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A STUDY OF ETHNOMEDICINAL USE OF PHYLLANTUS AMARUS BY HYPOGLYCEMIC ANALYSIS IN KIDNEY DISEASES

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ABSTRACT

Histological studies of the effects of oral administration of aqueous extract of *Phyllanthusamarus*commonly used in ethno medical practice in Africa for the management of various ailments such as kidney stonesand urogenital diseases on the kidney of adult Wistar rats were carefully studied. Rats of both sexes (n=24), average weight of 260g were randomly assigned into three groups: A, B and C of (n=8) in each group. Group A and B served as treatment groups (n=16) while group C (n=8) served as the control. The rats in the treatment groups (A & B) received 500mg/kg and 1000mg/kg body weight respectively of aqueous extract of *Phyllanthusamarus* orally through orogastric tube for twenty-eight days, while the control rats received equal volume of distilled water without the extract of *Phyllanthusamarus* added for the same period. The rats were fed with growers' mash purchased from Edo feeds and Flour Mill Ltd, Ewu, Edo state and were given water liberally. The rats were sacrificed on day twenty-nine of the experiment. The kidneys were carefully dissected out and quickly fixed in 10% formal saline for routine histological study after H&E method. The histological findings indicated that the treated sections of the kidneys showed hypertrophy of blood vessels, mild-severe infiltrate of chronic inflammatory cells and varying degrees of tubular necrosis when compared to the control sections. The findings indicated that the administration of *Phyllanthusamarus* extract has some adverse effects on the kidneys of adult Wistar rats. It is recommended that further studies aimed at corroborating these observations be carried out.

I INTRODUCTION

Plant materials as sources of medical compounds continue to play a dominant role in the maintenance of human health since antiquity. Over 50% of all modern chemical drugs are of natural plant product origin, and is essential in drug development programs of the pharmaceutical industry (Burton et al., 1983). Like any therapeutic agent, when overdosed or incorrectly used they also have the potential to induce adverse effects. The historic role of medicinal

herbs in the treatment and prevention of disease, and their role as catalysts in the development of pharmacology do not, however, assure their safety for uncontrolled use by an uninformed public (Matthews et al., 1999).

Phyllanthusamarus (*P. amarus*) is a broad spectrum medicinal plant that has received world- wide recognition (Srividiya and Perival, 1995). In Nigeria, it is called "Oyomokeisoamankedem" in Efik, "IyinOlobe" in Yoruba and "Ebebenizo" in Bini (Etta, 2008). *P. amarus* is generally employed to reduce pain, expel intestinal gas, to stimulate and promote digestion, as anti-helminthes to expel intestinal worms and act as a mild Laxative. *P. amarus* also has antiseptic, diuretic, antiviral, anti-diabetic, hypotensive and antipyretic properties, and is also used in the treatment of jaundice, diarrhoea, dysentery, wound, ulcers and urogenital diseases (Calixto et al., 1998; Santos et al., 1995). The plants of the genus *Phyllanthus* are widely distributed in most tropical and subtropical countries and have long been used in traditional medicine to treat chronic liver disease (Liu et al., 2003).

The histological effects of *P. amarus* on the kidneys have not been widely elucidated, as very few literature reports have been documented (Etta, 2008; Adeneye and Benebo, 2008). The traditional uses of *P. amarus*for kidney stones and gall bladder stones have been validated by clinical research, where *P. amarus* extract was found to exhibit a potent and effective non-concentration dependent inhibitory effect on calcium oxalate crystal formation, the building blocks of most kidney stones (Calixto, 2000). This response was present even at a very high (pathogenic) concentration. This may explain why it has long been used in traditional medicine as prevention against kidney stone formation (Campos and Schor, 1999). *P. amarus*has been found to be 94% successful in eliminating stones (Maxwell, 1990). Some Brazilian researchers in the mid 1980's reported on the antispasmodic activities of alkaloids in *P. amarus*, this explained the popular use of the plant for the expulsion of kidney and bladder stones. The alkaloid extract demonstrated smooth muscle relaxation specific to the urinary and biliary tract which the researchers surmised facilitates the expulsion of kidney and bladder calculi(Miller, 1998; Calixto, 1984).

II MATERIALS AND METHODS

2.1 Plant Materials

Fresh leaves of *Phyllanthusamarus* (voucher number UBAD-Pa 001) were collected in December, 2009 at Iduonomwina town, Ovia North-East local government area of Edo State. The plant was identified and authenticated at the Botany Department of University of Benin, Benin City. The harvested fresh leaves were sun dried and ground into a fine powder. The dried material (800g) was macerated in 10 liters of distilled water for 48hrs at 4°C in a refrigerator. The extract was sieved and the juice was filtered using Whatman No 1 filter paper. The filtrate was placed in a stainless-steel tray, and concentrated in an air-circulating oven at 42°C until totally dry. The resultant extract (18g) was placed into small glass dishes and stored at 28°C in an incubator for further studies.

