



FABRICATION AND EVALUATION OF GLIMEPIRIDE *CORDIA DICHOTOMA G.FORST* FRUIT MUCILAGE SUSTAINED RELEASE MATRIX TABLETS

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ABSTRACT

The main object of the present investigation was to develop a sustained release matrix tablets of glimepiride with *Cordia dichotoma G.Forst* fruit mucilage and to study its functionality as a matrix forming agent for sustained release. Physicochemical properties of dried powdered *Cordia dichotoma G.Forst* fruit mucilage were studied. Various formulations of glimepiride *Cordia dichotoma G.Forst* mucilage (CD-1, CD-2, CD-3, CD-4 and CD-5) were prepared. They were 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 *Cordia dichotoma G.Forst* fruit mucilage can be used as a matrix forming material for making sustained release tablets.

Key words: *Cordia dichotoma G. Forst*, Ethanol extract, Sustained release activity.

INTRODUCTION

Cordia dichotoma G. Forst belongs to *Boraginaceae* family. Glimepiride is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus. It belongs to sulfonyl ureas drug class. The recommended daily dose of glimepiride is 1-8 mg/ day; 2 mg q.i.d or 4 mg 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 dosing¹. 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 main objective of present investigation is to design and evaluate sustained

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release tablets of glimepiride using *Cordia dichotoma* G. Forst fruit mucilage as release retardant for making sustained release matrix tablets.

EXPERIMENTAL

Materials

Glimepiride was obtained as a gift sample from Dr. Reddy's Laboratories, Hyderabad, India. *Cordia dichotoma* G. Forst 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), sodium meta bisulfite (Antioxidant) were procured from SD Fine chemicals, Mumbai, India. All other chemicals used were analytical-reagent grade and double distilled water was used throughout the experiments.

Methods

Extraction of mucilage

The fresh fruits of *Cordia dichotoma* G. Forst were washed with water. Incisions were made on the fruits and left over night. The fruits were crushed and soaked in ethanol for 5–6 h, boiled for 30 minutes and left to stand for 1 h to allow complete release of the mucilage into the ethanol. The seeds were removed. This extract was further fractionated using petroleum ether (40-60%), ethyl acetate, butanol and butanone in succession². Then the mucilage was extracted using a multi layer muslin cloth bag to remove the marc from the solution. 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 and 45% relative humidity till use. This mucilage was tested for flow properties³ (Table 1). All values were found to be satisfactory.

Table 1: Flow properties of dried *Cordia dichotoma* G. Forst fruit mucilage

Parameter	Value
Bulk density (g/mL)	0.58
Tapped density (g/mL)	0.79
Carr's index (%)	26.58
Hausner's ratio	1.25
Angle of repose (°)	27.83
Number of experiments (n = 3)	

Preparation of sustained release matrix tablets

Sustained release matrix tablets of glimepiride with *Cordia dichotoma G. Forst* fruit mucilage were prepared by using different drug : mucilage ratios viz. 1 : 0.25, 1 : 0.5, 1 : 0.75, 1 : 10 and 1 : 1.25. *Cordia dichotoma G. Forst* was used as matrix forming material, while sodium bisulphite as antioxidant, micro crystalline cellulose as diluent and magnesium stearate as lubricant. All the ingredients used were passed through a # 100 sieve, weighed and blended. The above formulations were compressed by a direct compression technique, using 8 mm flat faced punches. Formulations of designed formulations are show in Table 2.

Table 2: Formulae of glimepiride- *Cordia dichotoma G. Forst* fruit mucilage matrix tablets

Ingredients (mg)	Formulations				
	CD-1	CD-2	CD-3	CD-4	CD-5
Glimepiride	8	8	8	8	8
Dried <i>Cordia dichotoma G. Forst</i> mucilage	2	4	6	8	10
Micro crystalline cellulose (Avicel)	182	180	178	176	174
Sodium meta bisulfite	5	5	5	5	5
Magnesium stearate	3	3	3	3	3
Total weight of tablet	200	200	200	200	200
Drug : mucilage	1:0.25	1:0.50	1:0.75	1:1.0	1:1.25

These matrix tablets were evaluated for their physical properties (Table 3).

Table 3: Physical properties of formulated matrix tablets

S. No.	Formulation code	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Drug content (%)
1	CD-1	5.6	5.70 ± 1.22	0.25	100.2 ± 0.10
2	CD-2	5.7	6.20 ± 1.50	0.20	101.7 ± 0.02

Cont...

S. No	Formulation code	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Drug content (%)
3	CD-3	5.7	5.10 ± 1.70	0.30	99.5 ± 0.40
4	CD-4	5.8	6.40 ± 1.33	0.50	99.8 ± 0.20
5	CD-5	5.7	6.30 ± 1.10	0.40	100.1 ± 0.09

Swelling behavior of sustained release matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulations CD-1, CD-2, CD-3, CD-4 and CD-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 the following formula^{4,5} -

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

Where, S.I. = Swelling Index, M_t = Weight of tablet at time 't' and M_0 = Weight of tablet at time 0.

