



ISSN: 2277- 7695

TPI 2016; 5(10): 56-59

© 2016 TPI

www.thepharmajournal.com

Received: 10-08-2016

Accepted: 12-09-2016

Thakur Rohit Singh

Asst Professor, Dept of
Pharmacology, MRIMS,
Hyderabad, Telangana, India

Dr. Jamuna Rani

Professor, Dept of
Pharmacology, MRIMS,
Hyderabad, Telangana, India

Dr. TS Hemlatha

Professor, Dept of
Pharmacology, MNR Medical
College, Kukatpally,
Hyderabad, India

Dr. Jyothsna

Asst Professor, Dept of
Pharmacology, MRIMS,
Hyderabad, Telangana, India

Study of hypoglycemic effect of corosolic acid & its comparative evaluation with standard drug glibenclamide in alloxan induced diabetes in female albino mice

Thakur Rohit Singh, Dr. Jamuna Rani, Dr. TS Hemlatha and Dr. Jyothsna

Abstract

Aims & objectives: To evaluate the antidiabetic effect of corosolic acid in comparison with standard drug glibenclamide.

Background: Diabetes mellitus, commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. The discovery of insulin and its crystallization has revolutionized the therapeutic goal for diabetic mellitus. The chief drawback of insulin is it must be given by injection. Orally active drugs have always been in searched. Many studies have been proved the hypoglycemic effect of corosolic acid in animals. But thorough evaluation of hypoglycemic effect of corosolic acid with standard hypoglycemic drugs have to be proved. Hence the present study aims in evaluating the hypoglycemic effect of corosolic acid in comparison with standard drug glibenclamide.

Methods: Adult swiss albino mice weighing between 25-35gms were taken. The mice were divided in three groups (n=10). Group I-control served with distilled water; Group II-test group treated with 2mg/kg b.w corosolic acid; Group III-standard group, treated with 2.5mg/kg b.w glibenclamide. FBS was taken before & after induction of diabetes in group II & III using glucometer and results were tabulated in comparison with mean FBS of control group (group I).

Results: The results were expressed as mean \pm S.D. Statistical difference was tested by using students t-test. A difference in the mean P value <0.05 was considered as significant. Corosolic acid produces consistent hypoglycemic effect at the end of 4th week in comparison with standard drug glibenclamide with extremely significant P value ($P<0.01$). Mean percentage FBS reduction with corosolic acid in comparison with control group was 18% with extremely significant P value (<0.01) at the end of 4 weeks treatment and glibenclamide produced mean percentage FBS reduction of 31% with extremely significant P value ($P<0.01$) at the end of 4th week in comparison with control group.

Conclusion: corosolic acid has produced marked hypoglycemia in comparison with standard drug glibenclamide at the end of 4th week.

Keywords: Corosolic acid; glibenclamide; alloxan induced diabetes; hypoglycemia

Introduction

The word medicinal herbs often leads to the thought of some super natural cures. In olden days, the medicines prescribed by saints earned more favour and reputation than the ones based on some test and experience. It has been estimated that nearly about 2000 drugs have been used in curing human ailments in India since ancient periods. Out of these 2000 drugs, 200 are of animal origin and 200 are of mineral origin. The rest about 1500 are of herbal origin. Tremendous progress have been made in research on herbal medicine viz pharmacognosy, phytochemistry, pharmacology of plant products all over the world. Hence for over all development of the drug research, pharmacological research studies have very important role to play ^[1]. Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period ^[2]. The word diabetes means a siphon or running through and mellitus is a Latin word means sweetened like honey, was used by aerates the Cappadocia in second century. A.D to describe polyurea. He also noted thirst and emaciation as features of this fatal disease ^[3, 4]. A description of diabetes mellitus provided by Galan (130.A.D) was almost similar to that of aerates ^[5]. Diabetes Mellitus is a syndrome which is characterized by persistent hyperglycemia with or without glycosuria and which results in a derangement in mechanisms of blood sugar homeostasis ^[6].

