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ANTIDIABETIC ACTIVITY OF ACACIA ARABICA LEAVES ON STREPTOZOTOCIN INDUCED RATS

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Abstract:

Diabetes mellitus (DM) is a major public health disorder affecting quite 400 million people worldwide. [1] It is group of common metabolic disorders that arising from variety of pathogenic mechanisms which are all results in high blood glucose level. Management of diabetes without any side effects is still a challenging for medical system which leads to an increasing search for improved antidiabetic drugs. The objective of this study was to evaluated antidiabetic activity of hydroalcoholic extract of Acacia arabica leaves. The hydroalcoholic extract of leaves of Acacia arabica were evaluated at different doses (100 mg/kg of body weight) for antidiabetic potential in streptozotocin induced rats. The extracts were administered for three weeks in different groups whereas glibenclamide (5 mg/kg body weight) was used as reference standard throughout study. All values are expressed as mean ± SEM. The differences were compared using one way analysis of variance (ANOVA) followed by Tukey Kramer Multiple comparison tests. P values < 0.05 were considered as significant. Chronic treatment with the hydroalcoholic extract of Acacia arabica at 100 and 200 mg/kg of body weight significantly (P < 0.001) causes decrease in blood glucose on 1ST, 7th, 14th and 21st day as shown in figure 1, 2, 3 and 4. The present investigation supports the hypoglycemic effects of extracts of ethnic folk medicine which mitigates pathological states like diabetes mellitus.

Key-words: Streptozotocin, acacia arabica, glibenclamide, hypoglycemia.

1 INTRODUCTION

Diabetes mellitus (DM) is a major public health disorder affecting quite 400 million people worldwide. [1] It is group of common metabolic disorders that arising from variety of pathogenic mechanisms which are all results in high blood glucose level. The number of individuals is rising rapidly throughout the world. Both genetic and environmental factors contribute its pathology which involves lowers in insulin secretion, decreased insulin sensitivity, increase in glucose production and abnormalities in fat and protein metabolism. Hyperglycemia may lead to acute symptoms and metabolic abnormalities. [2] But, rates of morbidity of diabetes increased due to chronic complications that arise from prolonged hyperglycemia including retinopathy, neuropathy, nephropathy and cardiovascular disease. These chronic complications can be mitigated in many patients by sustained control of the blood glucose and treatment of comorbidities such as hypertension and dyslipidaemia. [3] Management of diabetes without any side effects is still a challenging for medical system which leads to an increasing search for improved antidiabetic drugs. Few of plant treatments used in traditional medicine for diabetes received scientific scrutiny and WHO has recommended that this area warrants attention. [4]

Table.1 Classification of Diabetes

Sr. No.	Type	Characteristic features
1.	Type 1	Selective degradation of β-cells in genetically susceptible individuals. Self-antibodies damage our own body tissues unknown cause. [5]
2.	Type 2	Results in peripheral insulin resistance, thereby results in decreased insulin sensitivity to the skeletal muscles, adipose tissues and liver. [6]
3.	Gestational Diabetes	Diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation. [7]

Acacia arabica commonly known as babul or gum arabic tree [8] belongs to the family Mimosaceae [9] extensively found in India, Arabia, Sudan and Kordofan (North- East Africa), Sri Lanka, Morocco, and Senegal (West Africa). Sudan is the major producer of acacia gum and caters for about 85% of the world supply. [10] Acacia arabica possesses antiviral [11], antibacterial [12], antifertility [13], antimutagenic, antiproteolytic [14], antihypertensive, antidiarrhoeal, and galactagogue activities. [15] The objective of the this study was to evaluated antidiabetic activity of hydroalcoholic extract of Acacia arabica leaves.

2 MATERIALS AND METHODS

2.1 Chemicals and Drugs

Streptozotocin were purchased from M. P. Biomedical Navi Mumbai. Glibenclamide was gift from Cipla Pvt. Ltd. Methanol was procured from Thermosil Chemicals. Sodium hydroxide, lead acetate was procured from ACME Chemicals. Fehlings Solution, Ferric chloride Hydrochloric acid, Sulphuric Acid, Conc. Nitric acid were procured from SD fine chemicals Ltd.

2.2 Plant Material

The leaves of Acacia arabica were collected from Amravati District, Maharashtra, India. The plants were identified and authenticated by Namrata Kakpure, Department of Botany, Vidyabharati Mahavidyalaya, Amravati. The leaves were cleaned, dried in shade. The leaves were kept in air tight container for further studies.

