

EVALUATION OF ALBIZIA GUM, DAMMAR GUM AND MOI GUM IN THE FORMULATION OF CONTROLLED RELEASE MATRIX TABLETS USING FUROSEMIDE

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Abstract:

Background: Natural gums like albizia gum, dammar gum and moi gum were used in this work for the preparation of matrix tablets.

Objective: The main objective of the present work is to study the suitability of albizia gum, dammar gum and moi gum in different proportions for the preparation of controlled release matrix tablets using water insoluble drug like furosemide.

Method: Matrix tablets were prepared by direct compression method by using water soluble diluent like lactose and water insoluble diluent like dibasic calcium phosphate.

Results: In vitro release studies were performed in 0.1 N HCl for the first two hours and pH 6.8 phosphate buffer for the next ten hours. The retardation of drug release was influenced by concentration of gum and nature of diluents. No interaction between drug and gums were observed by using FTIR and DSC studies.

Conclusion: Among the selected three gum's dammar gum showed 100% drug release within 12 hrs and followed zero order kinetics with non-Fickian diffusion.

Key Words: Furosemide, albizia gum, dammar gum, moi gum, controlled release matrix tablets, lactose and dibasic calcium phosphate.

1. INTRODUCTION

Some of the natural gums obtained from plants have been investigated for diverse applications in the design of pharmaceutical formulations. However, still many of the natural polymers obtained from the plants and other sources are not fully explored for their pharmaceutical excipient activity. Albizia gum, dammar gum and moi gum were among them. These natural excipients have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available [1]. Natural excipients obtained from plants have diverse applications in drug delivery and they play different roles in dosage forms as binders, disintegrants, coating agents emulsifying agents and suspending agents [2-4]. Now a day's extensive studies are being conducted for finding the applicability of these natural excipients in the design of novel drug delivery systems.

Among all the types of dosage forms matrix tablets are widely used for oral controlled drug release systems as they are easy to prepare. Many natural gums have been investigated as matrix forming materials for the design and development of oral tablets to achieve sustained and controlled drug delivery. Hydrophilic polymers are the most suitable for retarding drug release [5-7]. These polymers when they come in contact with water get hydrated and forms gel. The drug release from this gel will be usually diffusion controlled and hence the release will be sustained over a prolonged period of time [8]. In the present study albizia gum, dammar gum and moi gum were evaluated as rate controlling matrix materials for controlled release.

Albizia gum is obtained from the incised trunk of the tree *Albizia zygia* (Family: Leguminosae) and is shaped like round elongated tears of variable color ranging from yellow to dark brown [9]. Wide spread in tropical Africa. In the Ghanaian traditional medicine, the leaves of *Albizia zygia* are used in the management of mental troubles [10]. The pounded bark is applied topically to treat yaws, sores, wounds, and toothache. Leaf decoctions are administered to treat fever and diarrhoea. Ground roots of the plant are added to food to treat cough and as an expectorant. The root bark juice is also used on wounds to promote healing [11]. In Nigeria, some communities use the plant for the treatment of waist pain and in Cameroon [12], decoction of the leaves and stems is used in the treatment of boils, diarrhoea, male sexual impotence, oedema, and fracture [13, 14]. Albizia gum is also used as tablet binding agent and suspending agent [15, 16].

Dammar gum is obtained from the plant *Shorea robusta* (Family: Dipterocarpaceae) in India and East Asia. It contains about 40% α - resin, 22% β - resin, 23% dammarol acid and 2.5% water. It is used in foods, as either a clouding or a glazing agent, in the making of incense, varnishing and in other processes. Dammar was first introduced as a picture varnish in 1826 [17], and is commonly referred to as dammar varnish. Dammar varnish is commonly used in oil painting, both during the painting process and after the painting is finished [18]. Dammar gum is also used as emulsifier, stabilizer in the production of color, paints, inks and water resistant coating [19, 20].

Moi gum was obtained from the plant *Lannea coromandelica* (Family: Anacardiaceae), which is commonly known as “The Indian Ash Tree” is a deciduous tree which grows up to 14 meters high [21]. It is widely distributed in India, Bangladesh and some other tropical countries. It is used as a lotion in eruptions, leprosy and obstinate ulcers. It is known to cure sprains, bruises, skin eruptions, heart diseases, dysentery and mouth sores. The decoction of the bark can be used to alleviate toothache traditionally used to treat impotency [22]. Moi gum is also used as microencapsulating agent and rate controlling material.

As these three gums were having good swelling properties and hydrophilic in nature, hence, these three gums can be used as polymers for the design of controlled release dosage forms.

Furosemide (4-chloro-2-furfurylamino-5-sulphamoyl benzoic acid) is a drug with a diuretic action which acts at the renal level on the ascending limb of the loop of Henle [23]. Furosemide, a widely used “high-ceiling” loop diuretic drug, is indicated for congestive heart failure, chronic renal failure, and hepatic cirrhosis [24]. This drug is used in the treatment of oedema of pulmonary, cardiac or hepatic origin as well as in the treatment of hypertension and in the chronic treatment of cardiac infraction [25]. Furosemide is water- insoluble drug and its bioavailability is very low from its crystalline form. For water- insoluble, low permeable drugs the rate of oral absorption is often controlled by the dissolution rate in the gastrointestinal tract.

The furosemide exhibits highly erratic and very low dissolution profile in gastric and intestinal fluids. This is possibly due to its very high hydrophobic character. The rate of absorption and/or the extent of bioavailability for such insoluble hydrophobic drug is controlled by the rate of dissolution in the gastrointestinal fluids. Furosemide is absorbed mostly in the stomach and upper small intestine possibly due to its weak acidic properties (pKa 3.9) and is characterized by a short half life of 1 to 2 hr. The bioavailability of furosemide after oral administration is about 60% and dose quite variable (20–80mg) owing to the presence of an absorption window in the upper intestinal tract. [26]

Because of the short biological half life and erratic absorption behavior due to its poor solubility there are reports of designing the controlled drug delivery systems of furosemide using hydrophilic polymers [27-29]. Hence, in the present research work, it is selected as a model drug for evaluation of suitability of the three selected gums in the design of controlled drug delivery systems.

2. MATERIALS AND METHODS

2.1. Materials

Furosemide was received as a gift sample from Lupin Pharmaceuticals, Pune, Maharashtra. Albizia gum, dammar gum and moi gums were purchased from Yarrow Chem Products, Mumbai. Lactose, dibasic calcium phosphate (DCP) and magnesium stearate were purchased from Loba Chemie Pvt. Ltd.

