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FABRICATION AND EVALUATION OF GLIPIZIDE *ABELMOSCHUS ESCULENTUS* FRUIT MUCILAGE POVIDONE CONTROLLED RELEASE MATRIX TABLETS

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ABSTRACT

The present investigation was aimed to prepare matrix type controlled release tablets of Glipizide with *Abelmoschus esculentus* fruit mucilage and Povidone. The polymers were studied for its functionality as a matrix forming property to sustain the Glipizide release from the dosage form. Physicochemical properties of dried powdered mucilage of *Abelmoschus esculentus* fruit mucilage and Povidone blend were studied. Various formulations of Glipizide *Abelmoschus esculentus* fruit mucilage and Povidone were prepared. The prepared tablets were found to have better pharmacopoeial parameters with low standard deviation values. The swelling behavior and release rate characteristics were studied. The *in-vitro* dissolution study proved that the dried *Abelmoschus esculentus* fruit mucilage and Povidone in combination can be used as a matrix forming polymers for making controlled release matrix tablets.

KEYWORDS: Glipizide, *Azadirachta indica,* Povidone, matrix tablets, evaluation, controlled release.

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INTRODUCTION

Abelmoschus 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]

Glipizide is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus.[2] Glipizide is a weak acid (pKa = 5.9) which is practically insoluble in water and acidic solutions but as per the Biopharmaceutical Classification System (BCS) it is highly permeable (class 2). The oral absorption is uniform, rapid and complete with a bioavailability of nearly 100% and an elimination half-life of 2–4 h.[3] Glipizide is reported to have a short biological half-life (3.4 ± 0.7 h) requiring it to be administered in 2 to 3 doses of 2.5 to 10 mg per day. Hence we have selected Glipizide for the development of once daily controlled release matrix tablets. The pharmacokinetics and dosage schedule supports once daily controlled release formulations for Glipizide for better control of blood glucose levels to prevent hypoglycemia, enhance clinical efficacy and patient compliance.

The objective of present investigation is to prepare and evaluate controlled release tablets of Glipizide using *Abelmoschus esculentus* fruits mucilage and Povidone combination as release retardant for making controlled release matrix tablets.

MATERIALS AND METHODS

Materials

Glipizide was obtained as a gift sample from Dr. Reddy's Laboratories, Hyderabad, India. *Abelmoschus 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. Povidone, 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.

Extraction of Mucilage

The fresh *Abelmoschus esculentus* fruits were collected and washed with water. The fruits were crushed and placed 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 (in the quantities of three times the volume of filtrate) was added to precipitate the mucilage[4]. The mucilage was separated, dried in an oven at 40^0C, collected, powdered, passed through a # 80 sieve and stored in air tight container till use.

Drug-Excipient Compatibility Studies

Differential Scanning Calorimetric (DSC) Analysis

DSC analysis was performed using Shimadzu DSC-60, Japan. A 1:1 ratio of drug and excipient was weighed into aluminum crucible. The sample was analyzed by heating at a scanning rate of 20^0C over a temperature range 40^0-200^0C under nitrogen environment.

Fourier Transform Infrared (FTIR) Spectroscopic Analysis

FTIR spectra were recorded on samples prepared in potassium bromide (KBr) disks using a Shimadzu Corporation, (FTIR-1601 PC, Tokyo, Japan). Samples were prepared in KBr disks by means of a hydrostatic press at 6-8 tons pressure. The samples were scanned at wavelength 500 to 4000 cm^{-1}.

Flow Properties of Formulation Blend

The formulation blend was evaluated for flow properties viz., Angle of repose, Loose Bulk Density, Tapped Bulk Density, Compressibility index and Hausner's ratio. The experiments were conducted in triplicate.

Preparation of Matrix Tablets

Controlled release matrix tablets of Glipizide with *Abelmoschus esculentus* fruit mucilage and Povidone were prepared by using different drug: mucilage ratios as shown in Table 2, *Abelmoschus esculentus* fruits mucilage and Povidone were used as matrix forming materials while microcrystalline cellulose as a diluent and Magnesium stearate as a lubricant[5]. All ingredients used were passed through a # 100 sieve, weighed and blended. The granules were prepared by wet granulation technique and compressed by using 10 mm flat faced punches. The compositions of formulations were showed in **Table 2**. These matrix tablets were evaluated for their physical properties as per official and Pharmacopoeial methods[6-8] which were shown in **Table 3**.

