Formulation and Evaluation of Glipizide *Prosophis cumanensis* Fruit Mucilage and Povidone Sustained Release Matrix Tablets

Hindustan Abdul Ahad*[1], Harinath R[2], Sreenivasulu R[1], Kishore Kumar Reddy B[1], Chandrasekhar A[1], Krishna Mahesh CH[1], Sushma K[2], Sairam T[2]

[1]College of pharmacy, Sri Krishnadevaraya University, Anantapur- 515003, Andhra Pradesh, India
[2]SVU College of sciences, Sri Venkateshwara University, Tirupati, Andhra Pradesh, India

ABSTRACT

The present research work was aimed to prepare matrix type sustained release tablets of Glipizide with *Prosophis cumanensis* fruit mucilage and Povidone. The polymers were studied for its functionality as a matrix forming property to sustain the Glipizide release from the dosage form. Physicochemical properties of dried powdered mucilage of *Prosophis cumanensis* fruits and Povidone blend were studied. Various formulations of Glipizide *Prosophis cumanensis* fruit mucilage and Povidone were prepared. The formulated tablets were evaluated for pre compression and post compression parameters which were found to satisfactory within the limits. The swelling behavior and release rate kinetics were studied. The *in-vitro* dissolution study proved that the dried *Prosophis cumanensis* fruit mucilage and Povidone in combination can be used as a matrix forming polymers for making sustained release matrix tablets.

Key words: Glipizide, *Azadirachta indica,* Povidone, matrix tablets, sustained release.

INTRODUCTION

Prosophis cumanensis (Fabaceae family) is a shrub or small weed plant grows all over the world. The tree grows to a height of up to 12 m and has a trunk with a diameter of up to 1.2 m. The plant has characteristic thorns and yellow flowers[1]. The bark exudates a good amount of gum round the year.

Glipizide is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus[2]. Glipizide is a weak acid (pKa = 5.9) which is practically insoluble in water and acidic solutions but as per the Biopharmaceutical Classification System (BCS) it is highly permeable (class 2). The oral absorption is uniform, rapid and complete with a bioavailability of nearly 100% and an elimination half-life of 2–4 h[3]. Glipizide is reported to have a short biological half-life (3.4 ± 0.7 h) requiring it to be administered in 2 to 3 doses of 2.5 to 10 mg per day. Hence we have selected Glipizide for the development of once daily sustained release matrix tablets. The pharmacokinetics and dosage schedule supports once daily sustained release formulations for Glipizide for better control of blood glucose levels to prevent hypoglycemia, enhance clinical efficacy and patient compliance.

Corrosponding author:
Email: abdulhindustan@rediffmail.com

The objective of present investigation is to prepare and evaluate sustained release tablets of Glipizide using *Prosophis cumanensis* fruits mucilage and Povidone combination as release retardant for making sustained release matrix tablets.

MATERIALS AND METHODS

Materials

Glipizide was obtained as a gift sample from Dr. Reddy's Laboratories, Hyderabad, India. *Prosophis cumanensis* 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. Povidone, Micro crystalline cellulose (Avicel**)** 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 *Prosophis cumanensis* fruits were collected and washed with water. The fruits were crushed and placed in water for 5–6 h, boiled for 30 minutes 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 (in the

Table 1: Formulae of matrix tablets

Ingredients (mg)	Formulations				
	F-1	F-2	F-3	F-4	F-5
Glipizide	10	10	10	10	10
Prosophis cumanensis fruits mucilage	2	4	6	8	10
Povidone	2	4	6	8	10
Micro crystalline cellulose (Avicel)	181	177	173	169	165
Magnesium stearate	5	5	5	5	5
Total weight of tablet	**200**	**200**	**200**	**200**	**200**

