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Fabrication and *in vitro* Evaluation of Glimepiride *Hibiscus esculentus* Fruit Mucilage Sustained Release Matrix Tablets

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Abstract: The main objective of the present study was to develop matrix tablets of Glimepiride with *Hibiscus esculentus* fruit mucilage and to study its functionality as a matrix forming agent for sustained release tablet formulations. Physicochemical properties of dried powdered mucilage of *Hibiscus esculentus* mucilage were studied. Various formulations of Glimepiride *Hibiscus esculentus* mucilage were prepared. They found to have better uniformity of weight and drug content with low SD values. The swelling behavior and release rate characteristics were studied. The dissolution study proved that the dried *Hibiscus esculentus* mucilage can be used as a matrix forming material for making Sustained release matrix tablets.
Key words: Glimepiride, *Hibiscus esculentus*, matrix tablets, sustained release.

Introduction and Experimental

Hibiscus esculentus, (*Malvaceae* family) is an annual or perennial climber, growing up to 2 m tall. The fruit is a capsule up to 18 cm long[1]. Glimepiride is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus. It is belongs to sulfonyl ureas drug class. The recommended daily dose of Glimepiride is 1-8 mg/ day; 2 mg q.i.d or 4mg b.i.d. The biological half life ($t_{1/2}$) of Glimepiride is reported as 2.3± 0.8 h after a single dose of 3 mg and increasing to 5.3± 3.0 h after multiple dosing[2]. The pharmacokinetics and dosage schedule supports once daily controlled release formulations for Glimepiride for better control of blood glucose levels to prevent hypoglycemia, enhance clinical efficacy and patient compliance. The objective of present investigation is to design and evaluate sustained release tablets of Glimepiride using *Hibiscus esculentus* fruit mucilage as release retardant for making sustained release matrix tablets.

Materials

Glimepiride was obtained as a gift sample from Dr. Reddy's Laboratories, Hyderabad, India. *Hibiscus esculentus* fruits were collected from plants growing in local areas of Anantapur, India. The plant was authenticated at the Botany Department of Sri Krishnadevaraya University, Anantapur, India. Micro crystalline cellulose (Avicel) and Magnesium stearate were procured from SD Fine chemicals (Mumbai, India). All other chemicals used were of analytical reagent grade and double distilled water was used throughout the experiments.

Methods

Extraction of mucilage [3]

The fresh *Hibiscus esculentus* fruits were collected and washed with water. Incisions were made on the fruits, left over night. The fruits were crushed and soaked in water for 5–6 h, boiled for 30 minutes and left to stand for 1 h to allow complete release of the mucilage into

the water. The mucilage was extracted using a multi layer muslin cloth bag to remove the marc from the solution. Acetone (three times the volume of filtrate) was added to precipitate the mucilage. The mucilage was separated, dried in an oven at 40°C, collected, ground, passed through a # 80 sieve and stored in desiccator at 30 °C & 45% relative humidity till use. This mucilage was tested for flow properties (Table 1). All values were found to be satisfactory.

Preparation of Sustained release matrix tablets [4]

Sustained release matrix tablets of Glimepiride with *Hibiscus esculentus* fruit mucilage were prepared by using different drug: mucilage ratios viz. 1:0.5, 1:1.0, 1:1.5, 1:2.0 and 1:2.5. *Hibiscus esculentus* mucilage was used as matrix forming material while microcrystalline cellulose as a diluent and Magnesium stearate as a lubricant. All ingredients used were passed through a # 100 sieve, weighed and blended. The granules were prepared by wet granulation technique and compressed by using 8 mm flat faced punches. The compositions of formulations were showed in (Table 2). These matrix tablets were evaluated for their physical properties as per I.P methods[5, 6, and 7] (Table 3).

Swelling behavior of sustained release matrix tablets [8]

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation GMA-1, GMA-2, GMA-3, GMA-4 and GMA-5 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, the tablet was withdrawn, kept on tissue paper and weighed then for every 2 h, till the end of 12 h.. % weight gain by the tablet was calculated by formula.

$S.I = \{(M_t - M_0) / M_0\} \times 100$

Where, S.I = swelling index, M_t = weight of tablet at time't' and

M_o = weight of tablet at time 0. Swelling behavior of Sustained release matrix tablets were represented in Figure-1.

Estimation of Glimepiride

An ultraviolet spectrophotometric method based on measurement of absorbance at 230 nm in alkaline borate buffer of pH 7.4. The method obeyed Beer-Lambert's law in the concentration range of 1-20 µg/ml. When a standard drug solution was assayed for 6 times, the accuracy and Precision were found to be 0.94% and 1.12% respectively. No interference was observed from the excipients used.

