

## Effect of Ethanolic Extract of *Abrus precatorius* Leaves on Liver Enzymes in Alloxan-Induced Diabetic Male Rats

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Diabetes; Liver; Metformin; *Abrus precatorius* leaves; AST; AL

## 1. Abstract

Increased metabolic disorders are generally linked to the progression of diabetes mellitus (DM). In this study, we looked into the effects of the ethanolic extract of *Abrus precatorius* (*A. precatorius*) leaves on liver enzymes and glycaemia in alloxan-induced diabetic male rats.

Alloxan-induced diabetic Sprague-Dawley rats were treated with either metformin (150 mg/kg/d) or *A. precatorius* (200 mg/kg/d and 300 mg/kg/d) for 28 days. At the end of the treatment period, the rats were humanely killed and blood was collected for biochemical analysis.

Blood glucose concentrations were compared between the treated and control rats. Blood glucose concentration was significantly different between treated rats and control (untreated); extract of *Abrus precatorius* (*A. precatorius*) leaves decreased blood glucose level and serum level of VLDL but elevated HDL level ( $P < 0.05$ ) at 28 days of treatment.

These findings suggest that the *A. precatorius* leaves confer protection against hyperglycemia due to diabetes in adult Sprague-Dawley rats.

## 2. Introduction

Diabetes mellitus (DM) is a devastating disease that poses severe threat to the public. The number of adults projected to suffer from the disease by the year 2030 is approximated to be 439 million [1]. Type 2 DM which is essentially due to insulin resistance and subsequent impaired  $\beta$ -cell function is the most common form of DM

[2]. In addition to hyperglycaemia, several organs such as the liver also develop complications in diabetes (glycogen-storage disease and steatohepatitis) [3]. During prolonged DM, liver function is impaired [4]. Liver function tests reveal that elevation of ALT (alanine aminotransferase) though uncommon in normal non-diabetic subjects, is common in patients with type 2 DM [5]. In a study that involved several clinical trials with type 2 diabetes patients, it was discovered that compared with non-diabetic control subjects, the diabetic patients had a significantly higher levels of ALT (alanine aminotransferase) and AST (aspartate aminotransferase) [6]. The liver is generally known to play an important role in the metabolism and regulation of glucose in the body. A function that has been shown to make it vulnerable in diseases such as diabetes mellitus [7], as increased activity of the liver and therefore liver enzymes has been associated with insulin resistance [8]. The structure and function of the liver change during prolonged DM. Hepatic examination in patients with type 2 diabetes reveals non-alcoholic fatty liver disease due to impaired insulin action [9].

More and more studies are suggesting that the use of herbal therapy including that of *Abrus precatorius*, also known as *werenjeje* or *oju olongbo* by locals in south-western Nigeria should be incorporated into the healthcare system of countries with natural endowment of diverse therapeutic botanical heritage so far they are made to pass through scientific verification [10].

A previous study suggested that the therapeutic effect of *Abrus precatorius* seeds is seen and used in the management of diabetes mellitus locally in Nigeria [11]. Evidence of usage of *Abrus*

*precatorius* in several ways by many tribes around the world for healing and to improve human health was revealed in a study by Umamahesh and Veeresham [12].

Though many studies have investigated the therapeutic properties of *Abrus precatorius* leaves, such as its; anti-inflammatory effect [13], antiasthmatic effect [14], anti-nephropathy effect [15], anti-oxidant effect [16], anti-microbial effect [17], only few have checked specifically the effect of *Abrus precatorius* leaves extract on liver enzymes and liver histology in diabetes. Increasingly, plant-based drugs are being considered due to their relative cheapness and availability despite being equally effective and safe in the management of DM. This study therefore sets out to ascertain the use of *Abrus precatorius* leaves as a therapy to ameliorate the destructive effects of diabetes mellitus on the body. Specifically, in the present study, we reported the blood glucose ameliorative responses of alloxan-induced rat models of diabetes to a regimen of *A. precatorius* leaves. Improved activities of hepatic alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were also reported. The results we obtained from the present study are interesting and could induce further research into the anti-diabetic effect of *Abrus precatorius* leaves.

