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ENHANCEMENT OF DISSOLUTION OF FUROSEMIDE BY SOLID DISPERSION USING HYDROPHILIC POLYMER AND MODIFIED NATURAL CARRIERS

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ABSTRACT

Furosemide (FRMD) is a loop diuretic, poorly water- soluble (BCS-Class II) drug. It is used for the treatment of edema associated with congestive heart failure, cirrhosis of the liver and renal disease, including the nephrotic syndrome. Besides this it is also used for the treatment of hypertension. In order to enhance the extent of absorption, it is necessary to improve its solubility. To increase its solubility and dissolution rate, various solubility enhancement methods like physical mixing, solvent evaporation, kneading and hot melt by using carriers such as Poloxamer 407 and Modified xanthan gum in different ratios were investigated. Drug-carrier interactions were investigated by FTIR spectroscopy and differential scanning calorimetry. The studies showed that solubility and dissolution rate of Furosemide were distinctively increased in the prepared drug carrier mixture compared to that of pure Furosemide. The studies showed that dissolution and solubility parameters progressively improved with increasing the polymer proportion in the drug carrier mixtures. Poloxamer 407 in 1:3 ratio with the drug showed an increase in solubility and dissolution compared to the other polymers.

KEYWORDS: Furosemide; Modified xanthan gum; Poloxamer 407; Solid dispersion; Dissolution enhancement; Physical mixing; Kneading; Solvent evaporation; Hot melt.

INTRODUCTION

There are many drug molecules which have sufficient potency to produce pharmacokinetic as well as pharmacodynamic effects, but because of slight changes in their physical and chemical properties the only problem faced by them is the inability to produce desired effects

and this is resultant of decreased solubility. Many of the synthesized drugs often have solubility related problems.[1] Therefore, if these drugs are not completely solubilised in the gastrointestinal area, they will have a low bioavailability. If drugs are naturally less permeable, the solubility issue causes deeper problems with much more retarded bioavailability. In the biopharmaceutical classification system (BCS) drugs with low aqueous solubility and high permeability are categorized as class-II drugs and often solubility is the rate limiting step for absorption of these drugs. There have been several researches going on to alleviate the solubility related problems of the drugs and make them into use, and these efforts come under the title of solubility enhancement. This has been supported by various strategies like solid dispersion, complexation, eutectic mixture formation and others. Solid dispersions are one of the most successful strategies to enhance solubility of poorly water soluble drugs.

In the present investigation, Furosemide a weekly acidic anti-hypertensive drug which is practically insoluble in gastric fluid and having high permeability through stomach was selected. The rational for selecting such type is "Drug which having highly permeability through stomach but due to its solubility limitation in gastric fluid it can't enter in to systemic circulation. Gastric empting time is ranging from 30 min to 2 hrs after this time drugs go in to small intestine where it is soluble but can't permeate through its membrane due to its permeation limitation." Furosemide is a loop diuretic drug indicated for treatment of oedema and hypertension having high permeability through stomach.

MATERIALS AND METHODS

Materials: Furosemide was obtained as a gift sample from Karnataka Antibiotics Pvt Ltd, Bangalore. Poloxamer 407 was procured from Sigma Aldrich, Mumbai. Xanthan gum was purchased from HiMedia Laboratories, Mumbai. All other chemicals used were of analytical grade.

Methods

Development of calibration curve for furosemide

Calibration of Furosemide was carried out in pH 1.2 buffer solution. Stock solution was prepared by dissolving 10 mg drug in 20 ml methanol and make up the volume with buffer solution up to 100 ml (100 µg/ml). From this solution withdraw 0.2, 0.4, 0.6, 0.8, 1 ml and make up to 10 ml with pH 1.2 buffer solution. Absorbance of these solutions was measured at 234 nm by U.V spectrophotometer. The study was performed in triplicate and

the results are reported as mean±SD.

Preparation of modified karaya gum

10 grams of powdered GK was taken in a porcelain bowl and subjected to heating using a sand bath for 2hr at 120^{o}C.[2,3]

Preparation of modified xanthan gum

Modified polysaccharide was prepared by suspending 5 gm of selected pure polysaccharide - Xanthan gum (XG) in a beaker of 250 ml capacity, containing 100 ml of distilled water. The suspension was stirred at 500 rotations per minute using lab stirrer for 24 hours. Obtained swollen mass was then spread out on enameled tray (10 inches × 12 inches), and dried at room temperature for 72 hours. The dried product was scrapped out using a stainless steel spatula and subjected to crushing in a glass mortar with pestle, to obtain coarse, non-free flowing and heterogeneous particles of treated polysaccharide namely treated xanthan gum (TXG). Treated polysaccharide was then co-grounded with mannitol (1:1) in a glass pestle mortar for 20 minutes and passed through sieve (#22) to get the modified polysaccharide - co-grounded treated xanthan gum (C-TXG) and stored in a desiccator till further use.[4]

Preparation of drug-carrier mixtures

Solid dispersions were prepared by following methods.

Hot melt method

Furosemide and carriers were mixed in different ratios as required and melted in a porcelain evaporating dish immersed in a water bath at 70◦C with continuous stirring to obtain a homogeneous dispersion. The melted mixture was then solidified rapidly in an ice-bath under vigorous stirring. The final solid mass was crushed, pulverized and sieved it through #60.[5]

Solvent evaporation

In solvent evaporation method, carrier was dissolved completely in Methanol in different ratio in a beaker. Furosemide was dispersed in the in drug: polymer solution. The resulting solution was kept on the thermostatically controlled water bath (at 60±0.5°C) to remove the solvent from resulting mixture. The obtained mass was dried in the desiccator for 24hrs. The resultant mass was pulverized using a glass mortar and pestle. The pulverized mass was sifted through #60, weighed and transferred to the glass vials.[6]

Physical mixture

Grinding the drug and carrier in mortar for 2 min at the required drug-carrier ratios. Then the powder was passed through the #60. The resulted product was stored in desiccator to carry out further analysis.

Kneading method

A mixture of drug and carriers in different ratios were wetted with solvent (methanol) and water (1:1 ratio) and kneaded thoroughly for 30 minutes in a glass mortar. The paste formed was dried in hot air oven for 24 hours. Dried powder was scrapped, crushed, pulverized and passed through sieve No. 60 and stored in a desiccator.[7]

Table 1: Drug-carrier mixtures were prepared using compositions as given below.

