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Research Article

Anti-Diabetic & Anti Hyperlipidimic Activity of *Artocarpus heterophyllus* Root on Alloxan-induced Diabetic Rats

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ABSTRACT

Purpose: The present study to evaluates Anti-Diabetic & Anti Hyperlipidimic Activity of *Artocarpus heterophyllus* Root on Alloxan-induced Diabetic Rats.

Methods: Diabetes mellitus was induced by single intraperitoneal injection of 150 mg/kg body weight of alloxan and the animals were orally administered with 250 and 500 mg/kg body weight ethanol extract of *A heterophyllus* root bark once daily for 15 days.

Results: At the end of the intervention, diabetic control rats showed significant ($p < 0.05$) weight reduction, high serum lipids (except high density lipoprotein) concentrations, when compared with non-diabetic control rats. All these alterations were reverted to normal after administered with different doses of ethanol extract of *Artocarpus heterophyllus* root bark most especially at 500 mg/kg body weight which exhibited no significant ($p > 0.05$) different with non-diabetic rats.

Conclusion: The results suggest that ethanol extract of *Artocarpus heterophyllus* root bark may be useful in ameliorating complications associated with diabetes mellitus patient.

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INTRODUCTION

The diabetes mellitus is causing deaths and debilitating disease in world. One hundred and sixty million people were suffering from diabetes .which is almost five times more than estimates one decade ago and it may double in the year 2030. Having population of 237.6 million people in 2010, Indonesia is the world 4 most populated country. Having 7 largest number Of diabetic patients (7.6 million), despite having low prevalence (4.8% including both diabetes type 1 and 2 in aged 20-79) in 2012. [1, 12, 13, 14, 15]

Diabetes mellitus is a chronic metabolic disorder characterized by derangements in carbohydrate, protein and lipid metabolisms, due to defective or deficiency in insulin secretion and action. Insulin is a hormone secreted by the beta cells of the Islets of Langerhans of the pancreas, it helps in glucose uptake by the cells, thereby prevents increase in fasting blood glucose levels. Diabetes mellitus is also associated with hyperglycaemia, which promotes oxidative stress through non-enzymatic glycation and glucose auto-oxidation. Diabetic causes complications like retinopathy, microangiopathy and nephropathy [14, 16, 17, 18, 19].

Artocarpus heterophyllus (jack fruit) is an example of plant that may be used in this regards, it belongs to a family of *Moraceae* and grown in tropical climates. *Artocarpus heterophyllus* has been considered a rich source of carbohydrates, minerals, dietary fiber and vitamins amongst others. Its root bark has also been reported to be of great importance in the management of diabetes mellitus locally. In addition, the inhibitory ability of *Artocarpus heterophyllus* stem bark on alpha-amylase and alpha-glucosidase has been documented.[2, 3, 11, 22]

The pulp and seeds are used as tonic, roots in diarrhea and fever, woods as sedative in convulsions, leaves as vermifuge. Leaf ash is used in wounds and ulcers [19, 22].

Therefore, the present study was designed to examine the anti-diabetic, anti-inflammatory effects of ethanol extract of *Artocarpus*

heterophyllus root bark on haematological parameters, serum lipid profiles, liver and kidney functions indices of alloxan-induced diabetic rats [2, 19, 22].

Materials and Methods

Chemicals

Alloxan used was a product of Sigma Aldrich (St. Louis, MO, USA). Glibenclamide used was a product of Sandoz SA (Pty) Ltd. (Gauteng, South Africa). All assay kits used were obtained from Randox while other chemicals used were purchased from Merck Chemical (Germany) [3, 5].

Collection of Plant Material

The fresh peeled root of *Artocarpus heterophyllus* were collected from jaunpur,uttar Pradesh india. This was then identified and authenticated at the botaniocal survey of india by prayagraj by gp sinha(head scientist) with Ref. No- BSI/CRC/T/2019 20/578s [4, 5, 6].

Extract preparation

The root bark of *Artocarpus heterophyllus* was shade-dried to a constant weight. Thereafter, kitchen blender was used to blend the dried root bark of *Artocarpus heterophyllus* into fine powder and stored in air-tight containers. Thereafter, 100 grams of powdered plant sample was extracted with 1 litre of 70% ethanol for 48 hours. The extract was then filtered with Whatman filter paper and the filtrate was evaporated to dryness using a freeze dryer. The extract (RBAH) was reconstituted in distilled water and used for subsequent analysis [7, 8, 9].

Qualitative phytochemical screening

EAH was subjected to phytochemical screening for ensuring phytochemical like alkaloids,flavonoids,tannins,carbohydrates,Glycoside,phenolic compound.

