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FORMULATION AND EVALUATION OF GLICLAZIDE MATRIX TABLETS USING *MORINGA OLIFERA MUCILAGE* AS A POLYMER

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ABSTRACT

The aim of this work was preparation and evaluation of gliclazide sustained released matrix tablets using various proportions of natural polymer Moringa olifera mucilage powder (i.e., drug : Polymer ratio – 1 : 0.2, 1 : 0.4, 1 : 0.6, 1 : 0.8, 1 : 1) as release controlling factor by wet granulation method. To study the influence of different proportions of polymer on *in vitro* drug release characteristics the dosage form was evaluated in 7.4 pH phosphate buffer for 12 hours. Also friability, weight varaiation, hardness, disintegration drug time, content uniformity was studied according to the Indian pharmacopoeia. All the formulations showed good fit in zero order kinetics along with diffusion mechanisms. *In vitro* release showed that formulation F3 contains D : P ratio – 1 : 0.6 gave prolonged release for 12 hours. Analysis of drug release rate from matrix system indicated drug release was by super case-II transport mechanism.

Key words: Sustained release matrix tablets, Gliclazide, Moringa olifera, Super case-II.

INTRODUCTION

Sustained drug delivery systems significantly improve therapeutic efficacy especially as matrix systems, which is the innumerable method used to developed a sustained formulation. Sustained release dosage forms would be most applicable for drugs having short elimination half lives[1]. This system helps to prolong and control the release of drug. A matrix system can be better defined as a well mixed system comprising of one or more drugs with gelling agent i.e. hydrophilic polymers. In such systems of matrix sustained release, drug release retarding polymers are the key performers in such systems. Various materials like waxes, hydrophilic polymers, hydrophobic polymers and gums have been employed in the formulations of matrix tablets. The present study has been undertaken to investigate the sustain property of polymer of natural origin i.e. Moringa olifera mucilage.

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The reason for choosing a natural polymer is due to non-toxicity, low cost, free availability, eco-friendly, potentially degradable mucilage. Moringa olifera has evaluated as matrix for sustained release preparation using different model drug like gliclazide. Gliclazide is an effective oral anti-diabetic agent that belongs to the sulphonylurea drug class. The recommended daily dosage of gliclazide is 30-120 mg in divided doses 2 to 3 times a day. The drug causes gastro intestinal disturbances such as gastric pain, constipation, nausea and vomiting if present in larger concentration in gastro intestinal tract. Controlled release formulation is needed[2] for glicalzide for better control of blood glucose levels to prevent hypoglycaemia and enhance clinical efficacy, to reduce gastrointestinal disturbances and to enhance patient compliance so, gliclazide is a suitable drug for oral controlled release tablets and it would be a great advantage to slow down its release in GI, where not only therapeutic action can be prolonged but minimize the side effects. To improve the therapeutic efficacy of gliclazide and reduce the severity of upper GI tract side effect through alternative dosage form of gliclazide, can be achieved by modifying release of the formulation to optimize drug delivery. Hence in present study, Moringa olifera was evaluated for its ability to sustain the drug release for a prolonged period of time in a matrix tablet formulation of gliclazide.

EXPERIMENTAL

Matrix tablets were prepared containing Gliclazide 80 mg of the labeled claim. All the tablets were found to be non disintegrating in 0.1 N HCl, water, phosphate buffer pH 6.8 for 45 min. The prepared tablets were of good quality with regard to drug content, hardness and friability and weight variation. All the tablets were formulated employing Moringa olifera as the retarding material.

Materials

Gliclazide obtained as a gift samples from Matrix Labs Ltd., Hyderabad, A.P., Moringa olifera mucilage was prepared in our institution. All other materials were of pharmacopeial grade.

