

COMPARATIVE ANTIDIABETIC ACTIVITY OF MARKETED GLICLAZIDE FORMULATION WITH GLICLAZIDE LOADED PELLETS CONTAINING GUM KONDAGOGU AS A DRUG RETARDING MATERIAL IN RATS

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Received: 7 September 2013, Revised and Accepted: 28 September 2013

ABSTRACT

Controlled drug delivery systems significantly enhances therapeutic efficacy of drugs. Drug retarding polymers are the key performers in such designed systems.

Objective: The main objective of study is to evaluate antidiabetic effect of gliclazide loaded pellets developed by green synthesis technique where in gum Kondagogu is used as natural drug retarding polymer and compared with existing Gliclazide Marketed formulation.

Methods: The study is carried out in Wistar rats with body weight ranging between 100-220g. Diabetes was induced in animals by injecting alloxan 150mg/kg/bodyweight intraperitoneally (i.p.). Animals were divided into four groups. Group I - Control, Group II- Diabetic Control, Group III- Diabetic treated with Gliclazide Marketed formulation, and Group IV- Diabetic treated with gliclazide loaded pellets orally. Fasting blood glucose levels were estimated at 0, 2, 4, 6, 8, 10, 12 and 24 hours to understand the release of the drug from polymer matrix.

Results: The results have shown that the on single oral administration of gliclazide loaded pellets coated with gum Kondagogu showed almost similar anti-diabetic activity when compared with marketed formulation. The maximum reduction in the glucose level were observed at 4th and 6th hour and later the glucose levels were sustained in the same pattern to that of marketed formulation.

Conclusion: In the present study, an effort has been made to evaluate the efficacy of gum kondagogu as a novel controlled release matrix forming material and thus it could be concluded that gum kondagogu could be a controlled release matrix polymer and be a suitable substituent to existing synthetic polymers for drug retardation in the pharmaceutical industry.

Keywords: Gum Kondagogu, Gliclazide, tree gum exudates, natural drug retarding material

INTRODUCTION

Diabetes mellitus (DM) is common endocrine disorder affecting more than 200 million people Worldwide. [1] It is a metabolic disorder characterized by hyperglycaemia, hypertriglyceridaemia and hypercholesterolaemia resulting from defects in insulin secretion or action or both [2]. Gliclazide is a second generation hypoglycaemic drug belongs to the sulfonylurea class of insulin secretagogues mainly used in the treatment of non insulin dependent diabetes mellitus (NIDDM). Gliclazide reduces blood glucose levels in patients suffering NIDDM by correcting both defecting insulin secretion and peripheral resistance [3]. Controlled drug delivery systems significantly enhances therapeutic efficacy of drugs. Drug release retarding polymers are the key performers in such designed systems. A wide range of polymers like natural, semi-synthetic and synthetic from various origins are investigated as drug retarding polymeric materials. The most common and effective synthetic polymers in combination used for sustained release/controlled release are ethyl cellulose, hydroxypropyl methylcellulose and eudragits [4, 5]. Recent investigation reveals that application of new natural hydrophilic polymers as drug carriers have received considerable attention because they are readily availability, safe, cost-effective, biocompatible, biodegradable and ecofriendly. Some natural gums such as xanthan gum, guar gum, gum karaya, olibanum resin, chitosan, gum copal and gum damar were used in controlled drug delivery systems but found to be unable to sustain the drug release for a longer time(>8hr), even at a higher concentration. Therefore the study of new natural polymers for retarding drug release alone and not in combination at a lower concentration is the motive of research and the other hand to compare the drug retarding property with respect to existing marketed formulation mostly composed of synthetic polymers. [6,7]. The natural drug retarding polymer selected for the study is Gum Kondagogu (GK). GK is a tree exudates gum obtained from the bark

Cochlospermum gossypium (DC) belonging to family Bixaceae. The biopolymer GK backbone is a polysaccharide composed of α -D-GalpA-(1 \rightarrow 4)- α -L-Rhap. GK is classified under rhamnogalactouronans type of gums and rich in galactose, rhamnose and uronic acids [8]. The past research acknowledged the use of gum kondagogu in combination with other natural and semi-synthetic polymers [9, 10] as a drug retarding polymeric material.

