Asian Journal of Chemistry Vol. 21, No. 8 (2009), 6271-6276

Formulation and Evaluation of *Aloe barbadensis* Miller Mucilage Based Controlled Release Matrix Tablets of Glimepiride

HINDUSTAN ABDUL AHAD*, J. SREERAMULU†, V. HIMA BINDU‡ and Y. PADMANABHA REDDY
Department of Pharmaceutics, Raghavendra Institute of Pharmaceutical Education and Research, Anantapur-510 001, India
Tel: (91)(8554)255646; E-mail: abdulhindustan@rediffmail.com

This work aims to investigate and formulating controlled release matrix tablets of glimepiride with the mucilage from the leaves of *Aloe barbadensis* Miller and to study its functionality as an excipient in pharmaceutical controlled-release tablet formulations. The mucilage was extracted from *Aloe barbadensis* Miller leaves and physico-chemical properties of dried powdered mucilage were studied. Various formulations of glimepiride with *Aloe barbadensis* mucilage F1, F2, F3, F4 and F5 (1:0.8, 1:1.6, 1:2.4, 1:3.2, and 1:4, respectively) were prepared. These matrix tablets were evaluated for their physical properties like general appearance, thickness, hardness, friability, weight variation and uniformity of drug content, as per IP method. All the prepared matrix tablets were found to have good physico-chemical properties with low SD values. The swelling behaviour and release rate characteristics of the formulations were studied. The rate of release was faster in batch F1 and slower in batch F5. The result showed that as the proportion of mucilage increased, the overall time of release of the drug from the matrix tablet increased The dissolution study proved that the dried mucilage of *Aloe barbadensis* miller can be used as an excipient for making controlled release tablets.

Key Words: Glimepiride, *Aloe barbadensis* Miller, Matrix tablets.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose concentration caused by insulin deficiency, often combined with insulin resistance[1]. Glimepiride is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus[2] belongs to sulphonyl urea drug class.

The oral absorption is uniform, rapid and complete with a bioavailability of nearly 100 % and a biological half-life of 2.3 ± 0.8 h[3] after single dose of 3 mg and increasing to 5.3 ± 3.0 h after multiple dosing. The recommended dosage[4] of glimepiride is 1-8 mg/day; 2 mg b.i.d. The pharmacokinetic and dosage schedules

†Department of Chemistry, Analytical Chemistry, Sri Krishnadevaraya University, Anantapur-515 003, India.
‡Center for Environment, IST-JNT University, Hyderabad-515 002, India.

supports once daily controlled release formulation for glimepiride for better control of blood glucose levels to prevent hypoglycemia, enhance clinical efficacy and patient compliance. Hence we have selected glimepiride for the development of controlled release matrix tablets. The mucilage of *Aloe barbadensis* Miller clinically and experimentally proved antidiabetic activity[5] and release retardant activity in the present study.

EXPERIMENTAL

Glimepiride was obtained as a gift sample from Doctor Reddy's Laboratories, Hyderabad, India. The leaves of *Aloe barbadensis* Miller were collected from the medicinal garden of Raghavendra Institute of Pharmaceutical Education and Research, Anantapur, India. The plant was authenticated at the Botany Department of Sri Krishnadevaraya University, Anantapur, India. Micro crystalline cellulose (Avicel) was procured from SD Fine Chemicals (Mumbai, India). All other chemicals used were analytical-reagent grade and double distilled water was used throughout the experiments.

Extraction of mucilage[2-4]: The fresh leaves of *Aloe barbadensis* Miller were collected. These leaves were washed with water to remove dirt and debris. Incisions were made on the leaves, left overnight. The leaves were crushed and soaked in water 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 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 45 °C, collected, ground, passed through a # 80 sieve and stored in desiccator at 30 °C and 45 % relative humidity before use[6]. This mucilage was tested for following physico-chemical properties (Table-1). Chemical test, particle size, weight loss on drying, viscosity, pH, density, charring, swelling ratio[7], bulk density[8], compressibility percentage[9], angle of repose[10], Carr's index[11]. All values were found to be satisfactory.

TABLE-1
FLOW PROPERTIES OF DRIED *Aloe barbadensis* 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 controlled release matrix tablets[5,6,9]: Controlled release matrix tablets of glimepiride with *Aloe barbadensis* mucilage were prepared by using different drug: mucilage ratios *viz.*, 1:0.8, 1:1.6, 1:2.4, 1:3.2 and 1:4. *Aloe barbadensis* mucilage

was used as matrix-forming material, while microcrystalline cellulose as diluents 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 were showed in Table-2.

