

Article

Comparative *in-vitro* dissolution study and infrared characterization of binary solid dispersion of diclofenac sodium

Sharmin Akhter^{1*}, Jewel Barua¹, Md. Salahuddin², Rupantar Dey¹, Joysree Das¹ and Anowara Jenny¹

¹Department of Pharmacy, BGC Trust University Bangladesh, Chittagong-4000, Bangladesh

²PhD Fellow, Faculty of Medicine, University of Hong Kong, Hong Kong

*Corresponding author: Sharmin Akhter, Lecturer, Department of Pharmacy, BGC Trust University Bangladesh, BGC Biddyanagar, Chandanaish, Chittagong, Bangladesh. E-mail: lira.pharmacy@gmail.com

Received: 07 August 2016/Accepted: 25 August 2016/ Published: 31 August 2016

Abstract: Diclofenac sodium, a non-steroidal antiinflammatory agent was selected as a model drug for the study, which is BCS class II drug (low soluble and high permeable). Poor water solubility of any drug is characterized by low dissolution rate and consequently reduced bioavailability. Numerous methods have been followed in literature to improve the dissolution rate of poorly water soluble drugs. The objective of the present study was to improve the water solubility and the dissolution rate of poorly water soluble diclofenac sodium by solid dispersion (SD) technique. Binary SDs of diclofenac sodium were prepared by physical mixing as well as solvent evaporation technique using a highly water soluble polymer Eudragit E-100 in different drug-to-polymer weight ratios (1:1 to 1:5). The effect of the carrier Eudragit E-100 on the solubility and *in-vitro* dissolution behavior were investigated spectrophotometrically at 273 nm. It was found that only 11.43% was released within 60 minutes from active diclofenac sodium on the other hand the release of diclofenac sodium from the binary SD formulation of solvent evaporation containing Eudragit E-100 in 1:5 ratio (code: S9) showed the best result which was 98.57% within the same period of time. Evaluation of the properties of the prepared SDs formulations were performed by using Fourier Transform Infra Red (FTIR) spectroscopy. The FTIR spectroscopic data showed that though the stability of drug was enhanced due to Eudragit E-100, but there was absence of considerable drug-polymer interactions. So solid dispersion may be an effective technique to enhance dissolution rate of diclofenac sodium.

Keywords: solid dispersion; poorly water solubility; diclofenac sodium; solvent evaporation technique; Eudragit E-100; FTIR

1. Introduction

Solubility is an important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response to be shown. Among all newly discovered chemical entities, most of the drugs are lipophilic and fail to reach market due to their poor water solubility (Jatwani *et al.*, 2012). Poorly soluble drugs are the ones which do not readily dissolve in the gastric environment and hence they are not available at the desired therapeutic effect for producing the desired action. If the aqueous solubility of a drug is less than 1mg/mL, it causes serious absorption problem. These drugs generally exhibit many difficulties in the development of pharmaceutical dosage forms due to their limited water solubility, slow dissolution rate and low bioavailability (Paul *et al.*, 2012). Now-a-days, pharmaceutical technology provides many approaches to enhance the dissolution rate of poorly soluble drugs. Physical modifications often aim to increase the surface area, solubility and/or wettability of the powder particles and are therefore focused on particle size reduction or generation of amorphous states (Kamalakkannan *et al.*, 2010). There are also many other ways to increase the aqueous solubility of such compounds, including micronization, salt formation and formulation of the drug as a solid dispersion (SD) (Tanaka *et al.*, 2006). Out of all these approaches solid dispersion have attracted

tremendous interest as an efficient means of improving the dissolution rate and hence the bioavailability to a number of hydrophobic drugs. This article reviewed the various preparation techniques and types of solid dispersion based on molecular arrangement. Finally some of the practical aspects have also been considered for the preparation of solid dispersions (Jatwani *et al.*, 2012). For many compounds, however, decreasing the particle size may not lead to a significant or adequate increase in bioavailability. Salt formation may also be problematic, particularly with neutral compounds and weak acids (Tanaka *et al.*, 2006).

Solid dispersion method has been widely employed to improve the dissolution rate, solubility and oral absorption of poorly water soluble drugs (Patel *et al.*, 2010; Duncan, 2012). It involves at least two different solid components, generally a hydrophilic and a hydrophobic components of which the hydrophilic component forms the matrix crystalline or amorphous while a drug represents the hydrophobic component. The drug can be dispersed molecularly, in amorphous particles (clusters) or in crystalline particles of the matrix (Tanaka *et al.*, 2006). Numerous solid dispersion systems have been demonstrated in the pharmaceutical literature along with various hydrophilic carriers, such as polyethylene glycols, polyvinylpyrrolidone, hydroxypropyl methylcellulose, gums, sugar, mannitol and urea (Dingra *et al.*, 2010). Diclofenac is a well-known nonsteroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic properties, comparable or superior to other NSAIDs. Diclofenac shows preferential inhibition of the cyclooxygenase-2 (COX-2) enzyme. It is mainly indicated in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis (Riess *et al.*, 1978; Hinz *et al.*, 2003). The objective of this work was to investigate the improvement in the aqueous solubility and dissolution rate of diclofenac sodium from SDs (Kavita *et al.*, 2013). Dissolution data will also be compared by using different release kinetic models (Zero order model, First order, Hixson-Crowell cube root law and Higuchi square root law).

