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Short Communication

Influence of ayurvedic antidiabetic agent on the pharmacodynamics of glimepiride

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ABSTRACT

The present study is planned to explore the influence of ayurvedic antidibetic drug Madhumehari on the pharmacodynamics of glimepiride. Wistar albino rats of either sex were induced diabetes with alloxan and were used. The study was done in two phases, acute phase and chronic phase. In acute phase the diabetic rats were divided into six groups each consisting of 6. The diabetic control (Group-I) was treated with 0.5%W/V CMC suspension orally. To the diabetic group II, III and IV glimepiride 4mg/kg body wt, madhumehari 100mg/kg body wt. and madhumehari 200mg/kg body wt. were administered orally respectively. Groups V and VI were given orally the combination of glimepiride 4mg/kg body wt + madhumehari 100mg/kg body wt and glimepiride 4mg/kg body wt + madhumehari 200mg/kg body wt. In chronic study the protocol was similar to that of acute study but treatment was given for 7 days. Blood samples were collected from retro orbital plexus at predetermined time intervals for serum glucose level estimation after the oral dosing of glimepiride. The combination of glimepiride + madhumehari has shown antidiabetic activity at 3rd hour. Glimepiride when administered along with madhumehari 100 & 200mg orally the fall in serum glucose level was found to be more significant when compared with the *per se* treatment of glimepiride, madhumehari 100 & 200mg in both acute and chronic studies. From the above study it may be concluded that there is additive type of Pharmacodynamic interaction is possible between glimepiride and madhumehari.

Key words: Diabetes, glimepiride, madhumehari, Pharmacodynamic, serum glucose level.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disease characterized by high blood glucose levels which results from defects in insulin secretion or action or both. Glimepiride is a second generation sulfonyl urea most commonly used for the management of Type II DM [1]. Nowadays herbal drugs are used along with prescriptions and OTC medications. Madhumehari an ayurvedic drug is used most commonly in the treatment of Type II DM [2].

Usually ayurvedic drugs are considered to be safe but they can interact with allopathic drugs and results in altered activity and toxicity. At present, information on ayurvedic herb-drug interaction is scanty, while there is a progressive increase in the use of ayurvedic drugs in India as well as in many parts of the world. Ayurvedic drugs can compete with other allopathic agents for absorption, distribution, metabolism and elimination and thereby affecting the bioavailability of co-administered drug which may lead to potentially severe adverse effects [3, 4]. Keeping this in view we studied the influence of ayurvedic drug madhumehari on the pharmacodynamics of glimepiride in diabetic Wistar albino rats.

MATERIALS AND METHODS

Chemicals and Reagents: The pure drug Glimepiride was obtained from Aurobindo Pharma, Hyderabad as gift sample. Madhumehari was purchased from local ayurvedic Pharmacy, Hyderabad. Glucose kit was obtained from SPAN Diagnostics Ltd, Surat. The other reagents were purchased from S.D. Fine Chemicals.

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Animals: Wistar albino rats of either sex weighing about 150-200g were used in the present study. The animals were provided with standard rat chow and water *ad libitum.* Diabetes was induced in rats by administering alloxan 150mg/kg ip in normal saline [5]. Three days later blood was collected from retro orbital plexus of rats. The serum was isolated by centrifugation of blood for 20min at 2000rpm and subjected to glucose estimation by GOD-POD method [6]. Rats with serum glucose levels of 200-350mg/dl were considered as diabetic and employed in the study [7]. Prior approval from IAEC was obtained to conduct the study (IAEC/ SUCP/02/2009). The study was done in two phases.

a. Acute study - Phase- I
b. Chronic study - Phase-II

Phase – I: Acute study

Diabetic rats were divided into six groups each consisting of 6 and treatment was given as follows.

Group I: Diabetic control 1ml of 0.5%W/V CMC orally

Group II: Glimepiride 4mg/kg body weight in 0.5%W/V CMC orally

Group III: Madhumehari 100mg/kg body weight in 0.5%W/V CMC orally

Group IV: Madhumehari 200mg/kg body weight in 0.5%W/V CMC orally

Group V: Madhumehari 100mg/kg body weight in 0.5%W/V CMC and 30min later glimepiride 4mg/kg body weight in 0.5%W/V CMC was administered orally.