### 3. Materials and Methods

#### 3.1. Drugs and Reagents

The *Abrus precatorius* leaves were obtained from south-western part of Nigeria where they were hand-picked from living stems of *Abrus precatorius* tree. Cross-identification with common names of *Abrus precatorius* was done before identification and authentication by a qualified taxonomist. The leaves were thoroughly dried under shade. The dried leaves were pounded into fine powder and stored in plastic containers until when needed. The alloxan used was a product of Sigma-Aldrich (Sigma, St. Louis, USA). The glucometer that was used in measuring blood glucose was on-call-plus (ACON Biotech, Hang Zhou, China). A standard sensitive weighing scale was used for weight determination. The kits used for lipid profile was by Randox (UK).

#### 3.2. Extract Preparation

A 100 g of powdered leaves was soaked in 500 ml of 95% ethanol for 3 days (72 hrs) to allow for proper extraction of the leaves into the ethanol). The mixture was filtered using a Buchner funnel. The filtrate was evaporated to dryness under low pressure and maximum temperature of 40°C using a rotary evaporator placed on a water bath. A dark-green pasty extract of *Abrus precatorius* leaves (EAPL) weighing 20 g was obtained and stored in a desiccator until use. The method employed here, in the preparation of *Abrus precatorius* leaves extract is based on the method that described in a publication by Umamahesh and Veeresham [12]. Phytochemical analysis – based on standard methods as described by Hussain et al. [18] – of EAPL used in this study revealed that it is composed of alkaloids, steroids, glycosides, saponins, tannins, triterpenes

and anthraquinones in appreciable amounts while other flavonoids and phlobatannins are present in minute amounts.

#### 3.3. Procurement and care of experimental animals

The laboratory animals used for this study were housed and raised in the animal house of the Faculty of Basic Medical Science, University of Ilorin, Nigeria under standard lab conditions and were allowed free access to standard rat food and water. The study was carried out in accordance with the ethical guidelines specified by the Ethical Committee of the Institution. The guidelines are in conformity with the Helsinki Principles for lab animal use and care. Rats, weighing between 150 g and 200 g were selected and used for the experiment.

#### 3.4. Establishment diabetes mellitus in rats using alloxan

The rats were fasted for 12 h after which diabetes was induced by injecting alloxan (120 mg/kg) dissolved in distilled water intraperitoneally. The rats were allowed free access to food and water. Diabetic state was determined 3 days after induction of diabetes with alloxan. A pinch of blood collected from the tail tip [19] was analyzed for glucose level in each animal using the on-call-plus glucometer [20]. Rats with consistent fasting blood glucose level higher than or equal to 250 mg/dl were identified as being hyperglycemic and selected for the diabetic group of animals [21].

#### 3.5. Grouping of animals

The animals were divided into five (5) groups:

- Group 1: Control; received distilled water
- Group 2: Untreated; received distilled water
- Group 3: Experimental A; received 200 mg/kg of EAPL as used by Boyea *et al.* [22]
- Group 4: Experimental B; received 400 mg/kg of EAPL as used by Boyea *et al.* [22]
- Group 5: Treated; received 150 mg/kg of metformin.

#### 3.6. Drug Administration

The EAPL was dissolved in water and administered orally and continuously for 35 days. The fasting blood glucose and weight of all rats were measured weekly for 5 weeks.

#### 3.7. Animal Sacrifice

After 35 days of treatment, animals were anesthetized and sacrificed by cervical dislocation and then dissected. Blood was obtained directly from the heart into heparinized and plain centrifuge bottles for plasma and serum samples, respectively.

For serum preparation, blood samples were allowed to stand for 30 min and then centrifuged at 3000 r/min for 15 min to obtain the serum. Obtained serum was analyzed for HDL and VLDL using commercial diagnostic kits (Randox, UK). Weekly levels of glucose was obtained using pinches of blood from the tip of the tails of the rats and dropped on the glucometer-strip which was prior inserted into the glucometer. The weights of the rats was measured

and recorded using a standard scale. Biochemical analysis for AST and ALT was by the method Reitman and Frankel, 1957 used.