2.3 Exerimental Animals

The albino rats of wistar strain of either sex weighing 160- 200 gm were procured from Hyderabad. They were kept at 24 ± 2 0C with 50% ± 10% of relative humidity and light/ dark cycle for 12 hours. All animals were fed with rodent pellets and water ad-libitum under strict hygienic conditions. Institutional Animal Ethics Committee (IEAC) approved all the protocol of the study.

2.4 Preparation of Extract

Dried leaves of Acacia arabica (100 gm) were extracted with methanol : water (1:1) [16] as solvent by Soxhlet extraction and solvents were evaporated and concentrated on water bath at controlled temperature. The yield of extract was found to be 10.58%.

2.5 Preparation of Diabetic Rats

Streptozotocin dissolved in 0.1M citrate buffer of pH 4.5 was injected in rats intraperitoneally at dose of 50 mg/kg body weight. Rats were fed with 5% dextrose solution to overcome overnight hypoglycemia. After 48 hours, rats with marked hyperglycemia were selected and used for the study. [17]

2.6 Acute Toxicity Study

The wistar albino rats of 150- 180 gm (n = 6) were used for the acute toxicity. The animals were fasted overnight prior to experimentation. The animals were kept at room temperature of 220 ± 30 C with relative humidity of 50- 60% and 12 hours light and 12 hours dark cycle. Acute toxicity study of extract of leaves of Acacia arabica was carried out by using fixed dose procedure of CPCSEA guideline no. 420. After the substance administration food was withheld for 3- 4 hours. Animals were monitored for one week for any sign of toxicity. [18]

2.7 Experimental Design

The rats were divided into five groups. Group I (controlled group) administered with 0.5 ml citrate buffer, Group II (untreated diabetic rats), Group III (diabetic rats receiving glibenclamide orally at 5 mg/kg body weight in saline), Group IV and Group V (receiving 100 mg/kg and 200 mg/ kg of body weight of test extracts respectively). Glibenclamide was used as the

standardantidiabetic throughout the experimentation. The were carefully monitored everyday. Animals described as fasted were deprived of food for at least 12 hours but allowed to free access for drinking water. Fasting blood glucose measurement was done on day 1, 7th , 14th and 21st of the study. Boold glucose levels were measured by glucometer. [19]

2.8 Statistics

All values are expressed as mean ± SEM. The differences were compared using one way analysis of variance (ANOVA) followed by Tukey Kramer Multiple comparison tests. P values < 0.05 were considered as significant.

3 RESULT

In streptozotocin treated diabetic rats, values of glucose were elevated to high level during the study where body weight decreased. Chronic treatment with the hydroalcoholic extract of Acacia arabica at 100 and 200 mg/kg of body weight significantly (P < 0.001) causes decrease in blood glucose on 1ST, 7th, 14th and 21st day as shown in figure 9, 10, 11 and 12.

Table No. 2 Average Blood Glucose Profile

Group/Treatment	Average blood glucose (mg/dl)			
	Day 1	Day 7	Day 14	Day 21
Untreated Normal	85.17± 0.7***	89 ± 1.23***	89.5 ± 0.99***	88.5 ± 0.76***
Untreated Diabetic	352.83 ± 3.49	356.3 ± 3.12	358.33 ± 3.12	362.3 ± 2.39
Diabetic+ Glibenclamide (5 mg/kg)	253.7±1.2***	152.2±2.12***	114.8 ± 1.4***	93.83± 1.7***
Diabetic+ Extract (100mg/kg)	304.5 ± 1.4***	225±1.4***	150.5±2.4***	120.3±1.2 ***
Diabetic+ Extract (200mg/kg)	320.2±1.4***	201.2±2.21***	128 ± 2.12 ***	113.8 ±1.3 ***

Values expressed as mean ± SEM: (n=6)

*p < 0.05, ***p < 0.001 compared with untreated diabetic rats

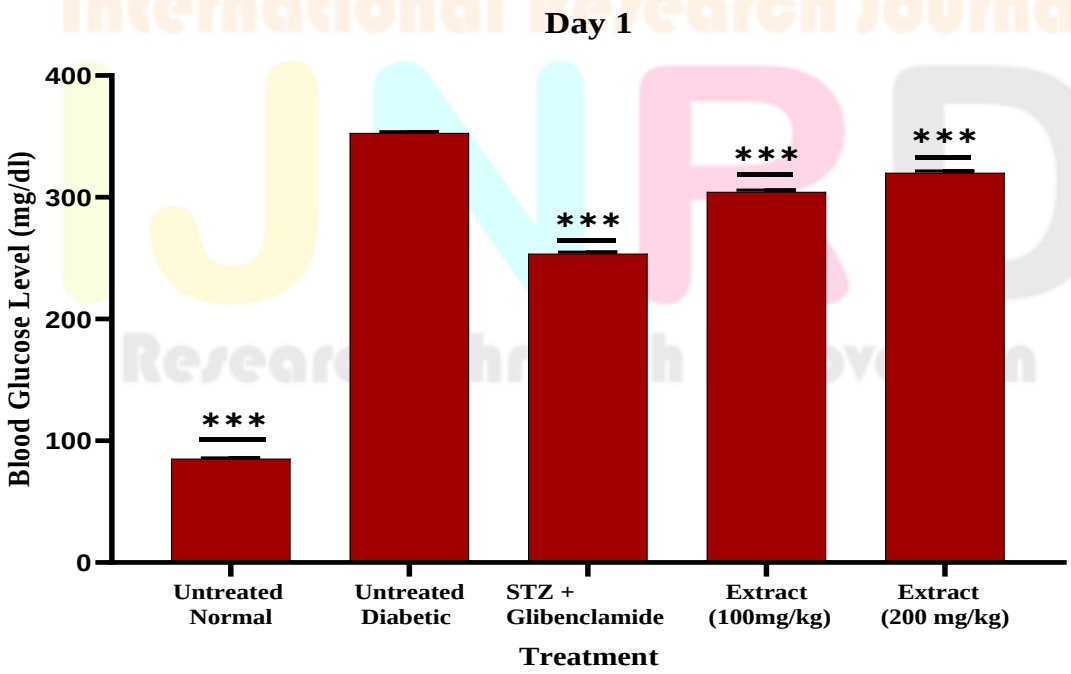

Figure No. 1 Effect of Acacia arabica on blood glucose level on 0 day.

All values are expressed as mean ± SEM (n=6). Statistical comparisons between each treatment and untreated diabetic rats were carried out by one way ANOVA followed by Tukey- Kramer Multiple comparison test. *** P< 0.001 when compared to untreated diabetic group.

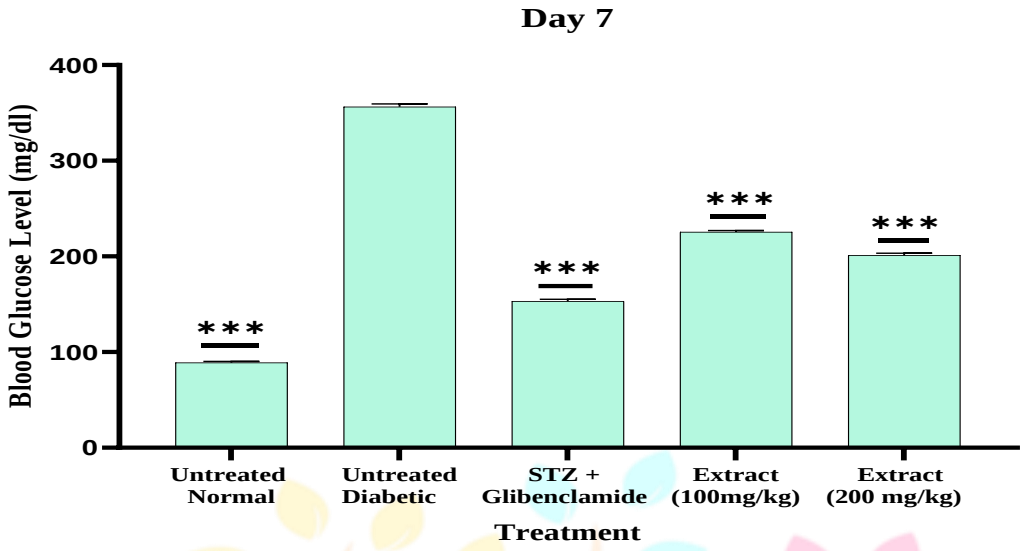

Figure No. 2 Effect of Acacia arabica on blood glucose level on 7 day.

All values are expressed as mean ± SEM (n=6). Statistical comparisons between each treatment and untreated diabetic rats were carried out by one way ANOVA followed by Tukey- Kramer Multiple comparison test. *** P< 0.001 when compared to untreated diabetic group.