Swelling behavior of sustained release matrix tablets are represented in Fig. 1.

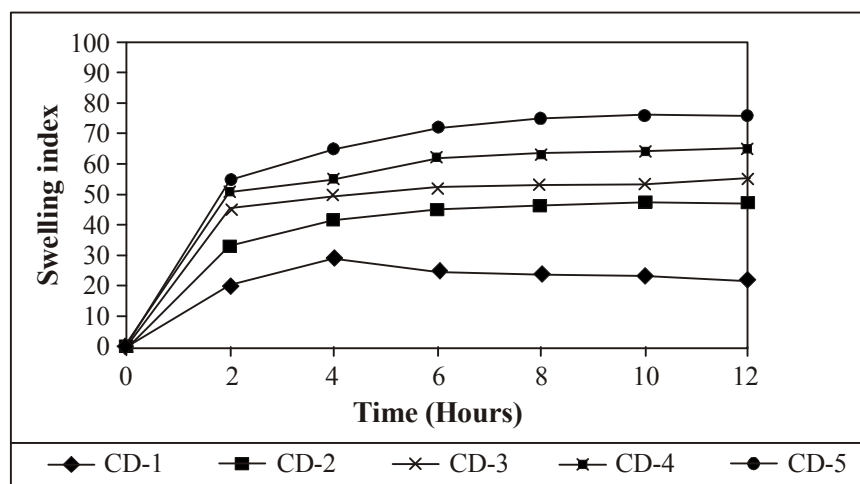


Fig. 1: Swelling index of formulated matrix tablets

Estimation of glimepiride

An ultraviolet spectrophotometric method based on measurement of absorbance at 230 nm in alkaline borate buffer of pH 7.4 was used. The method obeyed Beer-Lambert's law in the concentration range of 1-20 $\mu\text{g/mL}$. When a standard drug solution was assayed for 6 times, the accuracy and precision were found to be 0.9% and 1.10%, respectively. No interference was observed from the excipients used.

Drug release study

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 $37^\circ \pm 0.5^\circ\text{C}$. 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 are shown in Fig. 2.

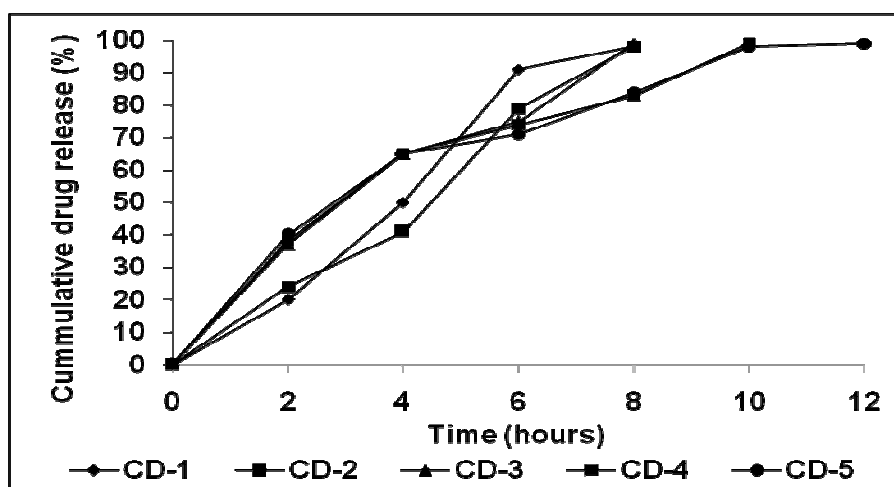


Fig 2: *In vitro* drug release profile of glimepiride from formulated matrix tablets

RESULTS AND DISCUSSION

The dried mucilage was evaluated as a matrix-forming material for oral sustained released tablets using glimepiride as a model drug. Matrix tablets, each containing 8 mg of

glimepiride, were prepared using dried mucilage in various drug–mucilage ratios (1 : 0.25, 1 : 0.5, 1 : 0.75, 1 : 10 and 1 : 1.25). The rate of release was faster in CD-1 and slower in CD-5. This result showed that as the proportion of mucilage was increased, the overall time of release of the drug from the matrix tablet also increased.

CONCLUSION

By performing the above study, the mucilage extracted from *Cordia dichotoma G. Forst* appears to be suitable for use as a pharmaceutical excipient in the formulation and manufacture of sustained release matrix tablets because of its good swelling, good flow and suitability for direct-compression formulations. From the dissolution study, it was concluded that the dried mucilage can be used as an excipient for sustained -release tablets.

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