Drug	Polymer	Method	Ratio	Formulation Code
Furosemide	Modified Xanthan	Physical Mixture	1:1	FXP1
			1:2	FXP2
			1:3	FXP3
		Solvent Evaporation	1:1	FXS1
			1:2	FXS2
			1:3	FXS3
			1:4	FXS4
		Kneading Method	1:1	FXK1
			1:2	FXK2
	Poloxamer 407	Physical Mixing	1:1	FPP1
			1:2	FPP2
			1:3	FPP3
		Solvent Evaporation	1:1	FPS1
			1:2	FPS2
			1:3	FPS3
		Hot Melt	1:1	FPH1
			1:2	FPH2
			1:3	FPH3

Compatibility study

Fourier transform infrared spectroscopy (FTIR)

FTIR spectra of the drug, solid dispersions and carriers were all carried out. Each formula (5 mg) was mixed with about 100 mg potassium bromide and compressed into discs. The IR spectra were scanned from 500cm^{-1} to 4000cm^{-1} using FTIR spectrophotometer (M-840, Shimadzu, Japan).[8]

Differential scanning calorimetry (DSC)

The DSC thermograms were recorded using a differential scanning calorimeter (DSC -60, Shimadzu, Japan). Approximately 2-5 mg of each sample was heated in a pierced aluminium pan from 50°C to 350°C at a heating rate of 10°C/min under a stream of nitrogen at rate 10ml/min.[9]

Evaluation

Characterization of xanthan gum and modified xanthan gum for viscosity and swelling index.[2,10]

Viscosity

A 0.5% aqueous solution of sample was added to the viscometer, pulled into the upper reservoir by suction and then allowed to drain by gravity back into the lower reservoir. The time that it takes for the liquid to pass between two etched marks, one above and one bellow the upper reservoir, is measured. The relative viscosity can be measured by using,

$\eta_{rel} = pt/p_o t_o$

Where ρ is the density, t is the time of outflow of the sample; ρ_o is the density, t_o is the time of the outflow of the reference liquid (water).[11] The study was performed in triplicate and the results are reported as mean±SD.

Swelling index

One gram of powder was accurately weighed and transferred to a 100 ml stoppered measuring cylinder and was made up to volume with distilled water. It was kept aside for 24 hrs or until constant swelling was observed. Then the volume to which the mass was swollen was noted.[3] The study was performed in triplicate and the results are reported as mean±SD.

$S.I = (V_f - V_i / V_i) \times 100$

Where S.I is the swelling index, V_f is the final volume and V_i is the initial volume.

Phase solubility study of furosemide with poloxamer 407

Phase solubility studies were carried out as described by Higuchi and Connors. An excess amount of FRMD was added to the flasks containing 25 ml aqueous solutions of each carrier in simulated gastric fluid (SGF, USP XXIII) containing increasing concentrations of the individual carrier (i.e., 0.5%, 1.0%, 2.5%, and 5.0% w/v). The flasks were sealed and shaken in a rotary shaker at for 24 hours. The samples were filtered with Whatman filter paper (0.12μm) and analyzed spectrophotometrically for the dissolved drug at 234 nm.[12] The study

was performed in triplicate and the results are reported as mean±SD.

Saturated solubility study

A saturated solution was obtained by stirring excess powdered solute for several hours at required temperature until equilibrium has been obtained. The solution was filtered using Whatman filter. After this period the amount of solute contained in sample of saturated solution was analyzed by UV-spectrophotometer at 234 nm. The study was performed in triplicate and the results are reported as mean±SD.

Drug content

Accurately weighed solid dispersions, equivalent to 10 mg Furosemide, was transferred into a 100 ml volumetric flask and sufficient amount of pH 1.2 buffer solution was added, shaken for 24 hour using rotary shaker and diluted to the 100 ml mark with same solvent. It was then filtered to obtain sample stock solution. 1 ml of the filtrate was further diluted to 10 ml with pH 1.2 buffer and then assayed for content of Furosemide using UV spectrophotometer at 234 nm. From the absorbance total drug content in the batches were calculated.[13] The study was performed in triplicate and the results are reported as mean±SD.

***In vitro* dissolution study of solid dispersions**

The dissolution was studied with accurately weighed amount of the formulations (Containing approx. 10 mg of Furosemide) using a USP apparatus II in 900 ml of pH 1.2 buffer solution for 1 hour. The rotational speed of the paddle was set at 50 rpm at 37 ± 0.5ºC temp. Aliquots (5ml each) were withdrawn at predetermined time intervals for 1h; sink conditions were maintained. The samples were analyzed for drug content at 234 nm using a UV spectrophotometer.[14] The study was performed in triplicate and the results are reported as mean±SD.

Preformulation studies

Angle of repose:[15]

A good flow of powder is required to assure efficient mixing. If a drug was identified at the preformulation stage to be “poorly flowable”, selecting appropriate excipients can solve the problem during preformulation evaluation of drug substance.

Procedure: A funnel was kept vertically in a stand at a specified height above a paper placed on a horizontal surface. The funnel bottom was closed and 10 gm of sample powder was

filled in funnel. Then funnel was opened to release the powder on the paper to form a smooth conical heap, was found by measuring in different direction. The height of the heap was measured by using scale. The study was performed in triplicate and the results are reported as mean±SD. The values of angle of repose are calculated by using the following formula.

$\theta = \tan^{-1}(h/r)$

Where, h: height of the heap.

r: radius of the heap.

Table 2: Standard value of angle of repose.

Angle of repose(Ɵ)	Type of flow
<25	Excellent
25-30	Good
30-40	Poor
>40	Very poor

Bulk Density[15]

Bulk density is defined as the mass of powder divided by the bulk volume. Bulk density was determined by measuring the volume of a known mass of powder sample that has been passed through a screen into a graduated cylinder or through a volumetric measuring apparatus into a cup.

Procedure: A known quantity of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, (Vo), to the nearest graduated unit. The study was performed in triplicate and the results are reported as mean±SD.

Calculate the bulk density, in gm per ml, by the formula.

Bulk Density = Bulk Mass/ Bulk Volume

Tapped Density[15]

Tapped density was determined mechanically tapping a measuring cylinder containing a powder sample. After observing the initial volume, the cylinder was mechanically tapped and volume readings are taken until little further volume changes were observed. The mechanical tapping was achieved by rewashing the cylinder and allowing it to drop under its own weight a specific distance. Device that rotates the cylinder during tapping may be preferred to minimize any possible separation of the mass during tapping down.

Cylinder dropping distance: 14±2 mm at a normal rate of 300 drops / minute. Unless otherwise specified, tab the cylinder 500 times initially and measure the tapped volume (Va), to the nearest graduated unit. Repeat the tapping an additional 750 times and measure the tapped volume, (Vb), to the nearest graduated unit. If the difference between the two volumes was less than 2%, (Vb) was the final tapped volume, (Vf). Repeat in increments of 1250 taps, as needed, unit the difference between measurements was less than 2%.

Tapped Density=Bulk Mass/ Tapped Volume

Hausner Ratio[16]

Hausner predicts the flow properties of powder by using inter particle friction. The study was performed in triplicate and the results are reported as mean±SD.

Hausner ratio=Tapped Density/Bulk Density

Table 3: Standard values for hausner ratio.

Hausner Ratio	Type of Flow	Hausner Ratio	Type of Flow
1.00-1.11	Excellent	1.35-1.45	Poor
1.12-1.18	Good	1.46-1.59	Very poor
1.19-1.25	Fair	>1.60	Very very poor
1.26-1.34	Passable	----------	----------

Compressibility[16]

The Carr's index is an indication of compressibility of a powder. It is indirectly related to the relative flow rate, cohesiveness and particle size. The study was performed in triplicate and the results are reported as mean±SD.

The compressibility index of all ingredients was determined by following equation

Carr's index = (Tapped density- Bulk density/ Tapped density) ×100

Table 4: Standard values of carr's index.