2. Materials and Methods

2.1. Materials

Diclofenac sodium was received as a gift sample from The ACME Laboratories Limited, Bangladesh. Eudragit E-100 was obtained from Eskayef Bangladesh Limited, Potassium di-hydrogen phosphate (MERCK, Germany), Di Potassium hydrogen phosphate (MERCK, Germany) and Methanol (Sigma-Aldrich, Germany) were procured from commercial sources. Distilled water were prepared in the laboratory (Department of pharmacy, BGC Trust University Bangladesh). All other chemicals and solvents used in this study were of analytical grade.

2.2. Determination of solubility of diclofenac sodium in water

Solubility studies were performed by placing single dose (50 mg) of the drug in 25 ml of screw-capped bottles containing 20 ml of water and placed in a water bath shaker. The bottle was capped tightly, thermostated at $37 \pm 0.2^\circ\text{C}$ and was shaken at 40 rpm. After 24 hr, 2 ml of the solution were filtered (using whatmann filter paper of pore size $0.45 \mu\text{m}$) diluted and assayed for diclofenac sodium spectrophotometrically at 273 nm using UV-Vis spectrophotometer (JENWAY, UK).

2.3. Preparation of solid dispersions (SDs) of diclofenac sodium

2.3.1. Preparation of SDs by physical mixing method

Solid dispersions (SDs) of diclofenac sodium were prepared by physical mixing method using Eudragit E-100 (carrier or polymer) at different ratios of diclofenac sodium to Eudragit E-100 (1:1, 1:3 and 1:5). Desired amount of diclofenac sodium and Eudragit E-100 was weighted out separately and accurately in an electronic balance (OHAUS CORP., China) for each of the ratios of drug to polymer as mentioned above. Then the drug and the polymer (Eudragit E-100) was placed in a mortar and mixed up by paste and grinded them well. The grounded powder particles were passed through a sieve of mesh size 40. The resulted mixed sample was the solid dispersions (SD). It was weighed and transferred in fresh glass vials with proper labeling. Finally, all the SDs formulations thus obtained in separate vials were stored in dessicator until further use. Table 1 shows the list of the physical mixtures of diclofenac sodium and its polymer Eudragit E-100.

2.3.2. Preparation of SDs by solvent evaporation technique

Binary solid dispersion of diclofenac sodium with Eudragit E-100 in different weight ratios of diclofenac sodium to Eudragit E-100 (1:1, 1:2 1:3, 1:4, and 1:5) were prepared by solvent evaporation technique. In case of this method, selection of solvent is of a prime necessity and drug and carrier is dissolved in a volatile organic solvent. Accurately weighted amount of diclofenac sodium and Eudragit E-100 for each of the ratios as mentioned above were taken separately in a screw capped test tube and was dissolved in minimum volume of methanol by magnetic stirrer to obtain a clear solution. This solution was then stirred robustly for uniform

mixing. The solution from the various ratios of drug to polymer thus obtained were kept in room temperature for few days until the solvent was evaporated from the solution. The viscous residues thus obtained were allowed to solidify and the solidified mixture was then triturated to convert powder particles with the help of mortar and pestle. Thus solid dispersion of diclofenac sodium was obtained. The powder particles were passed through sieve of mesh size 40. Then the resulted in each solid dispersion (SD) was weighted and transferred in a fresh glass vials with proper labeling. Finally all the SD formulations contained in separate vials were kept in a dessicator until the dissolution experiment was started. Table 2 shows the lists of the solid dispersions prepared by this technique.

2.4. Evaluation of diclofenac sodium solid dispersions

2.4.1. Determination of solubility of SDs of diclofenac sodium in water

Solubility studies were performed by placing the SD equivalent to one dose of the drug (50 mg) in 25 ml of water in different screw-capped solubility bottles and placed in water bath shaker. The bottles were capped tightly, thermostated at $(37 \pm 0.2)^\circ\text{C}$. After specific time interval the samples were withdrawn and filtered through membrane filters (Whatman filter paper pore size $0.45 \mu\text{m}$) and assayed spectrophotometrically at 273 nm.

