



Designing and Evaluation of Glibenclamide *Azadirachta indica* Mucilage Based Controlled Release Matrix Tablets

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Abstract

The aim of present study was to develop a Controlled release matrix tablets of Glibenclamide with the fruit mucilage of *Azadirachta indica* and to study its functionality as a matrix former for the controlled release of Glibenclamide from tablet formulations. Physicochemical properties of dried powdered mucilage of *Azadirachta indica* fruits were studied. Various formulations of Glibenclamide with *Azadirachta indica* fruit 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 vivo* release rate characteristics were studied. The dissolution study proved that the dried *Azadirachta indica* fruit mucilage can be used as a matrix forming material for making Controlled release Glibenclamide tablets.

Key words: *Azadirachta indica*, Glibenclamide, matrix tablets, 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 is a weak acid (pKa = 5.3) practically insoluble in water and acidic environment but highly permeable (class 2) according to the Biopharmaceutical classification System (BCS) [2]. 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 maximal recommended daily dose is 20mg [3].

Material and Methods

Glibenclamide was obtained as a gift sample from the Dr. Reddy's Laboratories, Hyderabad, India. The *Azadirachta indica* fruits 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.

Extraction of mucilage

The fresh *Azadirachta indica* fruits were collected and separately washed with purified water to remove dirt and debris. Incisions were made on them, left over night. The leaves/ fruits 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 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 35°C, collected, grounded, passed through a # 80 sieve and stored in desiccators at 30 °C & 45% relative humidity till use [4]. This mucilage was tested for following physicochemical properties, represented in table 1. All values were found to be satisfactory.

Table 1: Flow properties of dried *Azadirachta indica* fruit mucilage powder

Parameters	<i>Azadirachta indica</i> mucilage
Loose Bulk Density (g/ml)	00.63±0.15
Tapped Bulk Density(g/ml)	00.89±0.28
Carr's index (%)	29.21±0.21
Hausner's ratio	01.41±0.04
Angle of repose(⁰)	39.55±0.12
Number of trials(n) =3	

Preparation of Controlled release matrix tablets

Controlled release matrix tablets of Glibenclamide with *Azadirachta indica* fruit mucilage were prepared by using different drug: mucilage ratios viz. 1:0.5, 1:1.0, 1:1.5, 1:2.0 and 1:2.5. *Azadirachta indica* fruit 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 table2.

Table 2: Formulations of Glibenclamide *Azadirachta indica* mucilage matrix tablets

Formulation	Glibenclamide	AI	MCC	MS	TWT
AIG-1	10	5	182	3	200
AIG-2	10	10	177	3	200
AIG-3	10	15	172	3	200
AIG-4	10	20	167	3	200
AIG-5	10	25	162	3	200

These matrix tablets were evaluated for their physical properties⁴ like general appearance, thickness, Hardness, Friability, uniformity of weight and uniformity of drug content, as per I.P. method. These values were tabulated in table-3.

Table 3: Physical properties of formulated matrix tablets

Formulation	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Drug content (%)
AIG-1	5.5±0.15	6.50±1.35	0.51±0.03	99.7±0.41
AIG-2	5.6±0.09	6.70±1.87	0.45±0.04	99.2±0.23
AIG-3	5.8±0.28	8.70±1.45	0.21±0.11	100.8±0.09
AIG-4	5.7±0.06	7.80±1.24	0.36±0.01	99.4±0.41
AIG-5	5.6±0.02	8.40±1.15	0.38±0.23	99.1±0.27

Number of trials(n) =3, AIG - *Azadirachta indica* & Glibenclamide

Swelling behavior of controlled release matrix tablets [5]

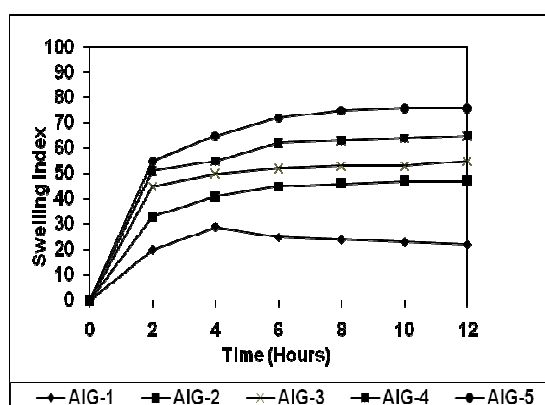
The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulations AIG-1, AIG-2, AIG-3, AIG-4 and AIG-5 were studied. One tablet from each formulation was kept in a Petri dish containing pH 7.4 phosphate buffer. At the end of 1 h, then for 2 h, the tablet was withdrawn, kept on tissue paper and weighed and the process was continued till the end of 12 h. The % 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_0 = weight of tablet at time t = 0. Swelling behavior of Controlled release matrix tablets were represented in fig.1.

