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Research Article

Antihyperglycemic activity of ethanolic extract of lantana camara linn leaves induce by STZ model on rats"

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Abstract

The study was aimed at investigating the effect of ethanol leaf extract of Lantana camara on the fasting blood glucose, body weight and kidney function indices of alloxan-induced diabetic albino Wistar rats. Thirty male albino Wistar rats of weight 100-181 g were randomly assigned six groups of five rats each. Group 1 was used as the standard control. Group 2-6 mice were induced with 150 mg/kg body weight (B.W) of alloxan monohydrate intraperitoneal.

Animals were deemed diabetic if their fasting blood glucose levels were 200 mg/dl or above 72 hours after induction. Glibenclamide at a dose of 50 mg/kg B.W. was administered to Group 3. For 21 days, 600, 800, and 1000 mg/kg B.W. of Lantana camara extract were administered orally to groups 4, 5, and 6. Using a glucometer, a blood sample was drawn via tail puncture once a week to measure glucose levels. When compared to untreated diabetic animals, animals treated with 600, 800, and 1000 mg/kg B.W. of the extract exhibited a substantial ($P<0.05$) drop in blood glucose, creatinine, urea, and uric acid.

When compared to the untreated group, the treated groups' body weight increased significantly ($P<0.05$). The outcomes were identical to those of the group treated with glibenclamide. This implies that the extract may be utilized to treat diabetes because it has antidiabetic properties.

Keywords: Diabetes; Lantana camara; alloxan; glucose; kidney function.

Introduction :

A pancreatic metabolic disease called diabetes mellitus causes abnormalities in insulin secretion or inactivity of insulin to glucose, which changes the metabolism of glucose [1]. Hyperglycemia, excessive thirst, and frequent urination are the condition's hallmarks. Antoimmune death of β-cells and subsequent insulin shortage (Type I) or loss in insulin activity (Type II) are the first of multiple aetiological progressions of diabetes mellitus. [2].

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But "the two forms of diabetes exacerbate the changes in the metabolism of proteins, fats, and carbohydrates, leading to microvascular and macrovascular complications" [3]. "Other complications of diabetes mellitus include but are not limited to retinopathy with potential loss of vision, cardiomyopathy, neuropathy, hepatocellular carcinomas, nephropathy, which leads to dysfunction of renal function architecture" [4].

One of the main causes of morbidity and death is acknowledged to be diabetes mellitus (DM). Between 2017 and 2045, the incidence of diabetes may increase by 48% worldwide, according to [5]. Thus, controlling blood sugar is a critical tactic for reducing hyperglycemia and the difficulties that come with it, as well as for enhancing the quality of life for diabetes patients [6].

Materials and Methods[6-13]

Collection of Preparation of Plant Extract

"Leaves of lantana camara were gathered from a Bhopal locality. A botanist from Barkatullaha University Bhopal's Department of Botany recognised and verified the leaves. After being separated from their stems, fresh Lantana camara leaves were sorted, cleaned with distilled water, cut into slices, and allowed to dry in the shade. An electric blender was used to grind the dried leaves into a fine powder. The powder was then extracted in 70% ethanol with intermittent stirring, macerated for 72 hours, and filtered using Whatman No. 4 filter paper, weighing 110 g. After being heated to 40˚C in a water bath, the filtrate was concentrated to paste and kept at 4˚C for analysis [7].

Induction of Diabetes

Thirty albino Wistar rats, weighing between 100 and 180 gm, were acquired from the Department of pharmacology animal house at Oriental College of pharmacy, Bhopal. Prior to the trial, the animals were acclimated for two weeks and given commercial feed and clean drinking water on an as-needed basis. The rats were split into two groups: the diabetic group and the non-diabetic control group [8].

After an overnight fast, 150 mg/kg body weight of alloxan monohydrates dissolved in 0.9% saline was administered intraperitoneally to the experimental rats to induce diabetes. Following induction, all rats were given unrestricted access to food and potable water.

A blood sample taken from the rats' tail tip puncture was utilised to confirm diabetes in the animals 72 hours after

induction. A glucometer was used to check for hyperglycemia. Albino Wistar rats were chosen for the experiment if their fasting blood glucose level was 200 mg/dl or more, which is termed diabetes. The Institute for Laboratory Animal Research's criteria were followed when using albino Wistar rats for the study [9].

