INTRODUCTION

Despite the availability of modern medicine, many people in the developing countries, especially in the rural areas still rely on traditional healers and medicinal plants to meet their primary healthcare needs and that of their domestic animals. In recent times, however, herbal remedies are becoming indispensable and constitute an integral part of primary health care systems in so many nations. Several documentations on the medicinal importance of traditional plants in Nigeria and their active ingredient(s) have been reported (Adesina, 1999). Ficus exasperata is a small tree or shrub up to 20m tall with scabrous, ovate leaves. It bears figs, which usually appear in pairs in the leaf axils. The bark is smooth, grayish cream with brown streaks and it exudes gummy sap. Several parts of F. exasperata have been used in traditional medicine for treatment of several pathological disorders (Keita, 1999; Ake, 1990; Akah et al., 1998). The ethnomedicinal uses of plants, especially F. exasperata would be useful to scientists for drug production (Fasola and Egunyomi, 2008). It is a high time that we began to conserve and domesticate through tissue cultured and kidney cortex revealed several damages, especially in the kidney cortex. This is an explicit indication that the use of F. exasperata leaf extract in herbal medicine without proper scientific evaluation might be dangerous to health. The efficacy of any drug is dependent on the non-toxic effects on the system of the recipient but exerting its positive effects on the target ailment. Most herbs (drugs) when taken are primarily metabolized by the liver and accumulation of their products can cause cell injury and death. Incidentally, this affects patients with liver diseases, where the processes of detoxification and excretion may have been dangerously altered. Interestingly, there are liver enzymes that act as indicators to either normal functioning or malfunction/dysfunction of the liver. Example is the alkaline phosphatase in the cells lining of the biliary duct of liver whose level in plasma may rise with large bile duct obstruction, interphatic cholestasis or infiltrative substances and diseases of the liver (Kelsey, 1980). The ratio of aspartate aminotransferase (AST) to alkaline phosphatase (ALP) is sometimes useful in differentiating causes of liver damages (MacSween and Whaley, 1992). Significantly, elevated levels of ALT often suggest the existence of other medical problem such as viral hepatitis, congestive heart failure, liver damage, biliary duct problems (MacSween and Whaley, 1992). It has also been reported that albumin level is decreased in chronic liver disease as well as in cirrhosis and nephritic syndrome (Varley et al., 1991). A study by Ijeh and Agbo (2006) indicated that high doses of the ethanolic leaf extract of F. exasperata could lead to toxic injury in the kidneys, which might interfere with renal tubular function and induce renal failure.

This present study is aimed at evaluating the impact of leaf extract of F. exasperata on liver biochemistry and its effect on cyto-architecture of the liver and kidney. This

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will help in no small measure to elucidating its suitability for use as a therapeutic herb.

MATERIALS AND METHODS

Plant collection and preparation of extraction
Leaves of *F. exasperata* was collected from Calabar Metropolis and certified by the herbarium unit of the Department of Botany, University of Calabar, Calabar, Nigeria. The leaves were washed and dried at room temperature (25°C) and subsequent drying in the oven (Continent, MG800G) for ten minutes. The dried leaves were then ground using an electric blender (Orbit, BL 919) to a powdery form. Two hundred grams of the ground material were soaked in 500ml of 98% ethanol for 48hrs stirring at intervals of 10 minutes. The extract was filtered through a muslin cloth and the concentrated extract was allowed to dry at room temperature and stored in a refrigerator at about 4°C until required.

Experimental animal and administration of extract
Thirty two clinically healthy male Wistar rats of about two months old weighing between 130-150g were housed in cages under standard laboratory condition of 12h light/dark cycle throughout the experimental periods. The rats were left to acclimatize for two weeks with free access to water and feed. Four experimental groups of eight rats each were used for the study. Rats in group 1 served as control and received 1ml of the vehicle (normal saline) and normal chow throughout the experimental periods. Group 2 rats received 50mg/kg BW of *F. exasperata* extract while rats in group 3 and 4 received 100mg/kg BW and 150mg/kg BW of the extract, respectively. The administration lasted for eight weeks through oral garvage. 24 hours after the expiration of the treatment regimen, the rats were sacrificed using chloroform anaesthesia. The liver and kidney were removed and weighed. Blood was taken from the heart through cardiac puncture and placed in heparinized sample bottles. The liver and kidney were stored in boun’s solution for histological studies.

Data Collection
Data on Aspartate Aminotransferase (AST), Alkaline Phosphate (ALP), Alanine Transaminase (ALT), Total Bilirubin and Conjugated Bilirubin were collected and subjected to analysis of variance (ANOVA) while Least Significant Different Test (LSD) was used to separate significant means (Obi, 2002).

