



## Fabrication and Evaluation of Gliquidone *Azadirachta indica* Fruit Mucilage and Poly Vinyl Pyrrolidone Sustained Release Matrix Tablets

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### ABSTRACT

*The purpose of the present investigation was to design matrix type oral tablets of Gliquidone with Azadirachta indica fruit mucilage and Poly Vinyl Pyrrolidone. The polymers were studied for its functionality as a matrix forming property to sustain the Gliquidone release from formulated matrix tablets. Physicochemical properties of dried powdered mucilage of Azadirachta indica fruit mucilage and Poly Vinyl Pyrrolidone blend were studied. Various formulations of Gliquidone Azadirachta indica fruit mucilage and Poly Vinyl Pyrrolidone were prepared. The designed tablets were found to have better pharmacopoeial parameters with low standard deviation values. The swelling behavior and release rate characteristics were studied. The in-vitro dissolution study proved that the dried Azadirachta indica fruit mucilage and Poly Vinyl Pyrrolidone combination can be used as a matrix forming polymers for making sustained release matrix tablets.*

**Key words:** Gliquidone, *Azadirachta indica*, Poly Vinyl Pyrrolidone, matrix tablets, sustained release.

### INTRODUCTION

The mucilage of *Azadirachta indica* fruits clinically and experimentally proved anti-diabetic activity [1] and release retardant property in the present investigation. Gliquidone is an oral hypoglycemic agent, which is a commonly prescribed drug for the treatment of patients with type II diabetes mellitus. It belongs to sulfonyl ureas drug class. Gliquidone is a weak acid with PKa of 5.3. Gliquidone is 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. The usual dose of Gliquidone is up to 180 mg daily [3]. The pharmacokinetics and dosage schedule supports

once daily sustained release formulations for Gliquidone for better control of blood glucose levels to prevent hypoglycemia, enhance clinical efficacy and patient compliance [4]. The objective of present investigation is to design and evaluate sustained release tablets of Gliquidone using *Azadirachta indica* fruits mucilage and Poly Vinyl Pyrrolidone combination as release retardant for making sustained release matrix tablets.

## MATERIALS AND METHODS

Gliquidone was obtained as a gift sample from Dr. Reddy's Laboratories, Hyderabad, India. *Azadirachta indica* 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. Poly Vinyl Pyrrolidone, 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 *Azadirachta indica* fruits were collected and washed with water. The outer shells were removed and the seeds with mucilage were placed 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 (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 40°C, collected, powdered, passed through a # 80 sieve and stored in desiccator at 30°C & 45% relative humidity till use [5]. The collected mucilage was tested for flow properties which were shown in Table 1. All values were found to be satisfactory.

### Drug-Excipient compatibility studies

#### Differential Scanning Calorimetry (DSC)

DSC analysis was performed using Shimadzu DSC-60, Shimadzu Limited Japan. A 1:1 ratio of drug and excipient was weighed into aluminum crucible. The sample was analyzed by heating at a scanning rate of 20°C over a temperature range 20<sup>0</sup>-300<sup>0</sup>C under nitrogen environment.

#### Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectra were recorded on samples prepared in potassium bromide (KBr) disks using a Shimadzu Corporation, (Tokyo, Japan) Model-1601 PC. Samples were prepared in KBr disks with the help of a hydrostatic press at 6-8 tons pressure. The scanning range was from 500 to 4000 cm<sup>-1</sup>.

### Preparation of matrix tablets

Sustained release matrix tablets of Gliquidone with *Azadirachta indica* fruit mucilage and Poly Vinyl Pyrrolidone were prepared by using different drug: mucilage ratios as shown in Table 2, *Azadirachta indica* fruits mucilage and Poly Vinyl Pyrrolidone were used as matrix forming materials while microcrystalline cellulose as a diluent and Magnesium stearate as a lubricant [6]. 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 2. These matrix tablets were evaluated for their physical properties as per I.P methods [7, 8] which were shown in Table 3.