Group VI: Madhumehari 200mg/kg body weight in 0.5%W/V CMC and 30min later glimepiride 4mg/kg body weight in 0.5%W/V CMC was administered orally.

Blood samples were collected from the retro orbital plexus of the eyes of rats at 0, 1, 2, 3, 4, 6, 8 and 10h after administration of glimepiride for the estimation of glucose level. Serum glucose level was estimated by GOD – POD method.

Phase II: Chronic study

The experiment was done similar to phase I but here drug treatment was given for 7 days. On 7th day 30min later glimepiride administration blood samples were collected and subjected to serum glucose estimation.

Statistical analysis: Statistical analysis was done using unpaired Student's t – test. The results are expressed as Mean ±SEM. In all test the criteria for statistical significance was $p<0.05$.

RESULTS

Glimepiride was used as a prototype drug of Sulfonylurea. It produced significant antidiabetic activity in both phase I & II studies at 3rd h. Madhumehari is commonly used antidiabetic agent in the Ayurvedic system. In the present study it also exhibited good antidiabetic activity by decreasing the blood glucose level in diabetic rats. The antidiabetic activity of madhumehari is dose dependent one. When glimepiride was co-administered along with madhumehari 100 & 200mg the combination exhibited more significant antidiabetic activity than *per se* treatment in both acute and chronic studies. The results were shown graphically in Fig: I and II for acute and chronic study respectively.

DISCUSSION

Madhumehari has a combination of 12 drugs. Apart from acting as antidiabetic agent this drug also supports the functions of pancreas, helps in digestion and as a rejuvenator. The ingredients of madhumehari includes *Gymnema sylvestre, Eugenia jambolana,Tinospora cardifolia & Ficus glomerata* which increases insulin level by regeneration of the β- cells of pancreas [8]. On the other hand *Momordia charantia* exhibits its antidiabetic activity by inhibiting glucose-6-phosphates besides fructose-1,6-biphosphate in the liver and stimulates hepatic glucose -6- phosphate dehydrogenase activity [9].

Fenu greek which is also one of the ingredients of madhumehari improves glucose homeostasis in both type I &II DM by delaying the carbohydrate digestion, absorption and enhancing insulin action [10]. Thereby if we administer both glimepiride and madhumehari for the management of type II DM together additive type of Pharmacodynamic interaction is possible which is beneficial. Hence this combination can be safely administered to type II diabetic patients.

The kinetics of madhumehari is not clear through the literature. So to find whether pharmacokinetic herb-drug interaction occurs between these combinations the results are yet to be confirmed by understanding the pharmacokinetic parameters like AUC, Cmax and Tmax of glimepiride after treatment with madhumehari.

CONCLUSION

From the light of above study it may be concluded that the ayurvedic drug madhumehari can be safely administered along with glimepiride in the management of type II diabetes mellitus.

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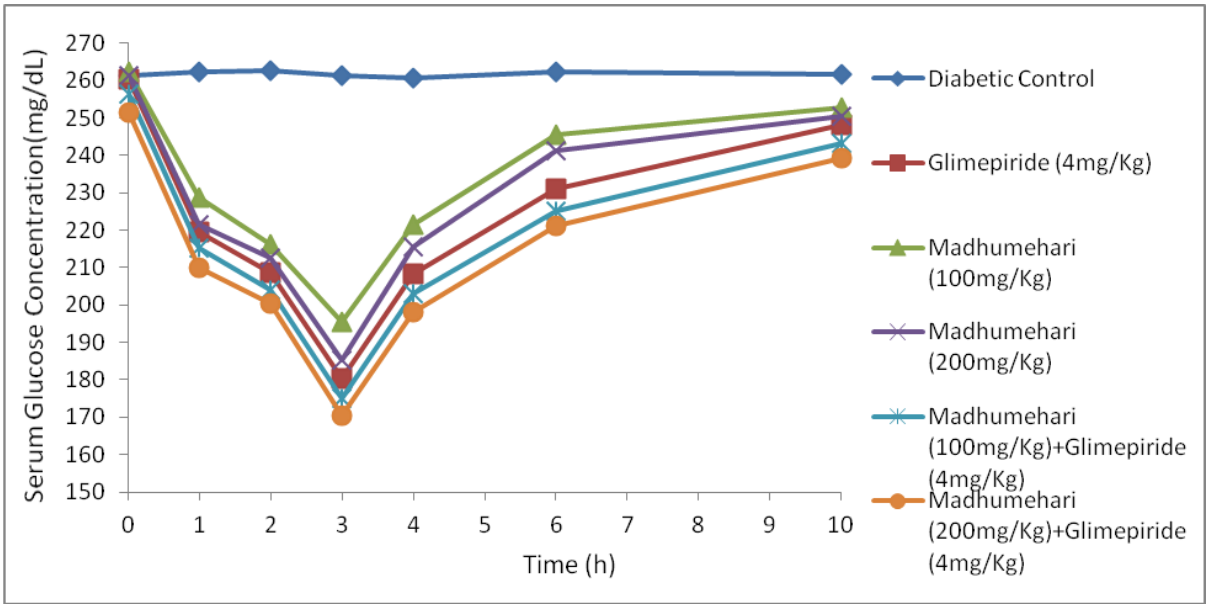

