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Research Article

Eenhancement of solubility and dissolution rate of Furosemide by ternary solid dispersion technique

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Abstract

Purpose: This investigation was carried out to determine if a solid dispersion of furosemide in different carrier such as poloxamer 407P, PEG 6000, and PVPK30 would enhance the dissolution properties of the drug.

Method: Solid dispersion of drug Furosemide, PEG 6000 & Poloxamer 407 and PVP K30 were prepared with a view to study the influence of polymer on solubility and dissolution of this poorly soluble drug furosemide. Solid dispersions of furosemide were prepared using different ratios of furosemide, PEG 6000, Poloxamer 407, pvpk30 as carrier by, solvent evaporation method. They were evaluated for percentage yield, drug content, FTIR spectral studies, DSC, XRD, solubility, and in-vitro dissolution. The dissolution studies were performed at 37 ± 0.5^{o}C and 50 rpm in simulated gastric fluid (0.1 N HCl).

Result: The solubility profile indicated that there is increase in solubility of furosemide when polymer concentration is increased. The solid dispersion complex of drug (1:4:4 ratios) of drug: poloxamer 407: pvpk30 was giving better dissolution profile as compared to pure drug and other solid dispersions. This in turn can improve the bioavailability. FT-IR, DSC shows the compatibility of drug and carrier.

Conclusion: Solid dispersion technique can be used to improve the dissolution of furosemide.

1. Introduction

Solid dispersions can be defined as molecular or amorphous mixtures of poorly water soluble drugs in hydrophilic carriers in which the polymer properties play an important role in the drug dissolution profile. It has been estimated that 40% of new chemical entities being discovered are poorly water-soluble. With recent advances in screening methods for identifying potential drug candidates, an increasing number of poorly water soluble drugs have been identified as potential therapeutic agents. Unfortunately, these drugs have poor bioavailability due to their poor solubility. This has limited the commercial potential of these drugs. The solid dispersion technique is one of the most efficacious to improve the bioavailability of drugs with low water solubility. Among the important factors increasing the solubility of drugs in solid dispersions, particle size reduction, reduced agglomeration, improved wettability and solubility, or dispersion of the drug as micro-fine crystals, amorphous materials or in a molecular form must be mentioned. These formulations offer many advantages over others and the most relevant are the lower cost of the adjuvants and the feasible industrial application. Solid dispersion in an inert carrier or matrix of solid state prepared mainly by the melting (or fusion) and solvent evaporation methods. The melting method involves heating a physical mixture of an active agent and a carrier until melted, followed by rapidly solidifying under vigorous mixing, resulting in super saturation of the drug by instantaneous solidification. On the other hand, the solvent evaporation method involves dissolving a physical mixture of two or more chemicals in a common solvent, followed by evaporation of the solvent. The proper selection of solvent and its removal rate

are crucial in determining the quality of the final dispersion. The release mechanism of drug from a variety of solid dispersions depends on the physical properties of carriers as well as drug substances and preparation methods.

Furosemide (FRMD) is 5-(aminosulphonyl)-4-chloro-2-[(2-fuanyl-methyl) amino] benzoic acid, a potent high ceiling (loop) diuretic, mainly used in the treatment of hypertension.2 The drug has been classified as class IV drug as per the biopharmaceutical classification system (BCS) and having low solubility and oral bioavailability, one of the major cause of the low oral bioavailability of FRMD is its solubility.8,9 Furosemide, a loop diuretic, inhibits water reabsorption in the nephron by blocking the sodium-potassium-chloride cotransporter (NKCC2) in the thick ascending limb of the loop of Henle. This is achieved through competitive inhibition at the chloride binding site on the cotransporter, thus preventing the transport of sodium from the lumen of the loop of Henle into the basolateral interstitium. Consequently, the lumen becomes more hypertonic while the interstitium becomes less hypertonic, which in turn diminishes the osmotic gradient for water reabsorption throughout the nephron. Because the thick ascending limb is responsible for 25% of sodium reabsorption in the nephron, furosemide is a very potent diuretic. The objective of the present study was to improve the solubility of FRDM by using eudragit polymer in three different ratio. The formulations were characterized by in vitro dissolution study to compare the effects of polymers on the preparation of solid dispersion and dissolution enhance.[1-5]

2. Material and Method

Furosemide is purchase for gift sample of Sanofi Aventis Andheri Mumbai, All other materials used were of pharmaceutical or analytical grade.

Instruments:- Schemadzu UV-vis spectrophotometry model 1800, laboratory, Perkin Emer Spectrum 68 FTIR, Dissolution tester (USP) TDT-08L (Electrolab),

2.1 Preparation of solid dispersion by solvent evaporation method [6]

Required amount of furosemide was dissolved in 20 ml of methanol. Accurately weighed carrier corresponding to different drug: carrier ratio by weight was dispersed in drug solution. Then the solvent was allowed to evaporate completely. The resulting solid mass was then pulverized in a mortar to get dry free-flowing powder. The powder was passed through a #80 mesh sieve. The resulting mass was transferred to desiccators containing CaCl2 and stored until completely dry. Solid dispersion of furosemide with polymers in the ratio (1:1:1, 1:2:2, 1:3:3, 1:4:4 and 1:5:5 resp.) was prepared.

