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Hepatic Enzyme Effects of an *Imperata cylindrica* Extract

M. O. Nwokike[1*], S. I. Ghasi[2], E. C. Ogbuagu[2], M. N. Ezenwaeze[3] and Akpotu E. Ajirioghene[4]

[1]Department of Pharmacology and Therapeutics, Ebonyi State University, Abakaliki, Nigeria.
[2]Department of Pharmacology and Therapeutics, University of Nigeria, Enugu, Nigeria.
[3]Department of Pharmacology and Therapeutics, Enugu State University College of Medicine, Enugu, Nigeria.
[4]PAMO University of Medical Sciences, Port-Harcourt, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

This study was performed to investigate the effects of aqueous *Imperata cylindrica* root extract on hepatic enzyme levels of alloxan-induced diabetic male Wistar rats. Forty (48) male wistar rats were divided into six groups consisting of eight animals each. Diabetes mellitus was induced using intraperitoneal administration 150 mg/kg body weight of alloxan and treatment was carried out for a period of 28 days. The first group served as the normal control and received only feed and water ad libitum. In Group 2 were diabetic rats without treatment with extracts. Group 3: diabetic rats treated with 200 mg/kg aqueous *Imperata cylindrica* root extract. Group 4: diabetic rats treated with 400mg/kg aqueous *Imperata cylindrica* root extract. Group 5: diabetic rats treated with 600mg/kg ethanol extract of aqueous *Imperata cylindrica* root extract. While Group 6 was diabetic rats treated with 0.5mg/kg Glibenclamide. The liver enzymes alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase levels were significantly ($p < 0.05$) changed in rats

**Corresponding author: E-mail: matthew.nwokike@gmail.com;*

treated with Alloxan (150mg/kg b.w.) while treatment with the respective dosages of extracts significantly changed the levels of these parameters to normal. The results obtained indicate that the different doses of aqueous *Imperata cylindrica* root extracts were beneficial in mending damages to the liver caused by Alloxan monohydrate in the male wistar rats.

Keywords: Aqueous Imperata cylindrica root extract; diabetic rats; Hepatoprotective; Alanine aminotransferase; Aspartate aminotransferase; alkaline phosphatise; acid phosphatase.

1. INTRODUCTION

Imperata cylindrica is important economically mainly because of its weedy characteristics. Holm et al. in 1977 classified this species as one of the ten worst weeds in the world [1]. The genus serves a host of productive functions ranging from its use for hay or grazing through the use as a thatching material to being a source of pulp for paper making [2]. Interest in its use for medicinal purposes gained wide appeal mainly because of its nearly worldwide distribution in the warm regions of both hemispheres [3]. A large number studies have been carried out to find the potential of *Imperata cylindrica* for medicinal use [4]. The leaves, rhizomes and roots have all been found to contain potent phytochemicals with medicinal value [5-7]. Ethanol extracts of *Imperata cylindrica* leaves exhibited a significant dose-dependent reduction in amplitude of smooth muscle contraction of rabbit jejunum. The heart pressure of cats was significantly reduced, with no effect on heart rate. The ethanol leaf extract exhibited vasodilative antihypertensive properties similar to the mechanism of adrenaline and suggests a potential use in the management of hypertension [8. This plant that is most noticeable as a weed has also been shown to possess significant anticoagulant activity [9]. Of most importance in the *Imperata cylindrica* studies are that no acute and sub chronic toxicities have been found in rats [10]. Plants are a resource bank for medicine and pharmacology and It has been estimated that between 60-90% of the populations of developing countries use traditional and botanical medicines almost exclusively and consider them to be a normal part of primary healthcare [11]. This is because of their efficacy, low incidence of side effects, and low cost. Based on the established safety of *Imperata cylindrica*, this study was carried out to investigate its possible hepatoprotective effect using established protocol with emphasis on the liver enzymes Alkaline Phosphatase, Alanine transaminase and Aspartate transaminase which are marker of hepatic function. With so many different animal models to choose from, it's imperative to carefully select the best model for the study goals. A Wistar rat model of diabetes mellitus was found appropriate to use for this study. The laboratory rat (Rattus norvegicus) is an indispensable tool in experimental medicine and drug development, having made inestimable contributions to human health due to the many advantages it offers, such as genome similarities, smaller body size and high rates of survival [12]. In a paper published in the April 1 issue of the journal *Nature 2004,* Gibbs et al. reported that, at approximately 2.75 billion base pairs, the rat genome is smaller than the human genome, which is 2.9 billion base pairs, and slightly larger than mouse genome, which are 2.6 billion base pairs [13]. However, they also found that the rat genome contains about the same number of genes as the human and mouse genomes. Furthermore, almost all human genes known to be associated with diseases have counterparts in the rat genome and appear highly conserved through mammalian evolution, confirming that the rat is an excellent model for many areas of medical research [14].