Methods

Gum was collected from the authenticated *Moringa* plant stems, dried, grounded and passed through sieve No. 80. Gum powder (10 g) was stirred in distilled water (250 mL) for 6-8 hours at room temperature. The supernatant was obtained by centrifugation. The residue was washed with water and the washings were added to the separated supernatant. Finally the supernatant was made upto 500 mL and treated with twice the volume of acetone by continuous stirring. The precipitated materials was washed with distilled water and dried at

50-60^{o}C under vacuum. The gum (10% w/w) mucilage was prepared by dispensing in distilled water. It was allowed to equilibrate for a period of 24 hrs.

Preparation of gliclazide matrix tablets

Matrix tablets each containing 80 mg of Gliclazide were prepared by wet granulation method using Moringa olifera mucilage. The tablets were prepared as per the formulae given in Table 1. The required quantities of medicament, matrix materials and diluents were blended thoroughly in a mortar by following geometric mixing technique. To the blend PVP (1%) is added to prepare dough mass and then pass through sieve No.: 12 to obtained granules. The granules were subjected to drying and to the resulting granules 2% talc and 2% magnesium stearate is added, which is previously passed through sieve No.: 100. The resulting mixture was compressed into tables on a rotatory multi-station tablet punching machine (Remek) to a hardness of 7.5-8 Kg/cm^2 using concave punches.

Table 1: Formulation of Gliclazide tablets

In gredients (mg/tab)	F1 +D : P (1 : 0.2)	F2 + D : P (1 : 0.4)	F3 + D : P (1 : 0.6)	F4 + D : P (1 : 0.8)	F5 + D : P (1 : 1)
Gliclazide	80 mg	80 mg	80 mg	80 mg	80 mg
***Moringa olififera mucilage**	16 mg	32 mg	48 mg	64 mg	80 mg
Lactose	378 mg	362 mg	346 mg	330mg	314 mg
Talc	13 mg	13 mg	13 mg	13 mg	13 mg
Mg. stearate	13 mg	13 mg	13 mg	13 mg	13 mg
Weight of tablet	500 mg	500 mg	500 mg	500 mg	500 mg

+D : P – Drug : Polymer (Moringa olifera mucilage)

Evaluation of tablets[3,4]

Hardness of the tablets was tested using a Monsanto hardness tester. Friability of the tablets was determined in a Roche friabilator. Disintegration time of the tablets was determined using a thermionic tablet Disintegration test machine using water, 0.1 N HCl and phosphate buffer of pH 7.4 as the test fluids. Weight variation and drug content uniformity were determined.

The properties of tablets were given in Table 2.

Table 2: Properties of Gliclazide matrix tables

Formulation	Drug content	Friability (%)	Hardness (Kg/cm^2)	Weight variation	Disintegration time
F_1	99.00	0.3	7.5	Pass	Non disintergrating
F_2	99.86	0.2	7.5	Pass	Non disintergrating
F_3	100.90	0.3	8.0	Pass	Non disintergrating
F_4	100.23	0.2	8.0	Pass	Non disintergrating
F_5	99.39	0.3	7.5	Pass	Non disintergrating

Estimation of gliclazide

An ultra-violet (U.V) spectrophotometric method based on the measurement of absorbance at 229 nm in phosphate buffer pH 7.4 was used for estimation of Gliclazide. The method was validated for linearity, precision and accuracy.

Drug release study

Drug release from the matrix tablets prepared was studied using a eight station dissolution rate solution rate test apparatus (electro lab) employing a paddle stirrer at 50 rpm and at 37 ± 1^oC, phosphate buffer pH 7.4 is used as dissolution fluid. A 5 mL aliquot of dissolution medium was with drawn through a filter (0.45 µm) at different time intervals and assayed spectrophotometrically by measuring absorbance at 229 nm. The drug release experiments were conducted in triplicates (n = 3).

Data analysis

Release data were analyzed as per zero order, first order, Higuchi[5], Ritger & Peppas[6] equation models to assess the drug release kinetics and mechanism from tablets[7]. Data analysis and release characteristics were shown in Tables 3 and 4.

