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Formulation and Evaluation of Glimepiride *Cordia dichotoma G. Forst* Fruit Mucilage Sustained Release Matrix Tablets

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The main aim of the present investigation is 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. Physico-chemical 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 found to have better uniformity of weight and drug content with low SD values. The swelling behaviour 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

Drug products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years[1]. Regular research is going on in field of use of natural occurring biocompatible polymeric material in designing of dosage form for oral controlled release administration[2,3]. Natural gums are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media and these have been used for the preparation of dosage form.

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 dosing[4]. 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 release tablets of glimepiride using *Cordia dichotoma G. Forst* (*Boraginaceae* family) fruit mucilage as release retardant for making sustained release matrix tablets.

EXPERIMENTAL

Glimepiride was obtained as a gift sample from 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 S.D. 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, left over night. The fruits were crushed and soaked in ethanol for 5-6 h, boiled for 0.5 h and left to stand for 1 h to allow complete release of the mucilage into the ethanol. The seeds were removed from the fruits. This extract was further fractionated using petroleum ether (40-60 %), ethyl acetate, butanol and butanone in succession[5]. 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 properties[6] (Table-1). All values were found to be satisfactory.

TABLE-1
FLOW PROPERTIES OF DRIED *Cordia dichotoma G. Forst* FRUIT MUCILAGE

Parameters	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 (º)	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, 1:1.0 and 1:1.25. *Cordia dichotoma G. Forst* was used as matrix forming material, while sodium bisulphide 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[7], using 8 mm flat faced punches. Formulations of designed formulations were showed in (Table-2). These matrix tablets were evaluated for their physical properties[8-10] (Table-3).

TABLE-2
COMPOSITION OF VARIOUS FORMULATIONS

Ingredients (mg)	Formulations				
	CD-1	CD-2	CD-3	CD-4	CD-5
Glimepiride	8	8	8	8	8
Dried *Cordia dichotoma G. Forst* mucilage	2	4	6	8	10
Micro crystalline cellulose (Avicel)	182	180	178	176	174
Sodium metabisulfite	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

TABLE-3
PHYSICAL PROPERTIES OF FORMULATED MATRIX TABLETS

Sl 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
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 behaviour of sustained release matrix tablets: The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behaviour 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[11,12].

$$SI = \{(M_t - M_0)/M_0\} \times 100$$

where, SI = swelling index, M_t = weight of tablet at time 't' and M_0 = weight of tablet at time 0.

Swelling behaviour of sustained release matrix tablets were represented in Fig. 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 0.9 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 ± 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 Fig. 2.

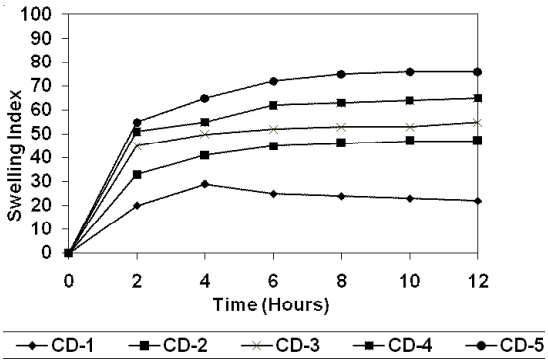

Fig. 1. Swelling index of formulated matrix tablets

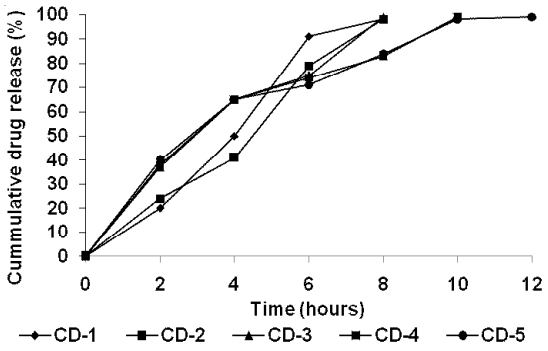

Fig. 2. *In vitro* drug release profile of Glimepiride from formulated matrix tablets

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, 1:1.0 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 increased, the overall time of release of the drug from the matrix tablet 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 is concluded that the dried mucilage can be used as an excipient for sustained-release tablets.

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