SHORT COMMUNICATION

INFLUENCE OF *ALLIUM SATIVUM* ON THE ANTIHYPERGLYCAEMIC ACTIVITY OF GLICLAZIDE IN DIABETIC RATS: AN HERB-DRUG INTERACTION STUDY

ABSTRACT

In this particular study, the objective was to examine how varying doses of gliclazide (1 mg kg^{-1}) and *Allium sativum* (104 mg kg^{-1}) affect interaction in rats with diabetes induced by alloxan. The diabetes was induced by intraperitoneal injection of alloxan at a dosage of 100 mg kg^{-1} of body weight. The results revealed that the administration of gliclazide at 1 mg kg^{-1} of body weight and *A. sativum* at 104 mg kg^{-1} body weight exhibited noteworthy antihyperglycemic effects. The objective was to determine whether an interaction exists between these two substances in the context of diabetic conditions. In combination the *A. sativum* significantly enhanced the antihyperglycaemic activity of gliclazide from 2nd to 8th h except at 4th h. Hence, there is existence of pharmacodynamic interaction between *A. sativum* and gliclazide.

Keywords: *A. sativum,* gliclazide, alloxan, antihyperglycaemic activity

INTRODUCTION

The current global diabetic population stands at 150 million individuals, and it is projected to exceed 300 million by the year 2025. This significant increase can be attributed to various factors such as sedentary lifestyles, the consumption of high-calorie foods, obesity, longer life expectancy, and other contributing factors. The use of numerous herbal medications has been suggested for the treatment of diabetes. Compared to synthetic pharmaceuticals, plant-based medications are frequently thought to be less toxic and less likely to cause side effects[1].

Since ancient times, people have employed the spicy flavoring ingredient known as garlic (*A. sativum L.*, Liliaceae). India has always grown garlic because of its distinctive flavor and therapeutic benefits. Drug-drug interactions can either increase or decrease blood glucose levels, which can have severe consequences and potentially lead to fatal outcomes for the affected individual.

Drug interaction studies often employ small animals like rabbits, rats and mice as commonly used models. These animal models allow for convenient investigation of pharmacodynamic and pharmacokinetic parameters at pre-clinical levels, with the ability to extrapolate the results to humans[2]. The goal of this study was to compare gliclazide, a reference standard, to the garlic used in rats with alloxan induced diabetes to experimentally evaluate its antihyperglycaemic activity.

MATERIALS AND METHODS

Animals

Adult Wistar rats, either male or female, were acquired from Ghosh Enterprises, Hyderabad, India. The study received the necessary approval from our Institutional Animal Ethics Committee (P2/IAEC/2/2021/VVIPS/SAB/Rats) prior to its initiation[3].

Drugs

A sample of gliclazide (5 g) was sourced from Wockhardt, Bangalore, India. The blood glucose kits (AUTOSPAN) utilized in the study were obtained from a local pharmacy and fabricated by Span Diagnostics Ltd., Surat, India. The standard animal diet used in the experiment was provided by Rayan Biotechnologies Pvt. Ltd., Hyderabad, India. For the preparation of the gliclazide solution, the compound was solvated in a slight amount of 0.1N sodium hydroxide and subsequently diluted with distilled water to reach the desired volume.

Alloxan was acquired from LOBA Chemie Pvt. Ltd., Mumbai, India. To specifically induce type II diabetes instead of type I, nicotinamide was administered half an hour before the administration of alloxan[4].

Preparation of *A. sativum* extract

A solution of *A. sativum* was prepared by dissolving it in distilled water.

Induction of diabetes

Male and female Wistar rats weighing between 200-250 g were subjected to an 18 h fasting period prior to

Table I: Blood glucose levels (mg dL^{-1}) in diabetic rats

Time (h)	Gliclazide (1 mg kg^{-1} of body weight) without *A. sativum*	*A. sativum* (104 mg kg^{-1} of body weight)	Gliclazide (1 mg kg^{-1} b.w.) in combination with *A. sativum* (104 mg kg^{-1} of body weight)
0	397.25 ±18.7	315.5 ± 28.3	363.6±27.7
1	409 ± 18.7	331.6 ± 25	373±34.4
2	302 ± 14.1	321.6 ± 26	209±26.1
3	220.5 ± 3.3	247 ± 18	223±13
4	252.5 ± 5.6	265.5 ± 18	225±23
6	225.5 ± 23.23	255 ± 10.4	208±27
7	202 ± 20.4	283.3 ± 14.4	145±15