2.4.2. *In vitro* dissolution studies of diclofenac sodium and solid dispersion

The *in-vitro* dissolution tests were performed for the pure diclofenac sodium (50 mg) and solid dispersions (50 mg equivalent of diclofenac sodium), using USP dissolution test apparatus type II (paddle type) where 900 ml of 0.05 M Phosphate buffer (pH = 6.8) worked as a dissolution medium. The temperature of the medium was maintained at $(37 \pm 0.5)^\circ\text{C}$ throughout the experiment. Paddle was set at a stirring rate of 50 rpm. A 5 ml aliquot was withdrawn from the dissolution test system at predetermined time intervals of 5, 15, 30, 45 and 60 minutes and then 5 ml of fresh dissolution medium was replaced to the dissolution system to maintain the constant volume of dissolution medium. The absorbance of the withdrawn fractions were, one by one measured at 273 nm using a UV-Vis spectrophotometer (JENWAY 6305, UK) against dissolution medium as a blank. Percentage of drug release was calculated using the equation obtained from the standard curve prepared with the standard diclofenac sodium in the media (Paul *et al.*, 2012).

2.4.3. Comparison of dissolution data by model dependent methods

Data obtained from *in vitro* drug release study were tested with the following mathematical model to study the release kinetics.

Zero order equation: The equation assumes that the cumulative amount of drug release is directly related to time. The equation may be as follows:

$$C = K_0 t \text{-----} (1)$$

Where, K_0 is the zero order rate constant expressed in unit concentration/time and t is time in sec. A graph of concentration vs time would yield a straight line passing through the origin and with a slope equal to K_0 .

First order equation: The release behavior of first order equation is expressed as log cumulative percentage of drug remaining vs time. The equation may be as follows (Wagner, 1969):

$$\text{Log } C = \text{Log } C_0 - kt / 2.303 \text{-----} (2)$$

Where, C = The amount of drug un-dissolved at t time, C_0 = Drug concentration at $t = 0$, k = Corresponding release rate constant.

Higuchi square root law: The Higuchi release model describes the cumulative percentage of drug release vs square root of time. The equation may be as follows (Higuchi, 1961):

$$Q = K\sqrt{t} \text{-----} (3)$$

Where, Q = the amount of drug dissolved at time ' t '. K is the constant reflecting the design variables of the system. Hence, drug release rate is proportional to the reciprocal of the square root of time.

Hixson-Crowell cube root law: It is the law that represents idea about the evaluation of drug release pattern changes with the surface area and the diameter of the particles. It is mentioned as the cube root of the percentage of drug remaining in the matrix vs time (Hixon and Crowell, 1931). The equation is as follows:

$$Q_0^{1/3} - Q_t^{1/3} = k_{HC} \times t \text{-----} (4)$$

Where, Q_0 = Initial amount of the drug in the tablets, Q_t = and k_{HC} = the rate constant for the Hixson-Crowell cube root law.

2.4.4. Fourier transform infra red (FTIR) spectroscopy

FTIR spectroscopy was used to study the possibility of an interaction between drug and polymer in solid-state. In this study, Fourier-transform infrared (FTIR) spectra were obtained by using an IR Spectrophotometer. The samples (Diclofenac sodium or SDs) were previously grounded and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:5 (Sample: KBr) ratio, respectively. The KBr discs were prepared by using corresponding machine. Scans were obtained at a resolution of 4 cm^{-1} , at wave numbers from 4000 to 500 cm^{-1} .

2.5. Preparation of standard curve for diclofenac sodium

10 mg of diclofenac sodium was accurately weighted and taken in 100 ml volumetric flask, and then buffer solution was added up to the mark and shaken properly. This solution was called mother solution. Then 10 ml of mother solution was taken in another volumetric flask and added buffer solution upto the mark. This was the stock solution. Serial dilution was carried out to get different drug concentrations. Then 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 ml of stock solution were gradually taken in the test tube. Then 9, 8, 7, 6, 5, 4, 3, 2, 1 and 0 ml of buffer solution were added respectively in those test tubes for the purpose of serial dilution. These were then analyzed by UV-Vis spectrophotometer at 273 nm and absorbance of each of the diluted solutions was noted. The absorbance values were plotted against drug concentrations. Standard curve for diclofenac sodium was thus produced (Figure 1).

3. Results and Discussion

3.1. Physical appearance

The Diclofenac sodium solid dispersions were prepared employing solvent evaporation method. All solid dispersions were white fine powders. No discolouration was observed during preparation of SD.

3.2. Solubility of pure diclofenac sodium, physical mixture and SDs in water

The solubility of diclofenac sodium and SDs were carried out in water. It showed that the solubility of diclofenac sodium was 0.014 mg/ml and 0.823 mg/ml from the SDs formulation. The mentioned solubility results were obtained from the standard curve (Fig-1) as below against the absorbance data of diclofenac sodium and SDs.

