation SD8 was significantly higher compared to conventional tablets in 20 min. Enhancement in dissolution rate of a drug supported by mean dissolution time (MDT), dissolution efficiency (DE), and relative dissolution rate (RDR). DE was observed as 61.63% and it was increased almost by 3.0 folds from SD8 ODT compared with conventional tablets. MDT for SD8 formulation was reduced to 8.79 min, compared with conventional tablet (25.76 min). The relative dissolution rate (RDR) of optimized SD8 formulation was found to be 2.09. These results demonstrated that faster release of FPN from SD8 formulation compared to SD4, marketed and conventional tablets.

FTIR spectra showed no interaction between FPN and PEG, as same principal peaks present in pure drug and optimised SD8 formulation. The results of DSC studies revealed that, the sharp endothermic peak of drug was broadened in optimised SD8 formulation indicating FPN was molecularly dispersed in carrier. XRD studies showed the sharp intense peaks of drug indicating FPN was in crystalline state. The decrease or disappearance of peaks intensity in optimised SD8 formulation indicated, either there is a reduction in the crystallinity of FPN or it has undergone solid state transition to amorphous form.

Stability studies of the optimised SD8 formulation was performed at accelerated condition. No significant variation ($p>0.05$) in concentration of drug was observed, when determined using paired t-test. Similarity index value of 89.59 indicated that the similarity in dissolution profile of freshly prepared and after storage of optimised SD8 formulation.

CONCLUSIONS

An attempt was made to enhance the solubility and dissolution of FPN using SDs of PEG. *In vitro* dissolution rate of formulations with PEG10000 manifested best

results compared with formulations with PEG 8000. Significant improvement ($p<0.05$) in percent drug release (Q_{20}) was observed with SD8 compared with SD4, marketed and conventional tablets containing pure drug. Enhancement in dissolution of FPN was observed possibly due solubilisation of drug in hydrophilic carrier or change in the crystallinity of the drug. The DE and MDT of SD8 formulation were also significantly improved compared with conventional tablets. In conclusion, formulation of PEG solid dispersions in less carrier ratio could be an alternative technique for enhancing solubility, dissolution and thereby improving the absorption of poor water soluble drugs like FPN.

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REFERENCES

Bhaskar D, Rama RT, Sateesh KV. Formulation and pharmacokinetics of gelucire solid dispersions of flurbiprofen. Drug Dev Ind Pharm. 2015;41(8):1254-62.

Bikiaris DN. Solid dispersions, part I: recent evolutions and future opportunities in manufacturing methods for dissolution rate enhancement of poorly water-soluble drugs. Expert Opin Drug Del. 2011;8(11):1501-1519.

Biswal S, Sahoo J, Murthy PN. Characterisation of gliclazide-PEG 8000 solid dispersions.Trop J Pharm Res. 2009;8(5):417-424.

Bolourchian N, Mahboobian MM, Dadashzadeh S. The effect of PEG molecular weights on dissolution behavior of simvastatin in solid dispersions. Iran J Pharm Res. 2013;12(Suppl):11-20.

Chauhan B, Shimpi S,Paradkar A. Preparation and evaluation of glibenclamide-polyglycolized glycerides solid dispersions with silicon dioxide by spray drying technique. Eur J Pharm Sci. 2005;26(2):219-230.

Chella N, Daravath B, Kumar D, Rama RT. Formulation and pharmacokinetic evaluation of polymeric dispersions containing valsartan. Eur J Drug Metab Pharmacokinet. 2016;41(5):517-26.

Christian L, Jennifer D. Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm. 2000;50(1):47-60.

Cwiertnia B. Effect of water soluble carrier on dissolution profiles of diclofenac sodium. Acta Pol Pharm. 2013;70(4):721-726.

Dong HO, Young JP, Jun HK, Chul SY, Han GC. Physicochemical characterization and *in vivo* evaluation of flurbiprofen-loaded solid dispersion without crystalline change. Drug Deliv. 2011;18(1):46-53.

Dordunoo SK,Ford JL,Rubinstein MH.Preformulation studies on solid dispersions containing triamterene or temazepam in polyethylene glycols or gelucire 44/14 for liquid filling of hard gelatin capsules. Drug Dev Ind Pharm. 1991;17(12):1685-1713.

El-Maghraby GM, Elsergany RN. Fast disintegrating tablets of nisoldipine for intra-oral administration. Pharm Dev Technol. 2014;19(6):641-650.

Faisal W, O'Hora TR, O'Driscoll CM, Griffin BT. A novel lipid-based solid dispersion for enhancing oral bioavailability of lycopene-in vivo evaluation using a pig model. Int J Pharm. 2013;453(2):307-314.

Horter D, Dressman JB. Influence of physicochemical properties on dissolution of drugs in the gastrointestinal tract. Adv Drug Deliver Rev. 2001;46(1):75-87.

Mathews BR. Regulatory aspects of stability testing in Europe. Drug Dev Ind Pharm.1999;25(7):831-856.

Ozkan Y, Doganay N, Dikmen N, Isimer A. Enhanced release of solid dispersions of etodolac in polyethylene glycol. Farmaco. 2000;55(6-7):433-438.

Patil MP, Gaikwad NJ. Preparation and characterization of gliclazide-polyethylene glycol 4000 solid dispersions. Acta Pharmaceut. 2009;59(1):57-65.

Sinha S, Ali M, Baboota S. Solid dispersion as an approach for bioavailability enhancement of poorly water-soluble drug ritonavir. AAPS PharmSciTec. 2010;11(2):518-527.

Suresh B, Subash J, Basanth BE, Rajeshri D, Raju J, Prabhakar RV. Physicochemical characterization and dissolution enhancement of loratadine by solid dispersion technique. Korean J Chem Eng. 2013;30(1)238-244.

Veerareddy PR, Vemula SK. Formulation, evaluation and pharmacokinetics of colon targeted pulsatile system of flurbiprofen. J Drug Target. 2012;20(8):703-714.

Vippagunta SR, Maul KA, Tallavajhala S, Grant JW. Solid state characterization of nifedipine solid dispersions. Int J Pharm. 2002;236(1-2):111-123.

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