2.2 Phyllanthusamarus administration

The rats in the treatment groups (A & B) received 500mg/kg body weight and 1000mg/kg body weight respectively of aqueous extract of *Phyllanthusamarus* orally through an orogastric tube on a daily basis. The control group received an equal volume of distilled water without the extract of *P. amarus* added for twenty-eight days.

III HISTOLOGICAL STUDY

Blood samples were collected and analyzed for blood urea nitrogen (BUN) and serum creatinine (Scr) by using the commercial kits (McClatchey, 1994) on the twenty-nine day of the experiment. After bleeding, the rats were sacrificed by cervical dislocation and the abdominal cavity was opened up using a pair of forceps to expose the kidneys which were quickly dissected out and fixed in 10% formal saline for routine histological techniques. The tissues were dehydrated in an ascending grade of alcohol (ethanol), cleared in xylene and embedded in paraffin wax. Serial sections of 7 microns thick were obtained using a rotatory microtome. The deparaffinized sections were stained routinely with hematoxylin and eosin (H&E) method (Drury et al., 1967). Photomicrographs of the desired sections were made for further observations.

IV RESULT

The result of this experiment revealed that administration of *P. amarus* caused significant ($P<0.05$) increase in functional nephrotoxicity indicators such as BUN and Scr in *P. amarus* -treated rats compared with control (Table 1). The control sections of the kidneys showed normal histological features. The section indicated a detailed cortical parenchyma and the renal corpuscles appeared as dense rounded structures with the glomerulus surrounded by a narrow Bowman's spaces.

Table 1 Effects of *Phyllanthusamarus* administration (500mg/kg and 1000mg/kg) on BUN and Scr concentration

	BUN (mg/dl)	Scr (mg/dl)
Control	14.34±2.4	0.71±0.24
Experimental group A (500mg/kg)	26.6±4.26	1.72±2.64
Experimental group B (1000mg/kg)	63±1.23	3.7±3.93

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Figure 1. Normal kidney showing glomeruli (G), cortical (B) and medullary tubules (C). [H&E] Mag. x 400

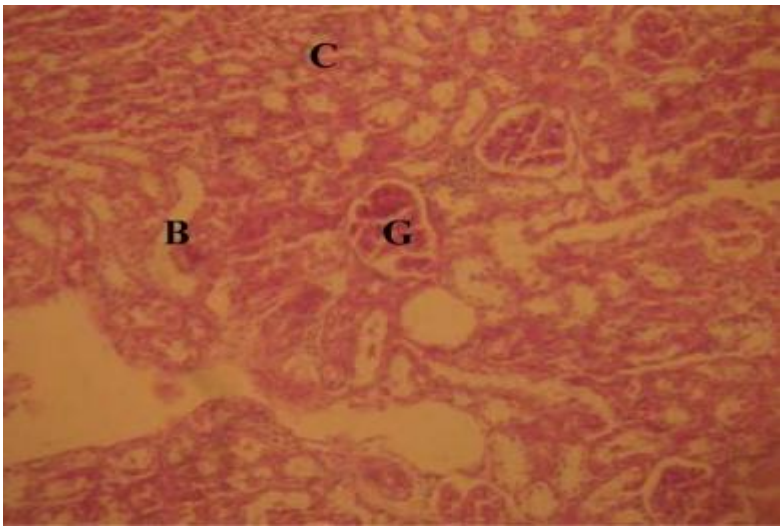

Figure1: Control section of kidney; this shows cortical parenchyma to consist of dense rounded structures, the glomeruli, surrounded by narrow Bowman's capsular spaces. H&E (Mag. X400).

Figures 2 & 3: Photomicrograph of treatment sections of the kidney of rats that received 500mg/kg body weight of *P. amarus* revealing some level of cyto-architectural distortion. H&E (Mag. X400)

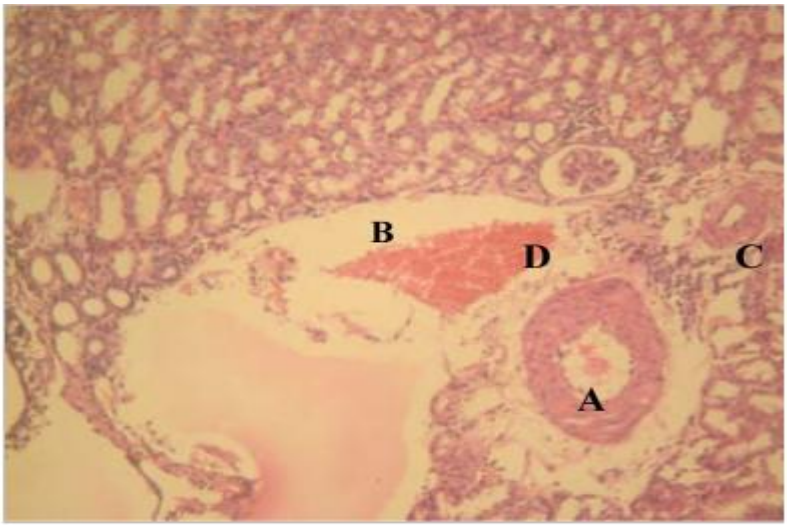

Figure 2. Group "A" treated kidney showing vascular hypertrophy (A), interstitial oedema (B), chronic inflammatory infiltrates (C) and haemorrhage (D) [H&E x 400]

