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Development and in Vitro Evaluation of Glibenclamide Aloe barbadensis Miller leaves Mucilage Controlled Release Matrix Tablets

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ABSTRACT: The main aim of the present study was to develop a Controlled release matrix tablets of Glibenclamide with the mucilage of *Aloe barbadensis Miller* leaves and to study its functionality as a matrix former for controlled release of Glibenclamide from tablet formulations. Physicochemical properties of dried powdered mucilage of *Aloe barbadensis Miller* leaves were studied. Various formulations of Glibenclamide with *Aloe barbadensis Miller* leaves mucilage were prepared by direct compression technique. The formulated matrix tablets were found to have better uniformity of weight and drug content with low statistical deviation. The swelling behavior and *in vitro* release rate characteristics were studied. The dissolution study proved that the dried *Aloe barbadensis Miller* leaves mucilage can be used as a matrix forming material for making Controlled release Glibenclamide matrix tablets.
KEY WORDS: *Aloe barbadensis Miller* mucilage, Glibenclamide, Swelling index, controlled release.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by high glucose concentration in blood, caused by Insulin deficiency, often combined with Insulin resistance[1]. Glibenclamide is an oral hypoglycemic agent, which is a drug for the treatment of patients with Non-Insulin Dependent Diabetes Mellitus (NIDDM) [2]. Glibenclamide inhibits ATP-sensitive potassium channels in pancreatic beta cells. This inhibition causes cell membrane depolarization, which causes voltage-dependent calcium channels to open, which causes an increase in intracellular calcium in the beta cell, which stimulates insulin release. Glibenclamide is a weak acid (p*K*a = 6.3) practically insoluble in water and acidic solutions but highly permeable (class 2) according to the Biopharmaceutical classification System (BCS) [3]. The oral absorption is uniform, rapid and complete with nearly 100% bioavailability. Therapy with Glibenclamide is usually initiated with 2.5mg given once daily.

The mucilage of *Aloe barbadensis Miller* clinically and experimentally proved anti-diabetic activity[4] and release retardant activity in the present study.

MATERIALS AND METHODS

Materials

Glibenclamide was obtained as a gift sample from the Dr. Reddy's Laboratories, Hyderabad, India. The *Aloe barbadensis Miller* leaves were collected from the local areas of Anantapur, India. The plant was authenticated at the Department of Botany, Sri Krishnadevaraya University, Anantapur, India. Micro crystalline cellulose 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[5]

The fresh *Aloe barbadensis Miller* leaves were collected and separately washed with purified water to remove dirt and debris. Incisions were made on them, left over night. The leaves were crushed and soaked in water for 5–6 h, boiled for 30 min and left to stand for 1 h to allow complete release of the mucilage into the water. The mucilage was filtered 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. The mucilage was separated, dried in an oven at 30°C, collected, grounded, passed through a # 80 sieve and stored in desiccators at 30 °C & 45% relative humidity till use. This mucilage was tested for flow properties[6] (Table1). All values were found to be satisfactory.

Preparation of Controlled release matrix tablets

Controlled release matrix tablets of Glibenclamide with *Aloe barbadensis Miller* leaves mucilage were prepared by using different drug: mucilage ratios viz. 1:1, 1:2, 1:3, 1:4 and 1:5. *Aloe barbadensis Miller* leaves 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 above formulations were compressed by a direct compression technique using 10 mm flat faced punches. Formulations of designed formulations were showed in (Table 2). These matrix tablets were evaluated for their physical properties[7,8] like general appearance, thickness, Hardness, Friability, uniformity of weight and uniformity of drug content, as per I.P. method (table 3).

Swelling behavior of Controlled release matrix tablets [9, 10, and 11]

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulations ABG-1, ABG-2, ABG-3, ABG-4 and ABG-5 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 10 h. (figure 1) % 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 t = 0.

In Vitro drug release studies [12]

Release of Glibenclamide from the formulated 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 Glibenclamide tablets in USP XXIV. A sample of Glibenclamide matrix tablets equivalent to 5 mg of Glibenclamide 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 226 nm for Glibenclamide content using a UV/ visible single-beam spectrophotometer-117 (Sistronics Corporation, Mumbai, India). The drug release experiments were conducted in triplicate (n = 3) (figure2).

RESULTS AND DISCUSSION

The dry, powdered *Aloe barbadensis Miller* leaves mucilage was evaluated for angle of repose, LBD, TBD, compressibility index, hasner's ratio and drug content (Table 1). The results of angle of repose and compressibility index (%) were 25.26±0.25, 10.64±0.01 respectively. The results of LBD and TBD were 0.74±0.08, 0.88±0.06 respectively. The result of Hausner's ratio was 1.12±0.07. The thickness of the tablets was ranged from 5.5±0.18 to 5.8±0.06 mm. The average percentage deviation of 20 tablets of each formula was less than ±5%. Drug content was found to be uniform among different batches of the tablets and ranged from 99.1±0.27to 100.8±0.09. The hardness of formulated tablets were ranged from 6.30±1.81to 7.51±1.45 kg/cm^2 and percentage friability of the tablets of all formulations were ranged from 0.21±0.05 to 0.68±0.07 (<1%), (Table 3). The results of dissolution studies of formulations ABG-1, ABG-2, ABG-3, ABG-4 and ABG-5 with *Aloe barbadensis Miller* leaves mucilage in 1:1, 1:2, 1:3, 1:4 and 1:5 ratios respectively (figure 2). The result of dissolution rate of matrix tablets was decreased as increase in mucilage concentration. Among the formulations, ABG-5 showed the least deviation from the theoretical release pattern.