In the present study, an effort has been made to evaluate the efficacy of gum kondagogu as a novel controlled release matrix forming material and gum ghatti is used as a binder in the formulation.

MATERIALS AND METHODS

Chemicals and Reagents

Gliclazide was purchased from Indus Laboratories, Hyderabad. Grade I Gum Kondagogu and Grade -I Gum Ghatti were procured from Girijan Co-Operative Corporation (GCC), Hyderabad, Alloxan monohydrate and all other analytical reagents were obtained from SD. Fine Chemicals.

Experimental Animals

Healthy, 6-8 week old Albino Wistar rats with body weight ranging between 100-220g were obtained from Albino Research Institute, Hyderabad, India were used in the investigation. The rats were allocated into four groups with approximately same mean body weights. Each animal were assigned a unique animal identification number which was tattooed in the ear. The animals were housed individually in plastic cages with sterilized sawdust. All animals were housed in single air conditioned room with 12hr light/dark cycles, and temperature was maintained at 27^oC \pm 2^o C with a relative humidity of 60 \pm 5%. From the arrival of the rats until the end of the experiment period, animal diet and water were provided *ad lib*. Experimental animals were acclimatization for

2 weeks before the start of the study. This study was conducted in accordance with Good Laboratory Practice and OECD -407 (Organization for Economic Cooperation and Development) guidelines and regulations. In addition, the study protocol and the use of experimental animals were reviewed and approved by the Institutional Animal Ethical Committee (25/50/2013/CPCSEA).

Experimental Design

Marketed formulation containing gliclazide and gliclazide loaded pellets coated with GK (drug retarding material) were suspended in about 2ml of water and were administered to animals orally by gavages. Animals were fasted they were deprived from food but not water for 12hr were used to assess the effect of Marketed tablets containing gliclazide and gliclazide loaded pellets [11].

Comparative anti-diabetic activity with marketed gliclazide tablets and with gliclazide loaded pellets (GK as drug retarding material) in Wistar Albino rats

Preparation of gliclazide loaded pellets

Pellets were synthesized by green technology. Gliclazide was coated with Gum Kondagogu as a drug retarding material and Gum Ghatti was added as binder. The mixture containing 10% gums was added slowly in the form of mucilage (20% w/v) and mixed uniformly and subjected to centrifugal force in a coating pan. A required gum solution as a binder is added to the pellets formed until a required coating is achieved. The obtained pellets are subjected to sieving #18/20 followed by #20/25. The obtained pellets were dried at 60° C for 12hrs in a convention oven and the dried pellets were stored in the air tight containers.

Selection of the Dose

The dose was selected using Animal equivalent dose (AED) calculation for gliclazide. The test and the reference formulation equivalent to 600mg/kg/bodyweight were administered as a single dose by gavage. Based on the respective body weight doses were administered. Food was withheld for 2-3 hr after the administration of dose [12].

Absolute Human dose = 60mg/70kg= 0.857

AED= $\frac{\text{Human Dose in mg/kg}}{\text{Animal weight in kg/human weight in kg}}$

(Animal weight in kg/human weight in kg)^{0.33}

Anti-diabetic activity

Healthy adult Albino Wistar male and female rats weighing 150-200g procured from Albino Research Institute, Hyderabad were used for the study. Diabetes was induced in animals by injecting alloxan 150mg/kg/bodyweight intraperitoneally (i.p.) freshly prepared in normal saline. The animals were tested for evidence of diabetes by estimating their glucose levels using glucometer Pulsatum; (Pulsatum Health Care private Ltd). The animals were divided into four groups. Each group consisted of 6 animals (3M, 3F). Group I - Control, Group II- Diabetic Control, Group III- Diabetic treated with Marketed gliclazide formulation, and Group IV- Diabetic treated with gliclazide loaded pellets orally. Blood samples from the rats were collected from the retro orbital plexus puncture method. Blood glucose level was estimated at 0, 2, 4, 6, 8, 10, 12 and 24 hours to understand the release of the drug from polymer matrix [13-16].