RESULTS

Aspartate Aminotransferase (AST)
The administration of *F. exasperata* leaf extract on male albino rats had significant effect (P < 0.05) on the Aspartate aminotransferase (AST) level. The trend was not consistent, though it seems dose dependant as the effect increased till 100mg/kg (582.33 µl/L) but reduced to 437.0 µl/L when the rats were administered with the extract dosage of 150mg/kg (Table 1).

Alkaline phosphate (ALP)
The effect of *F. exasperata* leaf extract on alkaline phosphate (ALP) level did not follow the pattern of the effect on Aspartate aminotransferase. When the rats were treated with 150mg/kg, the alkaline phosphate (ALP) level reduced significantly (P < 0.05) but at 50mg/kg, the ALP level increased at its peak, when compared with the control and other treatment groups (Table 1).

Alanine Transaminase (ALT)
There were significant differences (P < 0.05) between the levels of Alanine transaminase (ALT) among the treated groups compared to the control. The level of alanine transaminase was highest in the rats administered with 50mg/kg of the extract. However, there was no significant difference (P > 0.05) between the rats administered with 100mg/kg and 150mg/kg of doses of the leaf extract (Table 1).

Total Bilirubin/ Conjugated Bilirubin
The total bilirubin level differed significantly (P < 0.05) as the dosage of *F. exasperata* leaf extract administration increases while conjugated bilirubin did not differ significantly (P > 0.05) (Figure 1).

Histology of the liver
The normal liver cell showed central vein with it endothelium intact. It shows normal liver architecture with hepatocytes arrange in plates radiating outwards from the central vein, and separated by endothelial lined sinusoids (Plate 1). The sinuosids bear the liver macrophages known as kupffer cells. Treating rats with 50mg/kg of *F. exasperata* extract shows central vein with its endothelium intact though there are some areas of hepatocellular hypertrophy, hepetocellular hyperplasia and sinusoids sclerosis, indicating a damaging effect (Plate 2). When rats were treated with 100mg/kg of *F. exasperata* extract, the liver cells show denudation of the central veins endothelium. Hepatocellular hypertrophy and hyperplasia and sinusoidal sclerosis were also observed (Plate 3). There was central vein erosion when rats were treated with 150mg/kg of *F. exasperata* extract (Plate 4). The liver cells show areas of disorganized hepatocellular cyto-architecture having hepatic cells.

Histology of the kidney
Rats in the control group reveal kidney cortex with glomerulus, bowman’s capsules, proximal convoluted tubules and other normal cyto-architecture of the kidney (Plate 5). The kidney cortex of rats treated with 50mg/kg of *F. exasperata* extract show that there were segmental areas of glomerular tissue necrosis, reduced urinary space, denudation of proximal tubular epithelium and the presence of mononuclear cells in the renal cortical interstitial. This suggests chronic glomerulo-tubular necrosis (Plate 6). There was increase intra glomerular mesangial tissue of rats treated with 100mg/kg of the leaf extract of *F. exasperata*. The urinary space was widening, thickening of the Bowman’s capsule was seen and erosion of the tubular epithelial cells, interstitial edema and the presence of mononuclear cells in the interstitial (Plate 7). Micrograph of the kidney cortex of rats treated with 150mg/kg *F. exasperata* shows the presence of diffused necrosis of glomerular tissue and tubular epithelial necrosis (Plate 8). The kidney cortex shows areas of disorganized cyto-architecture of the renal cortical structures and diffused infiltration of the tissue with mononuclear cells.

DISCUSSION
Majority of the world’s population is dependent upon traditional medicine – the use of plants and plant extracts such as *Ficus exasperata*. This is particularly true of
Table 1: Effect of *Ficus exasperata* leaf extract on biochemical indices

<table>
<thead>
<tr>
<th>Biochemical parameters</th>
<th>Leaf extract dosage (mg/kg BW)</th>
<th>0</th>
<th>50</th>
<th>100</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartate (AST)</td>
<td>295.33±2.99</td>
<td>396.67±4.64</td>
<td>582.33±2.85</td>
<td>437.0±2.22</td>
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<tr>
<td>Alkaline Phosphate (ALP)</td>
<td>29.87±0.77</td>
<td>65.08±0.11</td>
<td>36.67±0.24</td>
<td>23.5±0.55</td>
<td></td>
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<tr>
<td>Alkaline Transaminase (ALT)</td>
<td>44.13±0.35</td>
<td>76.57±0.34</td>
<td>58.77±2.00</td>
<td>58.77±1.09</td>
<td></td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>5.27±0.27</td>
<td>9.97±0.09</td>
<td>14.50±0.44</td>
<td>37.57±0.90</td>
<td></td>
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<tr>
<td>Conjugated bilirubin</td>
<td>2.03±0.09</td>
<td>2.97±0.09</td>
<td>3.80±0.12</td>
<td>4.23±0.09</td>
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</tbody>
</table>