### Swelling behavior of matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation GPA-1, GPA-2, GPA-3, GPA-4 and GPA-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, 10]. 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 0. Swelling behavior of Sustained release matrix tablets were represented in Fig. 7.

### Estimation of Gliquidone

An ultraviolet spectrophotometric method based on measurement of absorbance at 225 nm in Phosphate buffer of pH 7.4. The method obeyed Beer-Lambert's law in the concentration range of 1-20 µg/ml. No interference was observed from the excipients used.

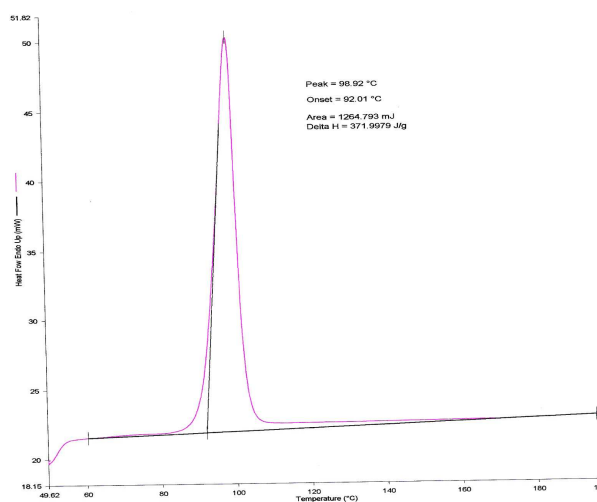
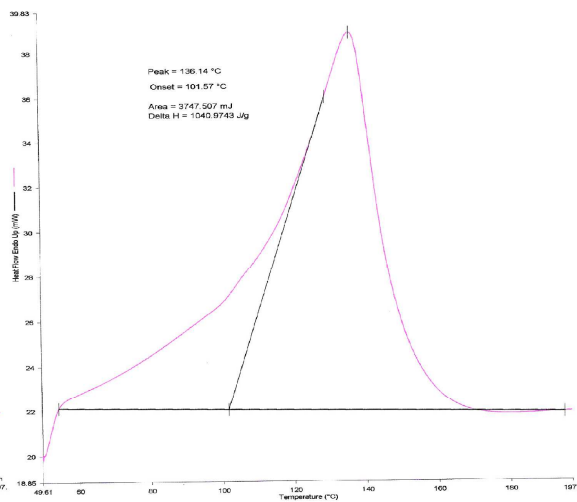
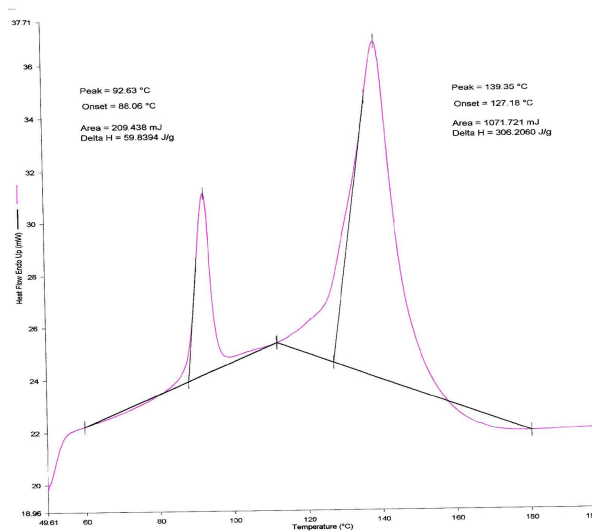
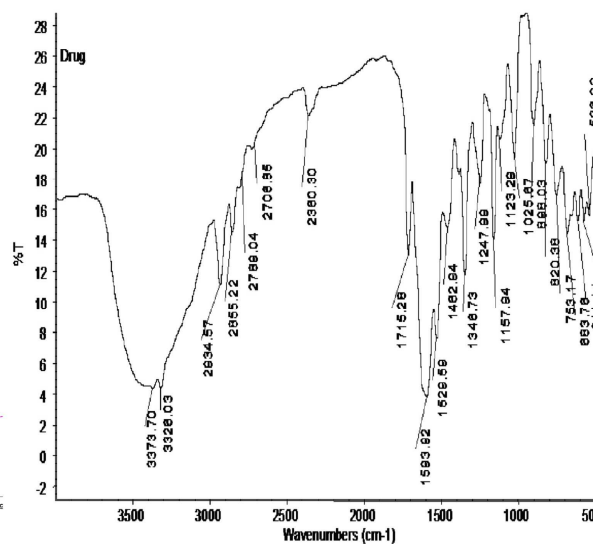
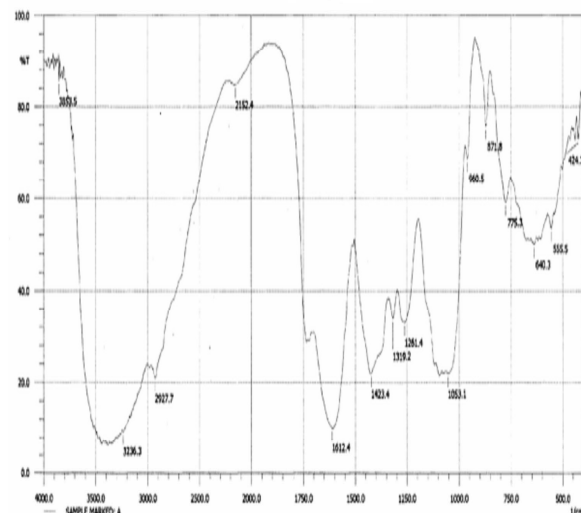
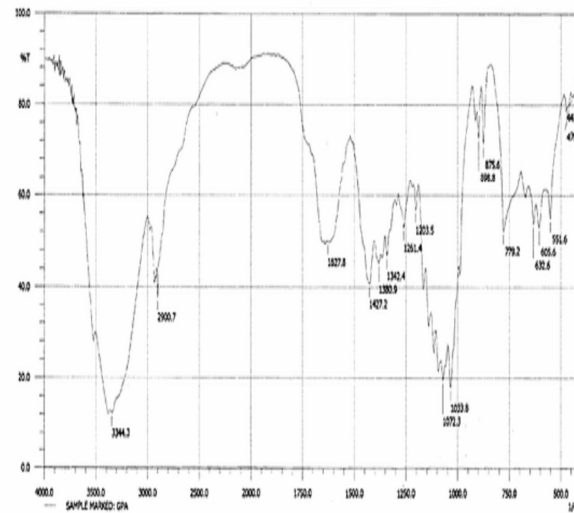
### In vitro drug release studies