Table 1: Formulation table of furosemide solid dispersion

Drug	**Furosemide**	**Furosemide**	**Furosemide**
Carrier	**PEG6000:POLOXAMER 407**	**POLOXAMER407:PVPK30**	**PEG6000:PVPK30**
SSD1	1:1:1	1:1:1	1:1:1
SSD2	1:2:2	1:2:2	1:2:2
SSD3	1:3:3	1:3:3	1:3:3
SSD4	1:4:4	1:4:4	1:4:4
SSD5	1:5:5	1:5:5	1:5:5

2.2 Preparation of solid dispersion tablet [7-10]

All ingredients weighed and materials except Talc and Magnesium Stearate were passed through sieve no. 40. Prepared blend was lubricated with Talc and Magnesium Stearate which was previously passed through sieve no. 80. Tablets were compressed using on BB tooling Compression machine. Tablet weight was maintained as per the solid dispersion polymer drug ratio. In addition to one or multiple filler binders and drug substances, generally a disintegrant, a lubricant and substance such as glidants are present in the tablet formulation.

Table 2:-Formulation of solid dispersion tablet

Sr no	Name of ingredients	Quantity required (mg)
1)	Furosemide	12
2)	Starch	8
3)	Avicel ph 102	82
4)	Magnesium stearate	0.5
5)	Talc	0.5

Total weight of the tablet - 100mg.

2.3 Evaluation Parameter of Solid Dispersion Tablet

1) % Practical Yield: [10,15]

Percentage practical yield is calculated to know about percent yield or efficiency of any method, thus its help in selection of appropriate method of production. Solid dispersions were collected and weighed to determine practical yield (PY) from the following equation.

$$PY(\%) = \frac{\text{Practical Mass (Solid dispersion)}}{\text{Theoretical Mass (Drug + carrier)}} \times 100$$

2) Drug content: [11,15]

10 mg of solid dispersions were weighed accurately and dissolved in 10 ml of methanol. The solution was filtered, diluted suitably and drug content was analyzed at 238 nm by UV spectrophotometer. Each sample analyzed in triplicate. Actual drug content was calculated for all batches using the equation as follows:

$$\text{Drug content \%} = \frac{Tact}{Tss} \times 100$$

$$= \frac{\text{Actual Simvastatin content in weight quantity of solid dispersion}}{\text{Theoretical amount of Simvastatin in solid dispersion}} \times 100$$

3) *In Vitro* dissolution study: [12,15]

Dissolution studies were performed assuring sink condition according to the paddle method (USP) using USP XXIII apparatus type-II (electrolab TDTO9T). The dissolution medium was 900 ml 0.1N HCl kept at 37°C ± 0.5°C. The solid dispersions containing 100 mg of Simvastatin was taken in a muslin cloth and tied to the rotating paddle kept in the basket of dissolution apparatus, the paddle was rotated at 50 rpm. Samples of 5 ml were withdrawn at specified time intervals and analyzed spectrophotometrically at 276 nm using Shimadzu-1800 UV-visible spectrophotometer. The samples withdrawn were replaced by fresh buffer solution. Each preparation
was tested in triplicate and then mean values were calculated.

4) Fourier transform infrared (FTIR) spectroscopy

FTIR spectra were recorded on samples prepared in potassium bromide (KBr) disks using a Shimadzu Corporation (Koyto, Japan) facilty (model - 8400S). Samples were prepared in KBr disks in a hydrostatic press at 6-8 tons pressure. The scanning range was 500 to 4000 cm -1.

5) Differential scanning calorimetry (DSC): [13,15]

Thermal analysis of Simvastatin, PVP K30 and the solid dispersion were carried out using differential scanning calorimetry method. Samples were examined using a Shimadzu TGA- 50 DSC instrument.

Samples equivalent to approximately 8 mg Simvastatin were placed in aluminum pans and heated from 40 to 250°C with a heating rate of 10°C/min.

6) X-ray Powder Diffraction (XRD): [14-17]

Furosemide was assessed by carrying out physical state analysis. The cavity of the metal sample holder of X ray diffractometer was filled with ground Sample powder & then smoothed out with a spatula.

X-ray Diffraction pattern of Simvastatin was obtained using the X-ray Diffractometer (Siemens‟, Germany D-5000).

3. Result and Discussion

Solid dispersions of Simvastatin were prepared by different methods using carriers like PEG 6000 and Poloxamer 407. In the present work, total 15 formulations were prepared and their complete composition is shown in Table-2. All the Solid dispersions prepared were found to be fine and free flowing powders.

Table 3: Result of percentage yield, & Drug content and *in vitro* dissolution of solid dispersion of furosemide

Sr. No	Formulation code	% practical yield	Drug content	% drug release 60min
1	SSD-A1	74.75	41.40	56.29
2	SSD-A2	74.3	45.26	77.24
3	SSD-A3	76.85	43.36	77.23
4	SSD-A4	73.47	40	69.34
5	SSD-A5	68.18	37.1	80.62
6	SSD-B1	63	64.4	71.88
7	SSD-B2	84.2	55	66.40
8	SSD-B3	61.53	58.83	58.00
9	**SSD-B4**	**88.47**	**82**	**82.71**
10	SSD-B5	79.88	38	81.66
11	SSD-C1	73.33	41.60	56.66
12	SSD-C2	81.4	46	62.63
13	SSD-C3	87.82	78	65.72
14	SSD-C4	82.22	81.33	75.11
15	SSD-C5	76.56	76.34	82.46

1) Percent practical yield

The results of percent practical yield studies are shown in Table No. 3 .The % Practical yield of the prepared solid dispersions was found to be in the range of 61.53- 88.47 % The maximum yield was found 88.47 % in SSD- B4 formulation.