### 3.8. Statistical Analysis

Data were analyzed by one-way analysis of variance followed by Tukey-Kramer post-hoc test. The software used was SPSS version 24. Results were presented as mean ± standard error of mean with statistical significance accepted at P = 0.05.

## 4. Results

### 4.1. Effect of *A. precatorius* on blood glucose

Table 1 compares average changes in the blood glucose levels across different groups of experimental animals at the end of this study. Induction of diabetes using alloxan increased blood glucose level until the first week in all animals excepting the Control group that was not given alloxan. Blood glucose level was reduced significantly (P<0.01) in the metformin and *A. precatorius* treated groups by the end of the experiment (35 days) when compared to the diabetic untreated group. There was also significant difference

in the final levels of blood glucose between both doses of *A. precatorius* with the higher dose (400 mg/kg) resulting in a significantly lower blood glucose level.

### 4.2. Effect of *A. precatorius* on Body Weight

In Table 2, it is noted that the body weight of animals in the diabetic untreated group decreased after 35 days while there was significant (P<0.01) increase in the body weights of animals in other groups.

### 4.3. Effect of *A. precatorius* on VLDL and HDL

Induction of diabetes significantly raised the serum level of VLDL (P< 0.001) and lowered the serum level of HDL significantly (P<0.001). Treatment with different doses of *A. precatorius* (200 mg/kg and 400 mg/kg) resulted in significant drop (P< 0.001) in the elevated level of VLDL; and a complementary significant increase (P< 0.001) in the depressed level of HDL when compared to the diabetic untreated group. Treatment with metformin, however, did not significant effect on VLDL level, but significantly raised the serum HDL level (P< 0.001) when compared to the diabetic untreated. See Table 3.

**Table 1:** Effects of *A. precatorius* extracts on blood glucose level of diabetic rats

Treatment group	Initial blood glucose (mg/dl)	Final blood glucose (mg/dl)	Change in blood glucose (mg/dl)	% Change in blood glucose
Control (distilled water)	93.80±9.43	86.6±3.02*	7.20±7.18*	7.44*
Diabetic untreated	490±5.00	459.1±2.03	30.90±12.50	6.36
200 mg/kg (EAPL)	430.80±15.16	133.18±22.20*	297.62±11.26*	67.98*
400 mg/kg (EAPL)	442.80±13.80	106.08±4.44*	336.72±10.70*	72.76*
Metformin (150 mg/kg)	380.40±19.35	145.0±12.43*	235.40±8.80*	60.30*

\*Indicates significant (reduction) change at P<0.001, compared with the untreated group, EAPL: Extract of *Abrus Precatorius* Leaves

**Table 2:** Effects of *A. precatorius* extracts on weight of diabetic rats

Treatment group	Initial weight (g)	Final weight (g)	Change in weight (g)	% Change in weight
Control (distilled water)	187.20±3.05	226.10±3.35	38.90±0.21 <sup>a</sup>	21.47 <sup>a</sup>
Diabetic untreated	142±4.41	109.00±2.00	-33.00±1.19 <sup>b</sup>	-21.91 <sup>b</sup>
200 mg/kg (EAPL)	212±3.21	213±1.10	1±1.29 <sup>a</sup>	0.50 <sup>a</sup>
400 mg/kg (EAPL)	150±4.24	168.70±3.82	18.70±3.01 <sup>a</sup>	11.76 <sup>a</sup>
Metformin (150 mg/kg)	168±5.96	186.10±7.00	18.10±1.26 <sup>a</sup>	11.75 <sup>a</sup>

<sup>a</sup>Significantly different from diabetic untreated; <sup>b</sup>Significantly different from normal control at P<0.01, EAPL: Extract of *A. precatorius* Leaves