3.3. Standard curve of Diclofenac sodium in 0.05 M Phosphate buffer (pH = 6.8)

Standard curve of carbamazepine is shown in Figure 1.

3.4. *In vitro* dissolution profile of Diclofenac sodium and SDs formulation in 0.05 M Phosphate buffer (pH = 6.8)

3.4.1. Dissolution profile of active Diclofenac sodium

50 mg of pure Diclofenac sodium was used for dissolution study by using 0.05 M phosphate buffer (pH = 6.8) as dissolution medium. It was found only 10.6% was released after 5 minutes and 11.43% was released 60 minutes. Figure 2 shows that dissolution profile of active diclofenac sodium is very poor.

3.4.2. Effect of Eudragit E-100 on release of diclofenac sodium

Physical mixtures of Diclofenac sodium and Eudragit E-100, P1 (1:1), P2 (1:3), and P3 (1:5) were used for dissolution study. It was found that P3 showed the best result in comparison of P1 and P2 which was 82.50% within 60 min. Comparison of dissolution profile of diclofenac sodium from binary solid dispersion containing Eudragit E-100 are shown in Table 3.

The rate of dissolution of solid dispersion of Di-Na prepared by solvent evaporation technique with Eudragit E-100 at 1:1 (S5), 1:2 (S6), 1:3 (S7), 1:4 (S8), and 1:5 (S9) ratios was compared with each other. When comparing the solid dispersion of Di-Na containing same polymer with different ratios, S9 & S8 gave the best result which was the release rate of 98.57% and 95.44% respectively (Table 4). Again all the solid dispersion formulations showed increased dissolution rates than their respective physical mixtures formulations (Figure 3 and Figure 4). It might be caused by the structural composition and higher molecular weight of Eudragit E-100. It has a lower content of quaternary ammonium groups and is considered as more permeable to water. The preliminary trials conducted revealed that SDs with low polymer ratio resulted in poor drug release whereas those prepared with

high polymer ratio exhibited quicker drug release. This observation indicated that the increased dissolution rate of diclofenac sodium solid dispersions may be due to the presence of drug in amorphous state as compared to the physical mixtures drug is present in crystalline state.

Table 1. Solid dispersion formulation of diclofenac sodium prepared by physical mixing method.

Serial No.	Polymers	Drug to polymer ratio	Summarized* form of SDs	Dispensing (mg)	Codes used
01	Eudragit E-100	1:1	Di-Na:Eu 1:1	300:300	P1
02	Eudragit E-100	1:3	Di-Na:Eu 1:3	300:900	P2
03	Eudragit E-100	1:5	Di-Na:Eu 1:5	300:1500	P3

*Diclofenac sodium: Eudragit E-100

Table 2. Solid dispersion formulation of diclofenac sodium prepared by solvent evaporation technique.

Serial No.	Polymers	Drug to polymer ratio	Summarized* form of SDs	Dispensing (mg)	Codes used
01	Eudragit E-100	1:1	Di-Na: Eu 1:1	300:300	S5
02	Eudragit E-100	1:2	Di-Na:Eu 1:2	300:600	S6
03	Eudragit E-100	1:3	Di-Na:Eu 1:3	300:900	S7
04	Eudragit E-100	1:4	Di-Na:Eu 1:4	300:1200	S8
05	Eudragit E-100	1:5	Di-Na:Eu 1:5	300:1500	S9

*Diclofenac sodium: Eudragit E-100

Table 3. Percent release of diclofenac sodium from pure drug and solid dispersion containing Eudragit E-100 with different ratio.

Time (minute)	Percent (%) release of drug			
	Pure drug	P1(Di: Eudragit) 1:1	P2(Di: Eudragit) 1:3	P3(Di: Eudragit) 1:5
After 5 min	10.6	23.44	47.76	59.03
After 60 min	11.43	49.05	60.26	82.50

Table 4. Percent release of diclofenac sodium from pure drug and solid dispersion of diclofenac sodium with Eudragit E-100 in different ratios prepared by solvent evaporation method.

