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*Original Paper*

# Kidney and Liver Function Parameters in Alloxan-Induced Diabetic Rats Treated with Aloe Barbadensis Juice Extract.

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**ABSTRACT**

*Aloe barbadensis* juice extract has been reported to possess hypoglycaemic property but the effects of its use on kidney and liver functions in diabetic animals have not been well investigated. This study investigated some biochemical parameters in the liver and kidney of alloxan-induced diabetic rats treated with *Aloe barbadensis* juice extract. Alloxan-induced diabetic rats were administered orally with *Aloe barbadensis* juice extract for seven days after which some biochemical indices in the serum, liver and kidney were measured and compared with the control. Serum alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea and creatinine of untreated diabetic group and treated diabetic groups were significantly elevated when compared with the normal control group with no significant changes in the levels of the enzymes in the liver and kidney. There were no significant changes ($p>0.05$) in the serum levels of Na+ and K+ in untreated diabetic group and treated diabetic groups when compared with the normal control rats which are not diabetic. These results suggest that administration of aqueous extract of *Aloe barbadensis* to diabetic rats did not have any adverse effect on the liver and kidney functions in rats showing that the extract is not toxic to man.

***Keywords: Aloe barbadensis*, Alloxan, Liver function, Kidney function, Diabetic rats.**

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## INTRODUCTION

Diabetes Mellitus is a complex metabolic disorder in which the pancreas produces insufficient amounts of insulin, or in which individual's system fail to respond appropriately to insulin. In people with diabetes, glucose levels build up in the blood and urine, causing excessive urination, thirst, hunger, and problems with fat and protein metabolism (Kathleen, 1996). The disease is ranked seventh among the leading causes of death and third in terms of its complications and is a major health problem in developed and developing countries (Seidell, 2000). The number of diabetic patients is increasing globally because of diverse changes in diets in all cultures. It has been predicted that the number of diabetic patients will double from 143 million in 1997 to about 300 million by 2025 largely because of dietary intake and other lifestyle factors (Seidell, 2000).

In the developing countries where majority of diabetic patients cannot afford effective but expensive drugs, the use of medicinal plants becomes an alternative therapy. A wide range of medicinal plants have been used by various cultures to treat diabetes mellitus because of their hypoglycaemic properties. Some of these medicinal plants include *Vernomia amygdalina* (Olagunju *et al*., 1998), unripe fruit of *Carica* papaya (Oloyede, 2005) and *Aloe barbadensis* (Adesokan *et al*., 2006).

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*Aloe barbadensis* (common name: Aloe vera) belongs to a class of plants called xeropids which have the ability to close their stomata completely to avoid loss of water (Artherton, 1997). Aloe vera is the source of the herbal preparations; the aloe gel and aloe latex. The aloe latex is commonly referred to as 'aloe juice'. The latex contains a series of glycosides known as anthraquinones (Tyler, 1994). The hypoglycaemic property of this extract has earlier been shown (Adesokan *et al*., 2006). It is therefore imperative to investigate the effects of this medicinal plant on liver and kidney functions in diabetic rats so as to ascertain its safety.

## MATERIALS AND METHODS

### Preparation of *Aloe barbadensis* juice extract

*Aloe barbadensis* plant was obtained from Sango area, Ilorin, Nigeria and identified at the Department of Biological Sciences, University of Ilorin, Nigeria. The leaves were washed thoroughly under a running tap water, after which they were cut open. The gel was scooped into a muslin cloth and then squeezed to obtain the juice. The extract was prepared daily for each administration over the seven days experimental period. 5.0mg/ml and 10mg/ml doses were prepared to deliver 500mg/kg and 1000mg/kg body weight concentrations respectively to rats daily.

### Handling of Experimental Animals and Grouping

Twenty four male albino rats (*Rattus novergicus*) with average weight of 160g were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin, Nigeria. The rats were kept in metabolic cages which were cleaned of metabolic waste twice a day. They were exposed to 12 hours each of natural daylight and darkness and given rat chow and water *ad libitum.* They were divided into four groups. Group A (normal control) were not induced with diabetes. Group B (diabetic control) were induced with diabetes but not treated with *Aloe barbadensis*. Groups C and D (diabetic test groups) were induced with diabetes and treated daily with 500mg/kg and 1000mg/kg body weight *Aloe barbadensis* juice extract respectively. Procedures followed in raising the animals are in accordance with the ethical standards laid down by the Ethical Committee of the College of Health Sciences, University of Ilorin, Nigeria and permission was granted by the Institution to undergo the study.