Experimental Design

The 30 albino rats were divided into 6 groups of 5 rats each.

Group 1 - Normal Control Group

Group 2 - Diabetic untreated group

Group 3 - Diabetic treated group (received 5 mg/kg body weight glibenclamide).

Group 4 - Diabetic rats received 600 mg/kg body weight of Lantana camara

Group 5 - Diabetic rats received 800 mg/kg body weight of Lantana camara

Group 6 - Diabetic rats received 1000 mg/kg body weight of Lantana camara

Treatment was administered once a day orally for 21 days.

Determination of Blood Glucose Concentration

During the trial, five fasting blood glucose readings were taken. Initially, prior to alloxan inducing diabetes. Second, 72 hours after diabetes was induced. During the first, second, and third weeks of treatment, the measurement was repeated. The albino Wistar rats' tails were sterilised with 10% alcohol, punctured with needles, and the released blood was allowed to come into contact with the test strip, which was then placed into a calibrated glucometer (fine test glucometer) to measure the blood glucose levels. After 9 seconds, a direct reading in mg/dL was obtained.

Measurement of Body Weight

Using an ordinal weighing scale, the animals' body weight was recorded five times over the 21-day treatment period: before the alloxan injection (baseline values), 72 hours after the injection, and during the first, second, and third weeks of the treatment period.

Sample Collection for Analysis

At the end of 21 days treatment, the rats were made to fast overnight and then euthanized under chloroform vapour and sacrificed. Whole blood was obtained by cardiac puncture into non-heparinized tubes and were allowed to clot for 1 hour 30 minutes. The sample was then centrifuged at 4000rpm for 30 minutes to recover the serum for the various biochemical assays.

Biochemical Assays

Determination of serum urea

This was carried out using the method of [10]. Standard commercial kit supplied by Randox was used. Ten microliters (10µl) each of standard and serum sample were pipetted into respective test tubes labelled standard and sample. Then one thousand microliters (1000 µl) of working reagent was added to each test tube labelled reagent blank, standard and sample and mixed. After 30 seconds, initial absorbance was read simultaneously. Again, absorbance was read after 1, 2 and 3 minutes at 340 nm.

Calculation:

$$\textbf{Serum Urea concentration} = \frac{\Delta \text{Asample}}{\Delta \text{Astandard}} = \textbf{standard concentration}$$

Determination of serum creatinine

This was carried out using the method of. Standard commercial kit supplied by Randox was used. Fifty microliters (50 µl) each of distilled water, standard and serum sample were pipetted into respective test tubes labelled reagent blank, standard and sample. Then Five hundred microliters (500 µl) of working reagent was added to each test tube and mixed. After 30 seconds, absorbance A1 of the standard and sample was read. Exactly 2 minutes later, absorbance A2 of standard and sample was read at 492 nm [11].

Calculation:

$$\textbf{Creatinine concentration} = \frac{\Delta \text{Asample}}{\Delta \text{Astandard}} = \textbf{standard concentration}$$

2.7.3 Determination of serum uric acid

This was carried out using the method of. Standard commercial kit supplied by Beacon was used. One thousand microliters (1000 µl) each of enzyme reagent was pipetted into respective test tubes labelled reagent blank, standard and sample. Then twenty-five microliters (25 µl) of standard and sample were added to the respective test tubes mixed well and incubated at 37˚C for 5 minutes. Then, absorbance of the standard and sample were measured against reagent blank at 505 nm[12].

Calculation:

$$\textbf{Urea concentration concentration} = \frac{\Delta \text{Asample}}{\Delta \text{Astandard}} = \textbf{standard concentration}$$

Statistical Analysis

Data analysis was performed using minitab statistical package. Values were expressed as mean + standard error of mean (SEM). Statistical significance of the results between groups was determined using ANOVA. Differences between means were considered significant at $P<0.05$.