Liver function tests (LFTs) are groups of blood tests that give information about the state of the liver. The liver transaminases; Aspartate and Alanine are useful biomarkers of liver injury [15 and 16]. Alanine transaminase (ALT) is used by the body to metabolize protein. If the liver is damaged or not functioning properly, ALT can be released into the blood. This causes ALT levels to increase. A higher than normal result on this test can be a sign of liver damage. Aspartate aminotransferase (AST) is another enzyme found in several parts of the body, including the heart, liver, and muscles. Since Aspartate transaminase levels aren't as specific for liver damage as Alanine transaminase, it's usually measured together with alanine transaminase to check for liver problems [17]. When the liver is damaged, Aspartate transaminase can be released into the bloodstream. A high result on an Aspartate transaminase test might indicate a problem with the liver or muscles [18]. The third parameter, Alkaline Phosphatase , is an enzyme in the cells lining the biliary ducts of the liver. High levels of Alkaline Phosphatase may indicate liver

inflammation, blockage of the bile ducts, or a bone disease [15 and 19]. Measurement of the effect of aqueous *Imperata cylindrica* root extract on these hepatic enzyme levels is a good assessment of its hepatoprotective effect or otherwise.

2. MATERIALS AND METHODS

2.1 Study Design

This research was based on an experimental design. A Wistar rat model of diabetes mellitus was used to determine the effect of treatment with *Imperata cylindrica* root extracts on diabetic rats [20]. *Imperata cylindrica* roots were harvested from Awha Imezi in Ezeagu Local government area of Enugu state and extracted with chloroform, methanol and water using standard procedures. Alloxan Monohydrate was used to induce diabetes mellitus. Forty eight adult male Wistar rats weighing between 150 and 200grams were obtained from the animal house of the department of pharmacology and therapeutics for the study. The Wistar rats were placed into diabetic and control groups and treatment given with the extracts, glibenclamide and water for a period of twenty eight days in each case (Table 1). The rats were sacrificed after the last treatment day and blood samples collected for analysis of the liver function enzymes using standard analytical procedures. A statistical analysis was made at the end of the study using Prism GraphPad 6 software [21 and 22]. This research project was reviewed and approved by the University of Nigeria Teaching Hospital-Enugu Health Research Ethics Committee with report No: NHREC/05/01/2008B-FWA00002458-1RB00002323.

(ETHICAL COMMITTEE REPORT)

2.2 Extraction Procedure of Plant Materials

Imperata cylindrica extracts was prepared as described previously described [23]. In this procedure 500 g of fresh *Imperata cylindrica* roots was washed with water to remove debris and sand and spread under shade to remove excess water. These were subsequently cut into small pieces and then crushed using a household blender. 50 g of coarsely powdered *Imperata cylindrica* was placed in a container with 100 ml of purified water and tightly sealed. The flask was labelled and kept for 3 days with occasional shaking and stirring. After 3 days of maceration the extract was filtered through (Whatman No. 4 filter paper) and the filtrate concentrated by evaporating the solvents alone The powder obtained was weighed and resuspended in dimethyl sulphoxide (DMSO-Sigma, USA) to prepare stock solutions for the study.

2.3 Effect of *Imperata Cylindrica* Roots Aqueous Extract on Liver Function Enzymes

Alkaline Phosphatase (ALP), Alanine Transaminase (ALT) and Aspartate Transaminase (AST) levels in rat serum were evaluated using assay kits (Randox Laboratories ltd. United Kingdom).