Fig I: Effect of Acute administration of Glimepiride, Madhumehari 100 and 200mg *per se* and the combination of Glimepiride + Madhumehari 100mg and Glimepiride + Madhumehari 200mg on Blood glucose level in diabetic rats.

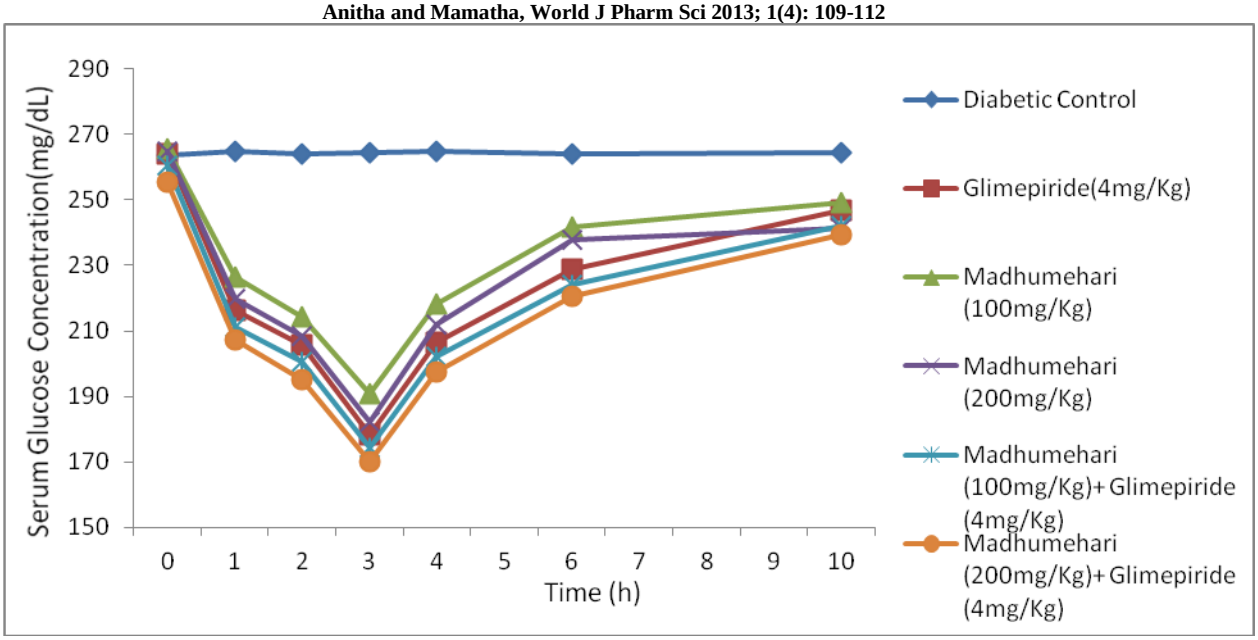

Fig II: Effect of Chronic Administration of Glimepiride, Madhumehari 100 and 200mg *per se* and the combination of Glimepiride + Madhumehari 100mg and Glimepiride + Madhumehari 200mg on Blood glucose level in diabetic rats.