2) Drug content

The actual drug content of all the 15 formulations are shown in Table No. 3 .The drug content of the prepared Solid dispersions were in the range of 40- 82 % indicating the application of the present methods for the preparation of Solid dispersions with high content uniformity. The maximum % drug content was found 82 % in SSD-B4 formulation.

3) *In vitro* dissolution study

Solid dispersion prepared by solvent evaporation method shows improved dissolution at the end of 60 min which is 82.71%. The ratio Drug: Poloxamer 407: pvp k30 (1:4:4) showed better in vitro release when compared with that of pure drug which is 28.78 % at the end of 60min. The solid dispersion prepared by solvent evaporation method and showed 1.5 fold increases in dissolution. This is due to increased wet ability and dispersibility of drug by the carrier. Hydrophilic carrier will help to improve wetting property and reduce the interfacial tension between hydrophobic drug and dissolution medium. The increase in dissolution rate was in the order of Poloxamer 407: pvpk30 > Poloxamer 407: PEG 6000 > PEG 6000: PVP K30.

Table 4: Caliberation of furosemide

Concentration	Absorption
5	0.5895
10	0.9382
15	1.232
20	1.564
25	1.876

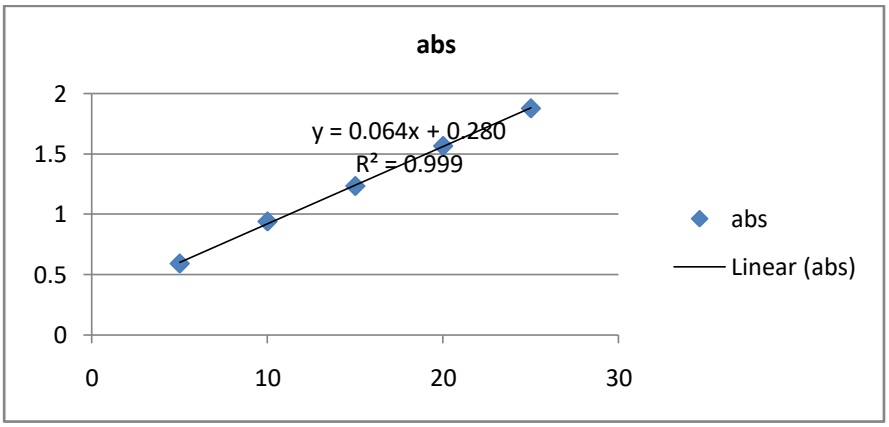

Fig 1: Calibration of furosemide

Table 5:-% drug release calculation

A1 Formulation batch

PEG6000: PVPK30		(1:1:1)						
Time	**abs**	**slope**	**intercept**	**conc**	**conc*900**	**conc*10**	**conc/1000**	**% drug release**
5	0.4432	0.064	0.28	2.55	2295	22950	22.95	38.25
10	0.4897	0.064	0.28	3.276563	2948.906	29489.06	29.48906	49.14844
15	0.5234	0.064	0.28	3.803125	3422.813	34228.13	34.22813	57.04688
30	0.532	0.064	0.28	3.9375	3543.75	35437.5	35.4375	59.0625
45	0.5785	0.064	0.28	4.664063	4197.656	41976.56	41.97656	69.96094
60	0.5543	0.064	0.28	4.285938	3857.344	38573.44	38.57344	64.28906
							Avg=	56.29297

1:2:2 A2 BATCH

Time	**Abs**	**slope**	**intercept**	**conc**	**conc*900**	**conc*10**	**conc/1000**	**% drug release**
5	0.5342	0.064	0.28	3.971875	3574.688	35746.88	35.74688	59.57813
10	0.543	0.064	0.28	4.109375	3698.438	36984.38	36.98438	61.64063
15	0.5949	0.064	0.28	4.920313	4428.281	44282.81	44.28281	73.80469
30	0.654	0.064	0.28	5.84375	5259.375	52593.75	52.59375	87.65625
45	0.6648	0.064	0.28	6.0125	5411.25	54112.5	54.1125	90.1875
60	0.6665	0.064	0.28	6.039063	5435.156	54351.56	54.35156	90.58594
								77.24219

1:3:3 A3 BATCH

Time	**Abs**	**slope**	**intercept**	**conc**	**conc*900**	**conc*10**	**conc/1000**	**%drug release**
5	0.498	0.064	0.28	3.40625	3065.625	30656.25	30.65625	51.09375
10	0.498	0.064	0.28	3.40625	3065.625	30656.25	30.65625	51.09375
15	0.598	0.064	0.28	4.96875	4471.875	44718.75	44.71875	74.53125
30	0.6754	0.064	0.28	6.178125	5560.313	55603.13	55.60313	92.67188
45	0.689	0.064	0.28	6.390625	5751.563	57515.63	57.51563	95.85938
60	0.6987	0.064	0.28	6.542188	5887.969	58879.69	58.87969	98.13281
								77.23047