Release of Gliquidone 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  $37^\circ \pm 0.5^\circ\text{C}$ . A sample of Gliquidone matrix tablets equivalent to 100 mg of Gliquidone 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 225 nm for Gliquidone content [11] 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. 8.

## RESULTS AND DISCUSSION

The DSC of Gliquidone Pure drug, *Azadirachta indica* fruits mucilage with Poly Vinyl Pyrrolidone and physical mixture were shown in Fig 1, 2 and 3 respectively. Infrared Spectrum of Gliquidone Pure drug, Infrared Spectrum of *Azadirachta indica* fruits mucilage with Poly Vinyl Pyrrolidone, Infrared Spectrum of formulation was obtained. The FTIR spectrums revealed that the formulation spectrum retains the peaks of drug used and these spectrums were represented in Fig. 4, 5 and 6 respectively.

Matrix tablets, each containing 100 mg of Gliquidone, were prepared using dried fruit mucilage of *Azadirachta indica* in various drug: mucilage ratios. *In-vitro* drug release profile of Gliquidone from formulated matrix tablets were studied using zero order, first order, Higuchi, Korsmeyer Peppas and Hixson-Crowell's Models which were shown in Fig. 8, 9, 10, 11 and 12 respectively. The rate of release was faster in GPA-1 and slower in GPA-5. The kinetic plots were perfectly fitting to the formulated *Azadirachta indica* fruits mucilage- Gliquidone matrix tablets. This result shown that as the proportion of *Azadirachta indica* fruits 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.1: DSC Spectra of Gliquidone****Fig. 2: DSC Spectra of polymers blend****Fig. 3: DSC Spectra of Physical Mixture****Fig. 4: Infrared Spectrum of Gliquidone****Fig. 5: FTIR spectrum of polymers****Fig. 6: Infrared Spectrum of the GPA-5**