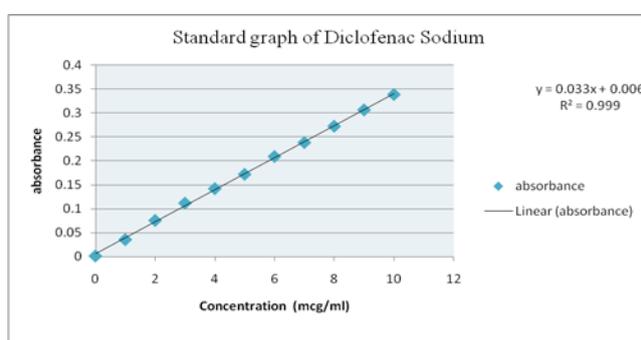
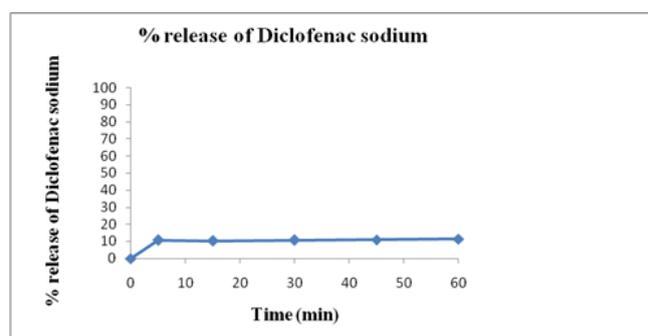
Time (min)	Percent (%) Release of drug					
	Pure Drug	S5 (Di:Eudragit) 1:1	S7 (Di: Eudragit) 1:2	S7 (Di: Eudragit) 1:3	S8 (Di: Eudragit) 1:4	S9 (Di: Eudragit) 1:5
After 5 min	10.6	72.1091	76.3766	71.3455	80.1818	85.4524
After 60 min	11.4347	94.0224	94.4893	94.7164	95.4424	98.5703

Table 5. Y-equation ($Y=aX+b$) and correlation co-efficient (R^2) from binary SDs formulation of diclofenac sodium.

Formulation Coding	Zero Order		1 st Order Kinetics		Higuchi model		Hixon Crowell model	
	Y equation	R ²	Y equation	R ²	Y equation	R ²	Y equation	R ²
Diclofenac sodium	0.113x+6.083	0.361	-0.00x+1.972	0.365	1.190x+3.835	0.607	-0.001x+4.544	0.364
S5	1.036x+41.25	0.508	-0.0155x+1.74	0.823	10.19x+23.78	0.745	-0.034x+3.8	0.721
S6	1.029x+43.71	0.476	-0.016x+1.7	0.811	10.26x+25.74	0.717	-0.035x+3.707	0.692
S7	1.087x+41.23	0.532	-0.017x+1.742	0.872	10.64x+23.15	0.772	-0.037x+3.801	0.760
S8	0.993x+47.60	0.416	-0.016x+1.617	0.728	10.22x+28.89	0.667	-0.034x+3.530	0.604
S9	1.018x+50.19	0.403	-0.023x+1.599	0.809	10.55x+30.70	0.655	-0.041x+3.437	0.652
P1	0.692x+12.04	0.837	-0.004x+1.925	0.820	6.267x+5.730	0.941	-0.013x+4.386	0.796
P2	0.677x+28.04	0.488	-0.005x+1.85	0.647	6.873x+14.72	0.776	-0.015x+4.155	0.608
P3	0.944x+34.60	0.548	-0.010x+1.786	0.786	9.418x+18.92	0.799	-0.026x+3.962	0.709

Table 6. Comparison of peaks present in Fourier Transform Infrared Spectra of pure diclofenac sodium & solid dispersion containing different polymer (Pavia *et al.*, 2001).

Serial Number	Diclofenac Sodium	P1 (Diclofenac sodium+ Eudragit E-100)	S9 (Diclofenac sodium + Eudragit E-100)	Indication with standard range of peak (cm^{-1}) in FTIR spectra
1.	Peak 3441.16	Peak 3448.72	Peak 3479.58 cm^{-1}	Peak N-H Primary & secondary amides (stretching) (3500-3100) cm^{-1}
2.	2925.17	2951.09	2927.94	C-H Symmetric stretching 2800 cm^{-1}
3.	1603.88	1635.64	1577.77	C=O asymmetric stretching 1600 cm^{-1}
4.	1470	1454.33	1454.33	C=C (aromatic) (1600-1475) cm^{-1}

**Figure 1. Standard curve of diclofenac sodium (API).****Figure 2. Percent release of active diclofenac sodium (API).**

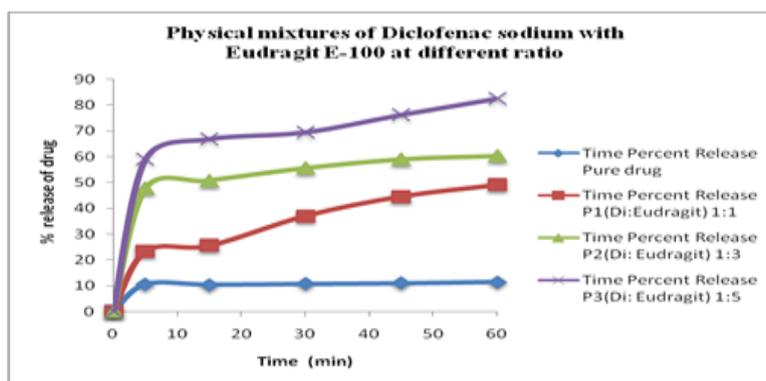


Figure 3. Average % release of drug from SD containing Eudragit E-100 (Physical Mixtures).

