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Full Length Research Paper

Toxicopathological effects of *Guiera senegalensis* extracts in wistar albino rats

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Toxicity of methanolic and water extracts of the plant *Guiera sengalensis* has been tested on rats. The methanolic extract was injected intramuscularly while the water extract was given orally. Rats receiving 1000 and 500 mg/kg/day of the methanolic extract died within one week. The 250 mg/kg/day dose resulted in enlargement of the liver and kidneys, although body weights of the treated rats were not significantly different from the control. Alterations of haematological and serological parameters were evident. The effect of water extract was less marked compared to that of methanolic extract. Treatment with *G. senegalensis* resulted in endotheliotoxicity, hepatonephropathy and pancreatic hyperplasia.

Key words: *Guiera sengalensis*, toxicology, pathology.

INTRODUCTION

The plant *Guiera senegalensis* is a member of family Combrataceae and is known locally as Ghubeish. The plant has been found to contain flavonoids, saponins alkaloids, tannins and mucilage. Ficarra et al. (1997) found four flavonoids in the leaves of *G. senegalensis*, namely catechin, myricitrin, rutin and quarterin.

El-Gazali et al. (1994) and El-Gazali (1997) stated that macerated leaves of the plant were used orally for treatment of febrifuge as well as for hyperglycemia and hypertension whereas the roots used mainly as antileprosy.

Silva et al. (1997) claimed that the plant is used by Fulani traditional healers to treat several disorders including venereal disease. He also stated that the plant has significant viricidal effect against Herps Simplex Virus type 1 (HSV1). Sanogo et al. (1998) reported that the plant posses anti tussive activity.

Although *G. senegalensis* has a wide range of traditional uses virtually up to now no data were available on its toxicity. These data were necessary before the use of the plant in large scale for medicinal purposes. Thus in this study experiments were setup in order to study the toxicity of the plant on rats.

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MATERIALS AND METHODS

Plant

The plant *G. senegalensis* was collected from the western part of the Sudan (El-Fashir) and authenticated in Medicinal and Aromatic Plant Research Institute (MAPRI), Khartoum, Sudan. The plant was dried in shade and the leaves were ground coarsely for the extraction.

Methanolic extract was prepared according to Harborne method (1980) and was dissolved in distilled water for injection. Water extract was prepared by maceration of coarsely ground leaves in distilled water.

Toxicity study

Two experiments were conducted; one for methanolic extract and the other for water extract of *G. senegalensis*. The water extract was given orally because it is the common route by which herbists used it for various treatments. However, the parental route was used to verify its safety if it was given as remedy.

In each experiment twenty male albino rats were used. The rats were divided randomly into four groups, of five rats each. Group I which was kept as control was injected intramuscularly with distilled water, whereas the other three groups received the methanolic extract at doses 250, 500 and 1000 mg/kg/day respectively for three weeks.

In the water extract study rats were similarly grouped as those in the previous experiment. The control group received distilled water orally and the other three groups received the water extract orally at the same doses as in the methanolic extract study. Clinical signs and mortality rates were recorded daily. Average body weights were determined in each group at time necropsy.

Table 1. Body weights and relative organ weight of male albino rats treated with methanolic and water extracts of *Guiera senegalensis* for three weeks.

Treatment (mg/kg/day)		Body weights (gms)	Relative organ weight (%)		
			Liver	Kidney	Heart
Methanolic extract (IM)*	0	136.3 ± 26.9^{NS}	3.5 ± 0.3^{NS}	0.6 ± 0.10^{NS}	0.4 ± 0.10^{NS}
	250	105.0 ± 28.3^{NS}	4.2 ± 0.1*	0.7 ± 0.02^{NS}	0.4 ± 0.04^{NS}
Water extract (PO)	0	116.7 ± 20.2^{NS}	2.8 ± 4.2^{NS}	0.7 ± 1.10^{NS}	0.26 ± 0.04^{NS}
	250	102.5 ± 21.0^{NS}	3.5 ± 0.4^{NS}	0.7 ± 0.05^{NS}	0.32 ± 0.06^{NS}
	500	101.3 ± 23.9^{NS}	3.3 ± 0.9^{NS}	1.0 ± 0.27^{NS}	0.36 ± 0.18^{NS}
	1000	101.7 ± 34.0^{NS}	3.5 ± 1.4^{NS}	0.6 ± 0.18^{NS}	0.36 ± 0.04*

*Rats dosed with 500 and 1000 mg/kg died within a week
Values are mean ± SD; NS : Not significant * P < 0.05.

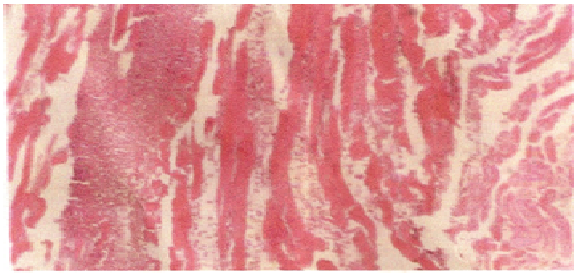

Figure 1. Muscle from rat receiving 500 mg/kg *Guiera senegalensis* methanolic extract. Note: Muscle fibers become homogenous with inflammatory cells infiltration. (H & Ex200).