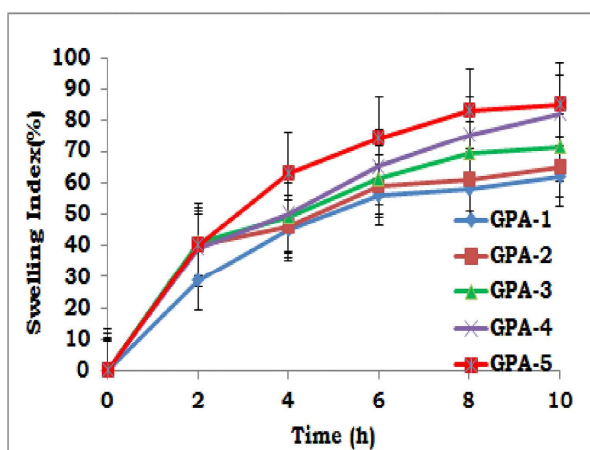


Fig. 7: Swelling Index of matrix tablets

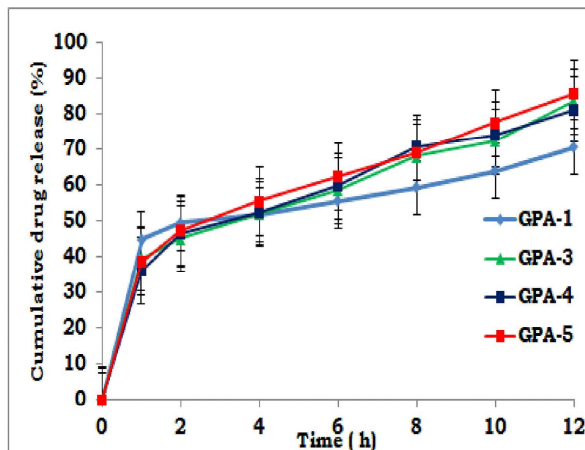


Fig. 8: Zero order release Plots

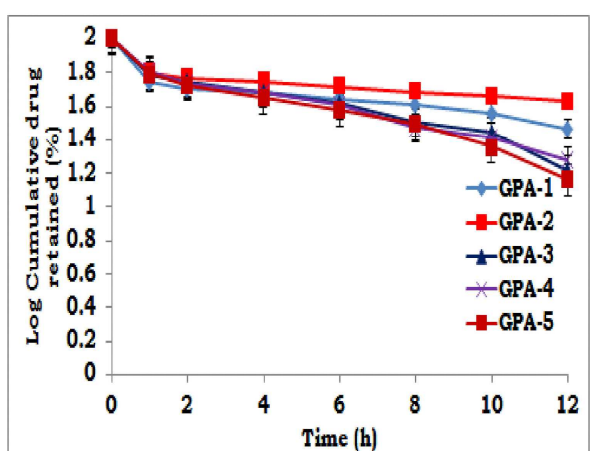


Fig. 9: First order release Plots

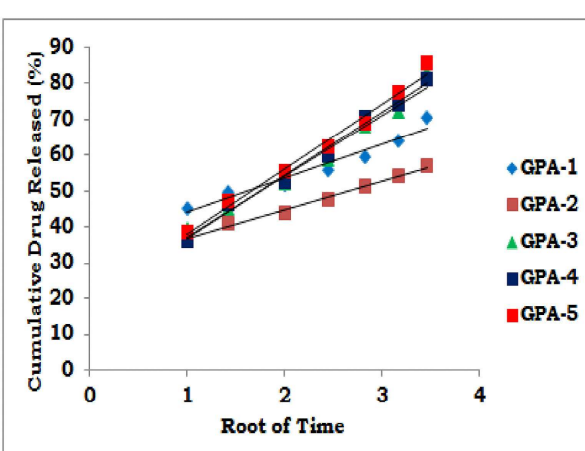


Fig. 10: Higuchi Plots

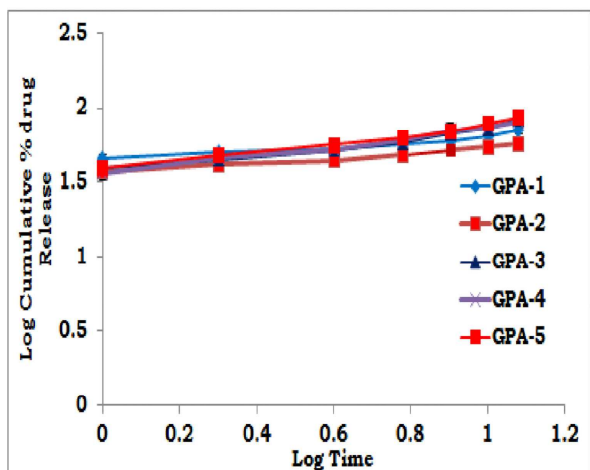


Fig. 11: Korsmeyer Peppas's Plots

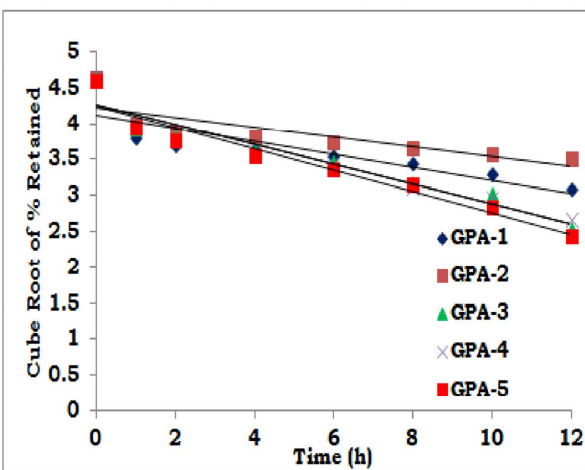


Fig. 12: Hixson-Crowell's Plots



## CONCLUSION

This study revealed that the combination of *Azadirachta indica* fruits mucilage and Poly Vinyl Pyrrolidone appears to be suitable as release retardants for making of sustained release matrix tablets because of its good flow properties and suitability for matrix formulations. From the dissolution study, it was concluded that dried *Azadirachta indica* fruits mucilage can be used as an excipient for making sustained release matrix tablets in combination with Poly Vinyl Pyrrolidone.

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

Parameters	Value
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
Angle of repose (°)	29.45±1.68
<b>Number of experiments (n)= 3</b>	

**Table 2: Formulae of matrix tablets**

Ingredients (mg)	Formulations				
	GPA-1	GPA-2	GPA-3	GPA-4	GPA-5
Gliquidone	100	100	100	100	100
<i>Azadirachta indica</i> fruits mucilage	2	4	6	8	10
Poly Vinyl Pyrrolidone	2	4	6	8	10
Micro crystalline cellulose (Avicel)	91	87	83	79	75
Magnesium stearate	5	5	5	5	5
<b>Total weight of tablet</b>	<b>200</b>	<b>200</b>	<b>200</b>	<b>200</b>	<b>200</b>

**Table 3: Physical properties of *Azadirachta indica* fruit mucilage Gliquidone matrix tablets**

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

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