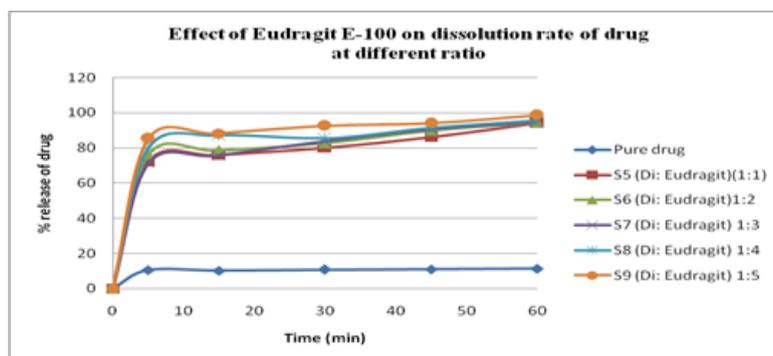


Figure 4. Average % release of drug from SD containing Eudragit E-100 (Solvent evaporation technique).

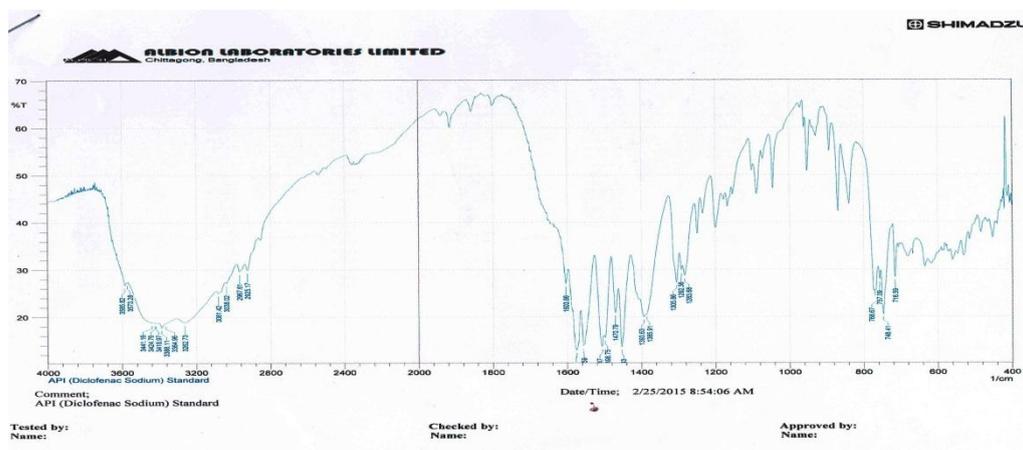


Figure 5. FTIR spectrum of pure Diclofenac sodium (API)

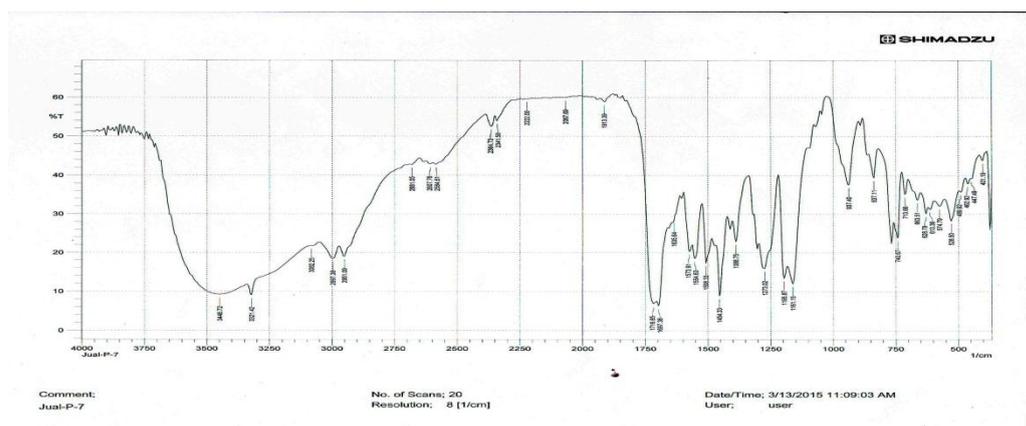


Figure 6. FTIR spectrum of solid dispersion containing Eudragit E-100 (1:1) (Formulation coding: P1).