The discovery of insulin and its crystallization has revolutionized the therapeutic goal for diabetic

Correspondence

Thakur Rohit Singh

Asst Professor, Dept of
Pharmacology, MRIMS,
Hyderabad, Telangana, India

mellitus. Insulin is chiefly required for rapid control of blood glucose like diabetic coma, diabetic ketoacidosis, pregnancy and other diabetic related complication. There have been several approaches for control of blood glucose level in maturity onset diabetes mellitus and in patients who are non-insulin dependent. One such approach has been discovery of oral antidiabetic drugs [7]. The chief drawback of insulin is it must be given by injection. Orally active drugs have always been in searched. The early sulfonamides tested in 1940s produced hypoglycemia as side effect taking this lead first clinically acceptable tolbutamide was introduced in 1957. Others followed soon after. In 1970s many so called second generation sulfonyl ureas have been developed which were 20-100 times more potent [8].

Corosolic acid is a triterpenoid compound isolated from leaves of plant *Lagerstroemia speciosa* L. (Lythraceae) commonly known as Crepe Myrtle, grows widely in Philippines, India, Malaysia, China. *Lagerstroemia speciosa* is a popular folk medicine in Philippines, a tea from the leaves has been used in the treatment of diabetes mellitus [9,10]. Many studies have been proved the hypoglycemic effect of corosolic acid in animals and *in vitro* models. But the comparative evaluation of corosolic acid with standard oral hypoglycemic agent need a thorough evaluation for which the present study aims at evaluation of antidiabetic effect of 1% corosolic acid in comparison with standard oral hypoglycemic agent glibenclamide.

Aim & objectives

To evaluate the antidiabetic effect of 1% corosolic acid in comparison with standard hypoglycemic drug glibenclamide.

Methodology of study

Ethical approval from Institutional Animal Ethics Committee was taken. Animals were divided into three groups v.i.z Group I (control); Group II (test); group III (Standard) each group comprising of 10 animals (n=10). The animals in group II and Group III were induced diabetes with alloxan. Animals were considered to be diabetic with 2-3 fold increase in glucose levels compared to control group.

Feeding of extract & standard drug glibenclamide in diabetic mice.

1% Corosolic acid extract 2mg/kg b.w (group II) and glibenclamide 2.5mg/kg b.w (group III) were administered to mice orally by polythene tube of diameter 2mm.

Group I –Control Mice

Group I mice served as control and all mice in this group received an equal volume (20ml/kg) of distilled water. Mice were fasted overnight but given ad libitum. Blood samples from mice were collected by orbital sinus puncture using heparinised capillary glass tube. The blood samples so collected were analysed for glucose levels employing glucostrips with glucometer at the end of each week for 4 consecutive weeks. Fasting blood sugar levels were analysed and readings were tabulated. (Table 1)

Group II-Test Mice

The mice in this group were administered intraperitoneally alloxan monohydrate (80mg/kg b.w) prepared in acetate buffer (0.15M, pH 4.5) 3 days before the start of experiment. Prior to administration animals were fasted overnight but given water ad libitum. After alloxan was administered within 24hrs all the animals were administered with 5% glucose orally as they were likely to go in a state of hypoglycemia during first 24hrs. Initial

hypoglycemia was followed by persistent and permanent hyperglycemia. At the end of 72hrs on 3rd day blood samples from mice were collected by orbital sinus puncture using heparinised capillary glass tube. The blood samples so collected were analysed for glucose levels employing glucostrips with glucometer. Then the mice were treated with 1% corosolic acid at a dose of 2mg/kg b.w suspended in 20ml of distilled water once a day orally for 4 weeks of duration. At the end of each week for 4 consecutive weeks fasting blood sugar levels were analysed by collecting blood samples by orbital sinus puncture, using glucometer and results were tabulated. (Table 2)

Group III-Standard Mice

Mice in this group were induced diabetes using alloxan monohydrate as described in group II. After induction of diabetes with alloxan, mice received standard drug glibenclamide 2.5mg/kg b.w. by oral route. The drug was dissolved in 20ml of distilled water (20ml/kg) and was administered for 4 weeks. At the end of each week for 4 consecutive weeks fasting blood samples were taken from mice and FBS was analysed using glucometer and results were tabulated. (Table 3)

Measurement tools

Type of study: Informal experimental design-before and after with control design.

