Extraction and Evaluation of *Mangifera indica* Gum as a Sustained Release Polymer in Glibenclamide Matrix Tablets

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**Abstract**

The aim of this study was to extract and evaluate *Mangifera indica* gum as sustain release polymer in glibenclamide matrix tablets. by using formal processes the gum of MI was tested for physicochemical and phytochemical properties and the results turned out favorable. The formulations were intended and evaluated for the various parameters like weight uniformity, friability, content percent, hardness and in-vitro dissolution studies. Moreover, all the matrix tablets formulations were within limits of the Pharmacopoeial standards. After a period of 24 h. in-vitro release studies, the findings of F1, F2, F3 and were 10.89%, 10.69%, 9.99% and 9.55%, respectively. the best sustained drug release among those formulations (of 10.89%) was been achieved with formulation F1 at the end of 24 h, which indicated that the drug release from the matrix tablets was dependent on gum concentration, also MI gum give effective results even with very low concentrations (below 1%).

**Keywords:** Extraction, *Mangifera indica* Gum, Sustain Release polymer, Evaluation, Matrix Tablets

**1 Introduction**

The means by which a medicinal product releases the drug and delivers it to its site of action are called drug delivery systems (DDS). These systems can be categorized according to its physical state, route of administration and mechanism of drug release¹ - ⁴. Basically, depending on the mechanism of drug release DDS are classified into immediate and modified drug release delivery systems.

Natural polymers lately raise huge interest, this is mainly because they are easily available, cheap and biocompatible also they are non toxic, non irritant and have soothing affect. Due to these features over semi synthetic and synthetic ones natural polymers significantly used in pharmaceutical industries as disintegrant, diluents, binders and many other applications. Demand for these substances is increasing, and new sources are being developed⁵.

*Sudan*, because of its geographical and environmental position, has traditionally been a good source for such products among the African countries still, large quantities are imported from Europe to meet increasing demand.

*Mangifera indica* tree belongs to genus Mangifera of the family Anacardiaceae. In demotic medicine MI tree has been used as a therapy against chronic dysentery, also in the prevention of cancer, scabies, asthma and bacteria. The bark exudates yield resin, gum, ash, and tannins⁶ - ⁸. MI gum resins spurt outside the mango trees trunk by the act of the wind, fire or any small injury on the trunk surface, after that those gum resin is collected and then purified to be used in pharmaceutical manufacturing to retard the release⁹.

*Mangifera indica* gum (MIG) is a dried gummy exudates polysaccharide obtained from the bark of *Mangifera indica* plant, studies were performed on this gum for its binding, sustained release, disintegrating properties an tablets containing this gum showed good appearance and better drug release¹⁰. MIG was incorporated as a binder in paracetamol tablets formulations. The results disclose that paracetamol tablets prepared by using MIG as a binder are more effective than the standard (5%w/w gum acacia). Therefore, it is concluded that the mango gum could be used well as a binding agent in the formulation of tablet dosage forms¹¹. MIG was isolated,
characterized and evaluated for its release retardant properties employing Lornoxicam as a model drug. Nicorandil sustained release matrix tablets were formulated by using MIG rate controlling factor and to evaluate drug release parameters as per various releases kinetic models. Hence use of natural gum Mangifera indica was successful in the formation of matrix tablets and it is effective in retarding the drug release at the same time. Therapy with Glibencalalide (GL) usually initiated with 2.5 mg given once daily due to its high bioavailability and rapid oral absorption, but because GL has short elimination half life (5-7 hrs.) its given three times per day. Also there is a variation in

The drug release and person to person variability. These complains certainly can be overcome by the sustained release multiunit dosage form. These reasons account for the choice of GL to formulate a matrix tablets using purified natural gum extracted from MI plant. Hence the aim of this research was to extract and evaluate a pharmaceutical grade Mangifera indica gum as excipient in sustain release oral dosage formulations using glibencalalide as a drug.

2 Materials and Methods

Materials are illustrated in table 1

### Table 1: Materials used in the research

<table>
<thead>
<tr>
<th>Material</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mangifera indica gum</td>
<td>Collected from the incised trunk of <em>Mangifera indica</em> in alfaki hashim (Khartoum, bahri)</td>
</tr>
<tr>
<td>Glibencalalide</td>
<td>Gift sample from Blue Nile pharmaceutical industry, sudan</td>
</tr>
<tr>
<td>Acetone</td>
<td>High purity was purchased from commercial market, sudan</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>From Omdurman Islamic University Labs</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>Gift sample from Blue Nile pharmaceutical industry, sudan</td>
</tr>
<tr>
<td>Isopropyle alcohol</td>
<td>From Omdurman Islamic University Labs</td>
</tr>
</tbody>
</table>

All the other solvents, reagents and chemicals used were of either Pharmacopoeial or analytical grade.