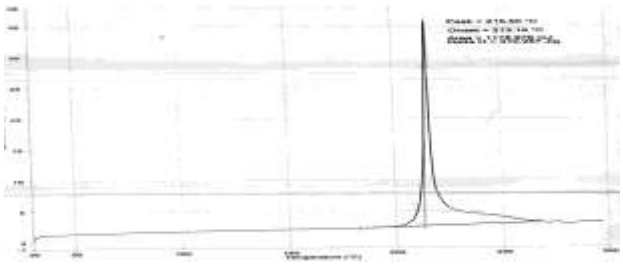

Figure 1: The DSC thermo gram of Glipizide

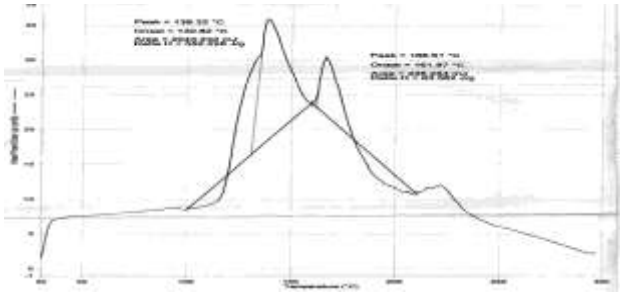

Figure 2: The DSC thermo gram of matrix tablets

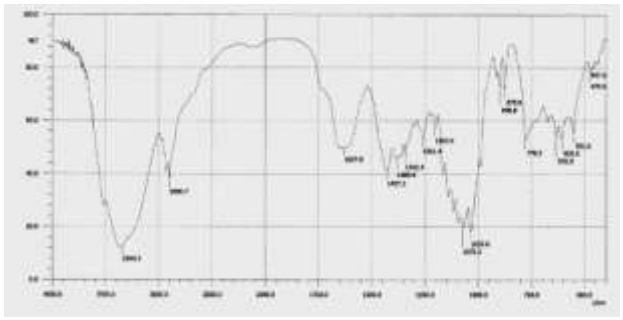

Figure. 3: IR Spectrum of Glipizide Pure drug

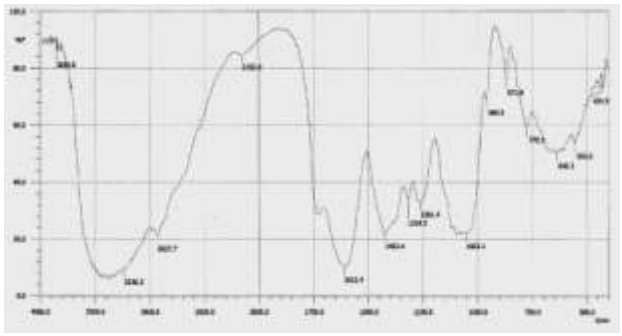

Figure. 4: IR Spectrum of Placebo tablets

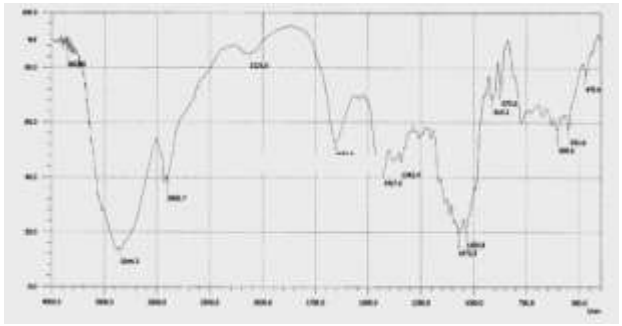

Figure. 5: IR Spectrum of formulated matrix tablets

quantities of three times the volume of filtrate) was added to precipitate the mucilage[4]. The mucilage was separated, dried in an oven at 40°C, collected, powdered, passed through a # 80 sieve and stored in air tight container till use.

Flow properties of formulation blend

The formulation blend was evaluated for flow properties viz., Angle of repose, Loose Bulk Density, Tapped Bulk Density, Compressibility index and Hausner's ratio. The experiments were conducted in triplicate.

Drug-Excipient compatibility studies

Differential Scanning Calorimetric (DSC) analysis

DSC analysis was performed using Shimadzu DSC-60, Japan. A 1:1 ratio of drug and excipient was

Table 2: Flow properties of formulation blend

Parameters	Value
Angle of repose (^{0})	29.45±1.68
Loose Bulk Density (g/ml)	0.578±0.08
Tapped Bulk Density (g/ml)	0.788±0.03
Compressibility index (%)	26.59±0.21
Hausner's ratio	1.24±0.04

All values are in mean ±S.D; Number of experiments (n)= 3

were prepared in KBr disks by means of a hydrostatic press at 6-8 tons pressure. The samples were scanned at wavelength 500 to 4000 cm^{-1}.