% COMPRESSIBILTY RANGE	FLOW DESCRIPTIONS
≤10	Excellent
11-15	Good
16-20	Fair
21-25	Passable
26-31	Poor
32-37	Very poor
>38	Extremely poor

RESULTS

The calibration curve of Furosemide was obtained in pH 1.2 buffer solution (Simulated Gastric Fluid without Enzymes) in the range of 2-10µg/ml at 234 nm (figure 1). It has shown good linearity with regression coefficient of 0.998 (r^2 value).

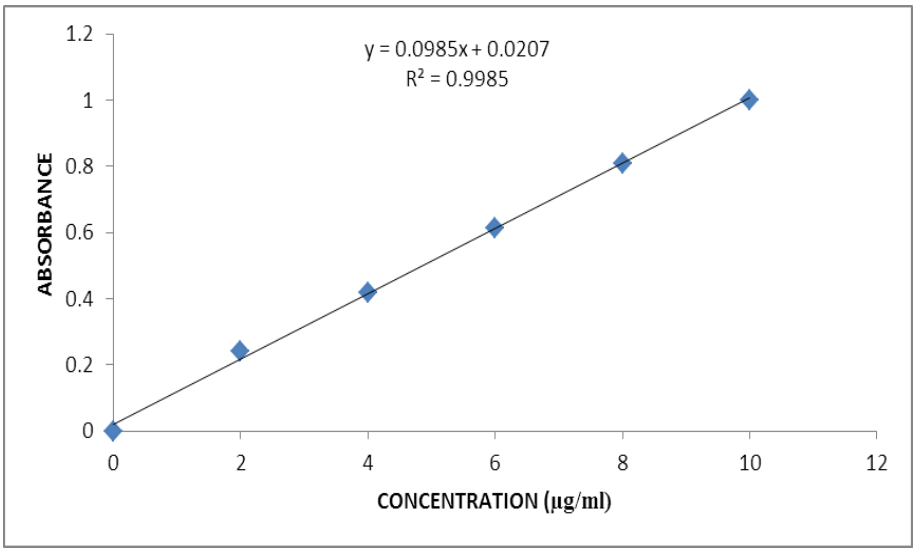

Figure 1: Calibration curve of furosemide.

Infrared spectrum of pure Furosemide is shown in figure 2. The characteristic absorption peak of Furosemide was obtained at 3397 and 3351 cm-1 due to N-H stretching vibration of NH_2 group; 3283 cm-1 due to O-H stretching vibration of COOH and 1675 cm-1 due to C=O stretching; 1494 cm-1 due to deformation of N-H group; 1323 cm-1 due to C-N stretching; 1239 cm-1 due to C-O stretching; 1057 cm-1 due to S=O stretching vibration; 583 cm-1 due to C-S stretching. The presence of all these peaks gives confirmation about the purity of the drug.

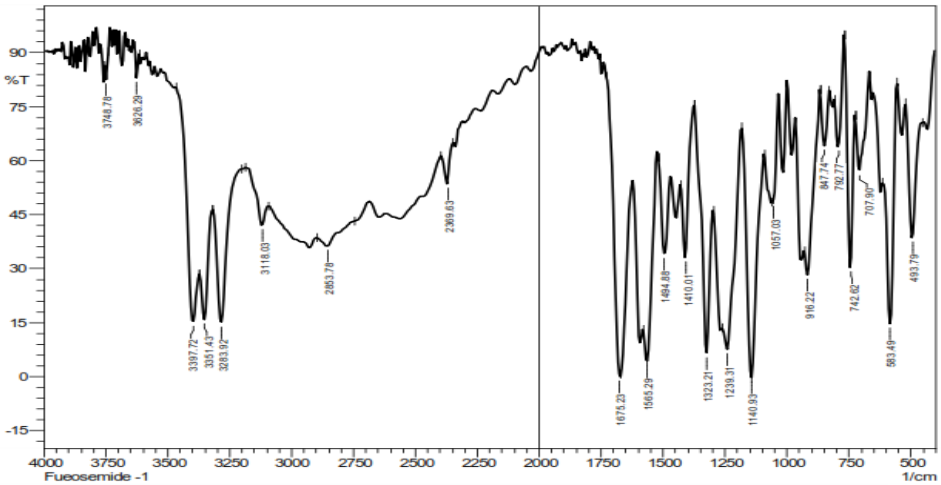

Figure 2: FTIR spectra of pure furosemide.

The peaks obtained in FTIR spectrum of xanthan gum (figure 3) were identical to that of peaks obtained for modified xanthan gum (figure 4). Hence no molecular changes or chemical interactions were observed.

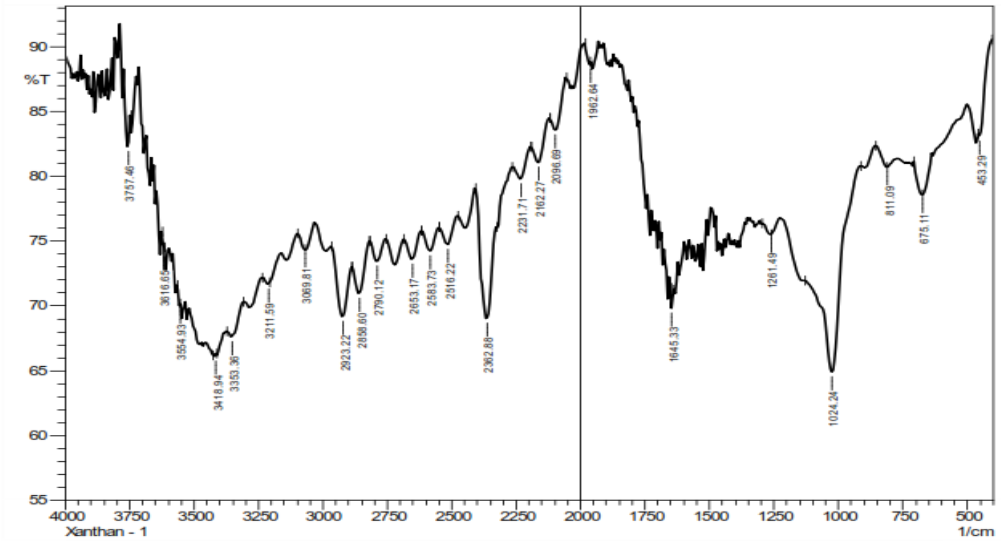

Figure 3: FTIR spectra of xanthan gum.

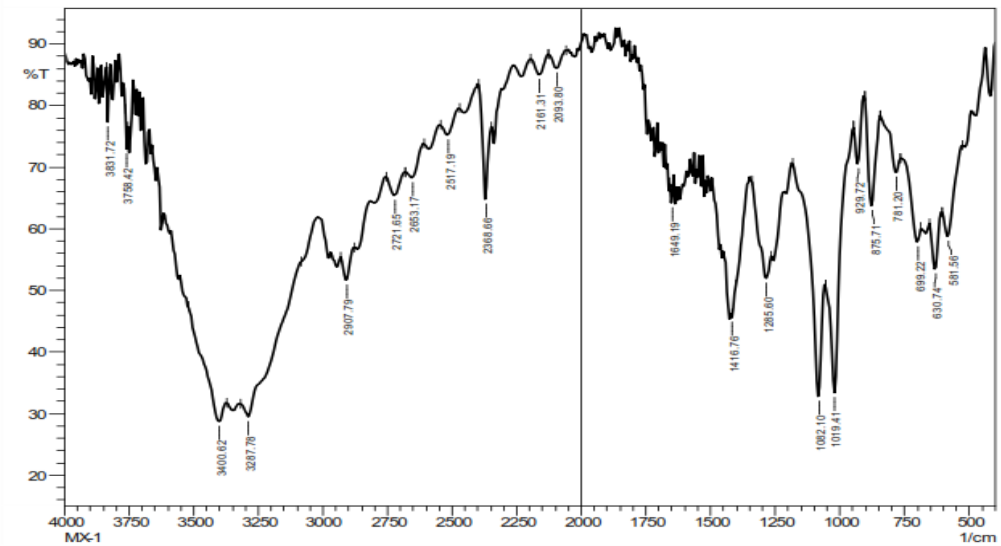

Figure 4: FTIR spectra of modified xanthan gum.