TABLE-2
FORMULATION OF GLIMEPIRIDE MATRIX TABLETS BY THE DIRECT-COMPRESSION METHOD

Ingredients (mg)	Formulations				
	F1	F2	F3	F4	F5
Glimepiride	5	5	5	5	5
Dried mucilage	4	8	12	16	20
Micro crystalline cellulose (Avicel)	188	184	180	176	172
Magnesium stearate	3	3	3	3	3
Total weight of tablet	200	200	200	200	200
Drug: mucilage	1:0.8	1:1.6	1:2.4	1:3.2	1:4

These matrix tablets were evaluated for their physical properties like general appearance, thickness, hardness, friability, weight variation test[12] and drug content, as per IP method. These values were showed in Table-3.

TABLE-3
PHYSICAL PROPERTIES OF GLIMEPIRIDE-*Aloe barbadensis* MILLER MUCILAGE MATRIX TABLETS

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	5.9	7.70 ± 1.25	0.80	101.2 ± 0.08
F2	6.2	8.10 ± 1.40	0.75	100.6 ± 0.30
F3	5.8	6.90 ± 1.35	0.46	99.8 ± 0.80
F4	6.0	6.80 ± 1.45	0.62	99.6 ± 0.50
F5	6.1	7.20 ± 1.30	0.72	100.8 ± 0.45

n = 5.

Swelling behaviour of controlled release matrix tablets[13]: The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behaviour of formulations F1, F2, F3, F4 and F5 were studied. One tablet from each formulation was kept in a Petri dish containing pH 7.4 phosphate buffer. At the end of 1 h, the tablet was withdrawn, kept on tissue paper and weighed then for 2 h. And every 2 h, weights of the tablet were noted and the process was continued till the end of 12 h. % weight gain by the tablet was calculated by the following formula.

$$SI = \frac{M_t - M_o}{M_o} \times 100$$

where, SI = swelling index, M_t = weight of tablet at time't' and M_o = weight of tablet at time t = 0. Swelling behaviour of controlled release matrix tablets were represented in Fig. 1.

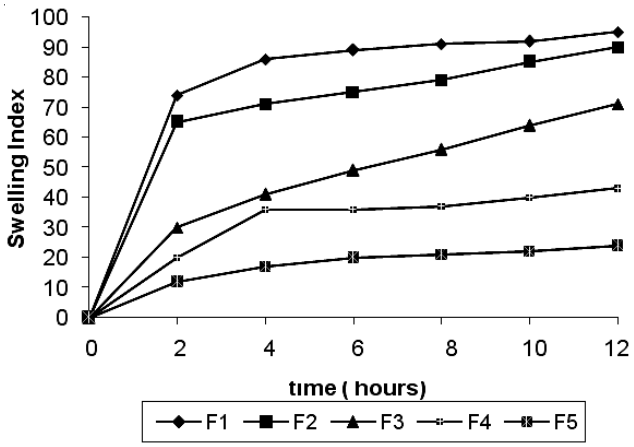

Fig. 1. Swelling index of glimepiride matrix tablets with *Aloe barbadensis* mucilage

In vitro drug release studies[14]

Estimation of glimepiride: Release of glimepiride from the matrix tablets was studied in phosphate buffer of pH 7.4 (900 mL) using a 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 °C as prescribed for glimepiride tablets in USP XXIV. A sample of glimepiride matrix tablets equivalent to 10 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.

RESULTS AND DISCUSSION

The dried mucilage was evaluated as a matrix-forming material for oral controlled released tablets using glimepiride as a model drug. Matrix tablets, each containing 10 mg of glimepiride, were prepared using dried mucilage in various drug-mucilage ratios (1:0.8, 1:1.6, 1:2.4, 1:3.2 and 1:4). An ideal modified-release dosage form should release a loading dose (18-25 %) in the first hour. Later, the remaining drug should be released at a constant rate over an extended period. An ideal release pattern was calculated according to these criteria. The *in vitro* dissolution profiles were shown (Fig. 1). F1, F2 and F3, at lower the ratios (1:0.8, 1:1.6 1:2.4), released