Biochemical inducers of rats reacted with *F. exasperata* (IU/l)

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Fig. 1. Effect of *Ficus exasperata* on liver enzymes of rats

Poorer section countries today tend to depend on herbal remedies which they believe is holistic in curing ailments. Oral drugs are meant to reabsorb in the intestine and transported to the portal vein in the liver. Substances such as these drugs are meant for metabolism (Biotransformation) by the liver and can occur in five pathways: Activation of pro-drug (inactive drug) from the inactive form to an active form, conversion of an active drug into an inactive product, increase activity of an active drug, increase / reduction in activity of an active drugs, and elaboration of a total new drug, different from the one taken, which aimed at detoxifying these drugs (Katzung, 2004, Kumar *et al.*, 2008).

Our results on AST, ALP and ALT indicated that as the doses of the extract increases, there was significant reduction in the levels of the enzymes in the liver. It does suggest that the liver cells have a mechanism of reducing the excess substances within the cells. At an optimal concentration of the extract in the system, the liver cells tend to metabolize it leading to the reduction of effect. This might be the reason underlying the low serum level of AST (437.0±µ/L), ALP (36.67 µ/L) and ALT (58.77 µ/L) observed when rats were administered with 150mg/kg, 100mg/kg and 150mg/kg, respectively of the *Ficus* extract. The extracts showed a dose-dependent effect on the total bilirubin. However, the effect of the extract on the liver enzymes tends to be enzyme-specific. Apparently, the biosynthetic pathways leading to their production are different and as such the extract may have acted upon them differently and at varying intensities.

There is no doubting the obvious that *F. exasperata* leaf extract contain different bioactive components at varying concentrations, which individually or synergistically might either boost or impede the production process of the different enzymes. Most of their contents are hepatic enzyme inducers that mean that they have the potential to cause an increase in the synthesis of the enzymes in the liver. When this happen the sizes of the liver cell increases...
PLATE 1  
H/E  
\( \times 400 \)
Photomicrograph of liver from control group (mg/kg showing the central vein (cv) with its endothelium intact. Hepatocytes (H) (polygonal shaped cells with one to two nuclei) are arranged in plates radiating outwards from the central vein, and separated by endothelial lined spaces Sinusoids (S). Within the sinusoids are seen the sinusoidal lining endothelial cells, red blood cells, and the resident liver macrophages Kupffer cells (K).

PLATE 2  
H/E  
\( \times 400 \)
Rats treated with 50mg/kg with F. exasperata, showing the central vein (cv) with its endothelium intact, areas of hepatic cellular hypertrophy (Hh), hepatocellular hyperplasia (Hs), sinusoidal sclerosis (Ss). \( X \) = Artifact

PLATE 3  
H/E  
\( \times 400 \)
Treated rats with 100mg/kg of extract of F. exasperata showing demodulation of the central veins endothelium (Cd), Hepatocellular hypertrophy (Hh) and hyperplasia (Hs) with a focus of sinusoidal sclerosis (Ss).

PLATE 4  
H/E  
\( \times 400 \)
Photomicrograph of rats treated with 150mg/kg, showing area of central vein erosion (Ce), areas of disorganized hepatic cellular cyto architecture having necrotic hepatic cells (Hn).

PLATE 5  
H/E  
\( \times 400 \)
Photomicrograph of the kidney cortex of rats in control group, treated with leaf extract of F. exasperata showing the glomerulus (g), Bowman’s capsule (B), TBM space (U), many proximal convoluted tubules (P) lined by simple cuboidal epithelial cells with brush borders, distal convoluted tubules (D) lined by simple cuboidal epithelium without brush borders, and the cortical interstitium (I).
Ikpeme et al., Biological response of male wistar rats to crude extract of Ficus exasperata (VAHL)

The results are an indication that medicinal plants, such as F. exasperata should be thoroughly screened before recommending it as therapeutic agents. It is arguable that these effects or distortions as reported in our results are negligible but unfortunately might have a gradual damaging effect unnoticed in the recipient, if proper caution is not taken.

REFERENCES