By comparing the FTIR spectrum of Furosemide with the drug-carrier mixtures (figure 5and 7) it can be seen that all the characteristic absorption bands of Furosemide were retained so it can be concluded that there was no chemical interaction between Furosemide and the carriers.

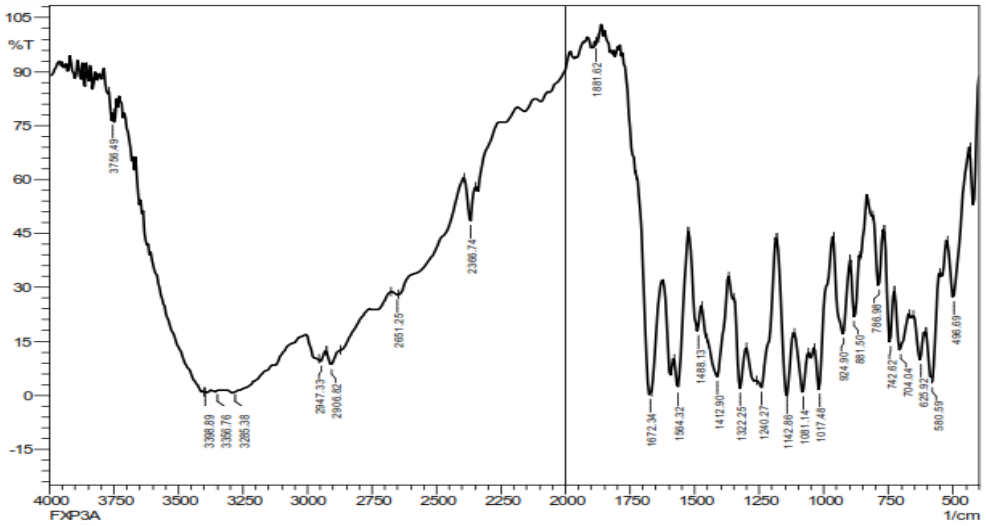

Figure 5: FTIR spectra of FXP3.

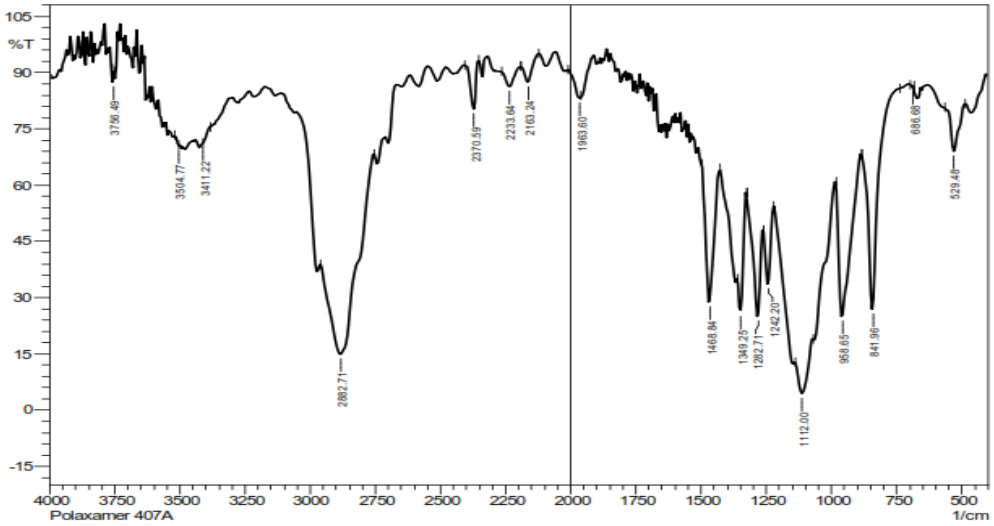

Figure 6: FTIR spectra of poloxamer 407.

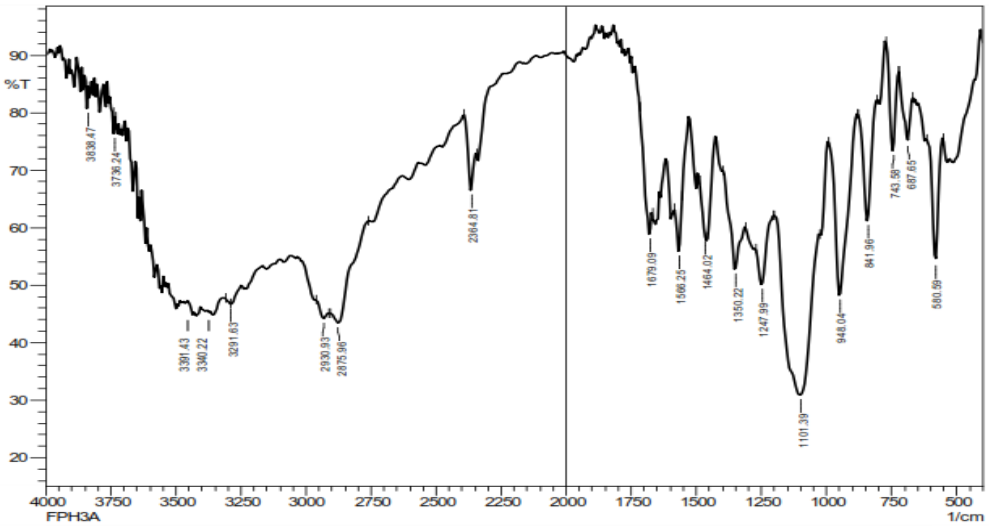

Figure 7: FTIR spectra of FPH3.

In figure 8, DSC thermogram of Furosemide shows a sharp characteristic endothermic peak (Tpeak = 224.05°C) corresponding to its melting, indicating its crystalline nature.