2.2. Preparation of standard curve of furosemide [30, 31]

Accurately weighed 50 mg of furosemide was dissolved in 100 mL of 0.1N HCl and pH 6.8 phosphate buffer to get a solution containing 500 μ g/mL of drug.

The stock solution was suitably diluted to obtain the furosemide concentration of 2, 4, 6, 8 and 10 μ g/mL with 0.1N HCl and 5, 10, 15, 20 and 25 μ g/mL with pH 6.8 phosphate buffers and the absorbance was measured at 271 nm against the respective reagent blank i.e. 0.1N HCl or pH 6.8 phosphate buffer using double beam UV visible spectrophotometer (Elico model SL-210). All estimations were done in triplicate and average values were reported with standard deviation. A standard curve was drawn between absorbance and the concentration and the values of correlation coefficient (r), slope (m) and intercept (c) were calculated.

2.3. Pre compression parameters

Powders normally flow under the influence of gravity; dense substances are generally less cohesive than lighter ones. Hence, differences in densities of various ingredients may lead to improper mixing and filling during manufacturing of formulation. This results in weight variation and variations in content uniformity of finished products. Hence, determination of density of any ingredient will be helpful in successful formulation development.

2.4. Preparation of matrix tablets

The three selected gums were used for the preparation of the controlled release matrix tablets of the model drug of furosemide using drug/polymer ratios of 1:0.25, 1:0.5 and 1:0.75. The compositions of the prepared tablets are shown in Table 1. Each time a batch of 300 tablets were prepared. Direct compression technique was used for the preparation of the tablets as all the gum powders showed good flow properties as per the initial studies carried out. Required quantities of powders were weighed and mixed in a geometric dilution pattern. The final powder blends ready for compression were further evaluated to conform the flow properties by using angle of repose, compressibility index and Hausener's ratio. The powder blends were compressed into tablets by using an Elite 10 station minipress with 8 mm diameter round punches with a compression force sufficient to obtain hardness in the range of 4-8 kg/cm².

| Formulation code | Furosemide | Albizia gum | Dammar gum | Moi gum | Dibasic calcium phosphate | Lactose | Magnesium stearate | Total wt of tablet (mg) |
|------------------|------------|-------------|------------|---------|---------------------------|---------|--------------------|-------------------------|
| AFD1 | 110 | 27.5 | | | 82.5 | | 5 | 225 |
| AFD2 | 110 | 55 | | | 55 | | 5 | 225 |
| AFD3 | 110 | 82.5 | | | 27.5 | | 5 | 225 |
| AFL1 | 110 | 27.5 | | | | 82.5 | 5 | 225 |
| AFL2 | 110 | 55 | | | | 55 | 5 | 225 |
| AFL3 | 110 | 82.5 | | | | 27.5 | 5 | 225 |
| DFD1 | 110 | | 27.5 | | 82.5 | | 5 | 225 |
| DFD2 | 110 | | 55 | | 55 | | 5 | 225 |
| DFD3 | 110 | | 82.5 | | 27.5 | | 5 | 225 |
| DFL1 | 110 | | 27.5 | | | 82.5 | 5 | 225 |
| DFL2 | 110 | | 55 | | | 55 | 5 | 225 |
| DFL3 | 110 | | 82.5 | | | 27.5 | 5 | 225 |
| MFD1 | 110 | | | 27.5 | 82.5 | | 5 | 225 |
| MFD2 | 110 | | | 55 | 55 | | 5 | 225 |
| MFD3 | 110 | | | 82.5 | 27.5 | | 5 | 225 |
| MFL1 | 110 | | | 27.5 | | 82.5 | 5 | 225 |
| MFL2 | 110 | | | 55 | | 55 | 5 | 225 |
| MFL3 | 110 | | | 82.5 | | 27.5 | 5 | 225 |

Table 1: Composition of matrix tablets of furosemide

2.5. Evaluation of prepared matrix tablets

The prepared matrix tablets were subjected to different quality control tests such as uniformity of weight, hardness, thickness, friability, drug content and in vitro dissolution studies.

2.5.1. Uniformity of weight [32]

This test was conducted according to the procedure given in Indian Pharmacopoeia.

2.5.2. Hardness [33]

Randomly five tablets were selected and the hardness of each tablet was determined by using Monsanto hardness tester.

2.5.3. Thickness

Test was conducted by selecting five tablets randomly; thickness of the each tablet was evaluated by Vernier callipers. Mean and standard deviation were calculated.

2.5.4. Friability [34]

Friability was determined by using Roche Friabilator. The loss in weight indicates the friability. The percent loss in weight should not be greater than 1.0 % is acceptable. The percent loss in weight or friability (f) was calculated by **Eq. 1** given below.

| | |
|---|----------------|
| $f(\%) = \left(1 - \frac{w}{w_0}\right) \times 100$ | -Eq. 1. |
|---|----------------|

2.5.5. Estimation of drug content [35]

Ten tablets were randomly selected from each batch, powdered in a mortar individually and the powder equivalent to dose of the one tablet (110 mg of furosemide) was taken in to a 100 mL volumetric flask containing 70 mL of pH 6.8 phosphate buffer. The flask was shaken occasionally for 30 minutes and the volume was made up to 100 mL mark with pH 6.8 phosphate buffer. About 10 mL of the solution was taken and filtered. The filtrate was suitably diluted and the absorbance was measured at 271 nm against a reagent blank using double beam UV visible spectrophotometer (Elico model SL-210).

2.5.6. In vitrodissolution studies [36]

Dissolution studies were conducted in triplicate for all the prepared tablets in an eight station dissolution apparatus (Veego) equipped with paddles by using the following dissolution conditions, medium for the first 2 hrs is 0.1N HCl and medium for the next 10 hrs is pH 6.8 phosphate buffer, revolutions per minute (RPM) maintained is 75, temperature is 37°C. 5 mL of sample was withdrawn for every one hour interwel and the same amount of medium was replaced to maintain the sink conditions.

Samples were suitably diluted and drug content was determined by measuring the absorbance at 271 nm as described earlier using double beam UV visible spectrophotometer (Elico model SL-210).

3. RESULTS AND DISCUSSION

3.1. Standard curve of furosemide

The method obeyed Beer's law in concentration range of 2-10 µg/mL for 0.1N HCl and 5-25 µg/mL for pH 6.8 phosphate buffers. The 'r' value was found to be more than 0.999 for both the media, which indicated a positive correlation between

the concentration of furosemide and the corresponding absorbance values. The concentration of both the media and corresponding absorbance's are given in Table 2 and 3. The standard curves are shown in Fig. 1 and 2 for 0.1N HCl and pH 6.8 phosphate buffers respectively. The standard deviation values given in the table were found to be low, which indicated that the method used was reproducible. Thus, the method was found to be suitable in present investigation for estimation of furosemide.