1:4:4 A4 BATCH

time	**Abs**	**slope**	**intercept**	**conc**	**conc*900**	**conc*10**	**conc/1000**	**%drug release**
5	0.4675	0.064	0.28	2.929688	2636.719	26367.19	26.36719	43.94531
10	0.4898	0.064	0.28	3.278125	2950.313	29503.13	29.50313	49.17188
15	0.5122	0.064	0.28	3.628125	3265.313	32653.13	32.65313	54.42188
30	0.5987	0.064	0.28	4.979688	4481.719	44817.19	44.81719	74.69531
45	0.689	0.064	0.28	6.390625	5751.563	57515.63	57.51563	95.85938
60	0.698	0.064	0.28	6.53125	5878.125	58781.25	58.78125	97.96875
								69.34375

1:5:5 A5 BATCH

time	**Abs**	**slope**	**intercept**	**conc**	**conc*900**	**conc*10**	**conc/1000**	**%drug release**
5	0.4532	0.064	0.28	2.70625	2435.625	24356.25	24.35625	40.59375
10	0.598	0.064	0.28	4.96875	4471.875	44718.75	44.71875	74.53125
15	0.6543	0.064	0.28	5.848438	5263.594	52635.94	52.63594	87.72656
30	0.6654	0.064	0.28	6.021875	5419.688	54196.88	54.19688	90.32813
45	0.675	0.064	0.28	6.171875	5554.688	55546.88	55.54688	92.57813
60	0.698	0.064	0.28	6.53125	5878.125	58781.25	58.78125	97.96875
								80.62109

B1 BATCH

POLO 407:PVPK30	1:1:1							
Time	**abs**	**slope**	**intercept**	**conc**	**conc*900**	**conc*10**	**conc/1000**	**%drug release**
5	0.4231	0.064	0.28	2.235938	2012.344	20123.44	20.12344	33.53906
10	0.5432	0.064	0.28	4.1125	3701.25	37012.5	37.0125	61.6875
15	0.567	0.064	0.28	4.484375	4035.938	40359.38	40.35938	67.26563
30	0.654	0.064	0.28	5.84375	5259.375	52593.75	52.59375	87.65625
45	0.6654	0.064	0.28	6.021875	5419.688	54196.88	54.19688	90.32813
60	0.6675	0.064	0.28	6.054688	5449.219	54492.19	54.49219	90.82031
								71.88281

1:2:2 B2 BATCH

Time	Abs	slope	intercept	conc	conc*900	conc*10	conc/1000	%drug release
5	0.6523	0.064	0.28	5.817188	5235.469	52354.69	52.35469	87.25781
10	0.5776	0.064	0.28	4.65	4185	41850	41.85	69.75
15	0.554	0.064	0.28	4.28125	3853.125	38531.25	38.53125	64.21875
30	0.5213	0.064	0.28	3.770313	3393.281	33932.81	33.93281	56.55469
45	0.5473	0.064	0.28	4.176563	3758.906	37589.06	37.58906	62.64844
60	0.5275	0.064	0.28	3.867188	3480.469	34804.69	34.80469	58.00781
								66.40625

1:3:3 B3 BATCH

time	Abs	slope	intercept	conc	conc*900	conc*10	conc/1000	%drug release
5	0.6523	0.064	0.28	5.817188	5235.469	52354.69	52.35469	87.25781
10	0.5776	0.064	0.28	4.65	4185	41850	41.85	69.75
15	0.554	0.064	0.28	4.28125	3853.125	38531.25	38.53125	64.21875
30	0.5213	0.064	0.28	3.770313	3393.281	33932.81	33.93281	56.55469
45	0.5473	0.064	0.28	4.176563	3758.906	37589.06	37.58906	62.64844
60	0.5275	0.064	0.28	3.867188	3480.469	34804.69	34.80469	58.00781
								66.40625

1:4:4 (best batch) B4 BATCH

Time	Abs	slope	intercept	conc	conc*900	conc*10	conc/1000	%drug release
5	0.5844	0.064	0.28	4.75625	4280.625	42806.25	42.80625	71.34375
10	0.633	0.064	0.28	5.515625	4964.063	49640.63	49.64063	82.73438
15	0.5949	0.064	0.28	4.920313	4428.281	44282.81	44.28281	73.80469
30	0.654	0.064	0.28	5.84375	5259.375	52593.75	52.59375	87.65625
45	0.6648	0.064	0.28	6.0125	5411.25	54112.5	54.1125	90.1875
60	0.6665	0.064	0.28	6.039063	5435.156	54351.56	54.35156	90.58594
								82.71875

1:5:5 B5 BATCH

Time	Abs	Slope	intercept	conc	conc*900	conc*10	conc/1000	%drug release
5	0.487	0.064	0.28	3.234375	2910.938	29109.38	29.10938	48.51563
10	0.554	0.064	0.28	4.28125	3853.125	38531.25	38.53125	64.21875
15	0.654	0.064	0.28	5.84375	5259.375	52593.75	52.59375	87.65625
30	0.6786	0.064	0.28	6.228125	5605.313	56053.13	56.05313	93.42188
45	0.698	0.064	0.28	6.53125	5878.125	58781.25	58.78125	97.96875
60	0.699	0.064	0.28	6.546875	5892.188	58921.88	58.92188	98.20313
								81.66406