Swelling Behavior of Matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation GPA-1, GPA-2, GPA-3, GPA-4 and GPA-5 were studied. One tablet from each formulation was kept in a Petri dish containing phosphate pH 7.4. At the end of 2 h, the tablet was withdrawn, kept on tissue paper and weighed, repeated for every 2 h till the end of 12 h.[9] The % weight gain by the tablet was calculated by eq. 1.

$$S.I = \{(M_t - M_0) / M_0\} \times 100 \quad (1)$$

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 Controlled release matrix tablets were represented in **Fig. 7**.

***In vitro* Drug Release Studies**

Release of Glipizide from the matrix tablets was studied in phosphate buffer of pH 7.4 (900 ml) using United States Pharmacopoeia (USP) 6-station Dissolution Rate Test Apparatus (Model Electro lab, TDT- 06T, Mumbai, India) with a rotating paddle stirrer at 50 rpm and 37 ± 0.5^0C. A sample of Glipizide matrix tablets equivalent to 10 mg of Glipizide 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 223 nm for Glipizide content[10] 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 **Fig. 8**.

RESULTS AND DISCUSSION

The DSC of Glipizide Pure drug, *Abelmoschus esculentus* fruits mucilage with Povidone and physical mixture were shown in Fig **1, 2 and 3** respectively. Infrared Spectrum of Glipizide Pure drug, Infrared Spectrum of *Abelmoschus esculentus* fruits mucilage with Povidone, Infrared Spectrum of formulation was obtained. The FTIR spectrums revealed that the formulation spectrum retains the peaks of Glipizide and these spectrums were represented in Fig. **4, 5 and 6** respectively.

The Angle of repose of formulated blend was 29.45^0±1.68 indicating good flow, The Loose Bulk Density was found to be 0.578±0.08 g/ml, Tapped Bulk Density was found to be 0.788±0.03 g/ml, Compressibility index was ranged from 26.59±0.21% and Hausner's ratio was found to be 1.24±0.04. All these values were shown in **Table 1**. The formulated tablets showed uniformity in swelling and the values plotted and shown in **Fig.7**. The thickness of formulated tablets were ranged from 5.7±0.23 to 6.2±0.19 mm, hardness was ranged from 5.85±1.55 to 7.56±0.52 kg/cm^2, the loss on friability was ranged from 0.19±0.04 to 0.80±0.01 % and drug content was ranged from 99.1±3.66 to 100.8±6.37 %. All these values were shown in **Table 3**. *In vitro* drug release profile of Glipizide from formulated matrix tablets were studied using zero order, first order, Higuchi, Korsmeyer Peppa's and Hixson-Crowell's Models which were shown in **Fig. 8, 9, 10, 11** and **12** respectively. The rate of release was faster in GPA-1 and slower in GPA-5. The kinetic plots were perfectly fitting

to the formulated *Abelmoschus esculentus* fruits mucilage, Povidone - Glipizide matrix tablets. This result shown that as the proportion of *Abelmoschus esculentus* fruits mucilage and Povidone 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.

CONCLUSION

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

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Table 1: Flow properties of formulation blend

Parameters	Value
Angle of repose (^{0})	29.45±1.68
Loose Bulk Density (g/ml)	0.578±0.08
Tapped Bulk Density (g/ml)	0.788±0.03
Compressibility index (%)	26.59±0.21
Hausner's ratio	1.24±0.04
Number of experiments (n)= 3	

Table 2: Formulae of matrix tablets

Ingredients (mg)	Formulations				
	GPA-1	GPA-2	GPA-3	GPA-4	GPA-5
Glipizide	10	10	10	10	10
Abelmoschus esculentus fruits mucilage	2	4	6	8	10
Povidone	2	4	6	8	10
Micro crystalline cellulose (Avicel)	181	177	173	169	165
Magnesium stearate	5	5	5	5	5
Total weight of tablet	**200**	**200**	**200**	**200**	**200**

Table 3: Physical properties of formulated matrix tablets

Sl. No	Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
1	GPA-1	5.9±0.19	6.52±1.04	0.70±0.08	99.8±7.51
2	GPA-2	5.8±0.48	7.52±1.18	0.80±0.01	100.8±6.37
3	GPA-3	5.7±0.23	5.85±1.55	0.19±0.04	99.9±5.81
4	GPA-4	6.1±0.16	7.56±0.52	0.53±0.04	99.1±3.66
5	GPA-5	6.2±0.19	6.92±0.29	0.64±0.01	100.4±2.55
Number of trials (n) = 5					

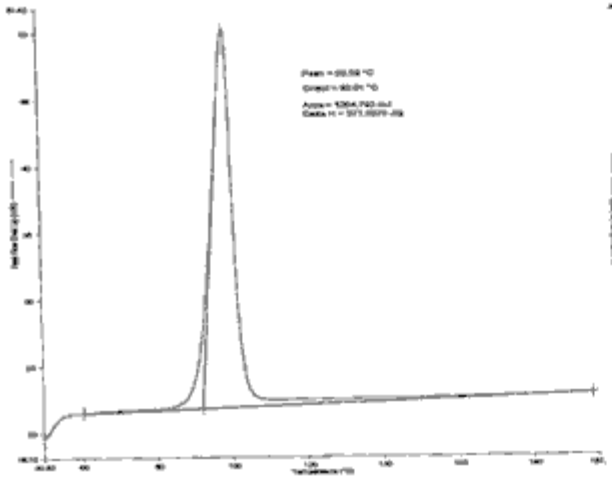
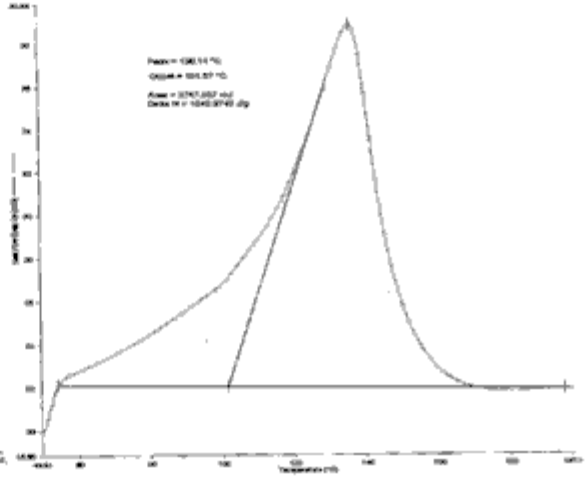


Fig.1



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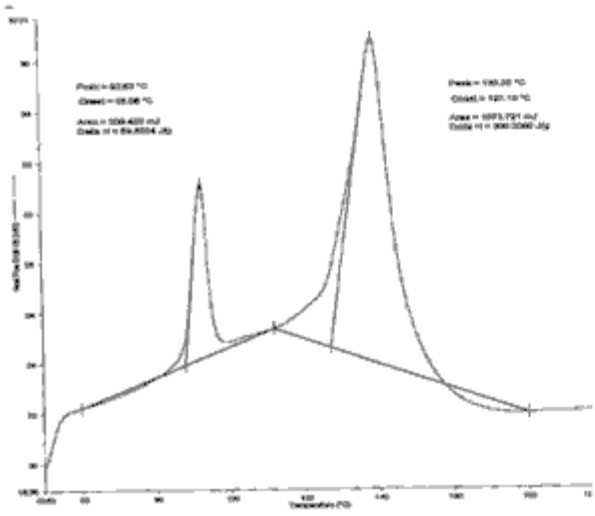
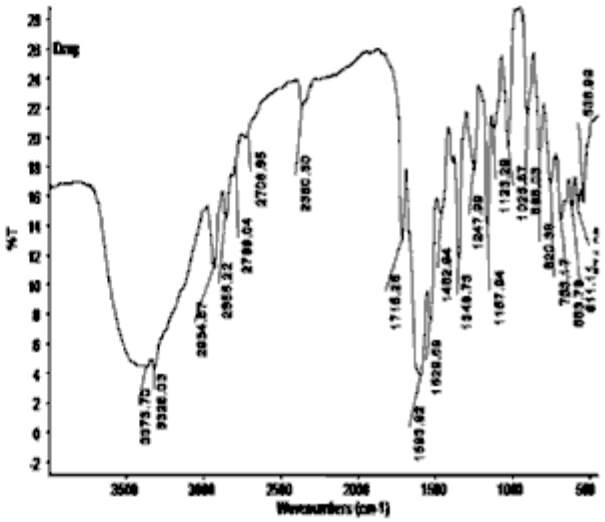


Fig. 3



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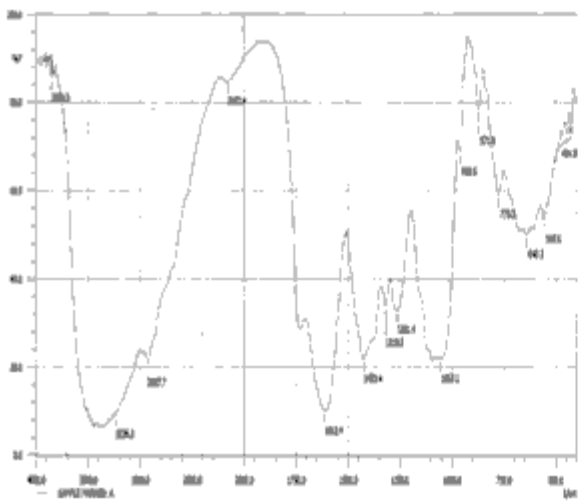

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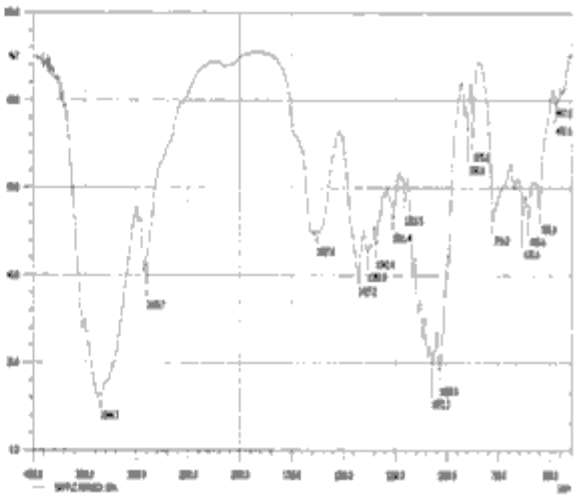

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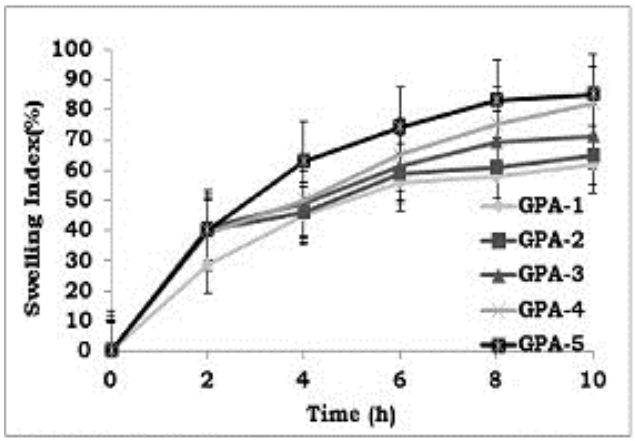


Fig. 7

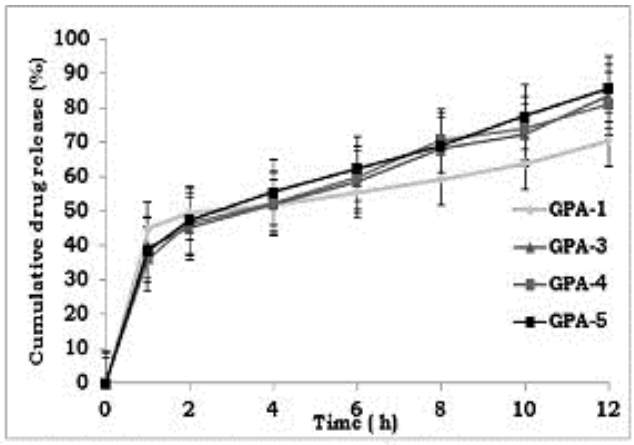
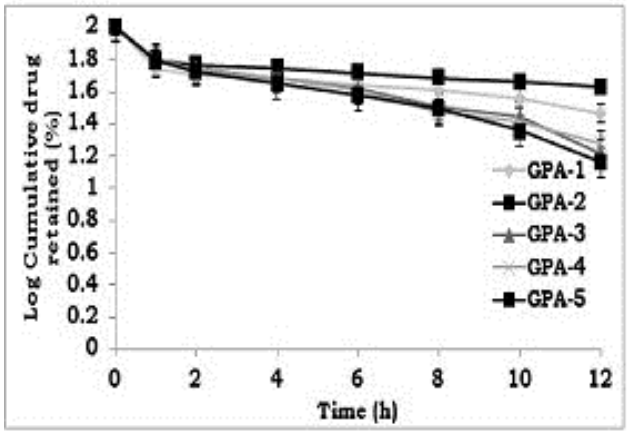


Fig. 8



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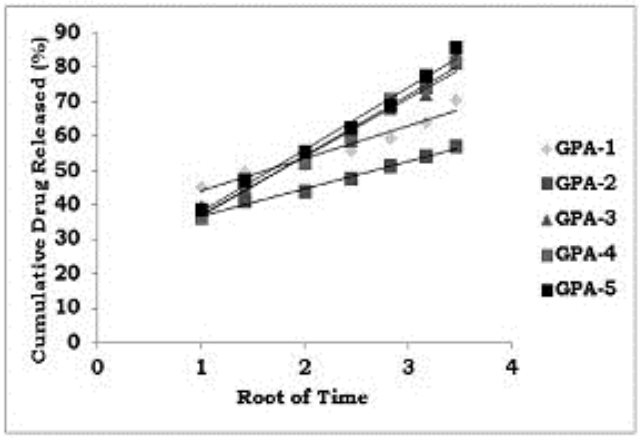

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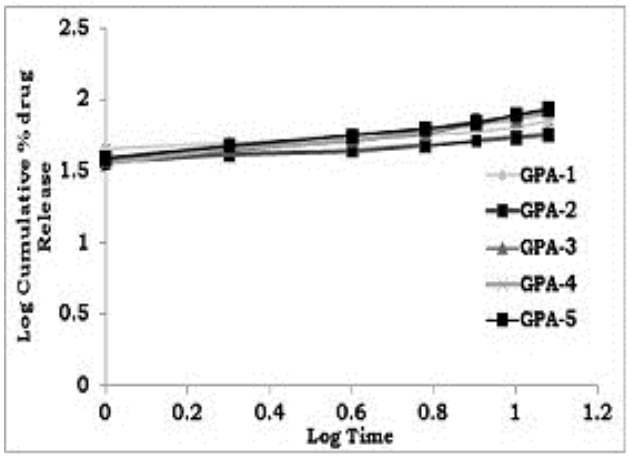

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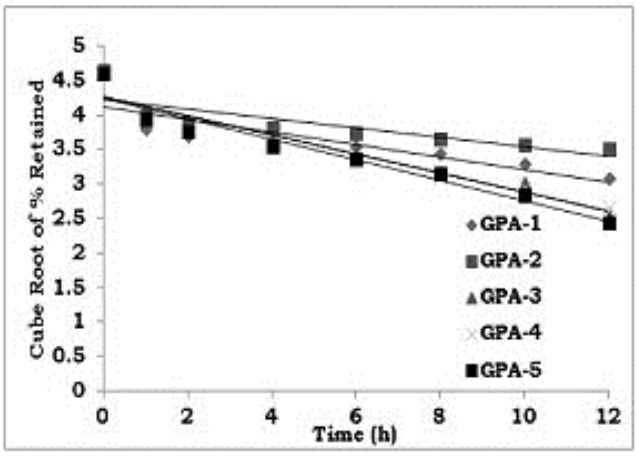

Fig.12

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