Experimental Animals

In vivo study was performed on Albino Wister rat (100-150gm) in the animal house of Shambhunath Institute of Pharmacy, Prayagraj with the prior approval from Institutional Animal Ethical Committee (IAEC) Ref. No-1632/PO/Re/S/12/CPCSEA/15 bearing approval number. From studies performed

according to CPCSEA. Healthy adult Albino Wistar rat (100-150gm) of either sex. The animals were housed under standard condition as prescribed and had a proper approach to water and feed, with the exclusion of food deprivation during the period of blood sampling throughout the experiment [20, 5, 4].

Induction of Diabetes

Freshly prepared alloxan monohydrate of 150 mg/kg body weight dissolved in 0.9% sterile NaCl of pH 7 was administered intraperitoneally to rats in group B to E to induce diabetes. Prior to this, their fasting blood glucose levels had been determined. Also, after 48 hours of alloxan induction, the rats fasting blood glucose levels were assessed with the aid of Acucheck Advantage II glucometer and those that had fasting blood glucose level ≥ 200 mg/dl were considered diabetic and used for the study. The rats were divided into five groups with six rats per group as follows:

Group A: Non-diabetic control rats received distilled water

Group B: Diabetic-control rats received distilled water

Group C: Diabetic rats received glibenclamide 5 mg/kg bw.

Group D: Diabetic rats received 250 mg/kg body weight of RBAH

Group E: Diabetic rats received 500 mg/kg body weight of RBAH^[19, 9]

Oral glucose tolerance test

Five days before the termination of the experiment, the oral glucose tolerance test (OGTT) was performed to assess the glucose tolerance. For this purpose, overnight (18 h) fasted rats were fed glucose (2 gm/kg) orally and blood was collected at 0, 30, 60 and 120 minute interval from orbital sinus for glucose estimation [21].

Assessment of Oral glucose tolerance test

Blood samples were collected from tail puncturing of each rat at 0 minute, 30 minute, 60 minute and 120 minute and blood glucose was estimated by glucose estimation kit.

Percent reduction in blood glucose was calculated with respect to the initial level [21].

Assessment of Anti-diabetic activity

Blood samples were collected from tail puncturing of each rat at 0 day, 1st day, 10th day and 15th day and blood glucose was estimated by glucose estimation kit. Percent reduction in blood glucose was calculated with respect to the initial level [3, 10, 11 4].

Assessment of Antihyperlipidemic activity

At the end of 15th day, blood was collected by heart puncture and serum was separated for the estimation of total cholesterol, HDL, LDL, VLDL, total Glycerides, total serum protein, albumin, globulin etc and the liver was isolated from the rats of all the groups and kept in 10% formalin solution and hence send for histopathological investigation [3, 4].

Statistical analysis

All analytical data represented as mean \pm SEM. one-way analysis of variance (ANOVA) followed by tukey's multiple comparison test was performed for statistical method. P value < 0.05 were taken significant difference.

RESULT

Preliminary screening (phytochemical) of each extract ensure the Presence of various chemical constituent like flavonoid, Glycoside, tannins, carbohydrates, alkaloids, Phenolic compound.

Acute toxicity study

No any death in animal was noticed at the dose 2000mg/kg. So the large fraction can be given due to low toxicity index.

Body weight differences

There are no significant difference was observed between the different group of experimental animal, but the diseased control group showed reduction in the weight profile in comparison to other animal group. Standard drug group successfully maintain the body weight profile till the experimental duration.

Antidiabetic activity of AH

Changes in BGL in different group are expressed statistically in the Table- 1.1. Upon

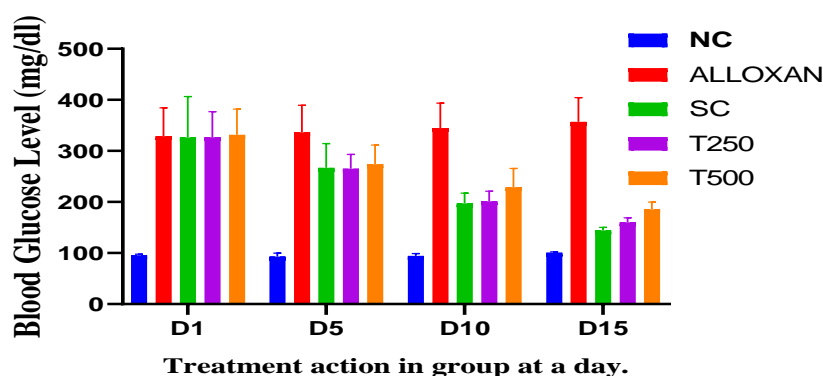
the administration of the Alloxan in diseased control group (G2) there was huge elevation in the BGL. The G2 significantly ($****p<0.0001$) increases the BGL (on 15th day) when compared to the standard control group (G3) The BGL elevated from normal (93 ± 1.20 mg/dl) to 329.00 ± 31.94 mg/dl on 1st day of experimentation period and it finally reaches to 356.66 ± 27.55 mg/dl on 15th day. The standard group (glibenclamide 5mg/kg) significantly ($****p<0.0001$) diminishes the level of blood