### Induction of Diabetes

Alloxan monohydrate (2, 4, 5, 6 tetraoxypyridine 5, 6-dioxyuracil) was obtained from BDH Chemicals Poole England. Five percent solution of the drug was prepared and used to induce diabetes in rats by intraperitoneal injection at a dose of 150mg/kg body weight. This drug has been reported to act by selectively destroying the beta cells of the pancreas thereby, reducing insulin secretion (Weaver *et al*., 1978). Diabetes was confirmed in the rats by measurement of blood glucose which was elevated.

### Preparation of Serum and Tissue Homogenate

Rats were anaesthetized with diethyl-ether vapour and blood was obtained by cardiac puncture. The blood was left to clot at room temperature for one hour and then put in a refrigerator for a further one hour. The serum was collected after centrifugation at 3000rpm for 5 minutes. This was kept at about $0^{O}C$ and used within 12 hour of preparation. After bleeding, animals were quickly dissected, the liver and kidneys removed and rinsed in ice-cold 0.25M sucrose solution. The tissues were thereafter cut finely with sterile blade before being homogenized in ice-cold 0.25M sucrose solution (1:5 w/v). The homogenate was kept frozen overnight to ensure maximum release of the enzymes (Akanji and Ngaha, 1989).

### Enzymes Assay and Measurement of Serum Metabolites

Alkaline phosphatase (EC. 3.1.3.1) activity was determined by the Para- Nitrophenyl phosphate (PNPP) method of Wright *et al*. (1972). Alanine aminotransferase (EC. 2.6.1.2), and aspartate aminotransferase (EC. 2.6.1.1) were assayed as described by Mohun and Cook (1957). Serum urea concentration was determined using the carbamidodiacetyl micro method of Veniamin and Varkirtzi-Lemonia (1970). Serum creatinine was determined by Jaffe reaction described by Tietz *et al*. (1994), while serum sodium and potassium ions were determined by flame photometry using the Jenway Clinical PFP7 Flame Photometer. Assay kits used were obtained from Quimica Clinical Applicada S.A. (QCA), Amposta Spain. All measurements were done using Spectronic 21 digital Spectrophotometer.

**Statistical Analysis**

Data was analyzed using Duncan multiple range test (Montgomery, 1976) following one-way analysis of variance (ANOVA). Differences at P<0.05 were considered significant.

**RESULTS**

Tables 1, 2 and 3 show the activities of ALP, ALT and AST respectively in the tissues and serum of the experimental animals. There were no significant changes (p>0.05) in the levels of ALP, ALT and AST in the liver and kidney of diabetic animals treated with plant extract (C and D) when compared with the non diabetic (A) and untreated diabetic group (B). However, the activities of the three enzymes in the serum of the diabetic groups (B, C and D) were significantly higher (p<0.05) than the normal control group (A). Values obtained for the three diabetic groups were not significantly different from one another.

Table 4 shows the serum concentrations of Na+, K+, urea and creatinine in the experimental rats at the end of seven days. There were no significant differences in Na+ and K+ levels of the control and diabetic groups. There was significant increase (p<0.05) in the serum urea and creatinine levels of the diabetic groups (B, C and D) when compared to the normal control group (A) as seen in Table 4. However, there were no significant differences in the values obtained for untreated diabetic group and treated diabetic groups.

**Table 1: Activities of alkaline phosphatase (ALP) in the liver, kidney and serum of alloxan-induced diabetic rats treated with *Aloe barbadensis* juice extract (IU/L)**

| Group | Liver | Kidney | Serum |
|---|---|---|---|
| A | 58.80±10.47 | 704.00±70.57 | 65.80±5.60 |
| B | 59.12±12.35 | 795.10±63.25 | 100.80±8.10 * |
| C | 67.60±9.24 | 691.00±68.25 | 102.80±6.40 * |
| D | 66.60±5.60 | 692.00±74.36 | 100.40±5.90 * |

Values are Mean ± SD, n=6.