Statistical analysis

The data obtained in present investigation was subjected to statistical analysis. All results are expressed as Mean \pm SD. The data was analyzed using Analysis of variance (ANOVA) and the group means were compared by Dunnet test. Values were considered statistically significant when $p < 0.05$. Graph Pad Instat was used for the analysis of data.

RESULTS

Evaluation of *In Vivo*- anti-diabetic study

There is an increase demand for controlled drug delivery system designed using natural polysaccharides as a retarding material. In the present investigation grade I gum Kondagogu and Grade I gum Ghatti

were used and shown in Fig. 1&2 respectively. Diabetes induced by Alloxan was treated by gliclazide which is a potent hypoglycemic drug used in the treatment of NIDDM. The anti-diabetic drug gliclazide loaded pellets coated with gum kondagogu was compared with marketed extended release gliclazide formulation. The results shown in Fig. 3 indicates that on single oral administration of gliclazide loaded pellets coated with gum Kondagogu showed almost similar anti-diabetic activity to that of marketed formulation. The maximum reduction in the glucose level were observed at 4th and 6th hour and later the glucose levels were sustained in the same manner similar to that of marketed formulation.



Figure 1: Specimen of grade I Gum Kondagogu



Figure 2: Specimen of Grade I Gum Ghatti

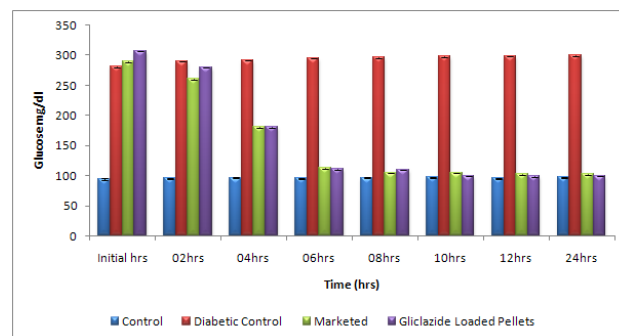


Figure 3: Anti-diabetic activity of gliclazide loaded pellets in comparison to marketed formulation in alloxan induced diabetic rats (n=6)

DISCUSSION

In order to have a better comparison between synthetic polymers and natural polymers, gliclazide was chosen as model drug and antidiabetic activity was evaluated. The evaluation was based on the sequence of drug release from the drug retarding matrices and ability to reduce the blood glucose levels. The experimental data shows increased plasma concentrations of glucose higher than 250mg/dl in alloxan treated albino Wistar rats which has been considered as severe diabetes. The present study revealed that the gliclazide loaded pellets (GK has a natural drug retarding material) had marked hypoglycemic effect in alloxan-induced diabetes. The maximum effect was observed in 4th and 6th hour and blood glucose levels were sustained till 24th hour similar to that of marketed formulation indicating alone gum kondagogu at a low

concentration is a potential natural drug retarding polymer which will be a suitable substitute for existing synthetic polymers in pharmaceutical industry.

CONCLUSION

The present study involves comparison anti-diabetic activity of marketed formulation usually composed of synthetic polymers and gliclazide loaded pellets which are formulated using gum Kondagogu as natural drug retarding material on alloxan induced diabetic Albino Wistar rats. The in vivo studies conforms reduction in the blood glucose level in the marketed and developed formulation showed similar data in control to diabetic induced animals. This further confirms that gum Kondagogu has an excellent drug retarding property and a potential controlled release excipient for pharmaceutical industry.

CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

ACKNOWLEDGEMENTS

The authors wish to acknowledge DST (WOS-A), Department of Science and Technology, New Delhi, for providing financial support to carry out this study.

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