In the present study, *Aloe barbadensis Miller* leaves mucilage has been employed to formulate sustained-release tablets of Glibenclamide. The matrix tablets were prepared according to the formula given in Table 2. The flow properties of *Aloe barbadensis Miller* leaves mucilage was evaluated for angle of repose, LBD, TBD, compressibility index and drug content (table 1). The results of angle of repose (<30) indicate good flow properties of the granules. This was further supported by lower compressibility index values(table 1). Generally, compressibility index values up to 15% result in good to excellent flow

properties. Bulk densities of all these results indicate that the *Aloe barbadensis Miller* leaves mucilage (dried) possessed satisfactory flow properties and compressibility. The matrix tablets of different formulations showed uniform thickness. The weights of matrix tablets were within the limits as prescribed in Pharmacopoeia. Good uniformity in drug content was found among different batches of the tablets and the percentage of drug content was more than 95%. Another measure of a tablet's strength is friability. Conventional compressed tablets that lose less than 1% of their weight are generally considered acceptable. In the present study, the percentage friability for all the formulations was below 1%, indicating that the friability is within the prescribed limits. All the tablet formulations showed acceptable pharmacopoeial properties for weight variation, drug content, hardness, and friability. The *In vitro* drug release profile of Glibenclamide from formulated matrix tablets were studied using zero order. This result shown that as the proportion of *Aloe barbadensis Miller* leaves 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

By performing the above study, the mucilage of *Aloe barbadensis Miller* leaves can be used 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 dried *Aloe barbadensis Miller* leaves mucilage can be used as an excipient for making controlled release tablets.

Table 1: Flow properties of dried *Aloe barbadensis Miller* leave's mucilage

Parameter	Value
Loose Bulk Density (g/cm^3)	0.74±0.08
Tapped Bulk Density (g/cm^3)	0.88±0.06
Carr's Index	10.64±0.01
Hausner's Factor	1.12±0.07
Angle of Repose (^{0})	25.26±0.25

Table 2: Formulae of Glibenclamide *Aloe barbadensis Miller* mucilage matrix tablets

Formulation	Glibenclamide	ABM	MCC	MS	TWT
ABG-1	5	5	187	3	200
ABG-2	5	10	182	3	200
ABG-3	5	15	177	3	200
ABG-4	5	20	172	3	200
ABG-5	5	25	167	3	200

ABG - *Aloe barbadensis Miller* & Glibenclamide, ABM- *Aloe barbadensis Miller* leaves mucilage, MCC- Microcrystalline Cellulose, MS- Magnesium stearate, TWT-Total weight of the tablet

Table 3: Physical properties of Glibenclamide *Aloe barbadensis Miller* mucilage matrix tablets

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
ABG-1	5.5±0.18	6.60±1.35	0.61±0.23	99.7±0.41
ABG-2	5.7±0.08	6.30±1.81	0.55±0.14	99.2±0.23
ABG-3	5.8±0.06	7.51±1.45	0.21±0.05	100.8±0.09
ABG-4	5.6±0.25	6.80±1.51	0.36±0.09	99.4±0.41
ABG-5	5.6±0.23	7.50±1.10	0.68±0.07	99.1±0.27

ABG - *Aloe barbadensis Miller* & Glibenclamide

Figure 1: Swelling Index of Glibenclamide- *Aloe barbadensis Miller* mucilage matrix tablets

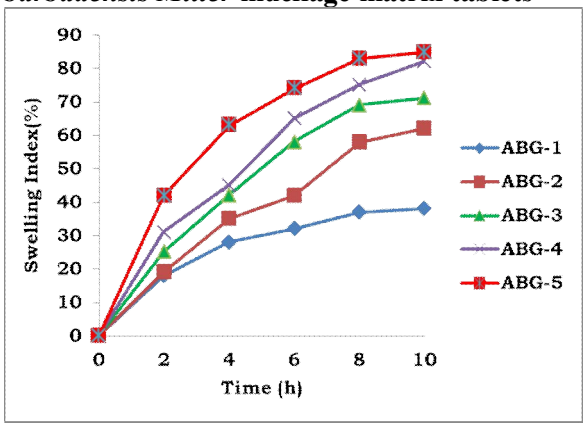
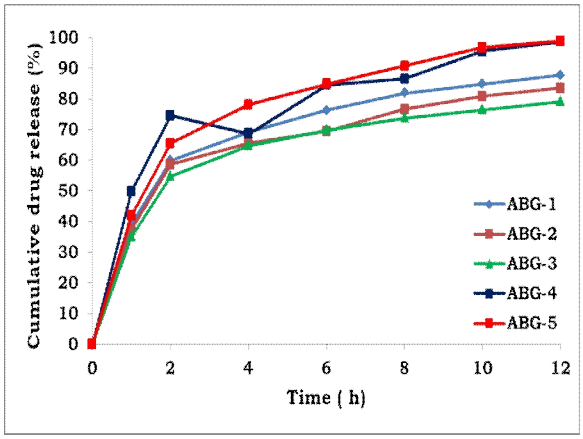


Figure 2: *In Vitro* drug release profile of Glibenclamide from matrix tablets



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