Result and Discussion

Diabetes is a metabolic alteration in blood glucose homeostasis due to insulin insufficiency, insensitivity or both. The control of glucose levels within the physiological milieu is necessary for effective functioning of the biological system. However, alteration of this biomolecule as a result of metabolic defects can lead to metabolic dysfunction. Alloxan is a diabetogenic agent that its mechanism of action is based on the destruction of the pancreatic beta cells through the generation of

reactive oxygen species . Uncontrolled diabetes is one of the predisposing factors to kidney dysfunction .

The study showed a non-significant difference in the fasting blood glucose of all the animals prior to induction of diabetes. However, post-diabetic induction indicated a significant increase in the fasting blood glucose of all the groups when compared to the normal control. Following 21 days treatment with leaf extract, the fasting blood glucose level decreased significantly when compared to the untreated diabetic group. These observations are in line with the report of [13].

The report also corroborates with the report of [14] who studied the antidiabetic activity of Lantana camara fruit in normal and streptozotocin-induced diabetic rats. The study also aligns with the report of [15] who documented that triterpenoid glycoside in Lantana camara exerted sugar lowering property in streptozotocin indued diabetic rats.

The increased in the glucose levels after diabetic induction suggest the destruction of pancreatic β-cells resulting in insensitivity of insulin receptor to insulin or loss of the efficacy of the pancreas to secret insulin required for glucose absorption. The reduction in blood glucose level of the animals treated with ethanol leaf extract of Lantana camara may be due to renewed β-cells and or increased sensitivity to insulin, activated by the constituent(s) of the plant extract. The mechanism of hypoglycemic effect of the extract may be attributed to increased insulin sensitivity and upregulation of insulin receptors or short activation of the beta-cells of the pancreas resulting to insulin release.

Furthermore, the hypoglycemic activity of this plant could be a resultant effect of the inhibition of hepatic glucose synthesis or activation of glucose utilization by peripheral tissues as well as inhibitors to tubular renal glucose re-absorption.

It was observed that 1000 mg/kg bw of L. camara extract administration reduced blood glucose comparable to glibenclamide. Bodyweight evaluation is one of the general indicators employed in assessing the metabolic regulation for diabetes mellitus. The study indicated a significant reduction in bodyweight of untreated diabetic group when compared to the normal. . The decrease in bodyweight may follow the fact that diabetes mellitus is associated with increased glycogenolysis, lipolysis and gluconeogenesis which result in muscle wasting and excessive breakdown of tissue proteins.

Treatment of the diabetic rats significantly increased the bodyweight back to normal as also seen in glibenclamide treated group when compared to the untreated group. However, the increase in bodyweight of the treated groups may be attributed to its shielding property in monitoring muscle wasting by reversing gluconeogenesis, lipolysis, glycogenolysis as well as appropriate control of glycemic status [30]. Furthermore, it could be suggested that there was a shift to carbohydrate as a source of energy with the preservation of proteins and fats which resulted in prevention of bodyweight decrease in diabetic rats treated with Lantana camara and glibenclamide. Serum creatinine, urea and uric acid of the untreated group 2 increased significantly when compared to the control group. This may be due to the deficiency or insensitivity of the insulin and subsequent inability of glucose to enter the extrahepatic tissues, thereby activating gluconcognenesis as an alternative route of glucose supply which further resulted to the generation of free glucogenic amino acids into the plasma.

These amino acids are then deaminated in the liver and then increase blood urea . Creatinine is a metabolic intermediate of muscle creatine and its concentrations in blood is a factor of body muscle mass. The increased level of creatinine in untreated diabetic group could be due to decreased body weight caused by muscle wasting as a result of the stimulation of lipolysis and proteolysis due to insulin defect.

The increase in uric acid concentrations observed in untreated group may follow the assertion of protein glycation which may also stimulate muscle wasting and increase the release of purine, the major source of uric acid. Administration of Lantana camara leaf extract decreased the levels of urea, creatinine and uric acid, regulated homeostatically glucose level and subsequently protect against renal impairment due to diabetes complications.

CONCLUSION

According to the study, a 1000 mg/kg body weight dose of Lantana camara ethanol leaf extract has nephroprotective and hypoglycemic effects that are on par with those of the chemotherapeutic antidiabetic medication glibenclamide. To precisely clarify the mechanism of the noted hypoglycemic and nephroprotective potentials, pharmacological research is advised.

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Calculation: