Effects of Leaf and Root Extracts of *Newbouldia laevis* on Hepatic and Renal Systems in Albino Rats

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ABSTRACT

Traditional medicine practitioners in Eastern Nigeria use various parts of *Newbouldia laevis* in treatment and management of several disorders. This research investigated possible toxicity of leaf and root extracts of the plant to liver and kidney in albino rats. Extractions were performed with deionized water and ethylacetate to produce deionized water leaf (DWL), deionized water root (DWR), ethylacetate leaf (EAL) and ethylacetate root (EAR) extracts. A total of 85 adult male albino rats, used in the study, were placed in 16 test and one control groups of five rats in each group. The test groups were given oral administration of 200, 400, 600 and 800mg/kg body weight of the extracts, the control received normal saline for 21 consecutive days. The activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and gamma glutamyltransferase (GGT) in the serum were used to assess hepatobiliary toxicity, while serum creatinine, urea and uric acid were used as renal toxicity indicators.

The activities of ALT, AST, ALP and GGT decreased insignificantly (P>0.05) in the groups given 200 and 400mg/kg of DWL extract, while the enzymes activity groups given 200 and 400mg/kg of other extracts increased insignificantly (P>0.05). The increases obtained at 600 and 800mg/kg of deionized leaf extracts were not significant (P>0.05), while those of ethylacetate extracts were significant (P<0.05). The concentration of creatinine, urea and uric acid obtained from serum of the animals treated with DWL extract was insignificantly higher (P>0.05), while the values recorded with other extracts were significantly higher (P<0.05) than in control. These results suggest that deionized water extracts of *Newbouldia laevis*, as used, may not be toxic to the liver and kidney, while those of ethylacetate may be. Doses of 200 and 400mg/kg DWL extract may be hepatoprotective.

Keyword: Liver enzymes; *Newbouldia laevis*; hepatobiliary toxicity; renal toxicity

INTRODUCTION

The use of plants in the management and treatment of diseases started with life. In more recent years with considerable research, it has been found that many plants do indeed have
medicinal value and these plants have been used to make modern medicines which are now presented by physicians and available for purchase at the drug stores. Today, traditional medicine has been brought into focus for meeting the goals of a wider coverage of primary healthcare delivery not only in Africa, but also, to various extents, in all countries of the world and is the first choice healthcare treatment for at least 80% of Africans who suffer from high fever and other common ailments [1].

In Nigeria many diseases were treated and are still being treated with medicinal plants with success. These diseases include malaria, epilepsy, infantile convulsion diarrhoea, dysentery, bacterial and fungal infections, mental illness, asthma, diabetes, worm infestation, pains and ulcers. Some of the medicinal plants used in Nigeria include *Garcina kola* used for the treatment of asthma; *Carica papaya* used as a remedy for hypertension; *Ocinum basilicum* as cure for typhoid fevers and *Cola nitida* for treatment of piles, etc [2][3][4]. The pharmacological properties of a medicinal plant stem from the chemical constituents of the plant. These compounds (phytochemicals, vitamins and minerals) have the ability to change physiological states [5].

*Newbouldia laevis* is a medium sized angiosperm in the *Bignoniaceae* family. It is found tropical Africa and grows to a height of about 10 meters with a cauliferous habit. It is ever green, though its leaves turn somewhat dark purple during the cold seasons. It is popularly known as the tree of life or fertility tree in Nigeria. Its local Nigerian names include *Akoko* (Yoruba), *Aduruku* (Hausa), and *Ogirisi* (Igbo). The root and leaves are used in the treatment of diseases such as fever, headache, convulsion, epilepsy, and manic disorders [6]. Detailed documented information on the applications of extracts of various parts of *Newbouldia laevis* are scarce. Further, like many medicinal plants, many of the uses and possible adverse effects of the plant by traditional medicine practitioners have not been investigated. Hence, this research investigated possible toxicity of leaf and root extracts of the plant on hepatic and renal systems.

**MATERIALS AND METHODS**

**Collection of Leaves and Roots of Newbouldia laevis**

Fresh leaves and roots of *Newbouldia laevis* were collected in the month of March, 2015 from Izzi in Abakaliki Local Government of Ebonyi State. The samples were identified by Prof. S. C. Onyekwelu of Applied Biology Department, Ebonyi State University, Abakaliki.

**Preparation of Extracts**

The samples were washed with distilled water, air-dried and ground into powder for extractions. The methods of extraction used by Agbafor [3] were adopted, utilizing deionized water and ethylacetate as solvents. The extracts were concentrated using rotor evaporator to get gel-like dark brown extracts.

**Experimental Animals and Handling**

Ethical approval for use of animals in research was given by Ebonyi State University Research and Ethics Committee. A total of eighty-five (85) adult male albino rats, placed in seventeen (17) groups (1-17) of five in each, were used. Groups 1, 2, 3, and 4 received oral administration of 200, 400, 600 and 800mg/kg body weight of DWL extract respectively for twenty one consecutive days, while group 17 was given normal saline. The other groups were treated the same way as summarized below.

- Groups 1 - 4 = DWL extract.
- Groups 5 – 8 = DWR extract.
- Groups 9 – 12 = EAL extract.
- Groups 13 – 16 = EAR extract.
- Group 17 = normal saline.

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Levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and γ-glutamyl transferase (GGT) in serum were be used to monitor the state of hepatic system. Renal toxicity was evaluated using serum levels of creatinine, urea and uric acid.

Serum activities of ALT and AST will be determined according to the method of Reitman and Frankel [7], as described by Akubugwo and Agbafor [8]. A manual two-point kit procedure using p-nitrophenylphosphate was employed in the determination of serum alkaline phosphatase activity [9]. The method of Rosalki and Tarlow [10], described by Tietz [9] was used to measure the serum activity of GGT. The method of Jaffe’s reaction described by Tietz [9] was used to measured serum creatinine. Serum urea was measured according to the method described by Fawcett and Scottie [11]. The method of Brown and Freier [12] was used for the determination of serum uric acid concentrations.

STATISTICAL ANALYSIS

Data generated were expressed as mean ± SD. Statistical significance of difference was determined using the program SPSS 12 (SPSS, USA) by performing one-way ANOVA with post-hoc comparisons between the control group and each of the treated groups by Ducan’s multiple comparison test. A p-value less than 0.05 was considered statistical significant.

RESULTS AND DISCUSSION

Figures 1, 2, 3 and 4 show serum Levels of ALT, AST, ALP and GGT of the rats after twenty one days of extracts administration. The activity of the enzymes decreased insignificantly (P>0.05) in the groups given 200 and 400mg/kg of DWL extract (1 and 2). From the figures, the activity of the enzymes recorded in 600 and 800mg/kg of DWL extract increased insignificantly (P>0.05). The increase in activity of these enzymes all the groups administered DWR extract was not significant (P>0.05). Administration of EAL extract produced an insignificant increase (P>0.05) in the enzymes activity at the dose of 200mg/kg, while the increase was significant (P<0.05) at the other doses. The extract doses of 200 and 400mg/kg of EAR extract recorded an insignificant increase (P>0.05) in the levels of the enzymes, while 600 and 800mg/kg gave a significant increase (P<0.05).

The decrease in activity of ALT, AST, ALP and GGT produced 200 and 400mg/kg DWL leaf extract suggests hepatoprotective potential. This may be due to the reported antioxidant property of the extracts [13]. Antioxidants scavenge free radicals and prevent lipid peroxidation of biomembranes thereby reducing the leakage of intracellular enzymes [14].

However, at higher doses of DWL extract and all doses of other extracts the serum levels of the enzymes increased linearly in a dose-dependent manner. This increase is an indication of toxicity. Clinical observations and experimental studies have shown that subtle changes in the membranes of hepatocytes are sufficient to allow passage of intracellular enzymes into the extracellular space. Cell damage increases membrane permeability, causing cytosolic enzymes to spill into circulation [14]. For instance, in liver disease associated with hepatic necrosis, serum ALT and AST levels are elevated even before the clinical signs and symptoms of the disease appear [14].

Several phytochemicals have been reported to exhibit hepatotoxicity. Pyrrolizidine alkaloids are metabolized in the liver to pyroles which are very toxic to hepatocytes, causing hepatocellular death and fibrosis [15]. Nwogu et al [16] reported the hepatotoxicity of pyrogallol, a hydrolysable tannin derived from simple phenolic acids like gallic acid. The levels of the enzymes obtained in the groups administered EAL extract were correspondingly
higher than other groups, suggesting higher toxicity. This may be due to higher concentrations of toxic phytochemicals. The results on examination of kidney function are presented in figures 5, 6 and 7. The concentration of creatinine, urea and uric acid obtained from serum of the animals treated with DWL extract was insignificantly higher ($P>0.05$) than in control. The increase in their concentration was also insignificant ($P>0.05$) at doses of 200, 400 and 600mg/kg of DWR extract, but significant ($P<0.05$) at 800mg/kg of the extract. The groups treated with EAL extract produced a significant increase ($P<0.05$) at all doses except 200mg/kg which was insignificant ($P>0.05$). In contrast, the values of these parameters obtained in the groups given EAR extract increased insignificantly ($P>0.05$) at doses of 200 and 400mg/kg, and significantly at 600 and 800mg/kg. The elevations in creatinine, urea and uric acid concentrations after administration of the extracts suggest possible renal toxicity. Measurement of blood urea is presently the most widely used screening test (with creatinine) for the evaluation of kidney function. Renal disorders that lead to high blood urea levels include chronic nephritis, polycystic kidney, tubular necrosis and obstruction of urinary tract [17]. Elevated serum creatinine levels are observed in impaired renal function caused by chronic nephritis, urinary tract obstruction, etc. Uric acid levels in the serum are elevated in conditions associated with decreased renal function [9]. The actual cause of this possible renal toxicity is still being investigated. However, some of the chemical constituents of the extracts may have contributed. Several studies [18][19] have indicated the possibility that the use of plant extracts in high doses could lead to toxic injury to the kidneys, which interfere with renal tubular functions and induce renal failure. Some pyrrolizidine alkaloids have been reported to contribute to renal damage due to megalocytosis of renal tubular epithelium and glomerulosclerosis [15]. The EAL extract showed highest toxicity.

![Fig. 1: ALT activity in the animals after twenty-one days of extract administration](image1.png)

![Fig. 2: AST activity in the animals after twenty-one days of extract administration](image2.png)
CONCLUSION
The leaf and root extracts may not be as toxic as many medicinal plants, especially when used at doses not greater than 400mg/kg. The DWL extract may be hepatoprotective at doses not greater than 400mg/kg body weight. Efforts are in progress in our laboratory to identify the compounds responsible for these observations.

CONFLICT OF INTEREST STATEMENT
The authors declare that they have no competing interests.

REFERENCES


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