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ANTIDIABETIC EFFECT OF *ACACIA CATECHU* IN NORMAL AND DIABETIC ALBINO RATS

Pharmacology

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ABSTRACT

Diabetes is a widely prevalent metabolic disorders which requires very prompt management. Like the efficacy of herbal products in other disorders, antidiabetic potency also has been observed in many plant products. *Acacia catechu*, also known as Katha, has been used since many years by the local healers to treat diabetic patients. This study has been conducted to prove the efficacy of antidiabetic effect of ethyl acetate extract of *Acacia catechu* in both normal and diabetic albino rats. The extract shows significant antidiabetic activity in both normal and diabetes induced rats. The presence of flavonoids, glycoside, terpenoids may be responsible for the effect.

KEYWORDS

Acacia catechu, Diabetes, streptozotocin, albino rat

INTRODUCTION:

Diabetes is a chronic metabolic disorder which is now prevalent throughout the world. The incidence of diabetes is increasing rapidly. In long term the diabetic patients are susceptible to series of complications that cause morbidity and premature mortality. On an average symptoms develop 15 – 20 years following the appearance of overt hyperglycaemia. The animal models also established long term complications related with both type 1 and type 2 diabetes[1]. According to WHO diabetes prevalence has increased from 108 million in 1980 to 422 million in 2014 worldwide. Almost of the death occurring in diabetics are below 70 years[2]. Treatment of diabetes consist of dietary regulation, insulin injections and oral hypoglycaemic drugs. Drugs of various groups with a wide variety of antidiabetic effect are available[3]. The main drawback of antidiabetic therapy is the requirement of lifelong treatment, and the risk of hypoglycaemia which is a very common occurrence[4].

There are also disadvantages for the present antidiabetic drugs including painful administration, lactic acidosis, oedema, gastrointestinal intolerance, insulin resistance etc. which is demanding development of new drugs for the management of diabetes[5]. In the research for novel drugs for diabetes, plants are having a very important role. Many plant extracts have been documented having antidiabetic therapy and have been used for long time by the local healers[6].

Acacia catechu, a moderate size tree commonly known as "Katha" is found in the forests of India and Burma. It has been reported that various phytochemicals contained in *Acacia catechu* is responsible for antibacterial, antioxidant, hepatoprotective property[7].

MATERIALS AND METHODS:

Animal: Healthy albino rats weighing 150 – 170 gm of either sex is taken for both the experiments.

Preparation of plant material: The whole plant was collected from the Imphal valley. Authentication of the plant was done by Dept of Life Science, Manipur University. Ethical approval was issued by IEAC, RIMS, Imphal.

Preparation of the extract: The plants were air dried under shade and dried plants were powdered by a mixer grinder. The extraction was done by using ethyl acetate after defatted with petroleum ether by soxhlet apparatus. Yield of the extract was 30% and stored in an airtight container at 4^0C for further use.

Experimental protocol:

Hypoglycaemic effect in normal rats: 24 healthy albino rats were weighed and grouped as described. They were kept fasting for 18 hours with free access to water and care was taken to prevent corpophagy. 1 ml of blood was collected from orbital sinus of each rat and serum glucose was estimated by glucose oxidase method as described by Barham et al. The animals were divided in 4 groups and treated as Table 1:

Table 1: Distribution of animals in different groups and treatment performed

Group	'0' hour after 18 hour fasting	Treatment orally '0' hour	2 hour
Vehicle control	Blood glucose estimation	Vehicle 0.6 ml/100 gm	Blood glucose estimation
Glibenclamide	Blood glucose estimation	Glibenclamide 0.5 mg/kg (0.6 ml/100 gm)	Blood glucose estimation
EEAC 250	Blood glucose estimation	EAAC 250 mg/kg (0.6 ml/100 gm)	Blood glucose estimation
EEAC 500	Blood glucose estimation	EAAC 500 mg/kg (0.6 ml/100 gm)	Blood glucose estimation

EEAC: Ethyl acetate extract of *Acacia catechu*

Hypoglycaemic effect in diabetic rats:

24 albino rats were weighed and grouped with 6 animals each. The animals were kept fasting for 48 hours. Diabetes was induced by intraperitoneal injection of streptozotocin (Sigma, St. Louis) dissolved in 0.1 M cold sodium citrate buffer at a dose of 55 mg/kg[8]. After 1-week the animals which showed glucose level >250 mg% were selected for the study. For the study the animals were divided in four groups as follows:

Table 2: Distribution of animals in different groups and treatment performed

Group	Treatment given	After 1 hour
Normal control	N/S 0.6 ml/100 gm without streptozotocin pre-treatment	Blood glucose estimation
Diabetic control	N/S 0.6 ml/100 gm in streptozotocin pre-treatment animal	Blood glucose estimation

Glibenclamide	Glibenclamide 0.5 mg/kg streptozotocin pre-treatment animal	Blood glucose estimation
EEAC 250	EAAC 250 mg/kg (0.6 ml/100 gm) streptozotocin pre-treatment animal	Blood glucose estimation
EEAC 500	EAAC 500 mg/kg (0.6 ml/100 gm) streptozotocin pre-treatment animal	Blood glucose estimation

RESULTS:

Solubility testing: The solubility of the ethyl acetate extract of *Acaccia catechu* was found to be 1 gm%.