Study area: Malla reddy institute of medical sciences.

Duration of study: 4 weeks.

Sample size- n=30; Group I (control group)-10 mice; Group II (test group)-10 mice.; Group III (standard group)-10 mice.

Chemicals

Alloxan was procured from light Kieran laboratories, Bombay. 1% corosolic acid was obtained from indfrag ltd, Bangalore. Glibenclamide from medreich PLC, UK. While other chemicals were of analytical grade obtained from E. Merch and Hi-media, India.

Study animals: Healthy adult swiss female albino mice approximately 4 months in age, weighing between 25-35 g were used for the study. All the animals were kept under ambient temperature on 12h light and 12 h dark cycle and were fed balanced mice feed.

Collection of plant material.

Crude extract of 1% corosolic acid was purchased from INDFRAG LTD, Bangalore, India. Its identification was made on botanical and pharmacological basis. The macroscopic study of drug was made with naked eye and confirmation was made on basis of literature description.

Preparation of extract.

1% crude extract of corosolic acid was pulverized in to fine powder and it was mixed with methanol at a ratio of 1:5. After 24hrs, the mixture was filtered. Filtrate was collected and the residue was again mixed with methanol at a ratio of 1:2 for 24hrs. After filtration, the filtrates were combined and evaporated to dryness using rotary evaporator. Preliminary phytochemical screening revealed the presence of triterpenoid, tannins, polyphenolic compounds.

Statistical Analysis

The results were expressed as mean \pm S.D. Statistical difference was tested by using students t-test with Spss statistical software.

A difference in the mean P value <0.05 was considered as significant.

Discussion

Previous studies have shown that corosolic acid possesses marked hypoglycemic effect which has been demonstrated in animals and *in vitro* studies. When genetically diabetic mice (type II) were fed a diet containing hot water extract for 5 weeks their elevated blood glucose levels was suppressed [11]. A dose dependent study of corosolic acid has been demonstrated in randomized clinical trial involving type II diabetes showed a significant reduction in blood glucose levels [12]. There are plants which exhibit properties similar to sulfonylurea drugs like glibenclamide, effecting hypoglycemia in normal animals by stimulating release of insulin from pancreatic β -cells [13, 14]. As a cytotoxic agent to the insulin-secreting cells of the pancreas, alloxan effectively induces diabetes in a wide variety of animal models [15]. Thus, it allows elucidation of antihyperglycemic agents in the treatment of diabetes. Alloxan-induced diabetes consistently produced the main characteristics of diabetes mellitus including polydipsia, polyphagia, polyuria, decreased insulin levels, weight loss and hyperglycemia. This study evaluated the blood glucose levels, in experimental diabetes induced by alloxan in mice. In control group only the mean FBS levels were maintained without induction of diabetes. All the mice in this group had well controlled glycemia for 4 weeks. The mean \pm SD for FBS at the end of each week for 4 consecutive weeks is shown in table 1 and fig 1. In our present study corosolic acid produces consistent hypoglycemic effect at the end of 4th week in comparison with standard drug glibenclamide with extremely significant P value ($P < 0.01$)

(Table 4). Mean percentage FBS reduction with corosolic acid in comparison with control group was 18% (fig2) with extremely significant P value (< 0.01) at the end of 4 weeks treatment (table 2) and glibenclamide produced mean percentage FBS reduction of 31% (fig 3) with extremely significant P value ($P < 0.01$) (table3) at the end of 4th week in comparison with control group (fig-3).

Results

Table 1: (group 1) control group.