Table 2: Standard curve data for furosemide in 0.1N HCl

| Concentration (µg/mL) | Absorbance at 271 nm (mean ± s.d., n=3) |
|-----------------------|---|
| 2 | 0.093 ± 0.0031 |
| 4 | 0.161 ± 0.0025 |
| 6 | 0.245 ± 0.0020 |
| 8 | 0.331 ± 0.0030 |
| 10 | 0.401 ± 0.0035 |

2.5.7. Drug release kinetics and mechanism of drug release from the matrix tablets

The analysis of drug release kinetics and mechanism of drug release from pharmaceutical dosage forms is an important process. The dissolution data was fitted to popular release models such as zero order and first order to determine the rate of drug release and Higuchi's and erosion equation, to assess the drug release mechanism from the matrix tablets prepared. If the mechanism of drug release is by diffusion it was further characterized by Korsemeyer- Peppas's equation to conform the diffusion type i.e. Fickian or non-Fickian or anomalous diffusion.

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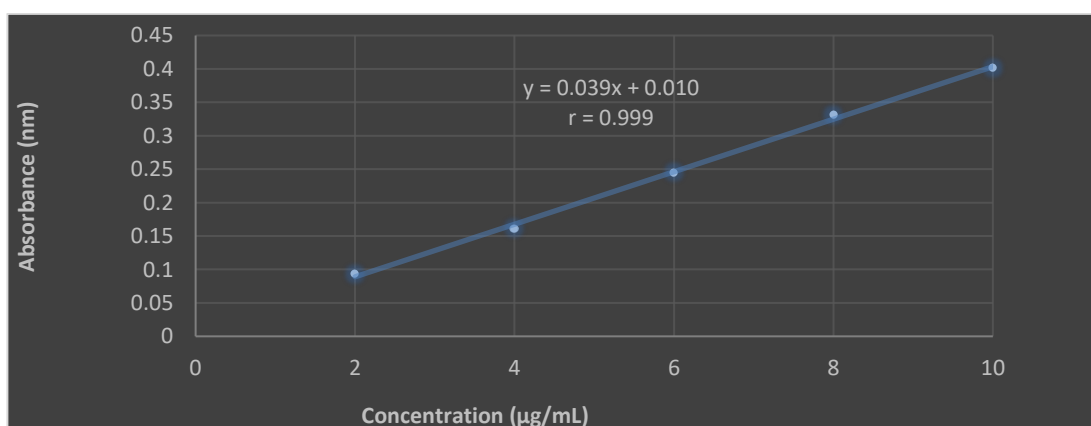


Fig. 1: Standard curve of furosemide in 0.1N HCl

Table 3: Standard curve data for furosemide in pH 6.8 phosphate buffer

| Concentration (µg/mL) | Absorbance at 271 nm (mean ± s.d., n=3) |
|-----------------------|---|
| 5 | 0.206 ± 0.0054 |
| 10 | 0.411 ± 0.0078 |
| 15 | 0.610 ± 0.0032 |

| | |
|----|--------------|
| 20 | 0.786±0.0061 |
| 25 | 0.988±0.0017 |

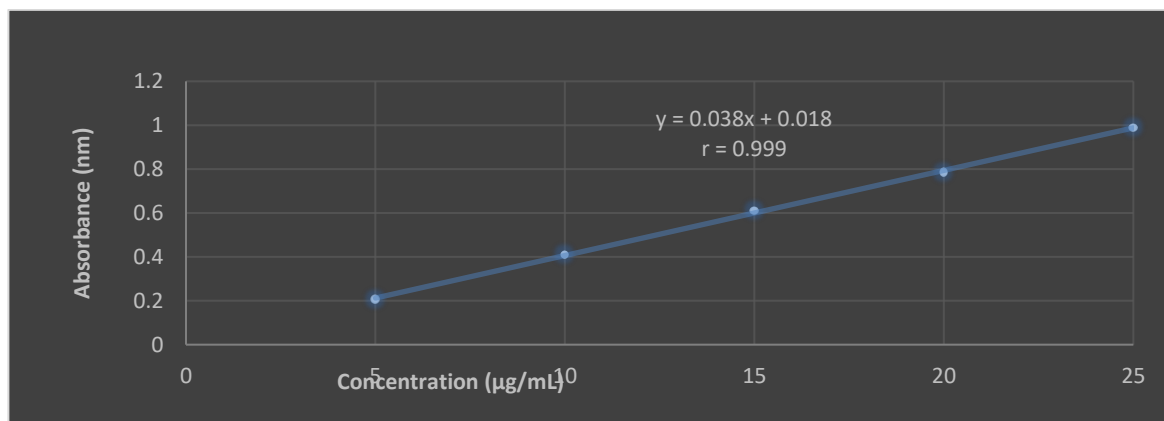


Fig. 2: Standard curve of furosemide in pH 6.8 phosphate buffer

3.2. Flow properties of the powder blend

The powder blends were subjected for evaluation of flow properties just before compression and results obtained were compressibility index was in the range of 8.63-9.89. Compressibility index values $\leq 10\%$ indicates excellent flow properties and desirable packing characteristics. Hausner's ratio was in the range of 1.01 – 1.67, angle of repose was in the range of 25 - 30° indicates excellent flow property of the powder. All the values were within the acceptable range for exhibiting good flow properties.

3.3. Evaluation of tableting properties of the prepared tablets

The results of uniformity of weight, hardness, thickness, friability and drug content for all formulations were calculated and results are given in Table 4. According to IP, the permissible level of deviation is ± 16.875 mg for 225 mg tablet. As the maximum deviation observed for all the tablets was found to be less than ± 2 mg and hence, all the tablets passed the test. Hardness of the tablets was in the range of 4-6.5 kg/cm². The thickness of tablets was in the range of 3.1 to 3.6 mm. Weight loss in the friability test was less than 1% in all the cases. The drug content in all the matrix tablets was found in the acceptable range of 91.90 to 99.47 and complies with the drug content test (90-110%). Thus the formulated matrix tablets were of good quality, fulfilling the official requirements of the tablets.

| Formulation Code | Uniformity of weight ^a (mg) | Hardness ^b (Kg/Cm ²) | Thickness ^b (mm) | Friability ^c (%) | Drug content ^d (%) |
|------------------|--|---|-----------------------------|-----------------------------|-------------------------------|
| AFD1 | 225±0.32 | 4.50±0.74 | 3.3-3.5 | 0.16±0.01 | 91.90 ±0.42 |
| AFD2 | 224±0.66 | 4.67±0.21 | 3.4-3.6 | 0.24±0.18 | 93.61 ±0.70 |
| AFD3 | 225±0.45 | 5.09±0.95 | 3.2-3.5 | 0.29±0.22 | 93.22 ±0.57 |
| AFL1 | 224±0.39 | 4.33±0.61 | 3.1-3.3 | 0.21±0.16 | 96.02 ±0.33 |
| AFL2 | 226±0.11 | 4.50±0.12 | 3.3-3.6 | 0.23±0.27 | 97.27 ±0.21 |
| AFL3 | 225±0.44 | 6.41±0.57 | 3.1-3.4 | 0.25±0.22 | 99.14 ±0.17 |
| DFD1 | 225±0.67 | 4.21±0.84 | 3.2-3.5 | 0.16±0.54 | 99.47 ±0.58 |
| DFD2 | 224±0.18 | 5.45±0.17 | 3.1-3.3 | 0.25±0.92 | 98.13 ±0.14 |
| DFD3 | 225±0.25 | 4.65±0.29 | 3.3-3.4 | 0.24±0.73 | 99.28 ±0.78 |
| DFL1 | 225±0.93 | 5.29±0.27 | 3.2-3.5 | 0.23±0.18 | 99.24 ±0.77 |
| DFL2 | 225±0.32 | 4.40±0.29 | 3.1-3.4 | 0.22±0.12 | 99.19 ±0.61 |
| DFL3 | 224±0.91 | 4.29±0.51 | 3.1-3.5 | 0.24±0.64 | 98.22 ±0.36 |
| MFD1 | 225±0.66 | 4.74±0.57 | 3.2-3.6 | 0.21±0.26 | 97.24 ±0.80 |
| MFD2 | 224±0.65 | 5.25±0.28 | 3.1-3.5 | 0.21±0.24 | 99.21 ±0.33 |
| MFD3 | 225±0.18 | 4.88±0.15 | 3.2-3.6 | 0.13±0.64 | 98.19 ±0.37 |

3.4. In vitro dissolution studies for furosemide matrix tablets

In vitro dissolution studies for furosemide matrix tablets were carried out and release profiles of different matrix tablets are given in Tables 5-7 and corresponding curves are shown in Fig. 3-5.

The dissolution studies were conducted only up to a period of 12 hrs irrespective of the complete drug release and only those formulations which are able to give 100 % of the drug release as contemplated were considered for further studies. Furosemide released from the matrix tablets formulated was affected by diluents. In the present work water soluble and water insoluble diluents were used. In case of soluble diluent like lactose, when the tablet is getting exposed to dissolution medium the soluble diluents gets dissolved in the dissolution medium and pores are created through which the dissolution

medium penetrates in to the core of the tablet there by enhancing the faster diffusion of the drug, where as in case of dibasic calcium phosphate, because it is an insoluble diluent the lag time for penetration of the liquid is more hence, the drug release is retarded.

As the goal of the present investigation is to complete the drug release in a uniform way with zero order, soluble diluent played its role in making it uniform drug release compared to the insoluble diluent. Uniformity of drug release is more appropriate with lactose hence, lactose is more suitable for water insoluble drug compared to dibasic calcium phosphate. Commercial formulations with this dose are not available so we have not compared with commercial tablets.

| Time (hrs) | Cumulative % drug released (mean \pm s.d., n=3) | | | | | |
|------------|---|------------------|------------------|------------------|------------------|------------------|
| | AFD1 | AFD2 | AFD3 | AFL1 | AFL2 | AFL3 |
| | DCP | | | Lactose | | |
| 1 | 11.32 \pm 0.16 | 10.22 \pm 0.14 | 11.52 \pm 0.71 | 14.65 \pm 0.91 | 13.41 \pm 0.51 | 15.60 \pm 0.52 |
| 2 | 17.23 \pm 0.16 | 15.71 \pm 0.52 | 17.40 \pm 0.47 | 26.45 \pm 0.32 | 17.50 \pm 0.27 | 21.71 \pm 0.37 |
| 3 | 25.29 \pm 0.22 | 32.40 \pm 0.27 | 25.32 \pm 0.19 | 37.6 \pm 0.67 | 25.26 \pm 0.33 | 25.33 \pm 0.74 |
| 4 | 27.11 \pm 0.62 | 37.68 \pm 0.44 | 34.21 \pm 0.42 | 50.68 \pm 0.93 | 33.16 \pm 0.51 | 27.27 \pm 0.18 |
| 5 | 33.37 \pm 0.13 | 41.24 \pm 0.32 | 39.86 \pm 0.51 | 61.51 \pm 0.82 | 39.22 \pm 0.24 | 31.23 \pm 0.41 |
| 6 | 37.53 \pm 0.29 | 45.29 \pm 0.27 | 43.73 \pm 0.61 | 68.64 \pm 0.33 | 46.13 \pm 0.48 | 37.69 \pm 0.36 |
| 7 | 45.27 \pm 0.31 | 52.57 \pm 0.57 | 49.21 \pm 0.52 | 74.19 \pm 0.11 | 49.31 \pm 0.49 | 47.01 \pm 0.63 |
| 8 | 55.47 \pm 0.58 | 57.22 \pm 0.43 | 53.44 \pm 0.76 | 79.51 \pm 0.57 | 52.14 \pm 0.64 | 52.85 \pm 0.34 |
| 9 | 63.77 \pm 0.39 | 60.39 \pm 0.63 | 57.86 \pm 0.48 | 84.35 \pm 0.64 | 63.16 \pm 0.67 | 65.52 \pm 0.85 |
| 10 | 70.18 \pm 0.23 | 63.52 \pm 0.11 | 62.32 \pm 0.62 | 90.57 \pm 0.53 | 74.46 \pm 0.72 | 77.26 \pm 0.44 |
| 12 | 79.17 \pm 0.32 | 69.47 \pm 0.52 | 64.47 \pm 0.18 | 98.38 \pm 0.72 | 88.36 \pm 0.45 | 84.55 \pm 0.56 |

Table 5: Drug release profiles of furosemide matrix tablets prepared employing albizia gum using DCP and lactose as diluents

Table 6: Drug release profiles of furosemide matrix tablets prepared employing dammar gum using DCP and lactose as diluents

| Time (hrs) | Cumulative % drug released (mean \pm s.d., n=3) | | | | | |
|------------|---|------------------|------------------|-----------------------------------|------------------|------------------|
| | DFD1 | DFD2 | DFD3 | DFL1 | DFL2 | DFL3 |
| | DCP | | | Lactose | | |
| 1 | 10.72 \pm 0.16 | 11.37 \pm 0.41 | 10.51 \pm 0.16 | 13.33 \pm 0.46 | 12.33 \pm 0.47 | 16.20 \pm 0.38 |
| 2 | 16.31 \pm 0.11 | 15.31 \pm 0.25 | 17.61 \pm 0.21 | 29.23 \pm 0.66 | 16.27 \pm 0.40 | 24.52 \pm 0.25 |
| 3 | 24.25 \pm 0.33 | 34.16 \pm 0.39 | 27.34 \pm 0.55 | 38.61 \pm 0.31 | 25.39 \pm 0.46 | 29.24 \pm 0.17 |
| 4 | 27.19 \pm 0.97 | 38.41 \pm 0.45 | 34.68 \pm 0.17 | 50.60 \pm 0.12 | 32.19 \pm 0.46 | 31.54 \pm 0.28 |
| 5 | 34.67 \pm 0.19 | 42.28 \pm 0.12 | 40.19 \pm 0.12 | 63.40 \pm 0.26 | 39.33 \pm 0.53 | 34.89 \pm 0.57 |
| 6 | 39.97 \pm 0.24 | 45.74 \pm 0.66 | 44.15 \pm 0.89 | 70.72 \pm 0.51 | 47.39 \pm 0.28 | 41.56 \pm 0.76 |
| 7 | 47.81 \pm 0.17 | 51.14 \pm 0.47 | 51.27 \pm 0.09 | 79.19 \pm 0.64 | 51.61 \pm 0.44 | 49.55 \pm 0.25 |
| 8 | 56.69 \pm 0.44 | 58.34 \pm 0.41 | 54.44 \pm 0.15 | 84.24 \pm 0.39 | 56.80 \pm 0.19 | 55.72 \pm 0.57 |
| 9 | 64.29 \pm 0.41 | 63.14 \pm 0.19 | 59.27 \pm 0.14 | 89.73 \pm 0.12 | 66.72 \pm 0.11 | 66.88 \pm 0.18 |
| 10 | 71.19 \pm 0.29 | 67.38 \pm 0.51 | 62.27 \pm 0.31 | 94.51 \pm 0.23 | 80.43 \pm 0.22 | 79.65 \pm 0.15 |
| 12 | 80.21 \pm 0.41 | 72.25 \pm 0.39 | 68.52 \pm 0.71 | 100.09\pm0.03 | 92.69 \pm 0.24 | 87.55 \pm 0.86 |

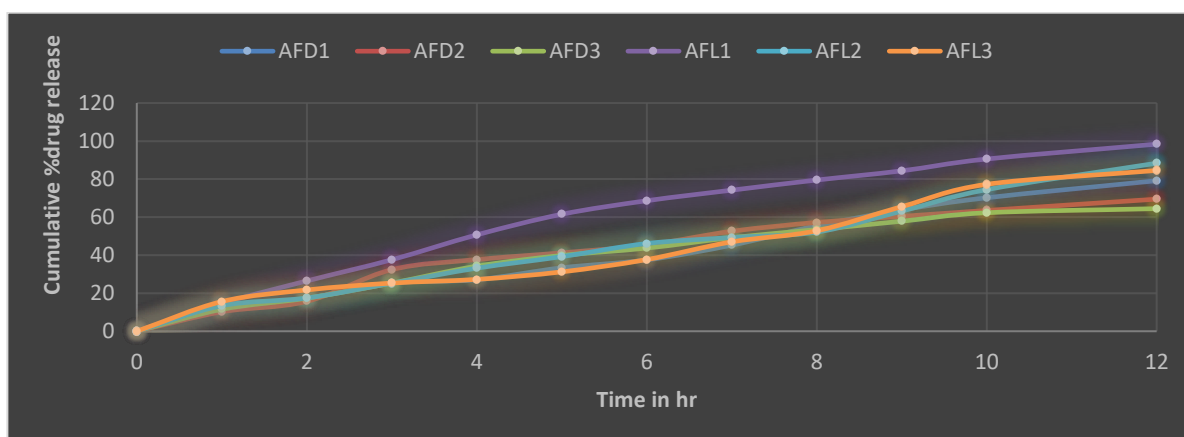


Fig. 3: Comparative dissolution profiles for formulations AFD1-AFD3 & AFL1-AFL3

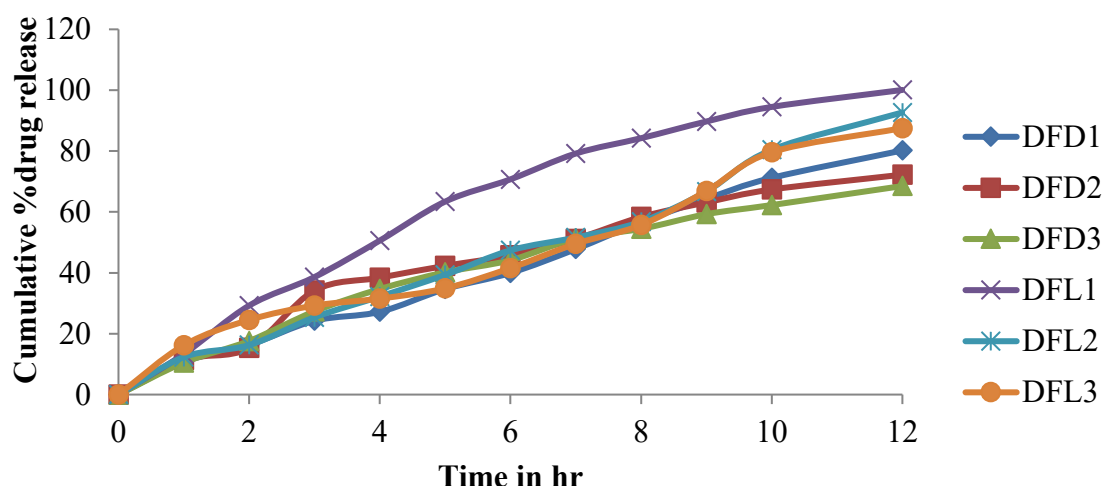


Fig. 4: Comparative dissolution profiles for formulations DFD1-DFD3 & DFL1-DFL3

| Time (hrs) | Cumulative % drug released (mean \pm s.d., n=3) | | | | | |
|------------|---|------------------|------------------|------------------|------------------|------------------|
| | MFD1 | MFD2 | MFD3 | MFL1 | MFL2 | MFL3 |
| | DCP | | | Lactose | | |
| 1 | 10.52 \pm 0.57 | 11.49 \pm 0.26 | 11.41 \pm 0.56 | 12.36 \pm 0.36 | 11.23 \pm 0.28 | 12.37 \pm 0.44 |
| 2 | 16.69 \pm 0.16 | 21.14 \pm 0.17 | 17.52 \pm 0.49 | 21.79 \pm 0.16 | 14.17 \pm 0.62 | 20.45 \pm 0.58 |
| 3 | 26.17 \pm 0.35 | 30.22 \pm 0.21 | 27.28 \pm 0.58 | 28.26 \pm 0.26 | 30.33 \pm 0.38 | 28.29 \pm 0.36 |
| 4 | 29.67 \pm 0.27 | 37.60 \pm 0.14 | 33.10 \pm 0.12 | 39.59 \pm 0.59 | 38.71 \pm 0.60 | 32.12 \pm 0.25 |
| 5 | 30.34 \pm 0.82 | 40.22 \pm 0.21 | 39.26 \pm 0.27 | 46.29 \pm 0.65 | 41.24 \pm 0.74 | 39.41 \pm 0.36 |
| 6 | 38.41 \pm 0.11 | 44.67 \pm 0.47 | 42.39 \pm 0.20 | 55.65 \pm 0.48 | 44.71 \pm 0.49 | 42.39 \pm 0.27 |
| 7 | 47.52 \pm 0.72 | 53.71 \pm 0.81 | 49.21 \pm 0.31 | 61.16 \pm 0.62 | 53.29 \pm 0.63 | 49.12 \pm 0.29 |
| 8 | 54.70 \pm 0.48 | 60.29 \pm 0.22 | 52.92 \pm 0.60 | 73.18 \pm 0.63 | 58.15 \pm 0.89 | 54.39 \pm 0.23 |
| 9 | 65.54 \pm 0.29 | 68.56 \pm 0.39 | 57.21 \pm 0.12 | 81.41 \pm 0.54 | 72.74 \pm 0.47 | 59.15 \pm 0.27 |
| 10 | 79.14 \pm 0.27 | 74.27 \pm 0.27 | 63.20 \pm 0.36 | 90.67 \pm 0.29 | 83.37 \pm 0.44 | 63.22 \pm 0.18 |
| 12 | 90.39 \pm 0.21 | 89.62 \pm 0.25 | 82.34 \pm 0.26 | 99.27 \pm 0.39 | 88.66 \pm 0.23 | 86.12 \pm 0.14 |

Table 7: Drug release profiles of furosemide matrix tablets prepared employing moi gum using DCP and lactose as diluents

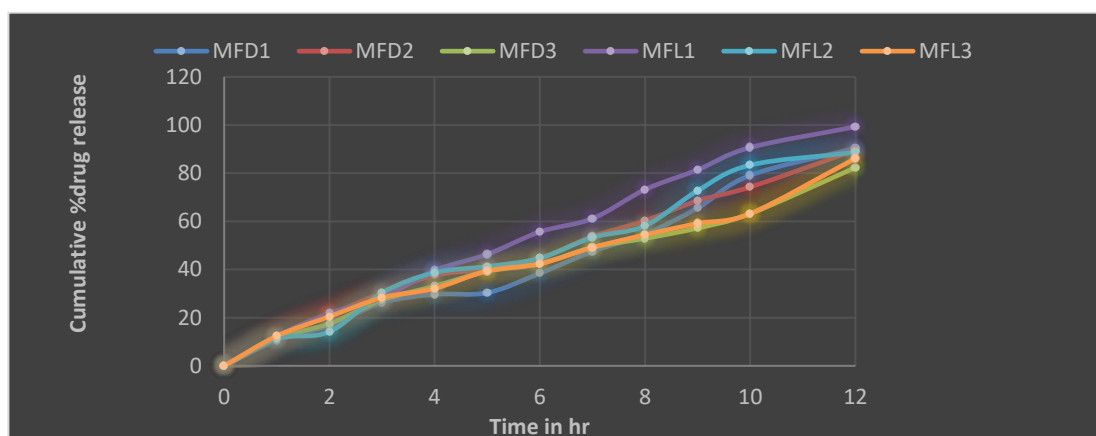


Fig. 5: Comparative dissolution profiles for formulations MFD1-MFD3 & MFL1-MFL3

3.5. Drug release kinetics of matrix tablets

Analysis of release data as per zero order and first order kinetic models indicated that the rate of drug release from the tablets followed first order kinetics in case of DCP as diluent, whereas zero order kinetics in case of lactose as diluent. The rate of drug release from optimized batch containing lactose as diluents (DFL1) was showed 'r' value as 0.9835 in case of zero order where as 0.8654 in case of first order kinetics this clearly indicating that the optimized formulation following zero order kinetics which is the desirable feature of controlled drug delivery systems.

3.6. Drug release mechanism of matrix tablets

When the release data was analyzed as per Higuchi's equation, the release was observed by diffusion mechanism, to conform the further type of diffusion i.e. Fickian or non-Fickian, data was analyzed with Peppas's equation, the release exponent "n" was in the range of 0.531 – 0.899 with all the matrix tablets indicating non - Fickian (anomalous) diffusion with erosion

3.7. Optimization

The drug release from the matrix tablets could be controlled by varying the proportion of drug-polymer in the matrix. The results of the study thus indicated albizia, dammar and moi gums could be used as rate controlling matrix in design of controlled release tablets. Both water soluble and water insoluble diluents can be included in the albizia, dammar and moi gums matrix tablets without affecting its rate controlling efficiency.

From the above dissolution studies it was observed that among all formulations, AFL1, DFL1, MFL1 showed near 100 % drug release over a period of 12 hrs, among these formulations DF1 showed 100 % drug release and followed expected zero order kinetics and non-Fickian diffusion and the tablet integrity was also maintained throughout prescribed time. Hence, among three gums employed in the present research work dammar gum showed optimized release, so it was concluded that dammar gum is more suitable for the formulation of controlled release matrix tablets for water insoluble drug like furosemide.

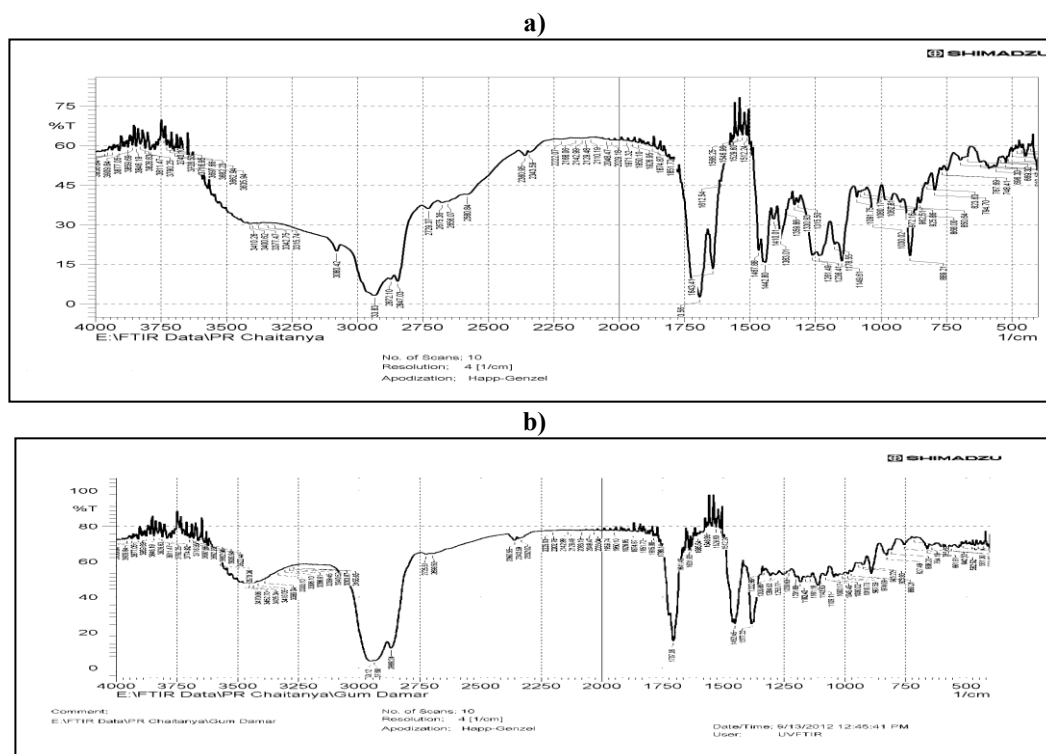
3.8. Drug-excipient compatibility studies

The concentration and characteristics of excipients can influence the final drug product. By the literature on furosemide did not show any interaction with dibasic calcium phosphate and lactose. The present study was aimed to investigate the suitability of albizia, dammar and moi gums for the preparation of controlled release matrix tablets. Generally drug-excipients compatibility studies were carried out for physical mixtures of drugs and excipients as per ICH guidelines. However there is possibility of drug-excipient incompatibility during compression due to heat and other processing variables rather than physical mixture. Hence compatibility studies were carried out for matrix tablets instead of physical mixture. For other polymers also compatibility studies were not done because these polymers were earlier reported their suitability with furosemide.

Drug- polymer compatibility studies were carried out for pure furosemide, albizia gum, dammar gum, moi gum and optimized formulation. The technique used was fourier transform infrared spectroscopy (FTIR). Differential scanning calorimetry (DSC) was done for pure lactose, dammar gum, furosemide and optimized formulation (DFL1) according to the procedure given in previous sections.

3.8.1. Fourier transform infrared spectroscopy (FTIR)

Albizia gum, dammar gum, moi gum, pure drug (furosemide) and optimized matrix tablet formulation DFL1 was subjected to FTIR spectroscopic analysis, to ascertain whether there is any interaction between the drug and the polymers used. The obtained spectra are given in Fig. 6. Characteristic peaks of pure gums were compared and the data was given Table 8. Characteristic peaks of pure drug (furosemide) were compared with the peaks obtained for the matrix tablet formulation DFL1. The data for the same is given in Table 9. The characteristic bands of furosemide were identifiable and there was no major shift in them when combined with polymers used in the preparation of matrix tablets. This indicates that the drug was intact and had not reacted with the excipients used in the formulations and hence they are compatible.