Table 1. Experimental Design

Group (N=8)	Designation	Treatment	Dose Mg//Kg body weight (b.w.)
A	Normal Control	Non-Diabetic Rats Treated With Distilled Water.	Ad Libitum
B	Diabetic Control	Alloxan-Induced Diabetic Rats Treated With Distilled Water.	Ad Libitum
C	Test Group1	Alloxan-Induced Diabetic Rats Treated With Aqueous Extract Of *Imperata Cylindrica* Root	200
D	Test Group 2	Alloxan-Induced Diabetic Rats Treated With Aqueous Extract Of *Imperata Cylindrica* Root	400
E	Test Group 3	Alloxan-Induced Diabetic Rats Treated With Aqueous Extract Of *Imperata Cylindrica* Root	600
F	Positive Control	Alloxan-Induced Diabetic Rats Treated With Glibenclamide	0.5

3. RESULTS

3.1 The Effects of Aqueous Extract of *Imperata cylindrica* Root on alanine aminotransferase (ALT)

The significant difference between the groups treated with *Imperata cylindrica* root extract and the diabetic control asserts that *Imperata cylindrica* root extract is able to decrease ALT levels in the diabetic Wistar rats. As shown in Fig. 1, both the high and low dosages of *Imperata cylindrica* root extract were equally effective in reducing ALT levels and no significant difference has been observed among them ($P < 0.05$). Treatment with *Imperata cylindrica* root extract show better effect than glibenclamide treated group and significant difference in mean values has been noticed between high dose of the extract (600 mg/kg b.w) and glibenclamide-treated groups ($P < 0.05$).

3.2 The Effects of Aqueous Extract of *Imperata cylindrica* Root on Aspartate Aminotransferase (AST) Levels

The results of statistical analysis show a significant difference in the mean value of AST levels in *Imperata cylindrica* root extract-treated and diabetic control groups ($P < 0.05$). This difference indicates the effectiveness of *Imperata cylindrica* root in reducing blood AST levels. As it is seen in Fig. 2 the effectiveness of *Imperata cylindrica* root extract significantly changes based on its dosage ($P < 0.05$) and the high dose of the extract (600 mg/kg) is seen to be more effective than glibenclamide in decreasing AST levels ($P < 0.05$).

3.3 The Effects of Aqueous Extract of *Imperata cylindrica* Root on Alkaline Phosphatase (ALP)

As seen in Fig. 3, both high and low doses of aqueous extract of *Imperata cylindrica* root significantly reduce ALP as compared with diabetic control group ($P < 0.05$). aqueous extract of *Imperata cylindrica* root, either in low (200 mg/kg b.w) or high (600 mg/kg b.w) doses, has been more effective than glibenclamide in reducing ALP and a significant difference has been observed between aqueous extract of *Imperata cylindrica* root treated and glibenclamide-treated groups ($P < 0.05$). The significant difference between mean of the high and low dosages of *Imperata cylindrica* root extract indicates that in diabetic rats, the high dose has been more useful in decreasing ALP levels to a value close to those of control non diabetic rats ($P < 0.05$). The effect of treatment with the extracts on ALP level is found to be dose dependent.

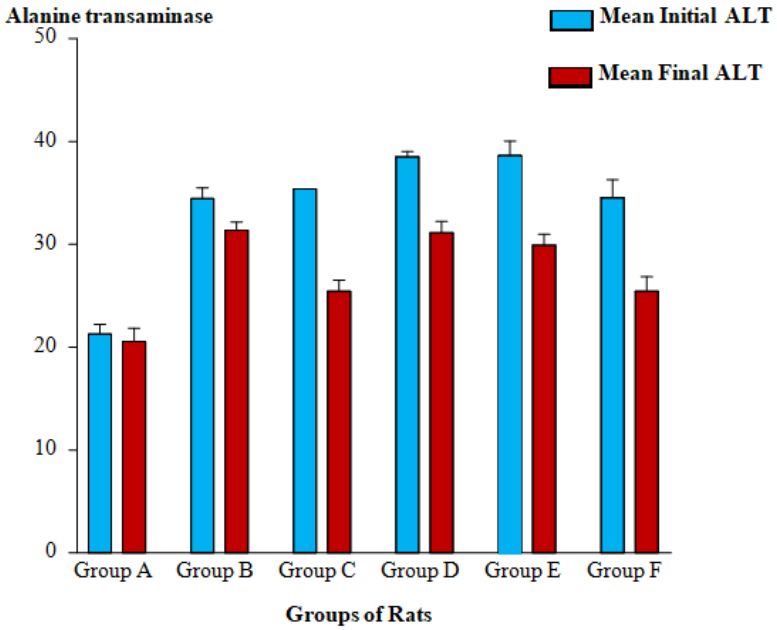

Fig. 1. Bar chart showing the effect of aqueous root extract of Imperata cylindrical on alanine transaminase (ALT) of both normal and alloxan-induced groups of Wistar rats