Hypoglycaemic effect: The effects of ethyl acetate extract of *Acacia catechu* on blood glucose levels were studied in normal as well as streptozotocin induced diabetic albino rats.

Fasting blood glucose of all the groups were measured 84.26 ± 7.02 mg%, 79.17 ± 4.23 mg%, 83.68 ± 7.82 mg% and 80.87 ± 6.67 mg% and in vehicle control, glibenclamide, EEAC 250 and EEAC 500 respectively. After 2 hours of drug treatment the glucose level was measured as 51.38 ± 4.34 mg%, 74.43 ± 3.37 mg% and 65.74 ± 6.86 mg% in glibenclamide, EEAC 250 and EEAC 500 groups respectively. There is no significant difference when compared to control in 2 hours. But there is highly significant difference with glibenclamide group.

Table 3: Effect on blood glucose level of different treatments in normal rats

Group	Serum glucose level (mg%)		
	Before treatment	After treatment	% reduction
Vehicle control	80.31 ± 1.00	80.51 ± 1.20	
Glibenclamide	82.70 ± 1.26	51.56 ± 0.19a***	37.65
EEAC 250	81.18 ± 0.64	71.39 ± 0.87a***b***	12.06
EEAC 500	81.46 ± 0.98	63.27 ± 0.72a***b***c***	22.33

All values are expressed as Mean ± SEM, n=6. a as compared to vehicle control, b as compared to glibenclamide group and c as compared to EEAC 250 group. *** = p<0.001. EEAC=Ethyl acetate extract of *Acacia catechu*

In streptozotocin induced diabetic albino rats, the extract of *Acacia catechu* at a dose of 250 mg/kg and 500 mg/kg reduced the fasting blood sugar level from 326.69 ±1.84 mg% to 135.16 ± 0.84 mg% and 324.40 ± 1.88 mg% to 103.60 ± 0.24 mg%. The reduction in the glibenclamide group was from 324.54 ± 1.59 mg% to 86.9 ± 0.41 mg%. The reduction of blood glucose level in all the groups were highly significant in comparison to the control group (271.96 ± 1.84 mg%). The results are depicted in table 4.

Table 4: Effect on blood glucose level of different treatments in streptozotocin induced diabetic rats

Group	Serum glucose level (mg%)		
	Before treatment	After treatment	% reduction
Normal control	81.68 ± 3.41		
Diabetic control	322.62 ± 1.84a***	271.96 ± 1.10	
Glibenclamide	324.54 ± 1.85	86.90 ± 0.41b***	73.22
EEAC 250	326.69 ± 1.59	135.16 ± 0.84b***c***	58.63
EEAC 500	324.40 ± 1.88	103.60 ± 0.24b***c***d***	68.06

All values are expressed as Mean ± SEM, n=6. a as compared to vehicle control, b as compared to glibenclamide group and c as compared to EEAC 250 group. *** = p<0.001. EEAC=Ethyl acetate extract of *Acacia catechu*, a as compared to normal control before drug treatment, b as compared to diabetic control after treatment, c as compared to glibenclamide and d as compared to EEAC 250.

DISCUSSION:

The emerging problem in diabetes worldwide warrants management in an extensive way, and the requirements of therapeutic approach cannot be ignored[2]. Treatment of diabetes consist of two main approach, a) To administer insulin, and b) To increase the efficacy of insulin by enhancing either the peripheral uptake or increasing sensitivity of muscle or liver to insulin[3]. Streptozotocin reversibly destroys the pancreatic β-cells decreases the amount of insulin in the body, and hemidiaphragm method evaluates the peripheral uptake of glucose in the tissues[9]. Estimation of blood glucose was done by glucose oxidase method, which has adequate sensitivity and it is specific for d-glucose with relatively little effect on other sugars present in blood[10].

Freshly prepared streptozotocin at a dose of 60 mg/kg s/c widely used to induce insulin dependent diabetes in rats. As the method is reversible, the animal usually recovers in 2 – 3 weeks. The blood glucose level was estimated in both normal and streptozotocin induced diabetic rats. in both models, the decrease of blood glucose level was very highly significant when compared to the control group. In the normal rats glibenclamide group decreased blood glucose level by 37.65%, while the reduction was 12.06 and 22.33% in EEAC 250 and EEAC 500 groups respectively. While in streptozotocin treated diabetic rats glibenclamide reduced blood glucose level by 73.22%, while EEAC 250 and EEAC 500 group showed reduction of 58.63% and 68.06% respectively. This shows enhanced response of *Acacia catechu* in diabetic animals compared to the normoglycaemic group. The higher dose (500 mg/kg) of *Acacia catechu* showed highly significant difference with the lower dose (250 mg/kg).

Many herbal remedies are now being used in the management of diabetes, and are becoming popular day by day. The phytochemicals attributed to the hypoglycaemic potential of these plants are glycoside, flavonoid, alkaloid, terpenoid etc[11]. The different parts of the *Acacia catechu* also contain flavonoids, alkaloids, glycosides and tannins[7]. The presence of these phytochemicals may be responsible for its hypoglycaemic potency.

CONCLUSION:

The ethyl acetate extract of *Acacia catechu* possesses significant hypoglycaemic potential, which is probably because of an insulin like effect which enhances peripheral uptake of glucose. The effect is more evident in higher dose (500 mg/kg). presence of flavonoid, glycoside, terpenoid could be responsible. However, further study need to be conducted to determine the exact mechanism as well as its possible use in human.

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