2.1 Extraction of *Mangifera indica* gum

The MI gum resin was collected from Mangifera indica trees (by injuring the trunk site). It was dried, ground, and passed through sieve no 80. Dried gum (85g) was stirred in distilled water (500ml) for 6-8 h at room temperature. The supernatant was obtained by centrifugation.

The residue was washed with water and the washings were added to separate a supernatant. The procedure was repeated four more times. Finally, the supernatant was made up to 500 ml and treated with twice the volume of acetone by continuous stirring. The precipitated material was washed with distilled water and dried at 50-60°C under vacuum. The dried gum was pulverized and stored in tightly closed container.

2.2 Physicochemical characterization of gum

The physicochemical properties such as organoleptic properties, solubility, swelling index, PH determination, loss on drying, Bulk Density, tapped density and Angle of repose were determined according to official Procedures.

2.3 Phytochemical examination of the gum

Preliminary tests were performed to confirm the nature of gum obtained. The chemical tests that were conducted are: Ruthenium red test, Molisch test, test for reducing sugars and Wagner's test.

2.4 Preparation of the matrix tablets

Matrix tablets were prepared by wet granulation method, glibencalmalide, MIG and MCC were mixed together and the mixture was passed through mesh (No. 60). Granulation was done using a sufficient isopropyl alcohol. The wet mass passed through mesh (No.30). The wet granules were air dried in the oven. The granules were then sized by mesh (No.35) and mixed with magnesium stearate.

Tablets were compressed using single rotary tablet press (lab press-1 / Shakti Pharmatech Pvt Ltd). Four different formulas, having different concentrations of MIG (1, 30, 40, and 50% w/w), were developed, the composition of the designed formulations were showed in table 2.

### Table 2: Composition of *Mangifera indica* gum Matrix Tablet Formulation

<table>
<thead>
<tr>
<th>Ingredients (mg)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glibencalalide</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>MIG</td>
<td>2</td>
<td>60</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>MS</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>MCC</td>
<td>175</td>
<td>117</td>
<td>97</td>
<td>77</td>
</tr>
<tr>
<td>TTW</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
</tbody>
</table>
2.5 Evaluation of the matrix tablets blend

The prepared powder blend was evaluated for various parameters like bulk density, tapped density, angle of repose, compressibility index and Hausner’s index\(^{17, 18}\).

2.6 Evaluation of the matrix tablets

All the tablets were evaluated for the following different parameters which includes\(^{17, 18}\):

2.6.1 General appearance

Five tablets from different batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated.

2.6.2 Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Erweka hardness tester. It is expressed in kg/cm\(^2\). Ten tablets were randomly picked from each formula and the hardness of the tablets was determined.

2.6.3 Friability

Friability of the tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution.

Pre weighed sample of ten tablets was placed in the friabilator for 4 minutes. Tablets were de dusted using a soft wiper and re weighed.

The friability \((f)\) is given by the formula:

\[
\text{Friability} (f) = 100 \left(\frac{W_o - W}{W_o}\right)
\]

Where \(W_o\) is weight of the tablets before the test and \(W\) is the weight of the tablet after the test

2.6.4 Weight variation test

Randomly twenty tablets were selected after compression, weighed individually and average weight was determined.

2.6.5 Drug content test

Ten tablets were weighed individually and powdered. The powder equivalent to average weight of one tablet was weighed and drug was extracted in Phosphate buffer pH 7.4, the drug content was determined using United State Pharmacopoeia (USP) high performance liquid chromatography (HPLC) method.

2.6.6 Swelling index

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling of formulations F1, F2, F3 and F4 were studied. One tablet from each formulation was kept in a Petri dish containing pH 7.4 phosphate buffer. At the end of 2 h, 4 h and 6 h, kept on tissue paper and weighed the process was continued till the end of 24 h, The % weight gain by the tablet was calculated by formula:

\[
S.I = \left(\frac{W_t - W_0}{W_0}\right) \times 100
\]

Where; \(S.I\) = swelling index, \(W_t\) = weight of tablet at time \((t)\), \(W_0\) = weight of tablet at time

2.6.7 In vitro drug release studies

Release of glibenclamide from the formulated matrix tablets was studied in phosphate buffer of pH 7.4 (900 ml) using a United State Pharmacopoeia (USP) 6 station Dissolution Rate Test Apparatus with a rotating paddle stirrer at 50 rpm and 37°C ± 0.5 °C as prescribed for glibenclamide tablets in USP.

A sample of glibenclamide matrix tablets equivalent to 20 mg of Glibenclamide was used in each test. Samples of dissolution fluid were withdrawn through a filter (0.45μm) every 2 for the first 6 hrs of the study period then a last sample of dissolution fluids were withdrawn at the 24. These samples were assayed against the reference standard using (USP) high performance liquid chromatography (HPLC) method at 230 nm. over a period of 24.

3 Results and Discussions

3.1 Physicochemical characterization of gum

The average yield of dried gum obtained from Mangifera indica tree was 31% w/w. The extracted gum was brown color powder. The powder was slightly soluble in water and virtually insoluble in acetone and ethanol.

The swelling characteristic of MIG was studied in phosphate buffer (pH 7.4) and water. The swelling ratio was determined as 15 for water and 10 for phosphate buffer. Generally, the results show that MIG has been high swelling index suggesting that the gum may perform well as binder/disintegrant/matrixing agent. The reading of the pH was (7.35).

The compressibility index, Hausner ratio and angle of repose of MIG were 22.5%, 1.3 and 26.5° respectively, implying that the MIG has a good flow with moderate compressibility.

The polymer of MI plant had the same wavelength range as the drug glibenclamide (213 – 232 nm) hence HPLC was used as detection method.

The gum obtained from Mangifera indica tree was subjected to physicochemical characterization and the results are in table 3

3.2 Phytochemical screening of the gum

Phytochemical tests that done on MIG assured that the gum lacks alkaloids and tannins and when the mucilage was mixed with ruthenium red it gave red color, which affirm the presence of the mucilage.

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Also on reaction with Molisch’s reagent a violet ring was formed confirming the presence of carbohydrates. There are no reducing sugars because the mucilage did not reduce Fehling’s solution. The results of phytochemical screening of the gum are in table 4.

### 3.3 Evaluation of the matrix tablets blend

The various flow parameters like the angle of repose, bulk density, tapped bulk density and compressibility index of the powder blends intended for compression were estimated. The angle of repose results indicating excellent flowability. The compressibility index range was found to be 21 to 25 and the Hausner ratio range was 1.26 to 1.34 indicating good flowability. The results were shown in table 5.

Table 3: Physicochemical characterization of *Mangifera indica* gum

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield (%)</td>
<td>31%</td>
</tr>
<tr>
<td>Odor</td>
<td>Characteristic odor</td>
</tr>
<tr>
<td>Taste</td>
<td>Tasteless</td>
</tr>
<tr>
<td>Color</td>
<td>Brown color</td>
</tr>
<tr>
<td>Solubility</td>
<td>Slightly soluble in water, practically insoluble in ethanol and acetone. Forms thick gel in water.</td>
</tr>
<tr>
<td>pH (1% w/v solution)</td>
<td>7.35</td>
</tr>
<tr>
<td>Swelling ratio</td>
<td></td>
</tr>
<tr>
<td>In water</td>
<td>15</td>
</tr>
<tr>
<td>In phosphate Buffer 7.4</td>
<td>10</td>
</tr>
<tr>
<td>Bulk density (g/cm³)</td>
<td>0.41±0.03</td>
</tr>
<tr>
<td>Tapped density (g/cm³)</td>
<td>0.53±0.02</td>
</tr>
<tr>
<td>Compressibility index</td>
<td>22.5%</td>
</tr>
<tr>
<td>Hausner ratio</td>
<td>1.3</td>
</tr>
<tr>
<td>Angle of repose (θ)</td>
<td>26.5±0.1</td>
</tr>
</tbody>
</table>

* Data was expressed as the mean ± SD, n=3

### 3.4 Evaluation of the matrix tablets

The GL matrix tablets were beige to brown in color, smooth, and flat shaped in appearance.

The hardness of the matrix tablets was found to be 3.47, 2.91, 2.50 and 2.37 kg/cm² for F₁, F₂, F₃ and F₄ respectively and the friability values were found below 1% for all the formulations, these results indicating that as the percent of the polymer increase, there is a decrease in the hardness values accordingly.

### 3.5 Swelling behavior of matrix tablets

The % weight gain by the tablet was used to estimate the magnitude of swelling. This was applied for all the formulations in-order to study their behavior. Figure 1 showed the swelling characteristics of MIG containing tablets. After calculating the swelling index with respect to time, a direct proportion was found. (as the time increases, the swelling index was increased).

### 3.6 In vitro drug release studies

The profile of GL matrix formulations *in-vitro* studies was shown in Fig 2. The results indicated release retardant property of the gum from all GL matrix formulations with an increase in the polymer concentration.

The sudden decrease in the cumulative % after the first two hours may be due to increase in the gel strength and hence, formation of gel layer with a longer path of diffusion compared to the diffusion coefficient of the drug, or the MIG polymer releases the drug as a “pulse” after a lag time (pulsatile effect).

A trial formula of glibenclamide immediate release tablet was prepared to exclude any problem in the dissolution of GL that may affect GL matrix tablet cumulative % results, the % release of this immediate tablets was found to be 45% in 30 minutes, this indicates that the cumulative % results of GL matrix tablets were only due to the sustaining effect of MIG polymer.

### 4 Conclusion

This study provided a clue about the evaluation of MIG as a release retardant in the formulation of sustained release matrix
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tablets because of its good swelling, good flow and suitability for matrix formulations. The results of this study demonstrated that MIG sustained the drug release. The polymer obtained was of high purity, and the method of extraction and characterization is economic and gave a high yield.

**Table 5: Results of flow properties of the matrix tablet blend**

<table>
<thead>
<tr>
<th>Formulations</th>
<th>F₁</th>
<th>F₂</th>
<th>F₃</th>
<th>F₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angle of repose (θ)</td>
<td>19.00±0.02</td>
<td>19.00±0.02</td>
<td>18.40±0.20</td>
<td>18.40±0.20</td>
</tr>
<tr>
<td>Bulk density (g/cm³)</td>
<td>0.44±0.02</td>
<td>0.44±0.03</td>
<td>0.44±0.04</td>
<td>0.44±0.02</td>
</tr>
<tr>
<td>Tapped density (g/cm³)</td>
<td>0.57±0.01</td>
<td>0.57±0.03</td>
<td>0.57±0.02</td>
<td>0.57±0.04</td>
</tr>
<tr>
<td>Compressibility index</td>
<td>22.8</td>
<td>22.8</td>
<td>22.8</td>
<td>22.8</td>
</tr>
<tr>
<td>Hausner ratio (HR)</td>
<td>1.28</td>
<td>1.28</td>
<td>1.28</td>
<td>1.28</td>
</tr>
</tbody>
</table>

*Data was expressed as the mean ± SD, n=3*

**Table 6: Results of physical properties of GL matrix tablets**

<table>
<thead>
<tr>
<th>Formulations</th>
<th>F₁</th>
<th>F₂</th>
<th>F₃</th>
<th>F₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness (kg/cm²) -(n=10)</td>
<td>3.47±0.37</td>
<td>2.91±0.50</td>
<td>2.50±0.50</td>
<td>2.37±0.17</td>
</tr>
<tr>
<td>Friability (%)(n=10)</td>
<td>0.152±0.011</td>
<td>0.096±0.008</td>
<td>0.050±0.013</td>
<td>0.048±0.018</td>
</tr>
<tr>
<td>Average Weight (mg) -(n=20)</td>
<td>196±0.95</td>
<td>201±1.02</td>
<td>198±0.55</td>
<td>203±1.22</td>
</tr>
<tr>
<td>Drug content (%) -(n=10)</td>
<td>112.5±1.7</td>
<td>93.9±1.2</td>
<td>87.4±3.1</td>
<td>82.7±3.5</td>
</tr>
</tbody>
</table>

**Fig 1: Results of swelling behaviour of different matrix tablets formulations**

**Fig 2: Results of in vitro dissolution profile of different matrix tablets formulations**

There is a fit reverse between the release from MIG matrix formulations and the ratio the gum present in that formulation, as the ratio increased the release is decreased. This may be result from an increase in the path length of the diffusion layer which in turn obtained from the formation of gel layer, resulting in reduction in a diffusion coefficient of the drug.

5 Acknowledgement

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6 Competing Interests

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Authors have declared that no competing interests exist.

7 Author’s contributions

ESY carried out the study, interpreted the results, and prepared the manuscript. ESE participated in the design of the study and was responsible for its coordination and contributed in the preparation of the manuscript. All authors read and approved the final manuscript.

8 References


