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TOXICITY STUDY ON ETHANOL EXTRACT OF *FISCUS PLATYPHYLLA DELLE* (MORACEAE) IN ALBINO RATS

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Abstract

*F*icus plytaphylla Del. (Moraceae) Gamji in Hausa, is a savanna tree commonly found in northern Nigeria; Sokoto, Borno, Bauchi, Zamfara, Adamawa etc. The plant possess *medicinal properties that are effective in the management of tuberculosis, cough and other ailments, and has been commonly used in traditional medicine. This study was undertaken to investigate the toxicity stem bark extract of Ficus platyphylla Del. so as to ascertain its safety in traditional medicine. Samples of the plant were collected from Madagali Local Government Area of Adamawa State, Nigeria, during fruiting and flowering season. It was air dried, powdered and extracted in ethanol. The extract was further distilled using rotary evaporator at the temperature of 45ºC to enhance its concentration. Different concentrations of the alcohol extract were prepared in distilled water; 1%, 2%, and 3% were administered orally to groups A, B and C respectively for 14 days. The reaction of the rats to the extract were investigated and compared with the control. The results obtained showed some degenerative changes in the brain, lungs, and intestine as well as*

175

EDITOR-IN-CHIEF
Prof. A.S. Hossein [Saskatchewan]

reduction in the red blood cells, white blood cells, packed cell volume and hemoglobin below their normal values. The result further showed that the severity of the extract was dose dependent.

INTRODUCTION

From the beginning of human civilization, people have used plants as medicine, perhaps, as early as Neanderthal man; plants were believed to have healing powers (Sayeed, 2010). Man being propelled by his belief on the potency of plants had continuously made efforts to explore both organic and inorganic compounds in his environment, interestingly plants and plant derived products have offered relief to many diseases (Yakubu, *et al.,* 2010) The use of these plants or herbs brought traditional medicine into existence (Sofowora, 1992) The proliferation of modern day medicine is anchored on plants and plants derived products. It has been reported that 80% of these medicines are derived from plants which have been investigated pharmacologically out of the 2000-2500 species of higher plants growing on earth (Farnsworth, 1996). *Ficus platyphylla,* Gamji in Hausa, is a savanna tree commonly found in northern Nigeria; Sokoto, Borno, Bauchi, Zamfara, Adamawa etc. It is about 18 m high, 6m in girth, with large widely spreading branches and a broad crown. The bark is rusty red, flaking off in scattered parches and greys beneath, slash pink. Branches very stout, twig stipples and young foliage finely velvety. Leaves are 7 – 40cm long by 10-28cm broad. Mostly broadly elliptic, round or blunt at the apex and narrowly cordate, thick finely velvety or globorous (Irvine, 1961; keal, *et al.,* 1989).It is called Epo obo among the Yarubas in South west, Nigeria and is commonly used in traditional medicine for convulsive disorder (Wakeel, *et al.,* 2004). The presence of bioactive components in its extract has made it potent in treating diseases of microbial origin (Gandidaza and Gaza, 1993).

Ficus plytaphylla, possesses medicinal properties that are effective in the management of tuberculosis, cough and other ailments (Kubmarawa *et al,* 2009). The plant has also been reported to possess in vitro antitrypanosomal activity (Wurochekke and Nok, 2004; Atawodi, 2005).

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MATERIAL AND METHODS
Sample collection and preparation

Samples of *F. platyphylla* were collected from Madagali local government Area of Adamawa State, Nigeria in the month of April. The collection was made at the flowering and fruiting season and identification made by John Akiniyi, Department of Chemistry University of Maiduguri, Borno state, Nigeria. The samples were thoroughly rinsed with tap water and distilled water before being air-dried at room temperature for 14 days. Then, the plant samples were ground to a fine powder and soaked in 96% ethanol for 4 days with frequent agitation at room temperature. The extract was filtered with Whatman filter paper no. 1 and the solvent distilled off by rotary evaporator at the temperature of 45°C.

Experimental Animals

Male and female Albino rats were used for the toxicity studies. The rats were obtained from the Biochemistry Research Laboratory, University of Maiduguri, Nigeria. The animals were acclimatized to laboratory conditions for 7 days prior to the experiments. The rats were maintained at a room temperature housed in a cage and were fed with pellet diet and tap water ad libitum.

Administration of extracts

The rats were divided into four groups (A,B,C and D) of four rats each. Group D, was used as control and received the vehicle only (water and feeds), while group 1,2 and 3 served as the test groups, were administered with 1%, 2% and 3% ethanol extracts of *Ficus   platyphylla* respectively. The administration continued for fourteen days.