Preparation of matrix tablets

Sustained release matrix tablets of Glipizide with *Prosophis cumanensis* fruit mucilage and Povidone were prepared by using different drug: mucilage ratios as shown in Table 1, *Prosophis cumanensis* fruits mucilage and Povidone were used as matrix forming materials while microcrystalline cellulose as a diluent and Magnesium stearate as a lubricant [5]. All ingredients used were passed through a # 100 sieve, weighed and blended. The granules were prepared by wet granulation technique and compressed by using 10 mm flat faced punches. The compositions of formulations were showed in Table 1. These matrix tablets were evaluated for their physical properties as per official and Pharmacopoeia methods [6-8].

Swelling behavior of matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation F-1, F-2, F-3, F-4 and F-5 were studied. One tablet from each formulation was kept in a Petri dish containing phosphate pH 7.4. At the end of 2 h, the tablet was withdrawn, kept on tissue paper and weighed, repeated for every 2 h till the end of 12 h[9]. The % weight gain by the tablet was calculated by eq. 1.

$$S.I = \{(M_t - M_0) / M_0\} X 100 \quad (1)$$

Where, S.I = Swelling Index, M_t = Weight of tablet at time 't' and

M_o = Weight of tablet at time 0.

***In vitro* drug release studies**

Release of Glipizide from the matrix tablets was studied in phosphate buffer of pH 7.4 (900 ml) using 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 Glipizide matrix tablets equivalent to 10 mg of Glipizide 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 223 nm for Glipizide content[10] using a UV/ visible double-beam spectrophotometer (Elico SL 210, Mumbai, India). The drug release experiments were conducted in triplicate (n = 3). The *in vitro* release data was mathematically treated with zero order, first order, Higuchi, Korsmeyer Peppa's and Hixson-Crowell's Models.

RESULTS AND DISCUSSION

The DSC of Glipizide Pure drug and physical mixture were shown in Figure 1 and 2 respectively. Infrared Spectrum of Glipizide Pure drug, Infrared Spectrum of *Prosophis cumanensis* fruits mucilage with Povidone, Infrared Spectrum of formulation was obtained. The FTIR spectrums revealed that the formulation spectrum retains the peaks of Glipizide. The IR spectrums of Glipizide pure drug, the polymers blend and the formulation blend are shown in Figure 3, 4 and 5 respectively.

The Angle of repose of formulated blend was 29.45^0±1.68 indicating good flow, The Loose Bulk Density was found to be 0.578±0.08 g/ml, Tapped Bulk Density was found to be 0.788±0.03 g/ml, Compressibility index ranged from 26.59±0.21% and Hausner's ratio was found to be 1.24±0.04. All these values were shown in Table 2. The formulated tablets showed uniformity in swelling and the values plotted and shown in Figure 6. The thickness of formulated tablets were ranged from 5.7±0.23 to 6.2±0.19 mm, hardness was ranged from 5.85±1.55 to 7.56±0.52 kg/cm^2, the loss on friability was ranged from 0.19±0.04 to 0.80±0.01 % and drug content was ranged from 99.1±3.66 to 100.8±6.37 %. All these values were shown in Table 3. *In vitro* drug release

Table 3: Post compression parameters of formulated matrix tablets

Sl. No	Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
1	F-1	5.9±0.19	6.52±1.04	0.70±0.08	99.8±7.51
2	F-2	5.8±0.48	7.52±1.18	0.80±0.01	100.8±6.37
3	F-3	5.7±0.23	5.85±1.55	0.19±0.04	99.9±5.81
4	F-4	6.1±0.16	7.56±0.52	0.53±0.04	99.1±3.66
5	F-5	6.2±0.19	6.92±0.29	0.64±0.01	100.4±2.55