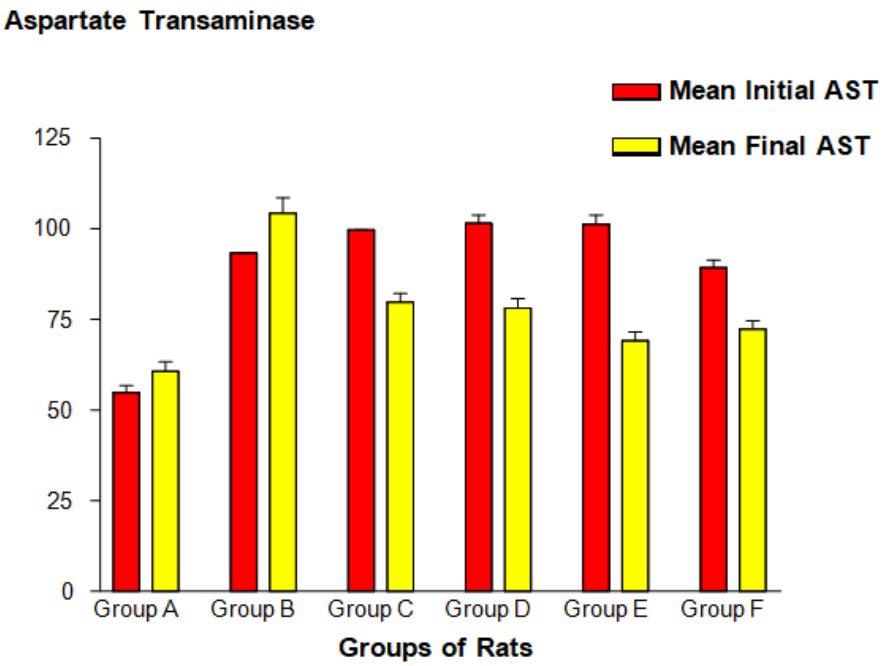

Fig. 2. Bar chart showing the effect of aqueous root extract of *Imperata cylindrical* on aspartate transaminase (AST) of both normal and alloxan-induced groups of Wistar rats

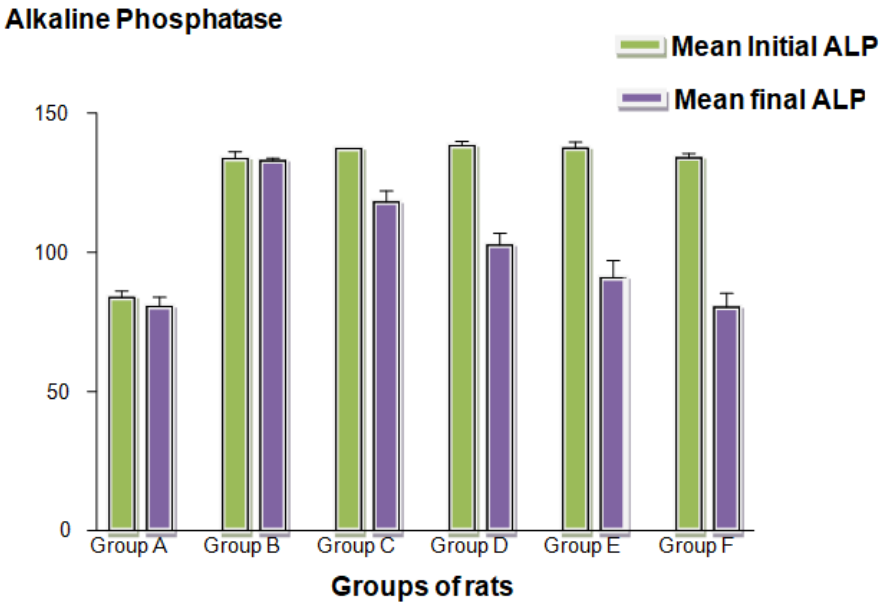

Fig. 3. Bar chart showing the effect of aqueous root extract of *Imperata cylindrical* on Alkaline Phosphatase (ALP) of both normal and alloxan-induced groups of Wistar rats