glucose when compare to the G2. Standard control group reduces BGL from 326.33 ± 46.33 (1st day) to 144.33 ± 3.28 (15th day). The significant reduction in BGL was initiated from 5th day of post treatment. EEAH 250 mg/kg (G4) also significantly ($****p<0.001$) on reduces the BGL (on 15th day) in contrast to the G2. EEAH 250 (G4) reduces BGL from 326.66 ± 29.05 (1st day) to 160.33 ± 4.91 (15th day) and EEAH 500 (G5) reduces BGL from 331.33 ± 29.15 (1st day) to 185.66 ± 8.21 (15th day).

Table 1

Group	Treatment	Fasting glucose level (mg/dl)				
		Initial	1 st day	5 th day	10 th day	15 th day
1	NORMAL		95.66 ± 1.20	93.33 ± 3.71	94.33 ± 2.72	100.66 ± 0.88
2	DISEASE CONTROL		329.00 ± 31.94	336.33 ± 30.55	344.66 ± 28.10	356.66 ± 27.55
3	GLIBENCLAMIDE		326.33 ± 46.33	266.66 $\pm 27.53^*$	197.33 $\pm 11.40^*$	144.33 $\pm 3.28^{****}$
4	T 250		326.66 ± 29.05	265.33 $\pm 16.12^*$	201.33 $\pm 11.26^*$	160.33 $\pm 4.91^{***}$
5	T 500		331.33 ± 29.15	274 ± 21.54	229.00 ± 21.07	185.66 ± 8.21

Each value expressed as Mean \pm SD, (n=6)
 $****p<0.0001$ compared with Disease Control



NC= Normal Control, Alloxan (diseased control),

SC= standard control (Rat received Glibenclamide 5mg/kg,

T 250= Rat were given 250 mg/kg of ethenolic extract of *A. heterophyllus*,

T 500= Rat were given 500 mg/kg of ethenolic extract of *A. heterophyllus*

Each value expressed as Mean \pm SD, (n=6)

$****p<0.0001$ compared with Disease Control

OGTT

Fasting glucose level profile in different group of animal are depicted statistically in table 1.2. Diseased control Group (G2) show significant (****p<0.0001) elevation in the BGL at all fixed time interval (0, 30, 60, and 120 min.) as compared to the normal control group (G1). The rat (G3) after treatment with standard drug

showed significant reduction in fasting BGL at all fixed time interval as compared to G2. EEAH administration at the dose 250 and 500 mg/kg also significantly reduces the level of BGL as compared to the G2. EEAH 250 and 500 mg/kg showed no any significant difference as compared to standard control.

Group	Treatment	Fasting glucose level (mg/dl)			
		Initial	30 min.	60 min	120 min
1	NORMAL	93.33 ±3.72	133.33 ±6.36	116.00 ±4.50	99.33 ±4.70
2	DISEASE CONTROL	359.00 ±27.46	394.00 ±28.36	406.66 ±26.90	370.00 ±29.10
3	GLIBENCLAMIDE	147.33 ±3.84****	203.33±4.41****	185.66±2.33****	153.66 ±1.45****
4	T 250	163.00 ±4.93****	221.33±4.33****	204.33 ±4.41****	173.66 ±4.66****
5	T 500	189.33 ±8.95****	254.00 ±11.06****	236.33 ±14.89****	194.33±12.33****

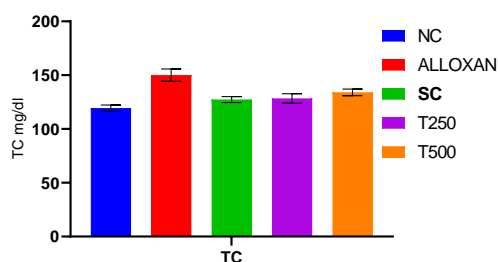
Each value expressed as Mean±SD, (n=6)
****p<0.0001 compared with Disease Control