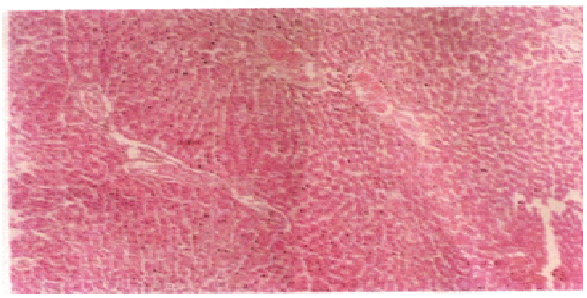

Figure 2. Liver from rat receiving 500 mg/kg *Guiera senegalensis* methanolic extract. Note: Congestion and dilated sinusoids. (H&Ex100).

Blood samples were collected weekly throughout the experimental period and at slaughter time for haematology and serum chemistry. Complete haemogram was determined according to Schalm (1965). Mean cell volume (MCV) and mean cell hemoglobin concentration (MCHC) were calculated.

Sera were analyzed for the activity of alkaline phosphate and cholesterol concentration using commercial kits according to Chemie (1972) and Richmond (1973) respectively. The concentration of total protein, calcium and phosphorus were determined according to Weichselbaum (1946), Trinder (1960) and Varley (193) respectively.

Post mortem examination was performed. The internal organs (liver, kidney and heart) were weighed and their ratios to bodyweight were calculated. Specimens from different organs were fixed in 10% neutral buffered formalin, embedded in paraffin wax, sectioned at 5 µm and stained with haematoxyline and eosin

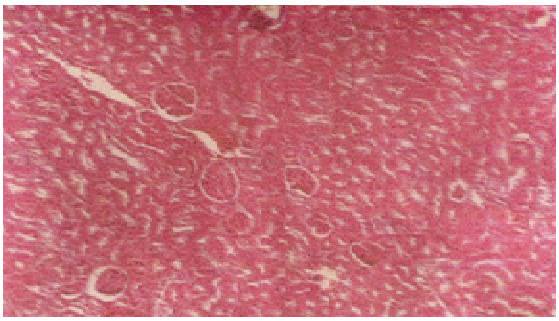

Figure 3. Kidney from rat receiving 1000 mg/kg *Guiera senegalensis* water extract. Note: Haemorrhage and isolated tubular necrosis (H&Ex100).

according to Drury et al. (1967).

Data were analyzed for significance using student's T-test according to Mendenhall (1971).

RESULTS

Rats receiving the methanolic extract of the plant *G. senegalensis* at the doses 1000 and 500 mg/kg/day died within one week but those receiving 250 mg/kg/day were depressed throughout the period of the study. There were no obvious signs observed in rats treated with water extract at different doses.

No significant difference was detected in body weights between the control and the rats treated by both extract. However, there was a significant increase in the relative weight of the liver in rats treated with 250 mg/kg/day methanolic extract and the heart in those treated with 1000 mg/kg/day water extract (P < 0.05), (Table 1). Congestion of the internal organs and fatty livers were the obvious gross lesions observed in both experiments.

There were no significant changes in blood cellular elements in rats receiving water extract of *G. senegalensis*. However, in those rats receiving methanloic extract of the plant, there was significant decrease in the mean values of RBC, Hb, PCV and MCHC at the dose 250 mg/kg/day (P< 0.05). A significant increase was also

Table 2. Haematologic and serum chemistry values of male albino rats treated with methanolic and water extracts of *Guiera senegalensis* for three weeks.

Parameters	Treatment (mg/kg)					
	Methanolic extract		Water extract			
	0	250	0	250	500	1000
PCV (%)	40.3±1.3 ^{NS}	38.0±0.0*	42.3±2.50 ^{NS}	43. ±2.30 ^{NS}	41.8±2.40 ^{NS}	42.0±1.00 ^{NS}
Hb (g/d)	10.8±0.4 ^{NS}	9.5±0.2*	11.9±0.17 ^{NS}	11.6±0.38 ^{NS}	11.6±0.15 ^{NS}	11.7±0.30 ^{NS}
RBCs(10^6)	5.4±15.5 ^{NS}	5.1±7.8*	4.9±0.42 ^{NS}	4.98±9.14 ^{NS}	5.0±0.09 ^{NS}	5.1±0.07 ^{NS}
WBCs(10^3)	1.4±0.1 ^{NS}	2.7±0.1**	1.6±0.08 ^{NS}	1.7±0.05 ^{NS}	1.6±0.60 ^{NS}	1.6±0.10 ^{NS}
MCV(fl)	74.2±2.2 ^{NS}	73.3±3.8 ^{NS}	87.2±5.60 ^{NS}	87.5±2.40 ^{NS}	83.3±4.60 ^{NS}	84.3±1.50 ^{NS}
MCHC (%)	26.7±0.6 ^{NS}	25.6±0.4*	28.2±1.70 ^{NS}	26.8±1.40 ^{NS}	27.9±1.60 ^{NS}	26.9 ±1.40 ^{NS}
TP(g/100ml)	7.6±0.3 ^{NS}	7.9±01**	7.2±0.30 ^{NS}	7.1±0.30 ^{NS}	7.7±0.50 ^{NS}	7.2±0.40 ^{NS}
ALP(U/l)	862.3±61.0 ^{NS}	1066.1±47.1***	855.3±72.60 ^{NS}	1027±78.90*	1069.7±72.20*	915.9±20.00 ^{NS}
Chol(mg/dl)	112.7±8.3 ^{NS}	156.8±30.1*	72.7±3.00 ^{NS}	105.2±15.40*	152.2±32.80*	93.1±5.30**
Ca(mg/100ml)	7.6±0.1 ^{NS}	7.9±0.1*	7.6±3.00 ^{NS}	7.7±3.00 ^{NS}	7.98±0.20*	8.2±0.20**
P(mg/100ml)	4.6±0.1 ^{NS}	4.8±0.2 ^{NS}	4.9±0.10 ^{NS}	4.8±0.2 ^{NS}	4.7±0.20 ^{NS}	4.9±0.20 ^{NS}