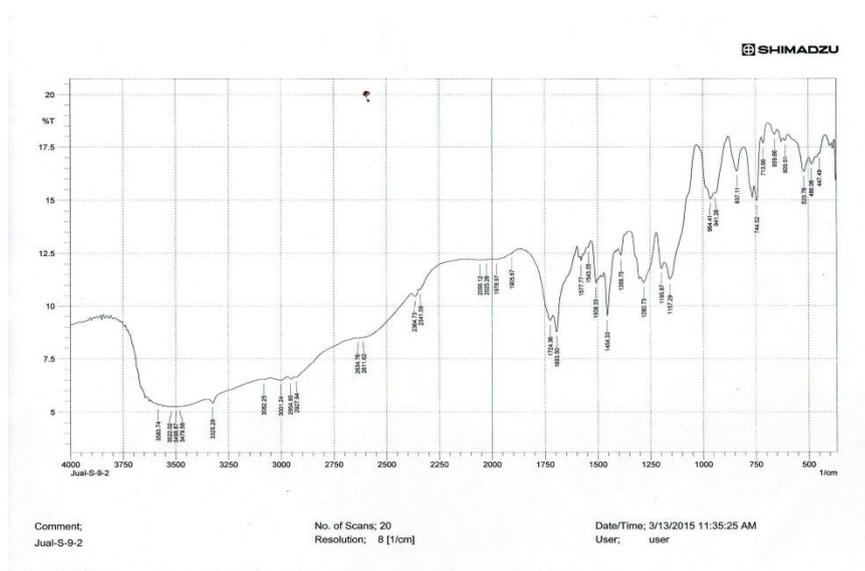


Figure 7. FTIR spectrum of solid dispersion containing Eudragit E-100 (1:5) (Formulation coding: S9).

3.5. Drug release kinetics

In this study, drug released from SDs formulation were analyzed by Zero order model, First order model, Hixson-Crowell cube root law and Higuchi square root equation. Y-equation ($Y=aX+b$) and correlation coefficient (R^2) of diclofenac sodium, different SDs formulation and physical mixtures are shown in Table 5. The data showed that active diclofenac sodium and the physical mixtures (Formulation coding: P1, P2 and P3) follows Higuchi release model. On the other hand, SDs formulation prepared by solvent evaporation technique (Formulation coding: S1, S2, S3, S4 and S5) followed 1st order release kinetics.

3.6. Fourier-transform infrared spectroscopy (FTIR) study

Fourier-transform infrared (FT-IR) spectroscopy was used to characterize possible interactions between the drug and the carrier in solid state. The FTIR spectra of SDs containing Eudragit E-100 (physical mixtures) showed in Figure 5 and SDs containing same polymer prepared by solvent evaporation showed in Figure 6 were compared with the standard spectrum of active diclofenac sodium showed in Figure 7. FTIR spectra of solid dispersion formulation of diclofenac sodium showed characteristic peaks at different wave numbers which was also found in the FTIR spectrum of pure diclofenac sodium. These characteristic peaks are given in Table 6.

The FTIR spectrum did not show presence of any additional peaks for new functional groups indicating no chemical interaction between drug and Eudragit E-100. Thus the FTIR spectra ensure the presence of drug in each formulation.

4. Conclusions

Diclofenac sodium is a poorly water soluble drug. The enhancement of oral bioavailability of poorly water soluble drugs remains one of the most challenging aspects of drug perfection. Various scientists achieved a complete dissolution of drug from solid dispersions (SDs) by using different hydrophilic carriers. The carriers acted as dispersing for the liberated drug, thus preventing the formation of any water-insoluble surface layers. In the present study, solid dispersions of diclofenac sodium with Eudragit E-100 in different ratios were prepared by physical mixing and solvent evaporation technique to improve water solubility and dissolution characteristics. The preparation of solid dispersion of diclofenac sodium by this method has been proven to be successful. This research showed that when diclofenac sodium was dispersed in suitable water-soluble carriers Eudragit E-100, its dissolution were enhanced compared with pure drug. Among all binary SD formulations, the Eudragit E-100 in 1:5 ratio gave the best result. The water soluble carrier may operate in the micro environment (diffusion layer) immediately surrounding the drug particles in the early stage of dissolution, since the carrier completely dissolves in short time thus enhancing the solubility & dissolution of drug. The Infrared spectroscopy study showed that there were no significant interactions between drug and carriers in the solid dispersion. However, the shape & surface morphology are important consideration for solid dispersion characterizations. So, further studies Differential Scanning Calorimetry (DSC), Scanning Electronic Microscopy (SEM) and X-ray diffractions (XRD) have to be conducted in this aspect to know the physicochemical characteristics of drug. Finally *In vivo* study is required for final selection of carrier and to produce a successful

drug delivery system. Solid dispersion preparation by the method demonstrated in this study thus may be an ideal means of drug delivery system for poorly water soluble drugs.