C1 BATCH

PEG6000: POLOXAMER 407	1:1:1							
Time	**abs**	**slope**	**intercept**	**conc**	**conc*900**	**conc*10**	**conc/1000**	**%drug release**
5	0.432	0.064	0.28	2.375	2137.5	21375	21.375	35.625
10	0.4453	0.064	0.28	2.582813	2324.531	23245.31	23.24531	38.74219
15	0.4567	0.064	0.28	2.760938	2484.844	24848.44	24.84844	41.41406
30	0.5564	0.064	0.28	4.31875	3886.875	38868.75	38.86875	64.78125
45	0.5876	0.064	0.28	4.80625	4325.625	43256.25	43.25625	72.09375
60	0.6547	0.064	0.28	5.854688	5269.219	52692.19	52.69219	87.82031
								56.74609

1:2:2 C2 BATCH

Time	Abs	slope	intercept	conc	conc*900	conc*10	conc/1000	%drug release
5	0.5162	0.064	0.28	3.690625	3321.563	33215.63	33.21563	55.35938
10	0.5072	0.064	0.28	3.55	3195	31950	31.95	53.25
15	0.5006	0.064	0.28	3.446875	3102.188	31021.88	31.02188	51.70313
30	0.316	0.064	0.28	0.5625	506.25	5062.5	5.0625	8.4375
45	0.7123	0.064	0.28	6.754688	6079.219	60792.19	60.79219	101.3203
60	0.7311	0.064	0.28	7.048438	6343.594	63435.94	63.43594	105.7266
								62.63281

1:3:3 C3 BATCH

Time	Abs	slope	intercept	conc	conc*900	conc*10	conc/1000	%drug release
5	0.4563	0.064	0.28	2.754688	2479.219	24792.19	24.79219	41.32031
10	0.4876	0.064	0.28	3.24375	2919.375	29193.75	29.19375	48.65625
15	0.4897	0.064	0.28	3.276563	2948.906	29489.06	29.48906	49.14844
30	0.564	0.064	0.28	4.4375	3993.75	39937.5	39.9375	66.5625
45	0.6753	0.064	0.28	6.176563	5558.906	55589.06	55.58906	92.64844
60	0.6897	0.064	0.28	6.401563	5761.406	57614.06	57.61406	96.02344
								65.72656

1:4:4 C5 BATCH

Time	Abs	slope	intercept	conc	conc*900	conc*10	conc/1000	%drug release
5	0.5432	0.064	0.28	4.1125	3701.25	37012.5	37.0125	61.6875
10	0.5543	0.064	0.28	4.285938	3857.344	38573.44	38.57344	64.28906
15	0.5546	0.064	0.28	4.290625	3861.563	38615.63	38.61563	64.35938
30	0.5687	0.064	0.28	4.510938	4059.844	40598.44	40.59844	67.66406
45	0.681	0.064	0.28	6.265625	5639.063	56390.63	56.39063	93.98438
60	0.7011	0.064	0.28	6.579688	5921.719	59217.19	59.21719	98.69531
								75.11328

1:5:5 C6 BATCH

Time	Abs	slope	intercept	conc	conc*900	conc*10	conc/1000	% drug release
5	0.5342	0.064	0.28	3.971875	3574.688	35746.88	35.74688	59.57813
10	0.5674	0.064	0.28	4.490625	4041.563	40415.63	40.41563	67.35938
15	0.6543	0.064	0.28	5.848438	5263.594	52635.94	52.63594	87.72656
30	0.6675	0.064	0.28	6.054688	5449.219	54492.19	54.49219	90.82031
45	0.6786	0.064	0.28	6.228125	5605.313	56053.13	56.05313	93.42188
60	0.689	0.064	0.28	6.390625	5751.563	57515.63	57.51563	95.85938
								82.46094

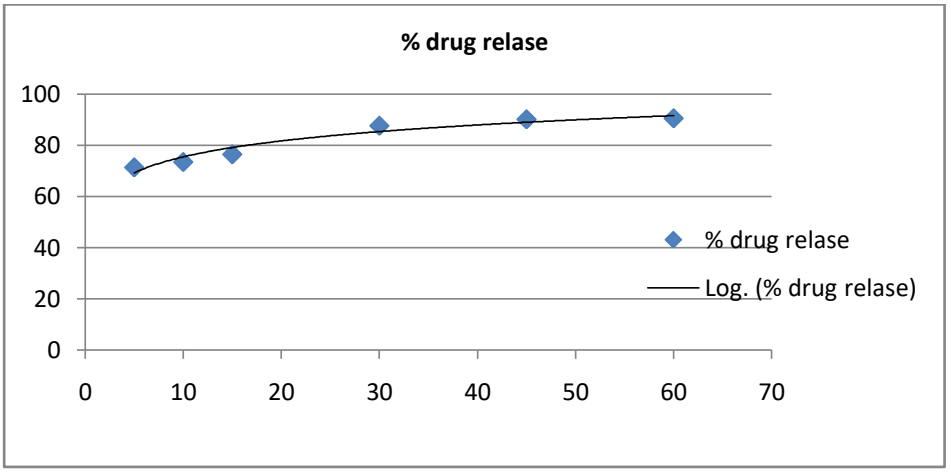

Fig 2: % drug release of furosemide: poloxamer 407:pvpk30.(1:4:4)

4) X-ray diffraction:-

The x-ray diffraction pattern of furosemide exhibited sharp, highly intense and less diffused peaks indicating the crystalline nature of drug, as shown in Figure. It showed diffraction peaks at 2θ degree. However the x-ray diffraction patterns of the physical mixture and solid dispersion were simply a superimposition of each component with with respect to the peaks of frusemide. Moreover, the relative intensity and 2θ angle of these peaks remained practically unchanged. Thus, there was no amorphization of the drug and which still retained its original crystalline form.