Fig.1. Swelling Index of formulated matrix tablets



In Vitro drug release studies

Standard Curve for Glibenclamide [6]:

The standard curve for Glibenclamide was prepared in phosphate buffer pH 7.4. Stock solution of 100µg/ml was prepared by dissolving accurately weighed quantity of 50mg Glibenclamide in 500 ml of phosphate buffer pH 7.4. Aliquots of 2,4,6,8,10,12,14,16,18 and 20ml were pipetted out separately into 100ml volumetric flask and made to volumes to get a concentration range of 2,4,6 till 20µg/ml respectively. The absorbance was measured at 226nm using Systronics U.V spectrophotometer-117.

Estimation of Glibenclamide [7]

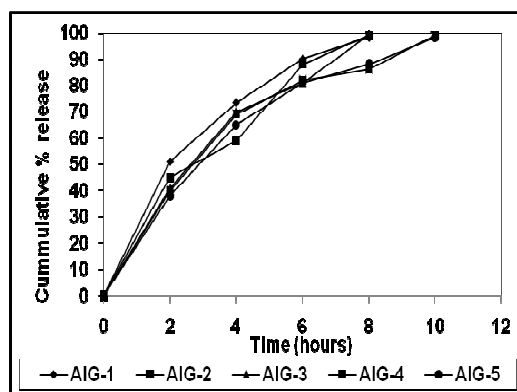
Release of Glibenclamide from the formulated matrix tablets was studied in phosphate buffer of pH 7.4 (900 ml) using a United States Pharmacopoeia (USP) 6-station Dissolution Rate Test Apparatus (Model Electro lab, TDT- 06T, Mumbai, India) with a rotating paddle stirrer at 50 rpm and $37^{\circ} \pm 0.5^{\circ}\text{C}$ as prescribed for Glibenclamide tablets in USP XXIV. A sample of Glibenclamide matrix tablets equivalent to 10 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 (Sistrionics 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 dry, powdered *Azadirachta indica* fruit mucilage was evaluated for angle of repose, poured density, bulk density, compressibility index and drug content (Table 1). The results of angle of repose and compressibility index (%) were 39.55 ± 0.12 and 29.21 ± 0.21 respectively. The results of loose bulk density (LBD) and tapped bulk density (LBD) were 0.63 ± 0.15 and 0.89 ± 0.28 respectively. The result of Hausner's ratio was 1.41 ± 0.04 . The thickness of the tablets ranged from 5.5 ± 0.15 to 5.8 ± 0.28 mm. The average percentage deviation of 20 tablets of each formula was less than $\pm 5\%$. Drug content was found to be uniform among different batches of the tablets and ranged from 99.1 ± 0.27 to 100.8 ± 0.09 . The hardness and percentage friability of the tablets of all batches ranged from 6.50 ± 1.35 to 8.70 ± 1.45 kg/cm^2 and 0.21 ± 0.11 to 0.51 ± 0.03 respectively, they were represented in table 3. The results of dissolution studies of formulations AIG-1, AIG-2, AIG-3, AIG-4 and AIG-5 with drug: *Azadirachta indica* fruit mucilage ratios as 1:0.5, 1:1.0, 1:1.5, 1:2.0 and 1:2.5 respectively were shown in fig. 2. The result of dissolution rate of matrix tablets was decreased as increase in mucilage concentration. Among the formulations, AIG-5 showed the least deviation from the theoretical release pattern.

In vitro drug release profile of Glibenclamide from formulated matrix tablets was by zero order, shown in fig. 2. This result shown that as the proportion of *Azadirachta indica* fruit 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.

Fig.2. In-Vitro drug release profile of Glibenclamide from matrix tablets



Conclusion

By performing the above study, the mucilage of *Azadirachta indica* fruits appears suitable for use as a pharmaceutical excipient in the formulation and manufacture of controlled release matrix tablets because of its good flow and suitability for direct compression formulations. From the dissolution study, it was concluded that dried *Azadirachta indica* fruit mucilage can be used as an excipient for making controlled release tablets.

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