INFLUENCE ON LIPID PROFILE

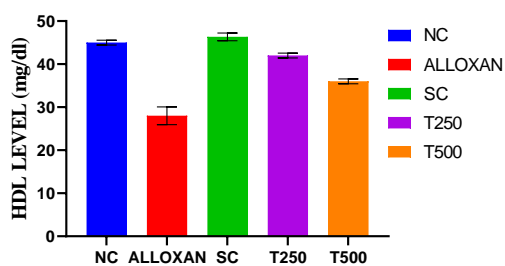
Lipidemic profile in different experimental group is depicted statistically in table 1.3. In alloxan induced animal (G2), significant (****p<0.0001) increment in the level of LDL, TC, and TG as compared to the normal control group (G1), however significant decrease in the HDL level was observed in the G2 as compared to the G1. Standard control group (G3) significantly (****p<0.0001) reduces the level of LDL, TC, and TG as compared to the G2, Standard drug improve the HDL profile (46.33±0.88 mg/dl) in comparison to the G2 (28.00 ±2.08 mg/dl). Administration of EEAH (250 and 500 mg/kg) in Group 4 and Group 5 respectively significantly (****p<0.0001) reduces the LDL, TC, and TG level. EEAH also significantly improve the HDL level (EEAH 250= 42.00 ±0.57mg/dl, and EEAH 500= 36.00 ±0.57 mg/dl) in comparison to G2.

Group	Treatment	Fasting glucose level (mg/dl)			
		TC	TG	LDL	HDL
1	NORMAL	119.33 ±2.96	121.33 ±1.45	83.66 ±7.88	45.00±0.577
2	DISEASE CONTROL	150.00 ±5.774	173.66 ±9.02	110.00 ±9.29	28.00 ±2.08
3	GLIBENCLAM,IDE	127.33 ±2.78*	133.66 ±0.88**	84.00 ±2.88	46.33±0.88****
4	T 250	128.33 ±4.410*	141.66 ±1.20**	79.66 ±17.34	42.00 ±0.57****
5	T 500	134.00 ±3.05	141.33 ±3.52**	103.33 ±0.88	36.00 ±0.57**

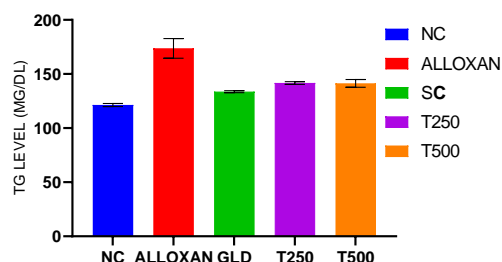
Each value expressed as Mean±SD, (n=6)
****p<0.0001 compared with Disease Control



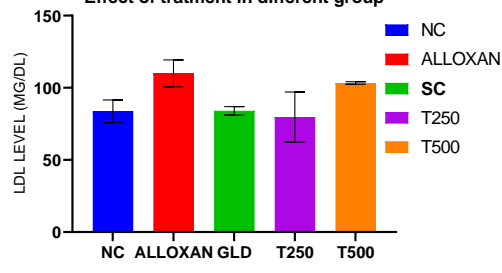
Effect of treatment in different group



Effect of treatment in different group



Effect of treatment in different group



Effect of treatment in different group

NC= Normal Control, Alloxan (diseased control),

SC= standard control (Rat received Glibenclamide 5mg/kg),

T 250= Rat were given 250 mg/kg of ethenolic extract of *A. heterophyllus*,

T 500= Rat were given 500 mg/kg of ethenolic extract of *A. heterophyllus*

Each value expressed as Mean \pm SD, (n=6)

****p<0.0001 compared with Disease Control

TG = Triglyceride

TC= Total cholesterol

LDL = Low density lipoprotein

HDL = High density lipoprotein

DISCUSSION

Alloxan is more common ingredient used for induction of diabetes in experimental animal, due to their beta cell toxicity in pancreas's langerhance. Weight loss of experimental animal is due to the destructive metabolism of the food material. Diabetes mellitus is the metabolic disorder which causes the elevated level of the blood glucose level, due to irregular insulin secretion or action. Each 250 and 500 mg/kg reduce BGL which was comparable to the standard "Glibenclamide". Lowering of blood glucose in experimental animal prove the BGL lowering property of the EEAH. EEAH 500 mg/kg showed more BGL lowering property in rats which showed the dose dependent potential of the AH [11, 12, 13, 14]. Natural drug are those drug which have least adverse effect with prove pharmacological action.

EEAH also help to manage hyperlipidemic condition. EEAH decreases, VLDL, LDL, TG, TC, and increases HDL level which prove antihyperlipidemic property of the AH [1,5].

CONCLUSION

The above experimental work conclude that AH posses antidiabetic activity due to BGL lowering property (Proven experimentally). It also possesses antiheperlipidemic activity due lipid lowering nature.

Further studies require proving its pharmacological property, and screening of single chemical constituent responsible for antidiabetic action.

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