***In vitro* drug release studies [9]**

Release of Glimepiride from the matrix tablets was studied in phosphate buffer of pH 7.4 (900 ml) using a United States Pharmacopoeia (USP) 8-station Dissolution Rate Test Apparatus (Model Electro lab , TDT- 06T,Mumbai,India) with a rotating paddle stirrer at 50 rpm and 37° ± 0.5°C. A sample of Glimepiride matrix tablets equivalent to 8 mg of Glimepiride was used in each test. Samples of dissolution fluid were withdrawn through a filter (0.45 µm) at different time intervals and were assayed at 230 nm for Glimepiride content using a UV/ visible single-beam spectrophotometer-117 (Systronics Corporation, Mumbai, India). The drug release experiments were conducted in triplicate (n = 3). The *in vitro* release rates were showed in Figure 2.

Results and Discussion

Matrix tablets, each containing 8 mg of Glimepiride, were prepared using dried fruit mucilage of *Hibiscus esculentus* in various drug: mucilage ratios (1:0.5, 1:1.0, 1:1.5, 1:2.0 and 1:2.5). *In vitro* drug release profile of Glimepiride from formulated matrix tablets were studid using zero order (Figure 2), first order (Figure 3), Higuchi plot (Figure 4), Peppas plot (Figure 5) and Hixon-Crowell Model (Figure 6). The rate of release was faster in GMA-1 and slower in GMA-5. The kinetic plots were perfectly fitting to the formulated *Hibiscus esculentus* fruit mucilage-Glimepiride matrix tablets. Infrared Spectrum of Glimepiride Pure drug (Figure 7), Infrared Spectrum of *Hibiscus esculentus* fruit mucilage (Figure 8), Infrared Spectrum of Glimepiride with *Hibiscus esculentus* fruit mucilage (Figure 9) shows the formation of matrix material without any negative interactions. This result shown that as the proportion of *Hibiscus esculentus* fruit mucilage increased, the overall time of release of the drug from the matrix tablet was also increased. Drug releases from matrix tablets were by drug dissolution, drug diffusion or a combination of both.

Conclusions

The present study revealed that *Hibiscus esculentus* fruit mucilage appears to be suitable for use as a release retardant in the manufacture of sustained release matrix tablets because of its good swelling, good flow and suitability for matrix formulations. From the dissolution study, it was concluded that dried *Hibiscus esculentus* mucilage can be used as an excipient for making sustained release matrix tablets.

Table 1. Flow properties of dried *Hibiscus esculentus* fruit mucilage

Parameters	Value
Bulk density (g/ml)	0.58±0.05
Tapped density (g/ml)	0.79±0.04
Carr's index (%)	26.58±0.21
Hausner's ratio	1.25±0.04
Angle of repose (^{0})	27.83±0.12

Number of experiments (n)= 3

Table2. Formulae of *Hibiscus esculentus* fruit mucilage -Glimepiride matrix tablets

Ingredients (mg)	Formulations				
	GMA-1	**GMA-2**	**GMA-3**	**GMA-4**	**GMA-5**
Glimepiride	8	8	8	8	8
Hibiscus esculentus dried mucilage	4	8	12	16	20
Micro crystalline cellulose (Avicel)	183	179	175	171	167
Magnesium stearate	5	5	5	5	5
Total weight of tablet	200	200	200	200	200

Table 3. Physical properties of *Hibiscus esculentus* fruit mucilage Glimepiride matrix tablets

Sl. No	Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
1	**GMA-**1	5.9±0.21	7.70±1.25	0.80±0.02	101.2±7.08
2	**GMA-**2	6.2±0.15	8.10±1.40	0.75±0.05	100.6±6.30
3	**GMA-**3	5.8±0.41	6.90±1.35	0.46±0.03	99.8±1.80
4	**GMA-**4	6.0±0.39	6.80±1.45	0.62±0.06	99.6±2.50
5	**GMA-**5	6.1±0.58	7.20±1.30	0.72±0.07	100.8±4.45

Number of trials (n) = 5

Table 4. Kinetic Values Obtained from *In-Vitro* Release Profile for Matrix Tablets of Glimepiride (Zero order and First order)

FORMULATION	ZERO ORDER KINETIC DATA			FIRST ORDER KINETIC DATA		
	Slope	Regression coefficient (r)	k value	Slope	Regression coefficient (r)	k value
GMA-1	6.3795	0.7080	9.5584	-0.0889	0.9796	-0.2198
GMA-2	6.3866	0.7811	9.0739	-0.0785	0.9821	-0.1901
GMA-3	6.754	0.9126	8.5804	-0.0775	0.9821	-0.1743
GMA-4	6.2864	0.9307	7.7607	-0.060	0.9852	-0.1385
GMA-5	6.7537	0.9204	8.4581	-0.0795	0.9819	-0.1705