Table 3: Analysis of Gliclazide release data

Formulation	Zero order (r)	First order (r)	Higuchi equation (r)	Peppas (n)
F_1	0.994	0.911	0.945	1.211
F_2	0.982	0.914	0.853	1.376
F_3	0.964	0.924	0.953	1.202
F_4	0.991	0.943	0.931	1.264
F_5	0.965	0.946	0.888	1.264

Table 4: Release characterstics of Gliclazide matrix tablets

Formulation code	K_O (mg/hr)	K_1 (hr^{-1})	T_{90} (h.)	T_{50} (h.)
F_1	15.00	0.407	5.24	3.30
F_2	11.27	0.384	8	5.10
F_3	8.54	0.209	10.42	6
F_4	5.64	0.096	--	9.30
F_5	4.03	0.055	--	12

RESULTS AND DISCUSSION

Matrix tablets each containing 200 mg of Gliclazide could be prepared employing different proportions (i. e, D : P ratio are 1 : 0.2, 1 : 0.4, 1 : 0.6, 1 : 0.8, 1 : 1) of moringa olifera mucilage by conventional wet granulation method. Hardness of the tablet was in the range of 7.5 to 8 Kg/cm^2. Weight loss in the friability test was less than 1% in all the cases. All the matrix tablets were non disintegrating in phosphate buffer of pH 7.4, water, 0.1 N HCl for 45 minutes. They were considered suitable for oral sustained release. Tablets are found to be sustained for 12 h. So they are considered to be suitable for oral sustained release.

Analysis of Gliclazide release profile of the matrix tablets prepared is shown in Fig. 1 to 3. Release parameters of the Tablets are summarized in Table 3 and 4, among all formulations F_3 formulation containing 1 : 0.6 Moringa olifera mucilage was slow and spread over 12 h, F_1 was spread over 7 h, F_2 was spread over 12 h, F_4 shows 69.9% drug release for 12 h and F5 shows 50% drug release for 12 h. When the release data were analyzed as per zero and first order kinetics, it was observed that the release from all the matrix tablets formulated (F1, F2, F3, F4, F5) employing Moringa olifera mucilage followed zero order kinetics because the correlation coefficient (r) values were higher in the zero order than the first order for all F_1, F_2, F3, F4, F5 (Table 3). Since the drug release is independent of concentration for all formulation, then the release data was analyzed as per peppas equation, the release exponent 'n' was more than 1 indicating Supercase II as the release mechanism from the entire matrix tablets prepared. Plots of percent release verses square root of time was found to be liner ($r > 0.9$) with all the tablets prepared indicating that the release from the Moringa olifera mucilage matrix tablets was diffusion control.

As the polymer concentration was increased, release rate was decreased. Good liner relationship was observed between percent polymer and release rate k_o or k_1. This drug

release from the matrix tablets prepared employing Moringa olifera mucilage could be controlled by varying the proportion of drug and polymer ratio.

Gliclazide matrix tablets formulated employing 1 : 0.6 Moringa olifera mucilage (F3) exhibit extended release up to 12 h when compared to other formulations, hence matrix tablets prepared employing 1 : 0.6 Moringa olifera mucilage (SR F3) are considered to be suitable for sustained release of gliclazide over 12 h.