Mean \pm Sd	1 st week	2 nd week	3 rd week	4 th week.
	78.6 \pm 12.03	79.4 \pm 12.30	80.1 \pm 11.33	80.3 \pm 11.54

Mean \pm SD for fasting blood sugar at the end of each week.

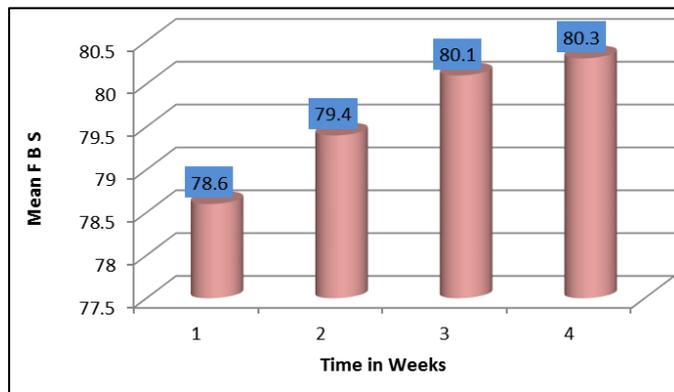


Fig 1: Control group mice mean fasting blood sugar level.

Table 2: Group II (test group) treatment with corosolic acid

Time in weeks	Before alloxan	After 72hrs,alloxan induction	1 st week	2 nd week	3 rd week	4 th week
Mean \pm SD FBS	97.8 \pm 29.61	194.5 \pm 7.7	132.2 \pm 31.1	120.6 \pm 21.5	111.2 \pm 40.4	104 \pm 19.2
P value	0.664	0.130	0.001	0.001	0.0305	0.0001

Mean \pm SD; P Value for FBS before alloxan & after 72 hrs of induction of alloxan and treatment with corosolic acid.

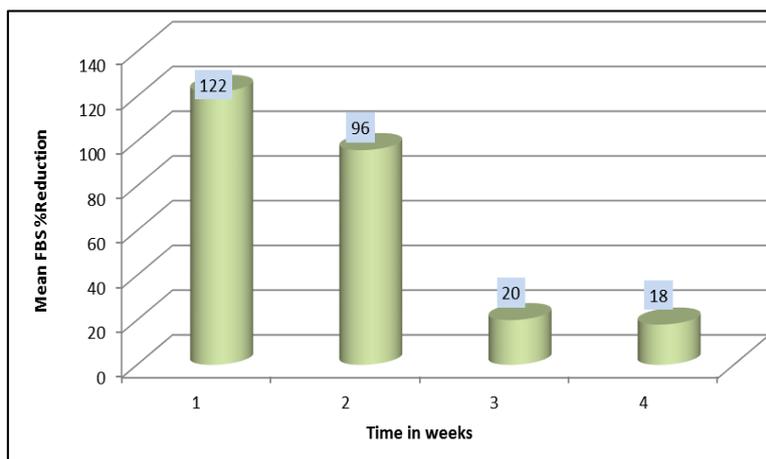


Fig 2: mean % FBS reduction –Control mice vs Corosolic acid (group II)

Table 3: Group III (Standard group)-Treatment with glibenclamide.

Time in weeks	Before alloxan	After 72 hrs of alloxan	1 st	2 nd	3 rd	4 th
Mean \pm SD, FBS	102.2 \pm 10.01	189.9 \pm 7.5	169.8 \pm 14.2	152.2 \pm 14.7	121.5 \pm 6.7	98.6 \pm 8.0
P value.	0.664	0.130	0.0001	0.0001	0.0001	0.0001

Mean \pm SD; P value for FBS before alloxan & after 72 hours of induction of alloxan and treatment with glibenclamide.