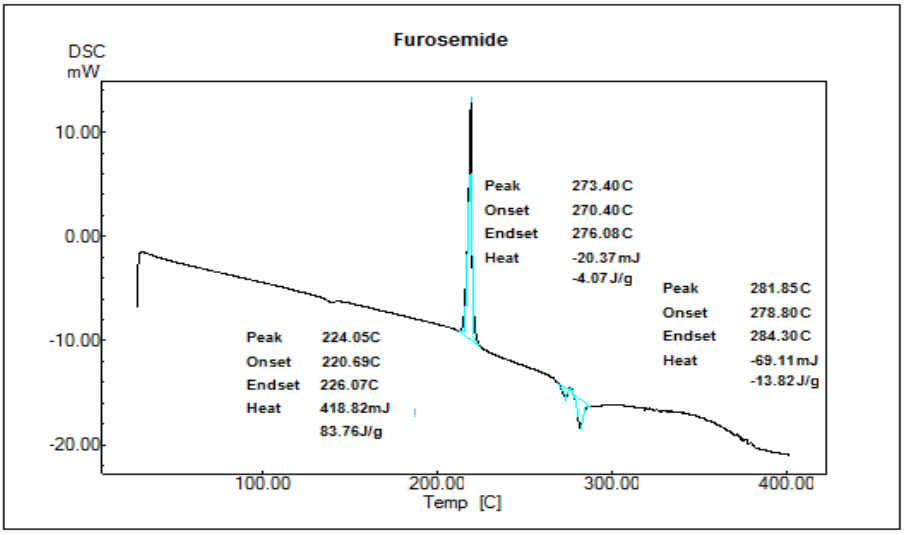

Figure 8: DSC thermogram of pure furosemide.

The DSC thermograms showed an increase in crystallinity of modified xanthan gum compared to xanthan gum (figure 9 and 10).

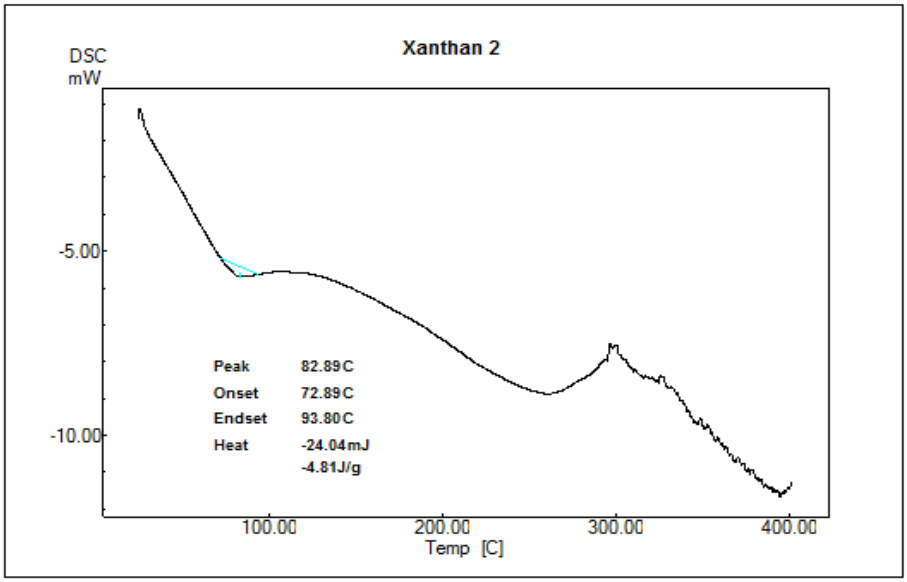

Figure 9: DSC spectra of xanthan gum.

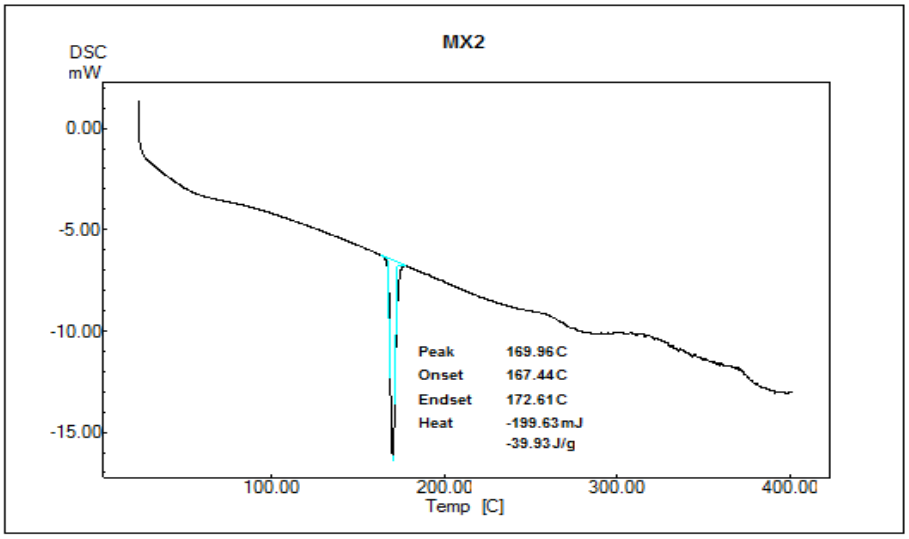

Figure 10: DSC thermogram of modified xanthan gum.

However, the characteristic endothermic peak corresponding to drug melting was broadened and shifted toward lower temperature with reduced intensity in the drug carrier mixture of 1:3 ratio prepared by physical mixing using modified xanthan gum and in the drug-carrier mixture of 1:3 ratio prepared by hot melt method using Poloxamer 407 (Figures 11 and 13). The DSC data show that there is complete absence of the sharp endothermic peak at 224.05°C. From the DSC results, a considerable reduction in crystallinity of Furosemide was observed in the prepared drug carrier mixtures. This indicates that Furosemide is converted in to amorphous form from its crystalline form in the FXP3 and FPH3 mixtures.

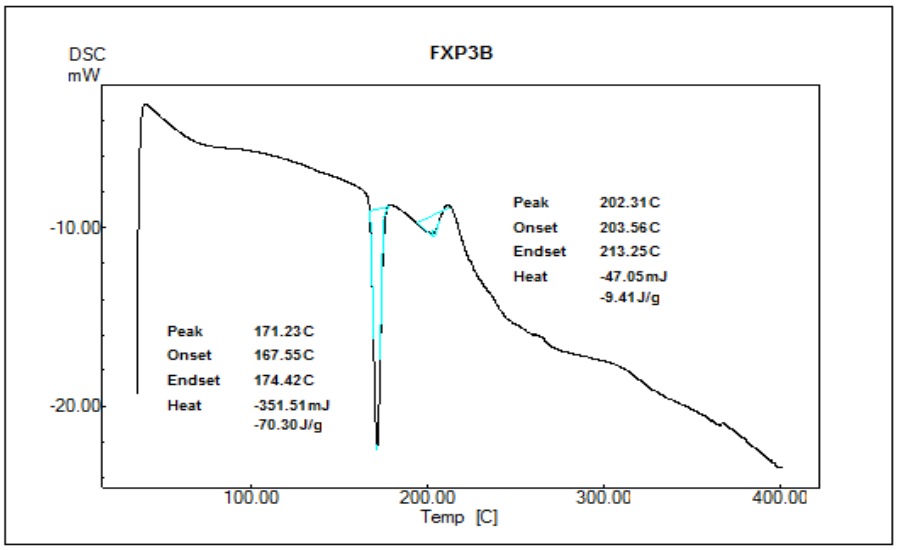

Figure 11: DSC thermogram of FXP3.