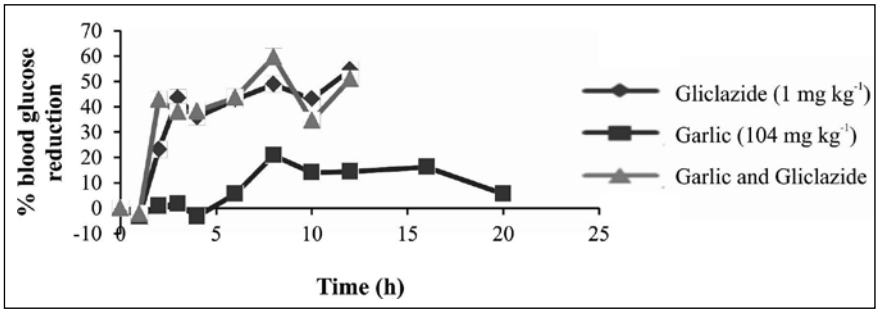

Fig. 1: Percent blood glucose reduction with gliclazide (1 mg kg^{-1} body weight) *A. sativum* (104 mg kg^{-1} body weight) and combination of gliclazide + *A. sativum* (1 mg kg^{-1} + 104 mg kg^{-1}) in diabetic rats (n=6)

alloxan injection. A solution of alloxan monohydrate was prepared by dissolving it in a saline solution. The prepared solution was induced intra peritoneally at a dosage of 100 mg kg^{-1} of body weight. To counteract the potential fatal hypoglycemia caused by alloxan's stimulation of excessive insulin release from the pancreas, the animals received oral administration of 10% dextrose to mitigate immediate hypoglycemic effects[5]. Blood sugar levels were assessed 24-48 h following alloxan treatment to evaluate the induction of diabetes.

Drug administration

The study included male and female Wistar rats weighing between 200-250 g after the induction of diabetes. A group of six rats, comprising both sexes, was selected based on their fasting blood glucose levels falling within the range of 200-400 mg dL^{-1} for the research. The rats were housed under standardized conditions, including consistent diet, room temperature, and a 12 h light-dark cycle. They were housed in polypropylene cages and provided unrestricted access to standard animal pellet diet and water[6].

Prior to the onset of the evaluation, the diabetic rats underwent an 18 h fasting phase with unrestricted approach to water. All over the duration of the experiment, water was hold back. A group of 6 diabetic rats were orally administered gliclazide at a volume of 1 mg kg^{-1}. Following a 1 week interval to eliminate any residual effects, the same group of animals received an oral dose of *A. sativum* at 104 mg kg^{-1}. Once again, after another 1 week washout period, the same group of rats were orally given *A. sativum* (104 mg kg^{-1}) 30 minutes before the oral administration of gliclazide (1 mg kg^{-1}).

Biochemical Assay

Blood samples were collected at defined time gap i.e., 0, 1, 2, 3, 4, 6 and 8 h from all the afore mentioned treatments. The collected blood samples were then subjected to analysis to measure blood glucose levels using the GOD-POD method[7].

RESULTS AND DISCUSSION

The successful induction of diabetes in the alloxan-treated rats was confirmed by the observed elevated blood glucose levels. However, there was a slight variation in the percentage of serum glucose depletion observed with the administration of gliclazide. The serum glucose levels achieved in diabetic rats with gliclazide (1 mg kg^{-1}) both prior and after therapy with *A. sativum* (104 mg kg^{-1}) were analyzed. Similarly, the percentage of blood glucose reduction obtained with gliclazide (1 mg kg^{-1}) prior and after therapy with *A. sativum* (104 mg kg^{-1}) in

diabetic rats was calculated. A graphical representation of these findings can be seen in Fig. 1. Additionally, the serum glucose levels and the corresponding percentage of serum glucose reduction achieved with the administration of *A. sativum* (104 mg kg^{-1}) were examined.

The administration of gliclazide at a dosage of 1 mg kg^{-1} of body weight demonstrated antihyperglycemic effects, with a mean percentage reduction of 220.5±3.3% at the 3rd h and 202±20.4% at the 8th h. *A. sativum,* given at a dosage of 104 mg kg^{-1} body weight, also exhibited antihyperglycemic activity, showing a mean percentage reduction of 247±18% at the 3rd h.

When used in combination, *A. sativum* significantly enhanced the antihyperglycemic activity of gliclazide from the 2nd to the 8th h, except for the 4th h. These findings indicate the existence of a pharmacodynamic interplay between *A. sativum* and gliclazide, as depicted in Table I[8,9].

CONCLUSION

The study's results provided evidence of an interaction between *A. sativum* and gliclazide in diabetic Wistar rats. Moreover, it was apparent that *A. sativum* had an independent effect on blood glucose levels. Hence, the observed interaction between gliclazide and *A. sativum* can be attributed to either pharmacodynamic or pharmacokinetic mechanisms.

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