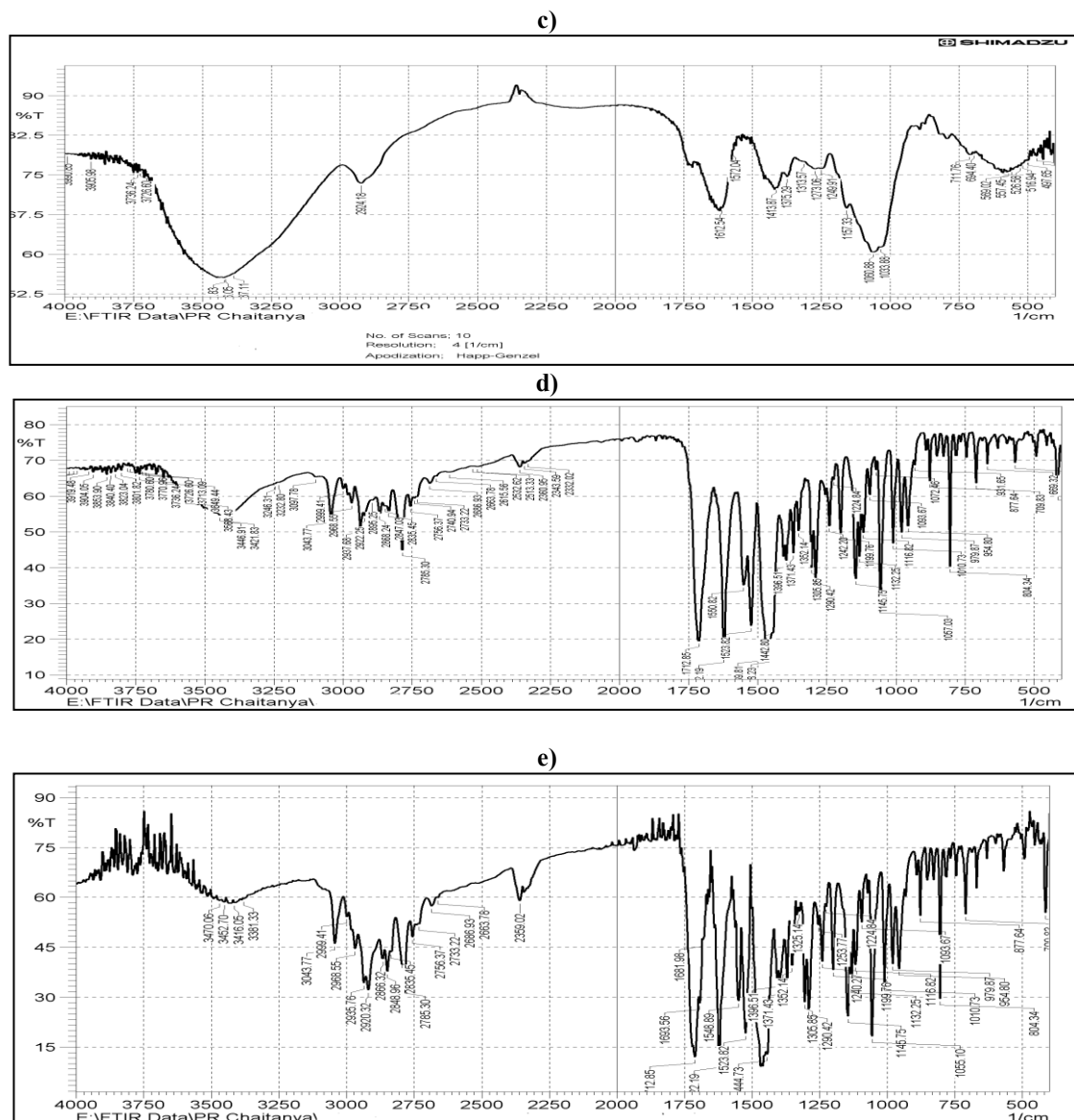


Fig. 6: FTIR spectra of (a) pure albizia gum (b) pure dammar gum (c) pure moi gum (d) pure furoseamide and (e) optimized formula (DFL1)

Table 8: FTIR spectral data of gums

| Name of the gum | Functional groups | Wave number of pure gums (cm ⁻¹) |
|-----------------|----------------------|--|
| Albizia gum | C-O Phenolic stretch | 1377.22 |
| | Ar-H | 1452.45 |
| | C=O stretching | 1707.06 |
| | OH Stretching | 3101.12 |
| Dammar gum | C-O Alcohol stretch | 1060.88 |
| | Ar-C=C | 1612.54 |
| | C-H stretch | 2924.18 |
| | OH Stretching | 3483.00 |
| Moi gum | C-H | 889.21 |
| | C-O Alcohol stretch | 1149.61 |
| | C-H bending | 1442.80 |
| | C=O stretch | 1695.18 |
| | OH Stretching | 3493.83 |

Table 9: FTIR spectral data of furoseamide pure drug and matrix tablet formulation DFL1

| Functional groups | Wave number of pure drug (cm ⁻¹) | Wave number of formulation (cm ⁻¹) |
|-------------------|--|--|
| C=O Stretching | 1712.00 | 1712.85 |

| | | |
|--------------------------------|---|---|
| C-Cl | 709.21 | 709.83 |
| N-H Stretching (2° Amine) | 3468.28 | 3470 |
| Ar-H | 3043.04 | 3043.77 |
| N-H Stretching(1°Sulphonamide) | 3232.16(Asymmetric) 3246.04(Symmetric) | 3381(Asymmetric) 3246.31(Symmetric) |
| S=O Stretching | 1352.14(Asymmetric) 1057.40(Symmetric) | 1352.14(Asymmetric) 1055.10(Symmetric) |
| S-N Stretching | 931.36 | 939.87 |

3.8.2. Differential scanning calorimetry (DSC) for furosemide

DSC studies were carried out for furosemide, dammar gum, lactose and optimized formulation DFL1 and the thermograms obtained are presented in Fig. 7. Thermogram of pure lactose showed a sharp peak at 145.6°C, dammar gum at 180.9°C and pure drug showed a sharp endothermic peak at 220.9°C, which corresponds to their melting points. Matrix tablet formulation DFL1 also showed endothermic peaks at 145.6°C, 180.9°C and 220.9°C. The evaluation of thermograms revealed no interaction between the drug and the excipients. From the thermograms, it was evident that the melting point of furosemide has not changed after it was formulated as a matrix tablet.

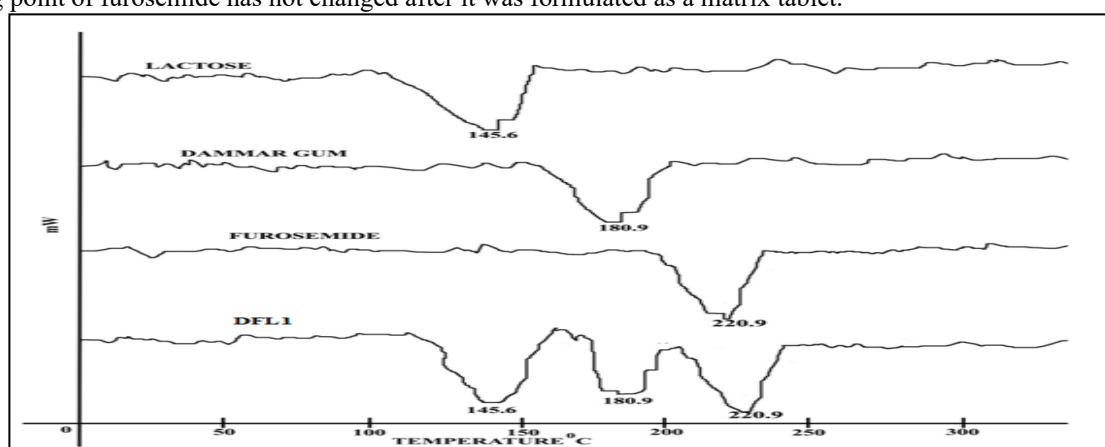


Fig. 7: DSC thermogram of pure lactose, dammar gum, furosemide and optimized formulation (DFL1)

CONCLUSION

Matrix tablets of albizia gum, dammar gum and moi gum were prepared in different concentrations. All the formulations were showed good tableting properties. Among three gums dammar gum was able to show the better controlled release of furosemide from matrix tablets over 12 hrs. The drug release was enhanced by using channeling agents like lactose and DCP. Among these two channeling agents lactose was showed better enhancement and controlled drug release. The drug release kinetics and mechanisms were evaluated. Compatibility studies were carried out for optimized formulations and the results proved that there was no interaction of drug and polymers.

Conflict of interest: The authors conform that this article content has no conflict of interest.

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