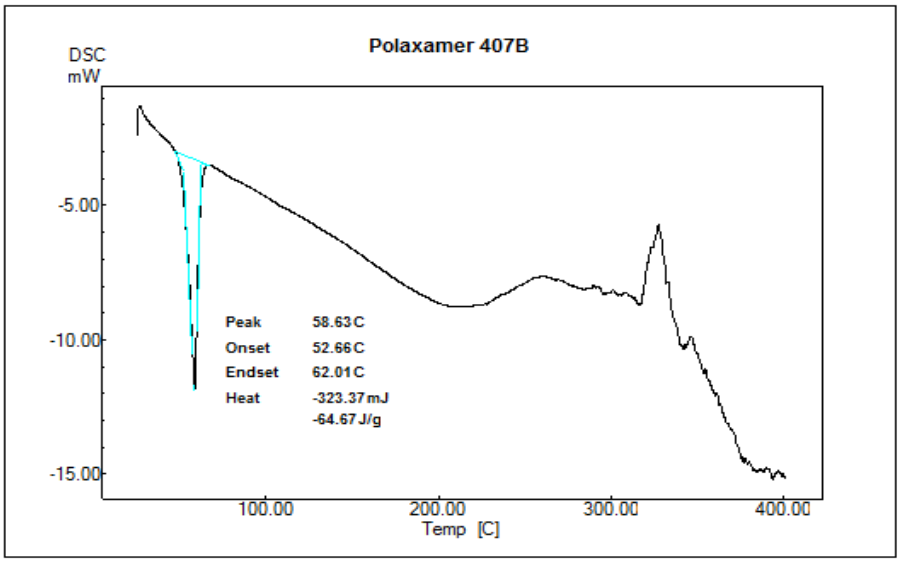

Figure 12: DSC thermogram of poloxamer 407.

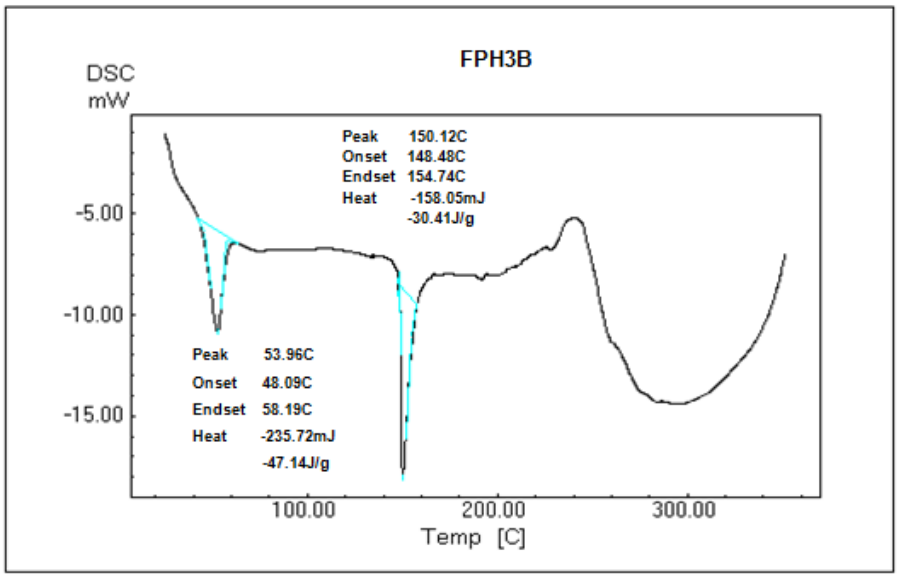

Figure 13: DSC thermogram of FPH3.

The viscosity and S.I of xanthan gum and modified xanthan gum is given in table 5. Xanthan gum was subjected to sequentially controlled modification of wetting and drying which resulted in the loss of its structural arrangement leading to reduced adhesive and cohesive force of attraction which helps to retain water and decease viscosity compared to xanthan gum.

Table 5: Viscosity and S.I values for XG and MXG.

Sample	Swelling Index (%) Mean±s.d	Viscosity (cps) Mean±s.d
Xanthan gum	866.6±2.1	12.66±4.89
Modified xanthan gum	859±1.9	4.51±2.24

Phase solubility diagram of Furosemide-Poloxamer 407 is shown in figure 14. Phase solubility diagrams showed a linear relationship between the amount of Furosemide solubilised and the concentration of Poloxamer in solution and followed A_L type curve. Furosemide-Poloxamer 407 having regression value of 0.997 indicated linearity. According to Higuchi and Connors this may be attributed to the formation of soluble Furosemide-Poloxamer 407 complex. Thus, it can be concluded that Furosemide with Poloxamer 407 enhanced dissolution property.

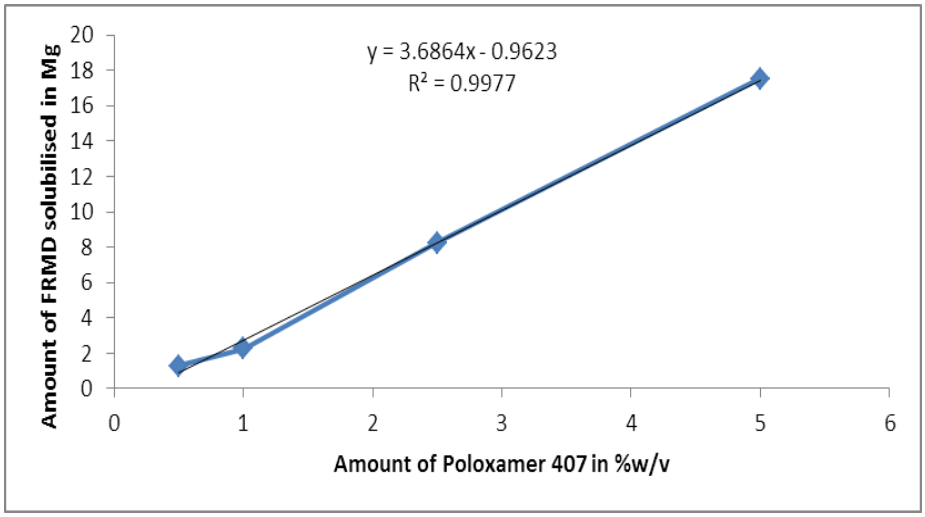

Figure 14: Phase solubility study of furosemide with poloxamer 407.

The solubilities of solid dispersions prepared by physical mixing, solvent evaporation and kneading methods by using modified xanthan gum as a carrier is given in table 6. All the drug-carrier mixtures showed an increase in drug solubility over the pure drug Furosemide. The solubilities of solid dispersions which were prepared by physical mixing, solvent evaporation and hot melt method by using Poloxamer 407 as a carrier is given in table . In all the above cases the solubility progressively improved with increasing the carrier proportion in the drug carrier mixtures.

Table 6: Saturated solubility studies of drug-carrier mixtures.

Formulation Code	Solubility (mg/ml)	Formulation Code	Solubility (mg/ml)
FXP1	0.189±0.01	FPP1	0.196±0.004
FXP2	0.215±0.004	FPP2	0.212±0.008
FXP3	0.280±0.003	FPP3	0.244±0.014
FXS1	0.165±0.007	FPS1	0.227±0.006
FXS2	0.174±0.008	FPS2	0.262±0.003
FXS3	0.183±0.003	FPS3	0.293±.0.009
FXS4	0.190±0.005	FPH1	0.288±0.011
FXK1	0.209±0.002	FPH2	0.305±0.009
FXK2	0.222±0.007	FPH3	0.324±0.009

Table 7 indicates percentage of drug content of all the mixtures. The results indicate the uniform drug dispersion within the carrier.