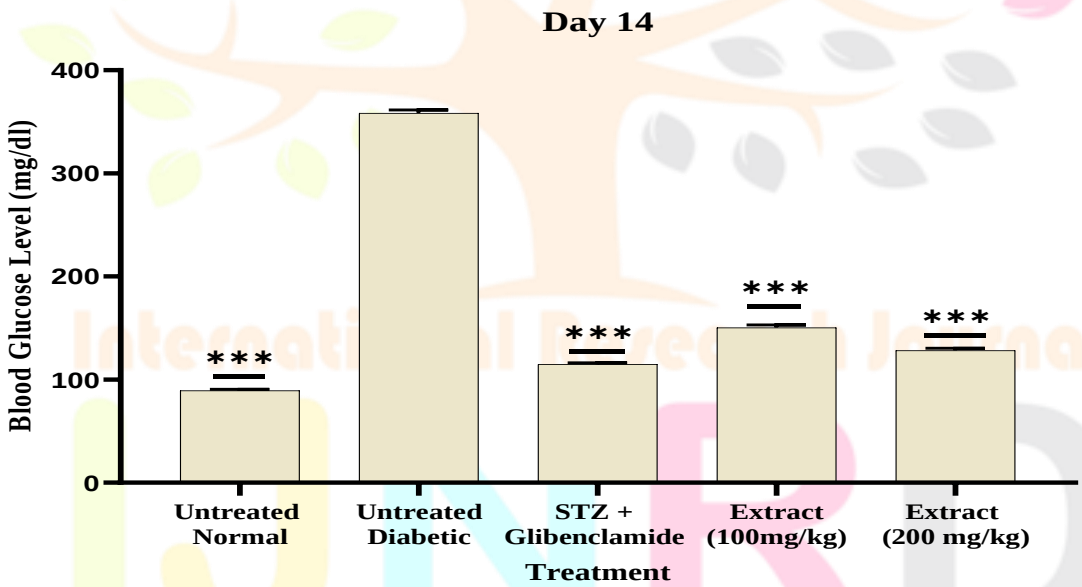

Figure No. 3 Effect of Acacia arabica on blood glucose level on 14 day.

All values are expressed as mean ± SEM (n=6). Statistical comparisons between each treatment and untreated diabetic rats were carried out by one way ANOVA followed by Tukey- Kramer Multiple comparison test. *** P< 0.001 when compared to untreated diabetic group.