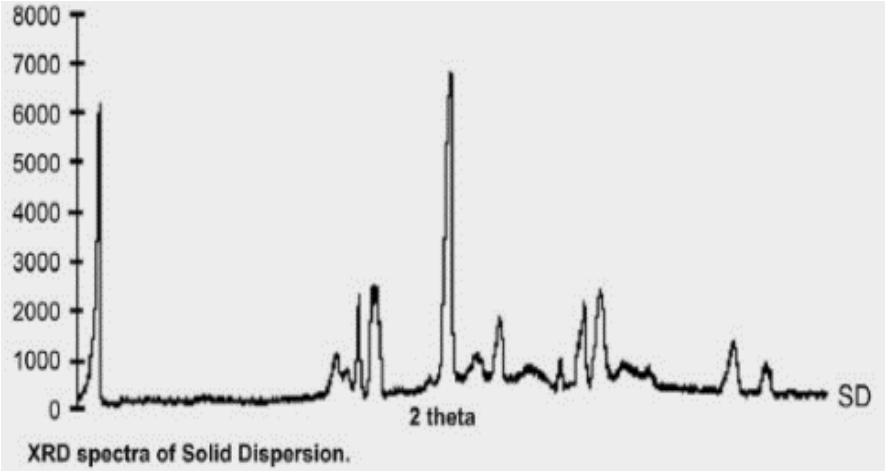

Fig 3: XRD spectra of solid dispersion.

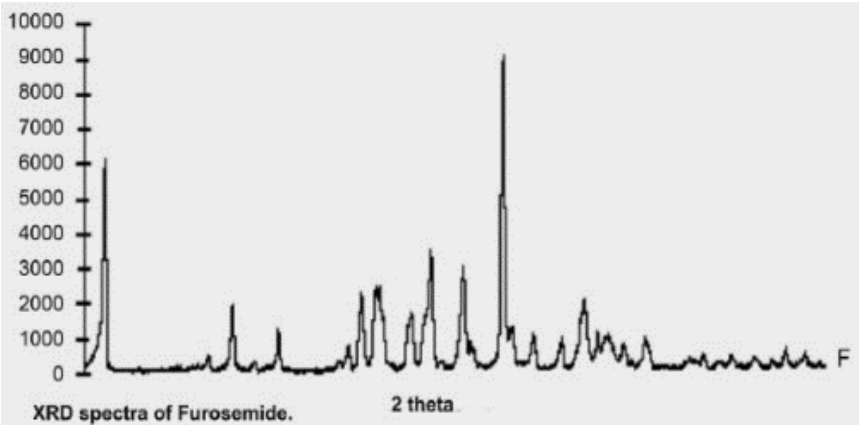

Figure 4: X-ray diffraction spectra of best formulation (F4)

5) DSC spectra of best formulation

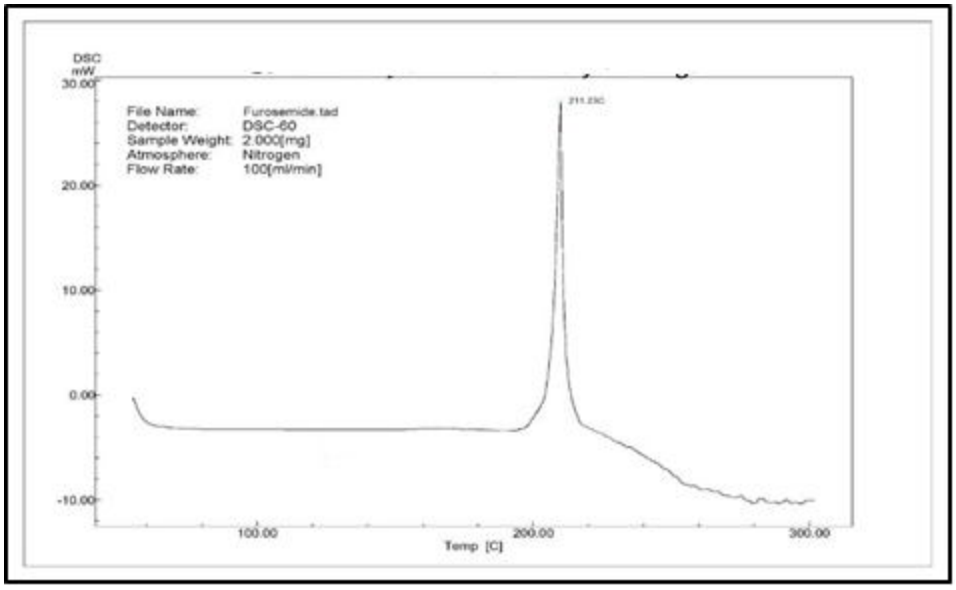

Figure 5: DSC Spectra of furosemide pure drug.