Table 7: Percentage drug content of furosemide in drug-carrier mixture.

Formulation Code	Drug Content (%)	Formulation Code	Drug Content (%)
FXP1	99.1	FPP1	97.3
FXP2	98.4	FPP2	97.5
FXP3	98.7	FPP3	96.6
FXS1	98.2	FPS1	97.7
FXS2	97.7	FPS2	98.3
FXS3	94.2	FPS3	98.0
FXS4	93.6	FPH1	96.7
FXK1	89.9	FPH2	96.8
FXK2	89.2	FPH3	97.9

The *in vitro* dissolution of Furosemide-carrier mixtures is shown in figure 15-20. This was achieved by using the various hydrophilic polymers and modified carriers such as Poloxamer 407 and modified xanthan gum. By observing the drug release studies it is evident that solid dispersions prepared by physical mixing using modified xanthan gum showed better *in vitro* drug release compared to kneading method and solvent evaporation. Solid dispersions prepared by hot melt using Poloxamer 407 as a carrier enhanced the *in vitro* drug release compared to physical mixing, solvent evaporation and solid dispersions prepared by modified xanthan gum.

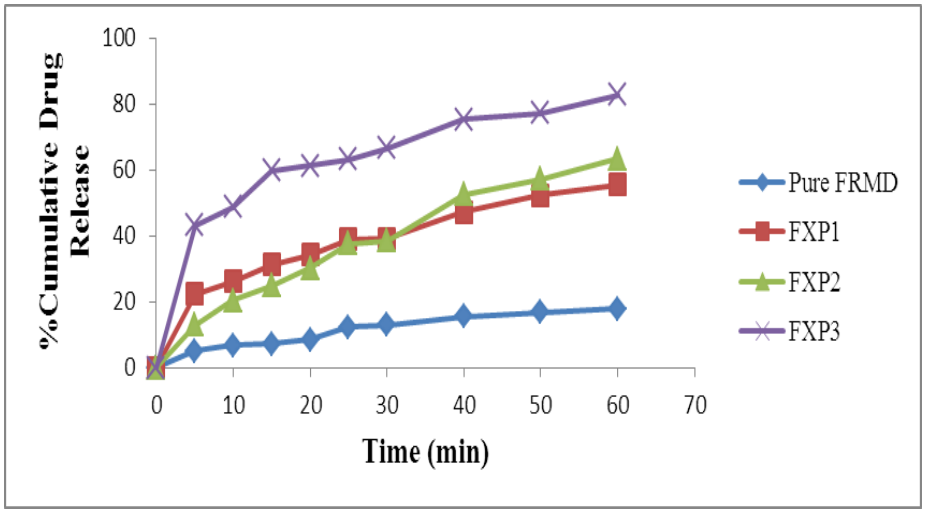

Figure 15: *In vitro* dissolution profile data of FRMD in pure form and FXP1, FXP2, FXP3.

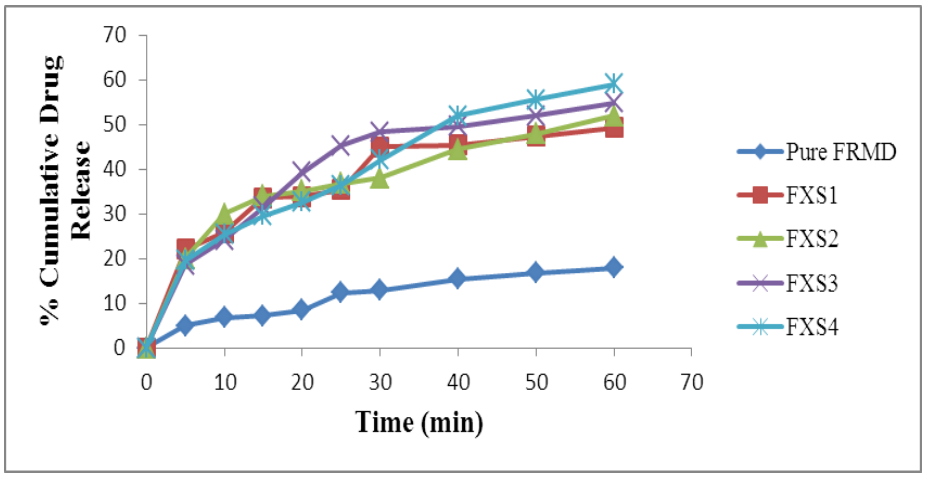

Figure 16: *In vitro* dissolution profile data of FRMD in pure form and FXS1, FXS2, FXS3, FXS4.

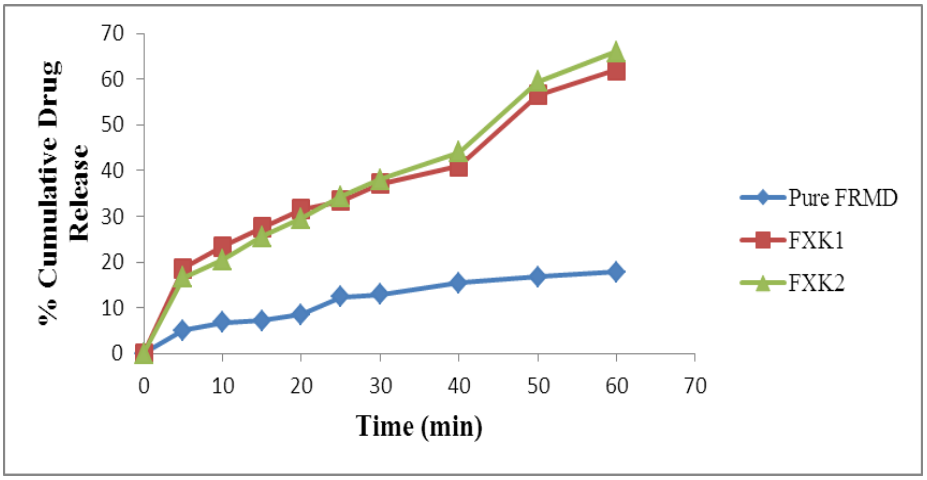

Figure 17: *In vitro* dissolution profile data of FRMD in pure form and FXK1, FXK2.

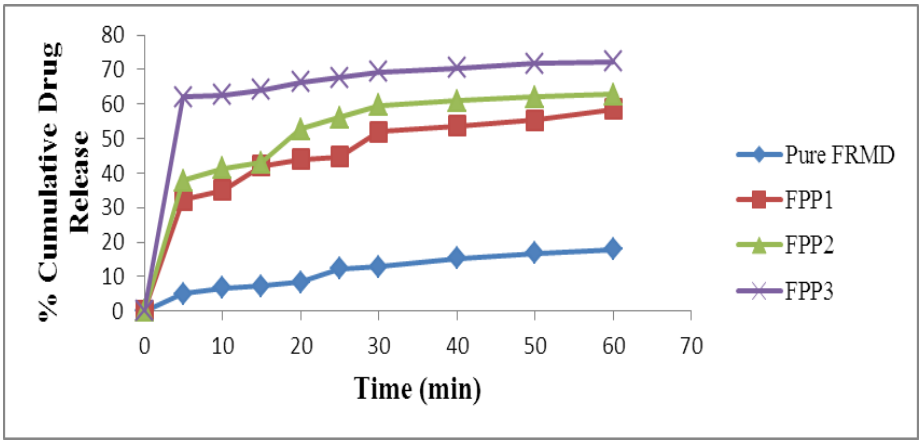

Figure 18: *In vitro* dissolution profile data of FRMD in pure form and FPP1, FPP2, FPP3.