All values are in mean ±S.D; Number of trials (n) = 5

profile of Glipizide from formulated matrix tablets were studied using zero order, first order, Higuchi, Korsmeyer Peppas and Hixson Crowell's models which were shown in Figure 7, 8, 9, 10 and 11 respectively. From these mathematical models the drug releasing mechanism was studied, when n = 0.5 indicates Fickian diffusion, while n = 0.5- 1.0 indicates Non-Fickian diffusion and when n = 1, the release is zero order. The formulations showed good linearity (r^2 = 0.9685 to 0.9951) with slope (n) between 0.5672 - 0.9643 which appears to indicate a coupling of diffusion and erosion mechanisms. This indicates the release of drug from the formulated matrix tablets was controlled by the swelling of the polymer followed by drug diffusion through the swelled polymer and slow erosion of the matrix tablet. From the release exponent in the Korsmeyer Peppas model it was revealed that the mechanism that led to the release of Glipizide was Non-Fickian diffusion with constant release rate for sustained release of drug from dosage form. The rate of release was faster in F-1 and slower in F-5. The kinetic plots were perfectly fitting to the formulated *Prosophis cumanensis* fruits mucilage, Povidone - Glipizide

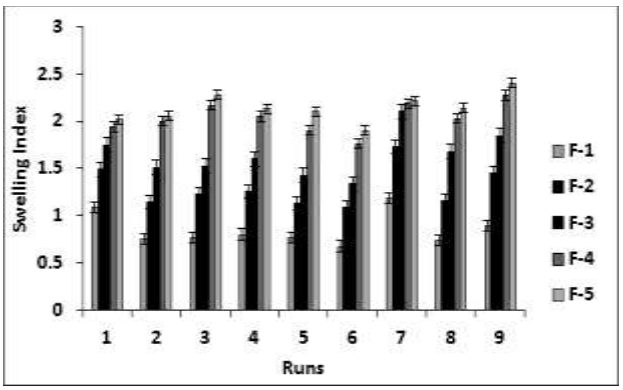

Figure 6: Swelling Index of matrix tablets

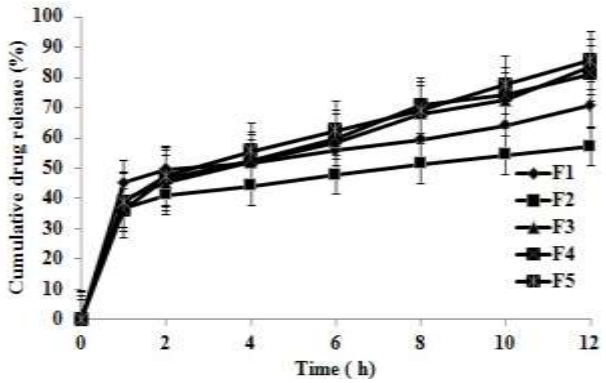

Figure 7: Zero order plots of matrix tablets

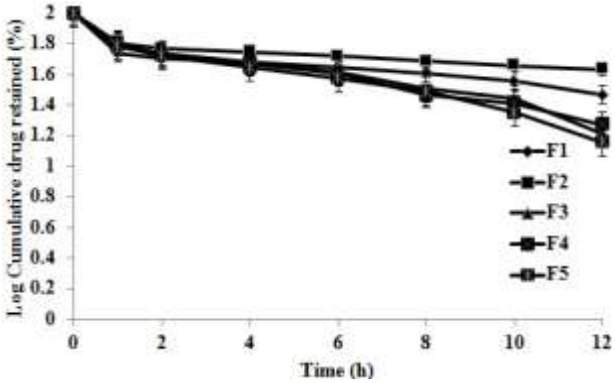

Figure 8: First order plots of matrix tablets

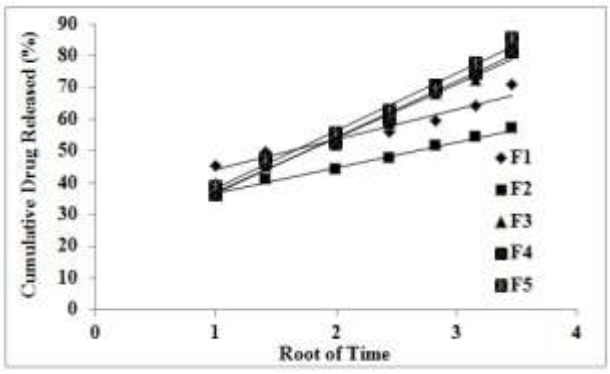

Figure 9: Higuchi plots of matrix tablets

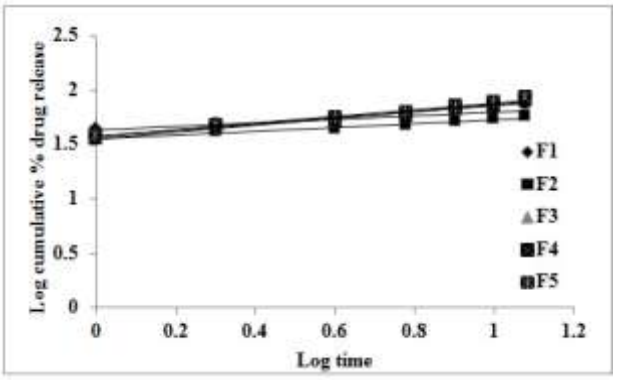

Figure 10: Korsmeyer Peppas plots of matrix tablets

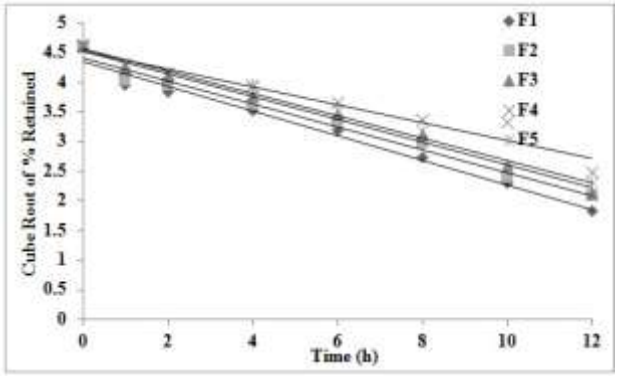

Figure 11: Hixson Crowell plots of matrix tablets

matrix tablets. This result shown that as the proportion of *Prosophis*

cumanensis fruits mucilage and Povidone 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.

CONCLUSION