Table 5. Kinetic Values Obtained from *In-Vitro* Release Profile for Matrix Tablets of Glimepiride (Higuchi, Hixon-crowell andPeppas models)

Formulation	HIGUCHI MATRIX KINETIC DATA			HIXON-CROWELL MODEL			PEPPAS KINETIC DATA			
	Slope	Regression coefficient (r)	k value	Slope	Regression coefficient (r)	k value	Slope	Regression coefficient (r)	k -value	n-value
GMA-1	25.23	0.979	28.491	0.1924	0.9542	-0.0528	0.3438	0.985	37.723	0.343
GMA-2	24.89	0.986	26.787	0.1801	0.9593	-0.0477	0.3786	0.978	33.665	0.370
GMA-3	25.68	0.994	24.849	0.1855	0.9867	-0.0443	0.4896	0.987	24.971	0.486
GMA-4	23.69	0.991	22.375	-0.1438	0.9855	-0.0732	0.5206	0.991	21.301	0.514
GMA-5	25.59	0.993	24.798	0.1807	0.9859	-0.04668	0.4798	0.986	23.591	0.479

Figure 1 Swelling Index of *Hibiscus esculentus* fruit mucilage Glimepiride matrix tablets

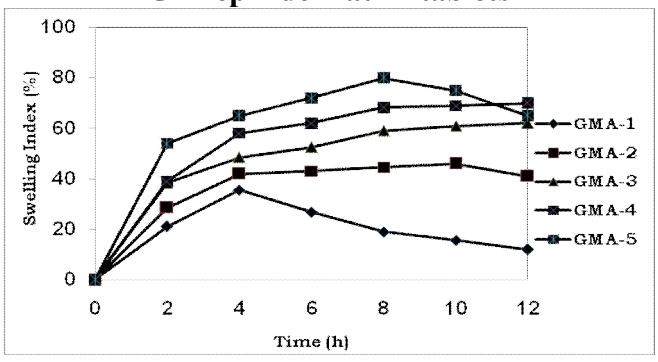


Figure 2. Zero order release Plot

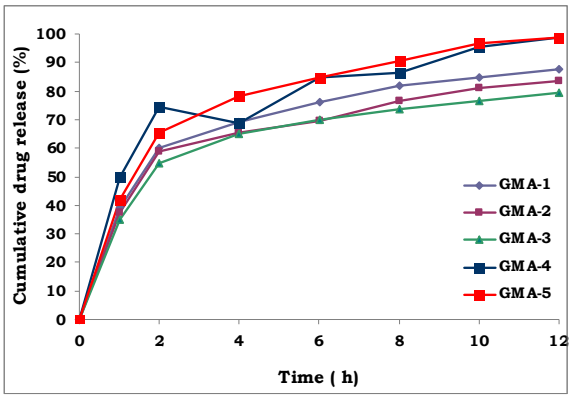


Figure 3. First order release Plot

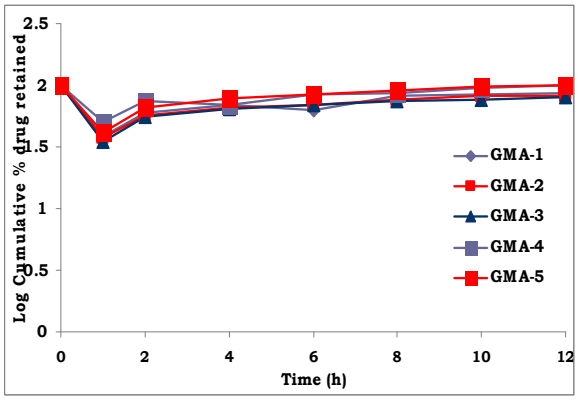


Figure 4. Higuchi Plot

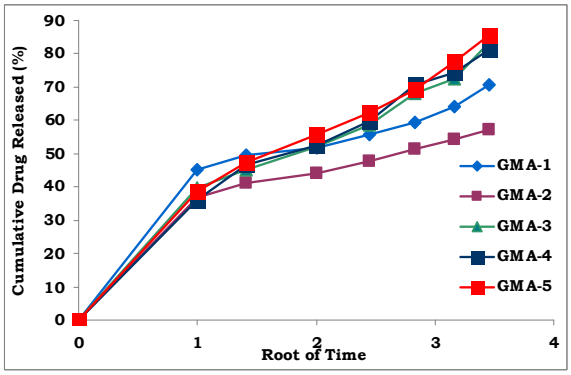


Figure 5. Peppas Plot

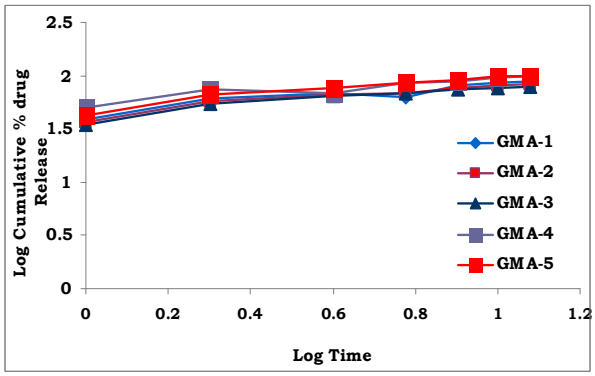


Figure 6. Hixon-Crowell Plot

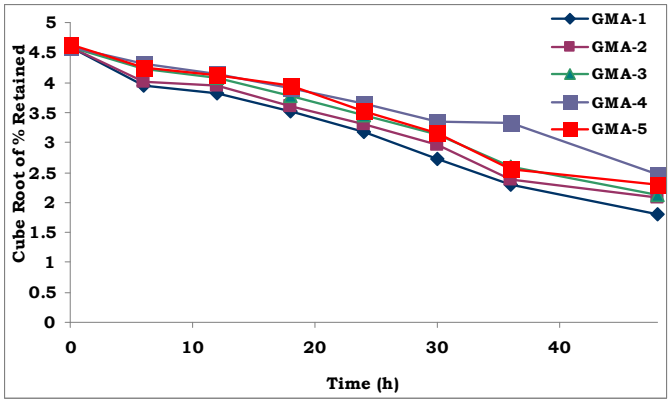


Figure 7 Infrared Spectrum of Glimepiride Pure drug

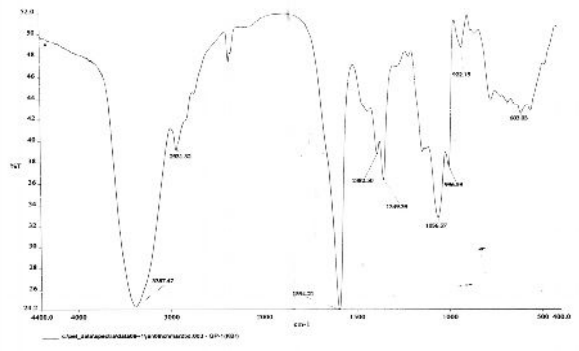


Figure 8 Infrared Spectrum of *Hibiscus esculentus* fruit mucilage

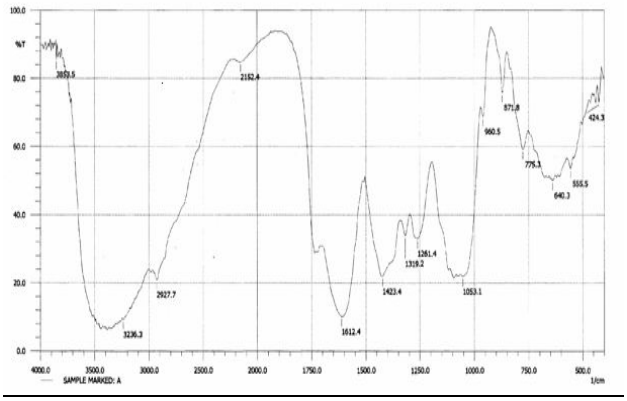
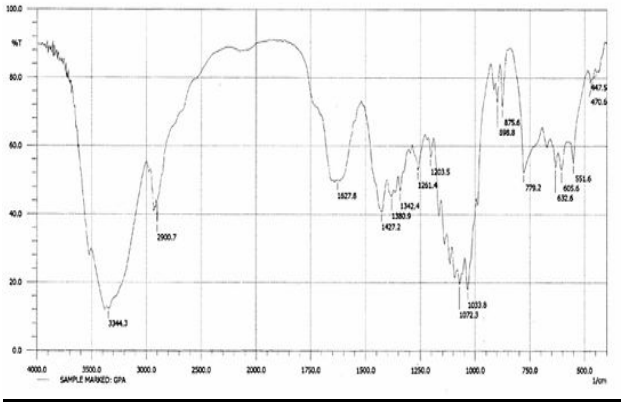


Figure 9 Infrared Spectrum of Glimepiride with *Hibiscus esculentus* fruit mucilage



Acknowledgements

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