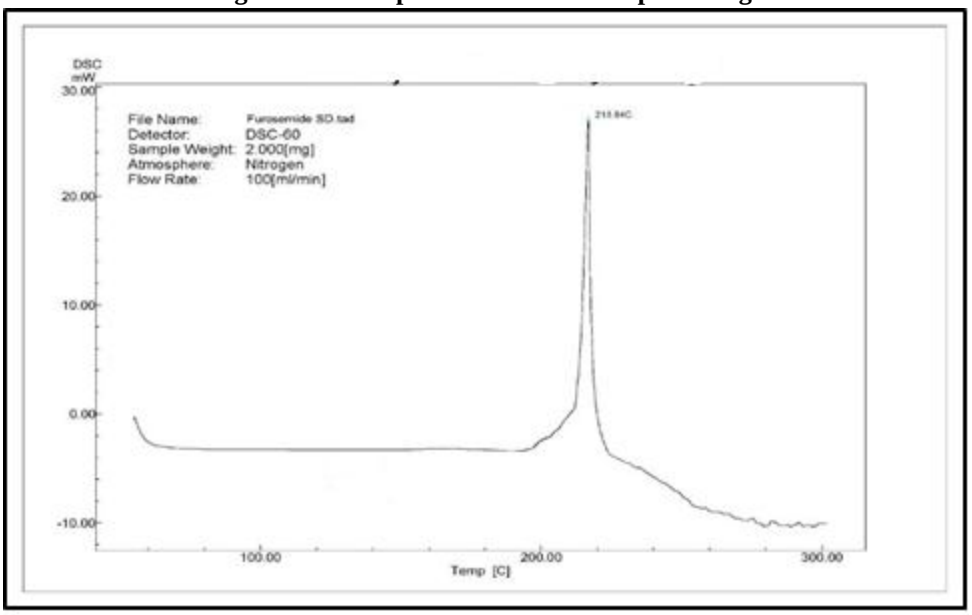

Figure 6: DSC Spectra of furosemide solid dispersion (F4)

DSC thermograms of furosemide and Solid dispersion of furosemide (F4, Poloxamer 407:PVPK30 1:4:4), in Figure 7 and 8 respectively. DSC studies, on the basis of the melting peak of furosemide solid dispersion (213.23 ^{o}C), indicate that there was not interaction between the drug and carrier. However, the characteristic melting peak of solid dispersion slightly shifted toward a higher temperature. This may be attributed to high polymer concentration and uniform distribution of the drug in the crust of the polymer, resulting in complete miscibility of the drug in the polymer. The similarity in the DSC of the Pure drug and solid dispersion suggests that the solvent evaporation method did not induce interaction at the molecular level.

6) Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectra were recorded on samples prepared in potassium bromide (KBr) disks. Samples were prepared in KBr disks by means of a hydrostatic press at 6-8 tons pressure. The scanning range was 500 to 4000 cm -1. IR spectra of FRMD and its binary systems with PEG-4000 are presented in Figure. Pure Furosemide spectra showed sharp characteristic peaks at 3400.27, 3122.54, 1665, and 1560 cm–1. All the above characteristic peaks appear in the spectra of all binary

systems at same wave number indicating no modification or interaction between the drug and carrier. The FTIR of FRMD, PM and SD (1:5) was given in figure 7.

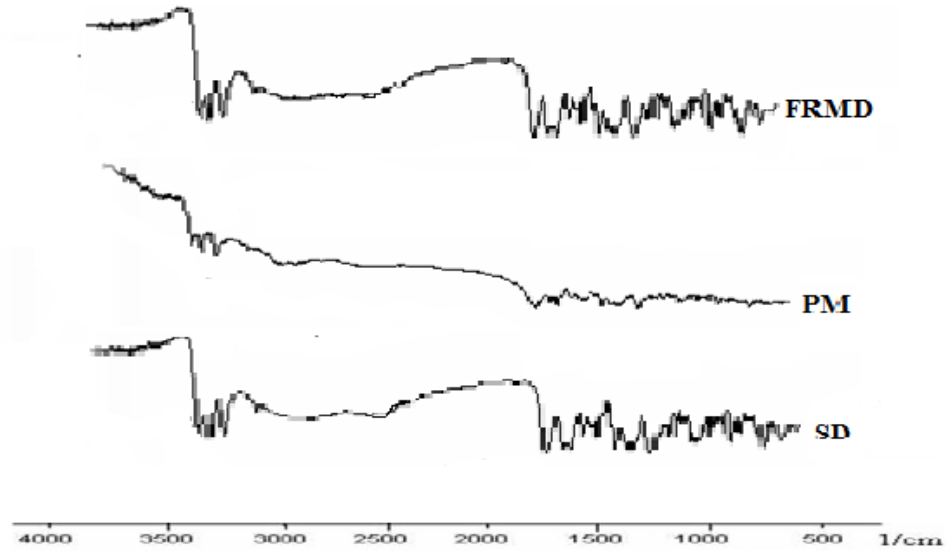

Figure 7: FTIR of furosemide and solid dispersion.