Acknowledgements

The authors are thankful to Pharmaceutical Technology Laboratory, Department of Pharmacy, BGC Trust University Bangladesh, Chittagong for their supports & co-operations. We are also thankful to Albion Laboratories Limited, Chittagong & University of Chittagong, Bangladesh for Fourier Transform Infra Red (FTIR) spectroscopy analysis.

Conflict of interest

None to declare.

References

- Dingra D, A Bhandari, RB Sharma, G Ranjana and G Sachin, 2010. Enhancement of dissolution rate of slightly soluble drug Clomophen Citrate by solid dispersion. *Int. J. Chem. Tech. Res.*, 2: 1691- 1697.
- Duncan QMC, 2002. The mechanism of drug release from solid dispersions in water- soluble polymers. *Int. J. Pharm.*, 231: 131-144.
- Higuchi T, 1961. Rate of release of medicaments from ointment bases containing drugs in suspension. *J. Pharm. Sci.*, 50: 847-875.
- Hinz B, T Rau, D Auge, U Werner, R Ramer, S Rietbrock and K Brune, 2003. Aceclofenac spares cyclooxygenase 1 as a result of limited but sustained biotransformation to diclofenac. *Clin. Pharmacol. Ther.*, 74: 222-235.
- Hixon AW and JH Crowell, 1931. Dependence of reaction velocity upon surface and agitation. *Ind. Eng. Chem.*, 23: 923-931.
- Jafari E, 2013. Preparation, Characterization and Dissolution of solid dispersion of diclofenac sodium using Eudragit E-100. *J. App Pharm. Sci.*, 3: 167-170.
- Jatwani S, AV Rana, G Singh and G Aggaral, 2012. An overview on solubility enhancement techniques for poorly soluble drugs and solid dispersion as an eminent strategic approach. *Int. J. Pharm Sci and Res.*, 3: 942-956.
- Kamalakkannan V, A Puratchikody, K Masilamani and B Senthilnathan, 2010. Solubility enhancement of poorly soluble drugs by solid dispersion technique- A Review. *J. Pharm. Res.*, 3: 2314-2321.
- Kavita K, A Mishra and B Jha, 2013. Extracellular polymeric substances from two biofilm forming *Vibrio* species: Characterization and application. *Carbohydr Polyme.*, 94: 882-888.
- Kuhlmann WD, 1979. Immune-electron microscopy of alpha-1-fetoprotein during development of rat hepatocytes. *J. Ultrastruct. Res.*, 68: 109-111.
- Murtaza G, M Ahmad and G Shahnaz, 2010. Microencapsulation of Diclofenac sodium by non-solvent addition technique. *Tropical J. Pharm Res.*, 9: 187-195.
- Najmuddin M, T Khan, AA Mohsin, S Shelar and V Patel 2010. Enhancement of dissolution rate of ketoconazole by solid dispersion technique. *Int. J. Pharm. Pharm. Sci.*, 2: 132-136.
- Patel T, LD Patel and S Makwana, 2010. Enhancement of dissolution of Fenofibrate by solid dispersion technique. *Int. J. Res Pharm. Sci.*, 1: 127-132.
- Paul PK, LR Dey, M Shahriar, I Dewan and SMA Islam, 2012. Comparative *in-vitro* dissolution study of Spironolactone from binary and ternary solid dispersion: Model dependent and model independent approaches. *JDDT*, 2: 73- 80.
- Pavia D, G Kriz and G Lampman, 2001. Introduction to spectroscopy: A guide for students of organic chemistry (3rd ed.), Washington: Brooks/Cole Thomson Learning, 13: 24.
- Riess W, H Stierlin, P Degen, JW Faigle, A Gerardin, J Moppert, A Sallmann, K Schmid, A Schweizer, M Sulc, W Theobald and J Wagner, 1978. Pharmacokinetics and metabolism of the anti-inflammatory agent Voltaren. *Scand J. Rheumatol. Suppl.*, 22: 17-29.
- Tanaka N, K Imai, K Okimoto, SR Jeda, YT Ibuki, K Higaki and T Kimura, 2006. Developments of novel sustain-release system disintegration controlled matrix tablet (DCMT) with solid dispersion granules of Niclapine (II): *in-vivo* evaluation. *J. Control. Rel.*, 122: 51-56.
- Wagner JG, 1969. Interpretation of present dissolved-time plots derived from *in-vitro* testing of conventional tablets and capsules. *J. Pharm. Sci.*, 58: 1253-1257.