4. DISCUSSION

Imperata cylindrica (L.) Beauv. (*Poaceae* family) is a perennial weed growing in tropical and subtropical areas and it is used in several herbal preparations to treat specific pathologic factors. Oral acute and sub-chronic toxicity screenings has demonstrated that it is safe at lower doses [24 and 25]. This work aimed to determine the hepatoprotective activities of the root water extract of this plant. Alloxan monohydrate was used to induce diabetes in this study as it is a well- known diabetogenic agent widely used to induce diabetes in animal models [26]. Alloxan is a urea derivative which causes selective necrosis of the pancreatic islet β-cells. Alloxan and its

reduction product dialuric acid establish a redox cycle with the formation of superoxide radicals. These radicals undergo dismutation to hydrogen peroxide. Thereafter, highly reactive hydroxyl radicals are formed by Fenton reaction. The action of reactive oxygen species with a simultaneous massive increase in cytosolic calcium concentration causes rapid destruction of beta cells [27 and 28]. Forty (48) male wistar rats were divided into six groups consisting of eight animals each. Diabetes mellitus was induced using intraperitoneal administration 150mg/kg body weight of alloxan and treatment was carried out for a period of 28 days. The first group served as the normal control and received only feed and water ad libitum. In Group 2 were diabetic rats without treatment with extracts. Group 3: diabetic rats treated with 200mg/kg aqueous *Imperata cylindrica* root extract. Group 4: diabetic rats treated with 400mg/kg aqueous *Imperata cylindrica* root extract. Group 5: diabetic rats treated with 600mg/kg ethanol extract of aqueous *Imperata cylindrica* root extract. While Group 6 was diabetic rats treated with 0.5mg/kg Glibenclamide. The animals were sacrificed and blood collected for analysis. The liver enzymes alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase levels were significantly ($p < 0.05$) increased in rats treated with Alloxan (150mg/kg b.w.) while treatment with the respective dosages of extracts significantly changed the levels of these parameters to normal. The induction of diabetes mellitus increased the levels of the liver enzymes from a mean value of alanine transaminase 31.38±0.7835, aspartate transaminase 93.35±0.05, and alkaline phosphatase 133.6±2.5 to alanine transaminase 34.44±1.067, aspartate transaminase 104.3±4.289, and alkaline phosphatase 132.9±0.8986. Aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) are biochemical markers of hepatic function. In diabetic condition increased liver enzymes is commonly observed among other factors. In the present study, induction of diabetes by alloxan produced increase in increased serum AST, ALT and ALP levels. The increased serum AST, ALT and ALP levels reported in diabetes may be due to liver dysfunction [29]. In this study the increased level of AST, ALT and ALP observed in alloxan-induced diabetic rats which may have occurred by leakage of enzymes from the liver cytosol into the blood stream and represents the toxicity of alloxan on liver. Diabetic rats treated with water extract of *Imperata cylindrica* root significantly reduced the enzyme levels which represents the protective action of the aqueous extract of *Imperata cylindrica* root in diabetic condition. Alloxan is a glucosamine-nitrosourea derived from *Streptomyces achromogenes* (gram-positive bacterium), and it is used for the treatment of pancreatic beta cell carcinoma. Alloxan induces diabetes, hyperinsulinemia, or hyperglycemia by damaging the pancreatic beta cells [30].

The increased serum aspartate transaminase, alanine transaminase and alkaline phosphatase levels in diabetes induced rats may be due to liver dysfunction which may have occurred by leakage of enzymes from the liver cytosol into the blood stream and this represents the toxicity of Alloxan on the liver [31 and 32]. ALT is specifically produced by hepatic cells [33 and 34], while AST is a less specific marker of liver function as it is produced by other organs as well. Diabetic rats treated with the aqueous extract of *Imperata cylindrica* roots significantly reduced both enzyme levels indicate the hepatoprotective action of *Imperata cylindrica* roots [35].

Alloxan treated rats showed elevated plasma levels of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP), but only the AST and ALT values were significant ($P< .05$) when compared to control (Fig. 1,2,and 3). Plasma levels of AST, ALT and ALP in *Imperata cylindrica* treated rats were significantly different compared to control. This finding agrees with the results of Saei et al. [36] showing the positive value of plant extracts in liver injury. The results obtained therefore give a strong indication that alloxan would induce hepatotoxicity in rats and the elevation of the hepatic enzymes by alloxan was prevented by treatment with aqueous extracts of *Imperata cylindrica* root.

5. CONCLUSION

In the present study, induction of diabetes by Alloxan produced elevated liver function enzymes but the administration of the extracts of *Imperata cylindrica* roots to Alloxan induced hyperglycaemic rat demonstrated prominent reduction in blood liver function markers. This study clearly showed the hepatoprotective effect of water extract of *Imperata cylindrica* root in alloxan-induced diabetes in male Wistar rats. The obtained results indicated that *Imperata*

cylindrica root may be a good natural source for protection against liver toxicity.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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