*Values are significantly different from the normal control group at (p<0.05)

A = Non diabetic rats not treated with *Aloe barbadensis* juice extract
B = Diabetic rats not treated with *Aloe barbadensis* juice extract
C = Diabetic rats treated with 500mg/kg body weight *Aloe barbadensis* juice extract
D = Diabetic rats treated with1000mg/kg body weight *Aloe barbadensis* juice extract

**Table 2: Activities of alanine aminotransferase (ALT) in the liver, kidney and serum of alloxan-induced diabetic rats treated with *Aloe barbadensis* juice extract (IU/L)**

| Group | Liver | Kidney | Serum |
|---|---|---|---|
| A | 538.00±52.15 | 200.00±25.50 | 10.60±1.82 |
| B | 545.34±51.57 | 210.40±30.20 | 33.40±4.30 * |
| C | 540.00±65.15 | 215.50±24.50 | 32.60±3.50 * |
| D | 546.10±50.25 | 220.40±28.80 | 34.50±4.20 * |

Values are Mean ± SD, n=6.

*Values are significantly different from the normal control group at (p<0.05)

**DISCUSSION**

The fact that the levels of the enzymes were maintained in the liver and kidney in all groups of the rat

means that the administered extract has no membrane labilizing effect on these organs. Enzyme activities in the tissues are often used as 'marker' to ascertain early toxic effects of administered foreign compounds to experimental animals (Akanji and Ngaha, 1989; Adesokan and Akanji, 2004). ALP is a membrane bound enzyme while ALT and AST are cytosolic enzymes. These enzymes are highly concentrated in the liver and kidney and are only found in the serum in significant quantities when the cell membrane becomes leaky and even completely ruptured (Cotran *et al*., 1989; Ngaha, 1981).

**Table 3: Activities of aspartate aminotransferase (AST) in the liver, kidney and serum of alloxan-induced diabetic rats treated with *Aloe barbadensis* juice extract (IU/L)**

| Group | Liver | Kidney | Serum |
|---|---|---|---|
| A | 1172.80±164.50 | 1276.00±204.70 | 121.20±2.28 |
| B | 1282.50±212.80 | 1234.00±280.90 | 186.20±4.41 * |
| C | 1402.00±202.40 | 1358.00±265.50 | 188.40±3.96 * |
| D | 1300.00±164.90 | 1326.00±260.50 | 190.60±3.55 * |

Values are Mean ± SD, n=6.
*Values are significantly different from the normal control group at ($p<0.05$)

**Table 4: Serum Na+, K+, urea and creatinine concentrations of alloxan-induced diabetic rats treated with *Aloe barbadensis* juice extract (mmol/L)**

| Group | $Na^+$ | $K^+$ | Urea | Creatinine |
|---|---|---|---|---|
| A | 141.20±2.28 | 4.14±0.62 | 3.54±0.34 | 44.40±5.81 |
| B | 142.20±4.41 | 4.72±0.49 | 12.60±1.20 * | 88.50±8.20 * |
| C | 141.40±2.70 | 4.82±0.26 | 10.80±0.90 * | 86.60±5.80 * |
| D | 141.20±3.96 | 4.62±0.55 | 11.80±0.80 * | 88.20±5.60 * |

Values are Mean ± SD, n=6.
*Values are significantly different from the normal control group at ($p<0.05$)

A rise in serum level or decrease in tissue level of these intracellular enzymes is an index of damage to liver and kidney cells (Moss and Rosalki, 1986).

The observed increase in serum enzyme levels without concomitant alteration in the tissue levels of the enzymes implied that the serum elevation in the diabetic groups might be from other sources apart from the liver and the kidney. Parenteral administration of alloxan at a dose of 150mg/kg body weight has been reported to cause oxidative damage to pancreatic beta cells in rats (Weaver *et al*., 1978). This increase might therefore arise from the damaged pancreatic cells caused by alloxan which was not reversed by *Aloe barbadensis* administration. The observed non alteration in serum electrolyte in animals treated with the extract compared with the control is an indication that the extract might not have altered renal function in the rats. Alteration in serum levels of Na+ and K+ has been associated with renal function impairment (Halpperin and Kamel, 1998; Orth and Ritz, 1998).

The significant increase observed in the serum urea and creatinine of all diabetic groups might be due to increased synthesis from the damaged pancreatic cells caused by alloxan injection and not as a result of kidney damage from *Aloe barbadensis* administration. This is so because rats in group B which were not treated with the extract also indicated similar increase in these serum metabolites.

## CONCLUSION

This study indicated that administration of *Aloe barbadensis* juice extract to alloxanized diabetic rats at the doses considered and the duration of administration did not have any adverse effects on the liver and kidney functions in rats.

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