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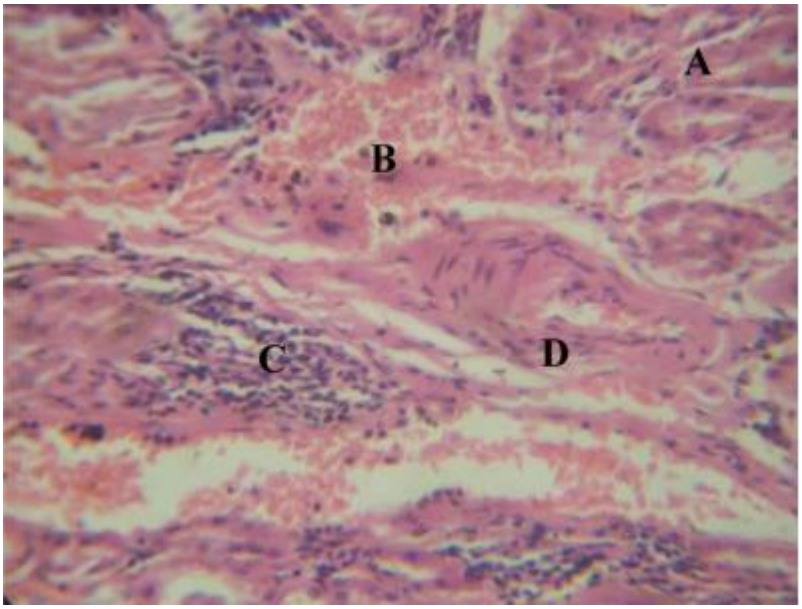

Figure 3. Group 'A' treated kidney showing Tubular necrosis (A), interstitial haemorrhage(B) Mild chronic inflammatory cell infiltrates(C) and Vascular hypertrophy (D) [H&E x 400]

V DISCUSSION

The result (H&E) revealed that administration of *Phyllanthusamarus* caused varying degree of cyto-architectural distortion and vasculogenic effect on the kidney which affected blood vessels, haemorrhagic and chronic inflammatory cells appearing in the treatment groups compared to the control group. Narrowing of the lumen also occurred with associated hypertrophic blood vessels and haemorrhage extending into the interstitium. There were several diffuse degeneration and necrosis of the tubular epithelial cells in the kidneys of the treated animals (500–1000 mg/Kg). The degenerative and atrophic changes where observed more in the kidneys of rats that received the higher dose (1000mg/kg) of *P. amarus*.

It may be inferred from the present results that higher doses of *P. amarus* may have resulted in degenerative and atrophic changes observed in the renal corpuscle. The histological effects observed in this experiment is in consonance with the report of Manjrekar *et al.* who observed that *P. amarus* induced deleterious changes on the renal tubules and testes of male rats (Manjrekar et al., 2008; Adedapo et al., 2005). It is noteworthy that *P. amarus* contains alkaloids and lots of antioxidants (Fernand, 1998; Naaz, 2007; Krithika and Verma, 2009), which has been given to apparently healthy animals. Our observation is consistent with the notion that antioxidant is associated with toxicities especially if taken arbitrarily (Miller, 2005). Although, antioxidants are essential for alleviation of oxidative stress, indiscrete intake of alkaloids and antioxidant constituents of *P. amarus* may present

their toxic effects by inducing oxidative stress (Atici et al., 2005; Galati and O'Brien, 2004). The possible deduction from these results is that secondary metabolites, which are largely responsible for therapeutic or pharmacological activities of medicinal plants (Perry, 1980), may also account for their toxicity when the dosage is abused. The actual mechanism by which *P. amarus* induced cellular degeneration observed in this experiment needs further investigation.

VI CONCLUSION

The results obtained in this study revealed that administration of *P. amarus* could affect the histology of the kidney of adult Wistar rat; causing disruptions and distortions of the cyto-architecture of the kidneys despite the fact that *P. amarus* is known to eliminate gall stones, kidney stones and other kidney related problems (Heyde, 1990). These results suggest that the functions of the kidney may have been adversely affected. It is recommended that caution should therefore be advocated in the intake of this product and further studies be carried out to examine these findings.

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