The present study revealed that *Prosophis cumanensis* fruits mucilage and Povidone combination appears to be suitable for use as a release retardant in the manufacture of sustained release matrix tablets because of its good swelling, good flow and suitability for matrix formulations. From the dissolution study, it was concluded that dried *Prosophis cumanensis* fruits mucilage can be used as an excipient for making sustained release matrix tablets.

Acknowledgement

The authors are thankful to Dr. Reddy's Laboratories, Hyderabad, India for providing the gift sample of Glipizide.

References

1. Duke, James A, 1983. *Prosopis juliflora* DC; Handbook of Energy Crops. Purdue University Center for New Crops & Plant Products.
2. KD Tripathi, 1999. Essentials of Medical Pharmacology. 4th ed. New Delhi: Medical Publishers (p) Ltd., 142-44.
3. Sweetman SC, 2005. Martindale, the complete drug reference. 34th ed. London: Pharmaceutical Press, 324-48.
4. Ahad HA et al., 2010. Fabrication and *in-vitro* evaluation of Glibenclamide and *Abelmoscus esculentus* fruit mucilage sustained release matrix tablets, Journal of Pharmacy research, 3(5), 943-946.
5. Ahad HA, Chitta Suresh Kumar, 2010. Formulation and *In-vitro* Evaluation of Once-Daily Sustained- Release Matrix Tablets of Glipizide, Der Pharmacia Lettre, 2 (1), 265-274.
6. Lachman L, Lieberman HA, Kanig JL, 1987. The Theory and Practice of Industrial Pharmacy. Philadelphia, PA: Lea and Febiger, 317-318.
7. Martin Alfred. Physical Pharmacy, 1991. 4th ed. Maryland, USA: Lippincott Williams & Wilkins, pp.423.
8. Aulton M.E. Pharmaceutics, 1988. The Science of Dosage Forms Design. 2nd ed. London: Churchill Livingstone, pp.600.
9. Killedar S.G,Bhagwat D.A, Adnaik R.S,More H.N.and D'souza J.I, 2008. Optimization of method for determination of swelling factor of Ispaghula husk seeds, Indian Drugs, 45 (4), 310–313.
10. The United States Pharmacopoeia 24, NF 19, 2000. United States Pharmacopoeial convention, Rockville, M.D. Asian Edi., 1462-5, 1913-4.