**Table 3:** Effect of treatment of diabetic rats with extract of *A. precatorius* (EAPL) on VLDL, HDL, AST and ALT

Treatment group	VLDL (mg/dl)	HDL (mg/dl)	AST (mg/dl)	ALT(mg/dl)
Control (distilled water)	28.46±0.88	37.14±0.78	114±1.12	33±8.71
Diabetic untreated	51.75±1.57 <sup>b****</sup>	18.21±1.07 <sup>b****</sup>	268±0.92 <sup>b****</sup>	125±5.53 <sup>b****</sup>
200 mg/kg (EAPL)	44.90±1.54 <sup>b****</sup>	42.00±1.51 <sup>a****</sup>	122±2.54 <sup>a****</sup>	35±4.49 <sup>a****</sup>
400 mg/kg (EAPL)	38.36±1.25 <sup>a****b****</sup>	34.00±0.73 <sup>a****</sup>	104±3.12 <sup>a****</sup>	33±0.37 <sup>a****</sup>
Metformin (150 mg/kg)	47.53±1.97 <sup>b****</sup>	33.55±2.42 <sup>a****</sup>	114±2.01 <sup>a****</sup>	120±8.68

<sup>a</sup>Significantly different from diabetic untreated; <sup>b</sup>Significantly different from normal control. \*P<0.05, \*\*P<0.01 and \*\*\*\*P<0.001. EAPL: Extract of *A. precatorius* Leaves, VLDL: Very low-density lipoprotein, HDL: High-density lipoprotein, AST: aspartate aminotransferase ALT: alanine aminotransferase.

#### 4.4. Effect of *A. precatorius* on Serum AST and ALT

The serum levels of the liver enzymes AST and ALT in all groups are displayed in Table 3. Both enzymes were elevated ( $P < 0.001$ ) significantly in the diabetic untreated group when compared to the normal control group. Administration of *A. precatorius* and metformin significantly decreased the elevated level of AST in comparison to the diabetic untreated group. However, though either dose of *A. precatorius* significantly reduced the level of ALT ( $P < 0.001$ ), metformin had no significant effect on the elevated level of ALT when compared to the diabetic untreated group.

#### 5. Discussion

For the study, we investigated the probable anti-hyperglycaemic effect of *A. precatorius* leaf extract on diabetic rats. The observed substantial diminish in blood glucose level in the *A. precatorius* treated groups suggests that intake of this extract may have some glucose-lowering effect. This glucose-lowering effect is due to the presence of certain bioactive component, and the effect it may have on pancreatic  $\beta$ -cells thereby enhancing their production of insulin. It may also be due to the effect such bioactive component may have in increasing the sensitivity to insulin at the peripheral tissues. It has been suggested earlier by Iwu et al. 1990 that glucose-lowering agents as observed in this study exert their effect either through direct or indirect mechanisms [24]. Due to the destructive effect of alloxan on pancreatic  $\beta$ -cells [25], it is likely that *A. precatorius* exerted its hypoglycaemic effect by stimulating the little remaining  $\beta$ -cells (after alloxan destruction) to increase their insulin production and secretion rather than by regeneration of dead pancreatic  $\beta$ -cells.

Disorders that are associated with lipid metabolism takes a special position in diabetes due to the tendencies to cause diabetic acidosis, coma and death. Administration of *A. precatorius* however, was able to arrest and even reverse hyperlipidemia by reducing the bad cholesterol (VLDL) and increasing the good cholesterol (HDL), hallmarks of lipid metabolic state. This observed anti-hyperlipidemic effect of *A. precatorius* is likely a direct resultant of the anti-hyperglycaemic effect of *A. precatorius*, halting and reversing the excessive catabolism of lipids that occur in diabetes.

Elevated levels of the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) signify disturbed functioning of liver cells [26]. Extract of the leaves of *A. precatorius* was able to attenuate increased levels of ALT and AST that occur in diabetes, and bring it down to close to normal levels especially with the 400 mg/kg dose of *A. precatorius*.

#### 6. Conclusion

In conclusion, the results that were gotten from this study show that the ethanolic extract of *A. precatorius* leaves attenuates hyperglycemia and the attending hyperlipidemia. It also offer some protection to the liver against diabetes. The observed action of *A. precatorius* leaves extract is likely due to the effect of a constituent

chemical compound or a combined effect of two or more constituent chemical compounds. Further chromatographical, biochemical and pharmacological analysis is necessary to determine the actual active chemical compound(s) responsible for the therapeutic effects observed in the leaf-extract of *A. precatorius*; and also determine the mechanism of action of such compound(s).

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