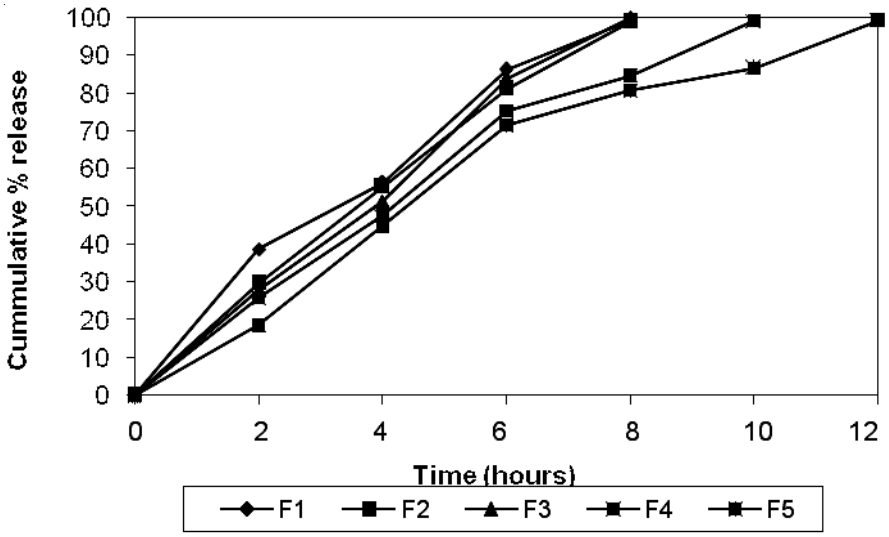

Fig. 2. *In vitro* drug release profile of glimepiride from glimepiride matrix tablets with *Aloe barbadensis* mucilage

38.75, 29.65 and 27.81 % of the drug in the first hour and the remaining drug was released within 6 h. This result occurred probably because of insufficient polymer was in the formulation. In F4, where the drug-mucilage ratio was 1:3.2, 25.80 % of the drug was released in the first hour and the remaining drug was released during 8 h. In F5, where the drug-mucilage ratio was 1:4, 18.55 % of the drug was released in the first hour and the remaining drug was released during 12 h. The rate of release was faster in F1 and slower in F5. This result showed that as the proportion of mucilage increased, the overall time of release of the drug from the matrix tablet increased. Drug release from swellable and erodible hydrophilic matrices can be attributed to polymer dissolution, drug diffusion through gel layer, or a combination of both.

Conclusion

By performing the above study, the mucilage extracted from *Aloe barbadensis* Miller appears to be suitable for use as a pharmaceutical excipient in the formulation and manufacture of controlled 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.

ACKNOWLEDGEMENT

The authors are thankful to Doctor Reddy's Laboratories, Hyderabad, India for providing the pure drug sample.

REFERENCES

1. C. Evans, Trease and Evans-Pharmacognosy, Elsevier Ltd., New York edn. 15, pp. 240-244 (2002).
2. R.K. Verma and S. Garg, *Eur. J. Pharm. Biopharm.*, **57**, 513 (2004).
3. R. Rosskamp, K. Wernickle-Panten and E. Draeger, *Diabetes Res. Clin. Practice*, **31**, S33 (1996).
4. B. Rosenkranz, V. Profozic, Z. Metelko,V. Mrzljak, C. Lange and V. Malerczyl, *Diabetologia*, **39**, 1617 (1996).
5. M. Ghannam and M. Kingston, *Horm. Res.*, **24**, 288 (1986).
6. S.K. Baveja, K.V. Rao and J. Arora, *Indian J. Pharm. Sci.*, **50**, 89 (1988).
7. S.G. Killedar, D.A. Bhagwat, R.S. Adnaik, H.N. More and J.I. D'souza, *Indian Drugs*, **45**, 310 (2008).
8. L. Lachman, H.A. Lieberman and J.L. Kanig, The Theory and Practice of Industrial Pharmacy, Philadelphia, PA: Lea and Febiger, pp. 317-318 (1987).
9. R.L. Carr, *Chem. Eng.*, **72**, 163 (1965).
10. R.K. Raghuram, M. Srinivas and R. Srinivas, *AAPS Pharm. Sci. Tech.*, [serial online]. 2003;4:E61. PubMed DOI: 10.1208/pt040461
11. M.E. Aulton and T.I. Wells, Pharmaceutics: The Science of Dosage Form Design, London, UK, Churchill Livingstone (1988).
12. Ministry of Health and Family Welfare, Government of India, Indian Pharmacopoeia, The Controller of Publications, New Delhi, edn. 5, p. A-89 (2007).
13. R. Reynold, S.N. Gehree, A.S. Hussain and L.S. Shenonda, *J. Pharm. Sci.*, **87**, 1115 (1998).
14. The United State Pharmacopoeia 24, NF 19, United State Pharmacopoeial Convention, Rockville, M.D. Asian Edition, pp. 1462-5, 1913-4 (2000).

(*Received*: 1 December 2008; *Accepted*: 26 May 2009) AJC-7607