Values are mean ± SD; NS: Not significant.
* P< 0.05; ** P < 0.01; *** P < 0.001.

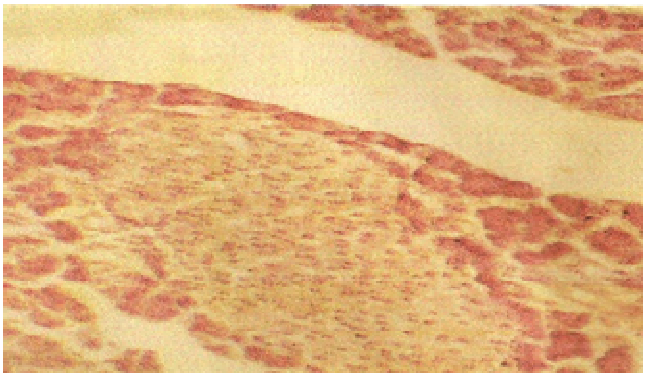

Figure 4. Pancreas from rat receiving 500 mg/kg *Guiera senegalensis* water extract. Note: Hyperplasia of islet of langerhans. (H&Ex400)

noted in the WBC at the same dose (P< 0.01), (Table 2).

Changes in serum constituents included significant increase in the activity of alkaline phosphate (AP) at the dose 250 mg/kg/day of the methanolic extract (P< 0.001) and at the doses 250 and 500 mg/kg/day the water extract (P< 0.05). Cholesterol concentration was raised significantly in rats receiving 250 mg/kg/day methanolic extract (P< 0.05), in rats receiving the water extract at the doses 250, 500 (P< 0.05) and at 1000 mg/kg/day (P< 0.01). The total protein increased only in rat treated with 250 mg/kg/day of the methanolic extract (P< 0.01). Calcium concentration was raised at the dose 250 mg/kg/day of the methanolic extract (P< 0.05) and at the doses 500 and 1000 mg/kg/day of the water extract (P< 0.05 and P< 0.01) respectively (Table 2).

Histopathologically, the dose 250 mg/kg/day of both extracts produced no adverse lesions in the internal organs. Hemorrhages, necrosis, loss of striation and infiltration of inflammatory cells were found in muscles of rats dosed with the methanolic extract (Figure 1).The lesions caused by the doses 500 and 1000 mg/kg/day were similar. These include congestion, haemorrhages and dilated liver sinusoids (Figure 2). Haemorrhages and isolated tubular necrosis of the kidney (Figure 3) and pancreatic hyperplasia (Figure 4) were also detected.

DISCUSSION

No research has been done to delineate the toxic effects of the plant *G. senegalensis*. In the present study, the methanolic extract of the plant was found to be fatal to male albino rats at a daily concentration of 1000 and 500 mg/kg/day after one week when given intramuscularly. Water extract was found to have some toxicity but no mortality was recorded. These may be due endotheliotoxic effect of the plant as reflected by the hemorrhage seen in the internal organs.

The dose 250 mg/kg/day of the water extract given per os had minor changes; hence people used this plant in the folk medicine. Nevertheless, the effect after long term use of this plant was not studied, so their adverse effect is unknown.

The changes seen histopatholoically in the liver included congestion, dilated sinusoids and hepatocytes necrosis may explain the elevated level of total protein concentration in rats that received the methanolic extract and the increased activity of the alkaline phosphatase in rats receiving both extracts. The decreased haematologic parameter in the intramuscularly treated rats may be attributed to the kidney damage that affected the erythropoietin production. The effect on the kidney is also reflected by the raised level of calcium in the two treated

groups.

The hyperplasia seen in the islets of pancreas may increase the production of insulin. This may elucidate the finding that the plant is hypoglycemic as stated by Ahmed (1999).

We may conclude that the plant *G.senegalensis* can be used safely at lower doses as hypoglycemic.

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