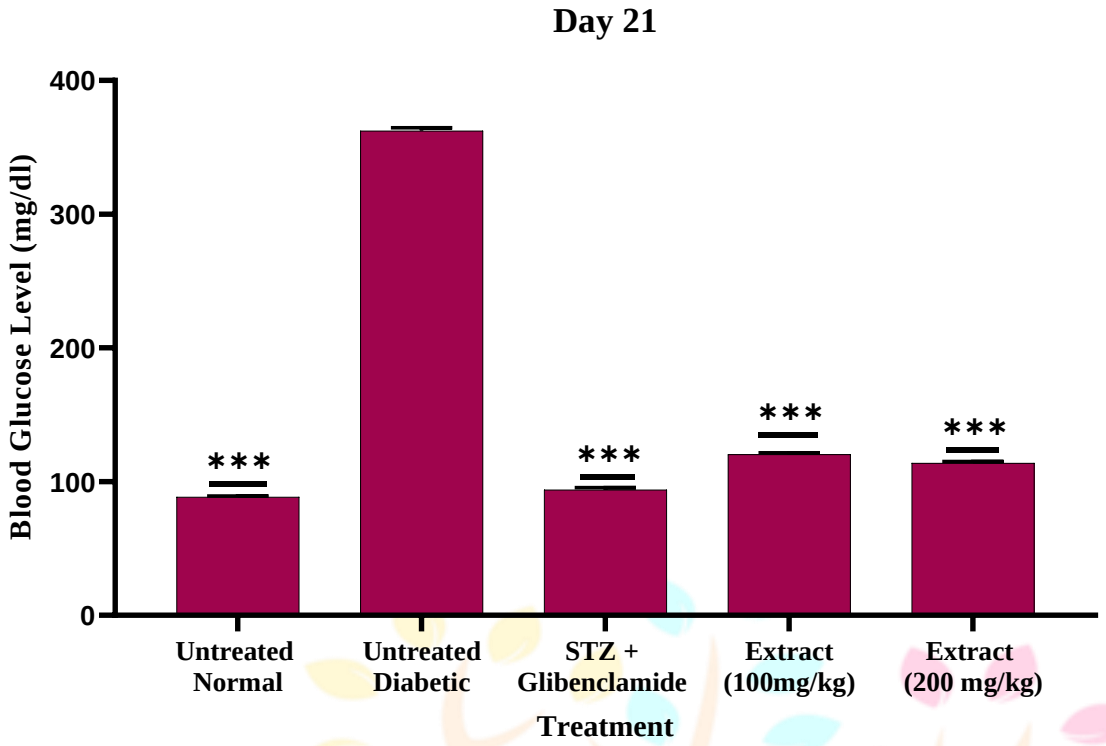

Figure No. 4 Effect of Acacia arabica on blood glucose level on 21 day.

All values are expressed as mean ± SEM (n=6). Statistical comparisons between each treatment and untreated diabetic rats were carried out by one way ANOVA followed by Tukey- Kramer Multiple comparison test. *** P< 0.001 when compared to untreated diabetic group.

4. DISCUSSION

Diabetes mellitus is chronic disorder caused by insulin deficiency or insulin resistance or both. Both genetic and environmental factors contribute its pathogenesis which involves decrease in insulin secretion, decreased insulin sensitivity, increase in glucose production and abnormalities in fat and protein metabolism. Insulin and oral hypoglycemic drugs, which are considered to be main line treatment of diabetes have many side effects and were not able to significantly control diabetic complication. Recently, attention was paid again to alternative and natural therapies. Currently, it is estimated that many plants are used traditionally for the treatment of diabetes. Streptozotocin is cytotoxic to the pancreatic beta cell thus it is an effective diabetes induction agent. Streptozotocin has been observed to cause a massive reduction of beta cell of islet of langerhans. [20]

In this study, hydroalcoholic extracts of Acacia arabica were evaluated for the management of streptozotocin induced diabetic model used in this study was type 2 diabetes since low dose of streptozotocin (50 mg/kg) destroys only part of pancreatic beta cells which secrete in adequate amount of insulin. In this study, continuous treatment with two different doses of hydroalcoholic extracts of Acacia arabica (100 and 200 mg/kg) for 21 days is given after the induction of diabetes mellitus. Glucose determination is done by glucometer on 1st, 7th, 14th and 21st day. Glucose levels decreases gradually during the continuous treatment of 21 days. After the induction of diabetes, glucose levels of rats were above 400 mg/dl which get reduced to about 304.5±1.4 mg/dl and 320.2±1.4 mg/dl after administration of extract at dose 100mg/kg and 200 mg/kg respectively on 1st day. On 7th day, the glucose levels were reduced up to 225.5±1.4 mg/dl and 201.2±2.21 mg/dl when dosed at 100 and 200 mg/kg respectively. On 14th day of the study glucose levels lowered up to 150.5±2.4 mg/dl and 128.2±2.12 mg/dl which fell up to normal level on 21st day i.e. 120.3±1.2 mg/dl and 113.8±1.3 mg/dl with dose of extract at 100 and 200 mg/kg respectively.

Observation in this study correlates with the previous research findings, in that the blood glucose levels significantly increased in streptozotocin induced untreated diabetic rats. In the present study, the continuous treatment of test compound for period of three weeks caused a significant decrease in blood glucose levels in treated diabetic rats.

5 CONCLUSION

In conclusion, the present investigation supports the hypoglycemic effect of extract of ethnic folk medicine which mitigates pathological state like diabetes mellitus. The hydroalcoholic extract of Acacia arabica improves the glucose levels and metabolic abnormalities in STZ induced rats through increasing insulin levels. Extract of Acacia arabica acts by suppressing the glucose level, reducing plasma cholesterol and triglycerides significantly and increasing hepatic glucokinase activity probably by enhancing the insulin release which acts as glucose sensor in the beta cell by controlling the rate of entry of glucose in glycolytic pathway and its subsequent metabolism. In the liver, glucokinase play a key role in the ability to store glucose as glycogen,

particularly in the postprandial state. Also, it inhibits alpha glucosidase that breaks down starch and disaccharides to glucose and decrease glucose transport through the intestinal epithelium. Efficacy of this extract is appreciably good when compared to standard drug glibenclamide. Therefore, it can be investigated for its efficacy in the treatment of diabetes in humans.

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