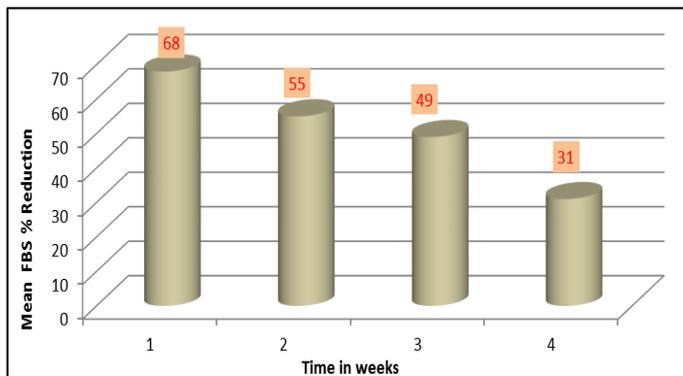


Fig 3: Mean % FBS reduction-Control mice vs Glibenclamide.

Table 4: P value - group II (test group) Vs group III (standard group)

Time in weeks	1 st	2 nd	3 rd	4 th
P value	0.0029	0.0012	0.435	0.0001

Conclusion

The readings obtained in laboratory suggest that corosolic acid has produced marked hypoglycemia i.e 18% FBS reduction in comparison with standard drug glibenclamide i.e 31% at the end of 4th week. Corosolic acid has not induced hypoglycemia even after 4weeks in comparison to glibenclamide. Experimentally corosolic acid have proved to be effective hypoglycemic agent with that of standard drug glibenclamide. Hence, furthur evaluation & clinical trial based studies are required to establish the efficacy of CA to that of standard drug glibenclamide. Furthur investigations are required to study its usefulness in type 1 diabetes mellitus and its actions in normal persons.

References

1. Anonymous: Wealth of India, A Dictionary of Indian Raw Material and Industrial Products, C.S.I.R. Publication and information directorate, New Delhi. 1976; X(P):78-81.
2. About diabetes. World Health Organization. Retrieved. 2014.
3. Cyril Akeele, Eric Nell, Norman Joels. Samson wrights applied physiology, Oxford University, Waltson street, Oxford; OX26DP, 13th Ed. 1992, 508.
4. Anonymous, Encyclopedia Britanica printed by university of Chicago, 5th Ed. 1992; 1:538.
5. Bynum WF. Companion encyclopedia of history of medicine, Rout ledge publication 11-New Fetterlave, London. 1994; P: 485-86.
6. William Boyd; Text book of pathology. Lea and Febriger, Philadelphia, 7th Ed. 1967, 837.
7. Goodman, Gilman. pharmacological basis of therapeutics, 8th Ed., 2(P):1463-1468.
8. Tripathi KD. Essentials of Medical Pharmacology. 15th Ed. 2003, 245-246.
9. Matsuyama F. Composition for inhibiting increase of blood sugar level or lowering blood sugar level. United states Patent application No.09/730,741; filed December 7,2000. 2001.
10. Quisumbing E. Medicinal plants of the phillippines. Katho publishing, Quezon city, 1978, 640-642.
11. Kakuda T, Sakane I, Takihara T, Ozaki Y, Takeuchi H, Kuroyanagi M. Hypoglycemic effect of extracts from lagerstroemia speciosa L. leaves in genetically diabetic KK-AY mice. Bioscience, Biotechnology and Biochemistry (Tokyo). 1996; 60:204-208.

12. William V Judy, Siva P Hari. Journal of Ethnopharmacology. 2003; 87:115-117.
13. Ivorra, MD, Paya M, Villar A. Hyoglycemic and insulin release effects of tormentric acid. A new hypoglycemic natural product. Plant medica. 1988; 54:282-286.
14. Davis SN, Granner DK. Insulin, oral hypoglycemic agents and the pharmacology of the endocrine pancreas. In: Goodman LS, Gilman AG. (Eds.), The Pharmacological Basis Of Therapeutics, 9th Ed. Mcgraw Hill, New York, 1996, 1487-1511.
15. Reyes BAS, Bautista ND, Tanquilut NC, Anunciado RV, Leung AB, Sanchez GC *et al.* 2006.