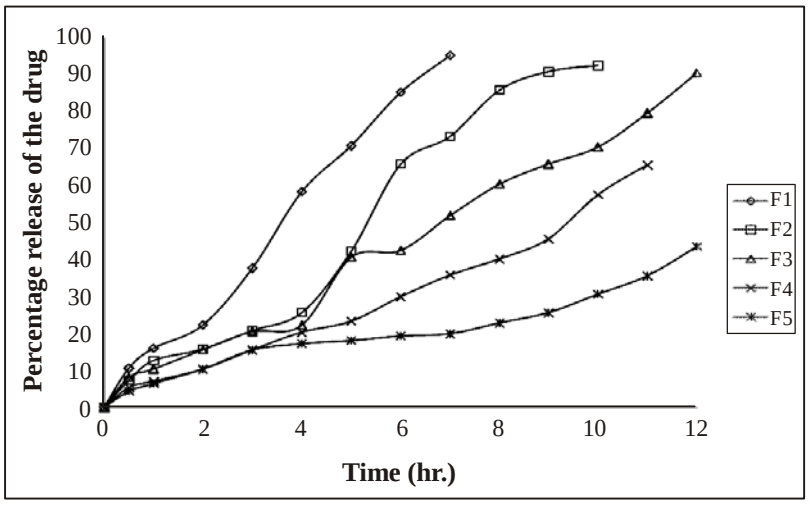

Fig. 1: Time Vs Cumulative percent drug release for Gliclazide tablets

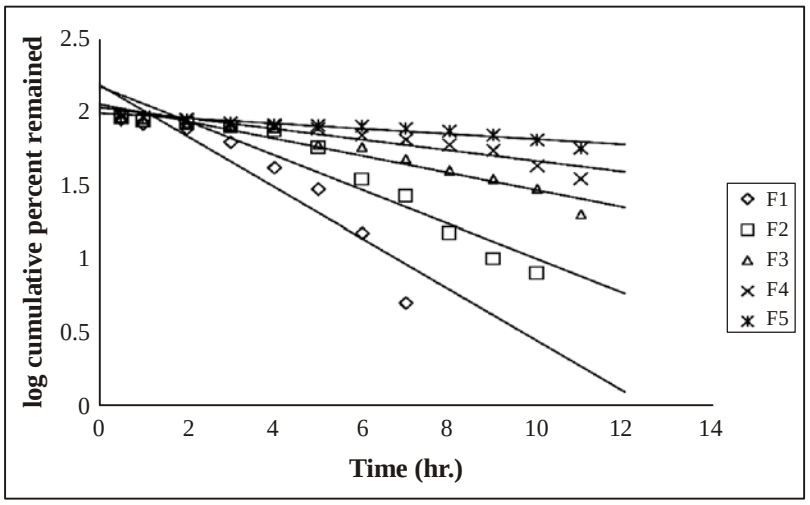

Fig. 2 First order plots for the matrix tablets of Gliclazide

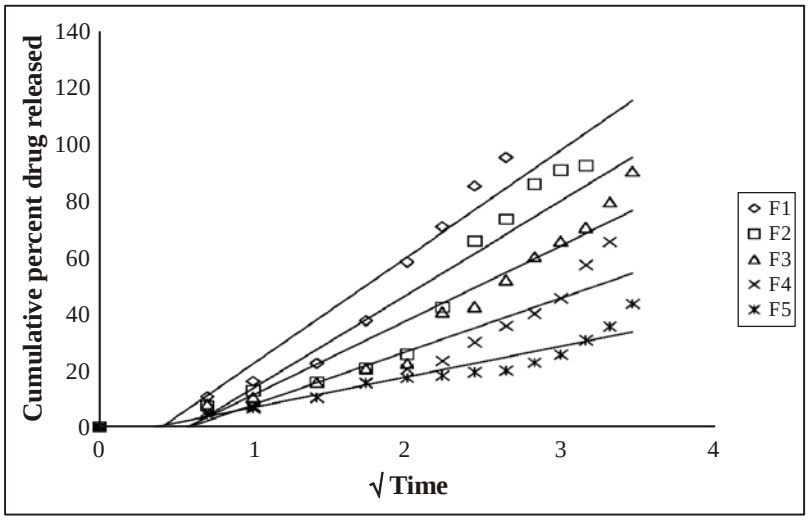

Fig. 3: Higuchi plots for the matrix tablets of Gliclazide

CONCLUSION

The sustained release Gliclazide drug delivery was promising approach to avoid greater fluctuations in plasma concentration. The present study reveals that among all formulations F3 (1 : 0.6 moringa olifera mucilage) was sustained for 12 hr and follows zero order and Supercase-II release mechanism.

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