4. Conclusion

The objective of the present study was to improve the solubility and dissolution behaviour of the poorly soluble drug, furosemide by solid dispersion technique using PEG 6000 and Poloxamer 407 as carrier. Solid dispersion of furosemide prepared by a Solvent evaporation method showed significantly higher drug solubility in comparison with pure drug. FTIR and DSC studies showed no evidence of interaction between the drug and carrier. XRD study shows amorphization of drug. Out of the 15 prepared formulation SSD- B4 showed marked increase in the solubility as well as the dissolution when compared to pure drug. Thus it can be concluded that the solubility of the poorly soluble drug, furosemide can be improved markedly by using solid dispersion technique and the carrier Poloxamer 407 and PVPK30 has increased the dissolution of the drug without any interaction.

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Conflict of interest

Conflict of interest declared none.

Reference

[1] Lipinski C.A.; Avoiding investment in doomed drugs, is poor solubility an industry wide problem, *Curr. Drug Discov*; 2001; 17–19.

[2] T. Vasconcelos, B. Sarmento, P. Costa; Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs, Drug Discov. Today; 2007; 12(23-24); 1068–1075.

[3] Q.M.D. Craig; The mechanisms of drug release from solid dispersions in water soluble polymer; *Int. J. Pharm.*; 2002; 231(2); 131–144.

[4] F. Frizon, J.O. Eloy, C.M. Donaduzzi, M.L. Mitsui, J.M. Marchetti; Dissolution rate enhancement of loratadine in polyvinylpyrrolidone K-30 solid dispersions by solvent methods; Powder Technol.; 2013; 235; 532–539.

[5] W.L. Chiou, S. Riegelman; Pharmaceutical applications of solid dispersion systems; *J. Pharm. Sci.*; 1971; 60(9); 1281–1302.

[6] A.T. Serajuddin; Solid dispersion of poorly water-soluble drugs: early promises, subsequent problems, and recent breakthroughs; *J. Pharm. Sci.*; 1999; 88(10); 1058–1066.

[7] Bhanja SB, Ellaiah P, Roy HK, Samal BK, Tiwari S And Murthy KVR; Formulation And Evaluation Of Perindopril Sublingual Tablets; *International Journal Of Research In Pharmaceutical And Biomedical Sciences;* 2011; 2(3); 1193-1198.

[8] Inara Staub, Elfrides ES Schapoval, Ana M Bergold; Microbiological assay of Ketoconazole in shampoo; *Int. J. Pharm* 2005; 292(1-2); 195-199.

[9] Bhumika Patel et al; Enhancement of dissolution of Telmisartan through use of solid dispersion technique surface solid dispersion; *Journal of Pharmacy and Bioallied Sciences*; 2012; 4(5); S64-S68.

[10] Sachin R Patil, Rani Kumar, Patil MB, Mahesh S Paschapur and Malleswara Rao VSN.; Enhancement of Dissolution rate of aceclofenac by solid dispersion technique; *Int. J. PharmaTech Res*; 2009; 1(4): 1198-1204.

[11] Venkates Kumar K, Arunkumar N, Verma PRP, Rani C.; Preparation and *In-vitro* characterization of valsartan solid dispersions using skimmed milk powder as carrier; Int. J. PharmaTech Res; 2009; 1(3): 431-437.

[12] Norbert Rasenack and Bernd W Miiller.; Dissolution Rate Enhancement by *in Situ* Micronization of poorly Watersoluble Drugs; *Pharmaceutical Research;* 2002; 19(12); 1894-1900.

[13] Malleswara Rao VSN, Shyam T, Appa Rao B and Srinivasa Rao Y.; Formulation and characterization of meloxicam solid dispersions; *The Indian Pharmacist*; 2008; 70; 67-70.

[14] Guanhao Ye, Siling Wang, Paul Wan Sia Heng, Ling Chen, Chao Wang; Development and optimization of solid dispersion containing pellets of itraconazole prepared by high shear pelletization; *Int. J. Pharm*; 2007; 337 (1-2);80-87.

[15] Kothawade S. N.et al; Formulation and Characterization of Telmisatan Solid Dispersions; *International Journal of PharmTech Research*; 2010; 2(1): 341-347.

[16] Garima chawla, Arvind K. Bansal; Improved dissolution of poorly water soluble drug in solid dispersions with polymeric and non polymeric hydrophilic additives; *Acta Pharma;* 2008, 58(3); 257-274.

[17] Yuichi T, Atsutoshi I, Hiiroko S, Toshio O, Keiji Y; Characterization and quantitation of Clarithromycin polymorphs by powder X-Ray diffractometry and solid state NMR spectroscopy; *Chemical & Pharmaceutical Bulletin* 2002; 50(8); 1128-1130.

[18] Yamashita K, Nakate T, Okimoto KA. Establishment of new preparation method for solid dispersion formulation of tacrolimus. *Int J Pharm* 2003; 267:79-91.

[19] Makiko F, Hideko O, Yu suke S, Honami T, Masuo K, Yoshiteru W. Preparation, characterization, and tableting of a solid dispersion of indomethacin with crospovidone. *Int. J. Pharm* 2005; 293: 145–153.

[20] Loganathan S, Maimaran S, Rajasekaran A, Reddy MVP, Sulaiman A. The effect of solid dispersions on (solubility) dissolution rate of ibuprofen. *The Eastern Pharmacist.* 2000; 513: 115 - 116.