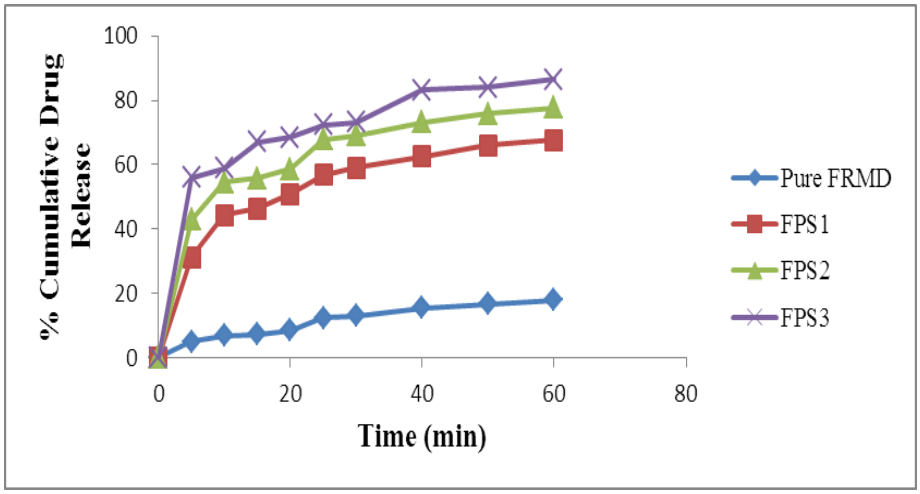

Figure 19: *In vitro* dissolution profile data of FRMD in pure form and FPS1, FPS2, FPS3.

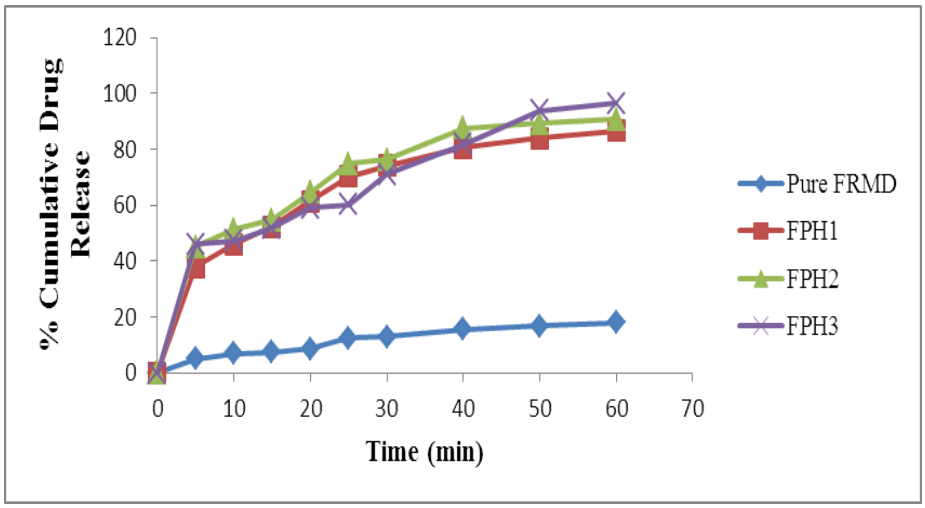

Figure 20: *In vitro* dissolution profile data of FRMD in pure form and FPH1, FPH2, FPH3.

Bulk densities, tapped densities, hausner ratio, angle of repose and carr's index values of Furosemide and its solid dispersions is given in table. From the results (table 8) it is concluded that majority of the furosemide solid dispersions had good flow properties and are within the USP limits compared to that of pure drug furosemide.

Table 8: Preformulation Parameters of Furosemide and its Solid Dispersions.

Batch name	Bulk density (g/cc)	Tapped density (g/cc)	Hausner ratio	Angle of repose (θ)	Carr's index (%)
Pure Drug	0.17±0.011	0.23±0.052	1.3±1.42	37.0°±0.23	26.6±0.64
FXP1	0.54±0.025	0.63±0.038	1.17±0.4	29.1°±0.52	14.2±0.72
FXP2	0.49±0.012	0.60±0.029	1.22±0.4	30.1°±0.24	18.3±0.81
FXP3	0.43±0.019	0.54±0.087	1.24±0.5	31.7°±0.13	20.3±1.22
FXSI	0.54±0.021	0.61±0.091	1.13±0.3	28.5°±0.16	11.4±0.33
FXS2	0.49±0.030	0.56±0.052	1.14±0.4	29.2°±0.48	12.5±0.42
FXS3	0.50±0.022	0.58±0.092	1.15±0.6	28.9°±0.34	13.8±0.55
FXS4	0.45±0.027	0.54±0.041	1.20±0.5	30.1°±0.37	17.6±0.63
FXK1	0.43±0.031	0.52±0.063	1.21±0.1	29.4°±0.43	17.5±0.64
FXK2	0.48±0.043	0.59±0.072	1.22±0.1	32.5°±0.52	19.1±0.37
FPP1	0.49±0.028	0.57±0.056	1.15±0.3	33.1°±0.41	13.2±0.46
FPP2	0.52±0.044	0.62±0.083	1.18±0.5	31.3°±0.33	14.3±0.71
FPP3	0.47±0.029	0.55±0.088	1.16±0.4	29.4°±0.28	10.6±0.59
FPS1	0.50±0.020	0.65±0.074	1.33±1.2	36.1°±0.25	24.0.±0.58
FPS2	0.45±0.016	0.63±0.062	1.39±1.4	36.6°±0.18	29.7±1.57
FPS3	0.38±0.028	0.54±0.055	1.42±1.1	38.1°±0.29	30.1±1.21.
FPH1	0.44±0.034	0.53±0.075	1.21±0.4	26.7°±0.31	17.5±0.65
FPH2	0.47±0.014	0.58±0.093	1.23±0.5	27.2°±0.46	10.8±0.54
FPH3	0.55±0.018	0.62±0.086	1.12±0.7	24.2±0.32	12.0±0.73

CONCLUSION

Furosemide is a BCS class II drug and it has very poor water solubility and insufficient dissolution rate.

Physical mixing, solvent evaporation and kneading methods were employed for the preparation of solid dispersions with modified xanthan gum as a carrier. Here all the methods were good because of its enhancement in the solubility and dissolution rates. An increase in the ratios of the drug and carrier enhanced the solubility and dissolution rates. Further increments had a retarding effect on the dissolution rates.

Physical mixing, solvent evaporation and hot melt method were also employed with Poloxamer 407 as a carrier. Here, hot melt method and Poloxamer 407 as a carrier was observed to be the best for enhancement of solubility and dissolution rates compared to other

two methods and a modified carrier. A considerable increment in the solubility and dissolution rates were observed with increasing ratios of drug and carrier.

The solid dispersion prepared by using Poloxamer 407 has good solubility and dissolution rate at 1:3 ratio.

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