Blood sample collection

At the end of the experimental period, blood samples were collected by cutting the tip of the tails of the rats using scissors. The blood samples were introduced into clean dry (EDTA) bottles for hematological parameters. The

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Prof. A.S. Hossein [Saskatchewan]

white blood cells (WBC) were estimated using improved Neubauer counting chamber as described by Dacie and Lewis (1991). The hemoglobin (Hb), concentration was determined by the Cyameth haemoglobin Method. While the Packed Cell Volume (PCV), was determined by Micromethod as described by Dacie and Lewis (1991)

Hispatholigical Studies

The liver, kidney, lungs, brain and intestines were immediately harvested and perfuse with 10% formalin which were then used for histopathological studies. Sections of the tissues were viewed under light microscope (Nikin microscope Eclipse E400 model 115 Japan).

Statistical Analysis

The data were statistically evaluated by one way ANOVA

RESULTS

Table I: Effect of *Ficus Platyphylla* extract on Red Blood Cells (RBC) (Anova Analysis of RBC data) Anova: Single Factor

SUMMARY

Groups	Count	Sum	Average	Variance
Column 1	16	9609	600.5625	29211.73
Column 2	16	9431	589.4375	3545.996
Column 3	16	11902	743.875	19351.58
Column 4	16	9708	606.75	22001
Column 5	16	8920	557.5	25216.8

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Groups	331808.1	4	82952.03	4.175699	0.004161	2.493696
Within Groups	1489907	75	19865.42			

EDITOR-IN-CHIEF
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Total	1821715	79				

F (Calculated) 4.175699 is greater than F (Critical), 2.493696 showing a significant difference (reduction) in RBC values

Table II: Effect of *Ficus Platyphylla* extract on white blood cells (WBC) (Anova Analysis of WBC data)
Anova: Single Factor.
SUMMARY

Groups	Count	Sum	Average	Variance
Column 1	16	3758	234.875	8608.383
Column 2	16	3645	227.8125	7432.296
Column 3	16	3086	192.875	8320.517
Column 4	16	2694	168.375	4687.983
Column 5	16	2660	166.25	4370.467

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
BetweenGroups	66568.2	4	16642.05	2.49986	0.050284	2.493696
Within Groups	501294.7	75	6683.929			

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Prof. A.S. Hossein [Saskatchewan]

Total	567862.9	79			

F (Calculated) 2.49986 is greater than F (Critical) 2.493696 which shows significant difference (reduction) in values of the white blood cells.

Table III: Effect of *Ficus Platyphylla* extract on packed volume cells (PCV) (Anova Analysis of PCV data)

Anova: Single Factor

SUMMARY

Groups	**Count**	**Sum**	**Average**	**Variance**
Column 1	16	775	48.4375	3.4625
Column 2	16	717.6	44.85	15.95333
Column 3	16	645	40.3125	52.72383
Column 4	16	595.6	37.225	77.83
Column 5	16	582.8	36.425	86.13667

ANOVA

Source of Variation	**SS**	**df**	**MS**	**F**	**Pvalue**	**F crit**
Between Groups	1676.485	4	419.1213	8.875688	06	2.493696
Within Groups	3541.595	75	47.22127			
Total	5218.08	79				

F(Calculated), 8.875688 is greater than F(Critical) 2.493696 which shows a significant(reduction) difference in the values of Packed Cell Volume

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Table IV: Effect of Ficus Platyphylla extract on hemoglobin (Anova Analysis of hemoglobin)
Anova: Single Factor
SUMMARY

Groups	Count	Sum	Average	Variance		
Column 1	16	234.7	14.66875	1.539625		
Column 2	16	224.4	14.025	1.375333		
Column 3	16	210.5	13.15625	2.006625		
Column 4	16	204.6	12.7875	2.5145		
Column 5	16	200.1	12.50625	3.988625		

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	51.67325	4	12.91831	5.653673	0.000495	2.493696
Within Groups	171.3706	75	2.284942			
Total	223.0439	79				

Figure I: Animals in group A treated orally with 1% extract showing hemorrhage, congestion, oedema and bronchopneumonia in the lungs of the test rats.

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Figure 2: Animals in group B treated orally with 2% extract showed that there was hemorrhage, congestion, oedema and bronchopneumonia, neuronal necrosis with gliosis characterized by aggregation of glial cells found on the central cortex (brain) of the test rats.

Figure 3: Animals in group C treated orally with 3% extract showed that there was subacute L enteritis characterized by L submucosal (mainly lymphococytes). The infiltration of leucocytes L increased the number of globlet cells, epithelial necrosis and villus atrospy in the intestine.

DISCUSSION

In this study, leaves extract of *Ficus platyphylla Del.* was administered orally to three groups of four rats each for the period of fourteen days. Clinical

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signs were observed in the test rats. It was quite noticeable that the extracts induced sleep in the test rats, thus, reducing their locomotive activities. This agrees with similar work conducted by Chindo *et al.*, 2003 and Chinenye *et al.*, 2011). An investigation conducted by (Zia, 1995 and Wakeel *et al*, 2004) further showed sleeping in test rats. The increase in dose orally administered on each group resulted in depression of weight when compared to the control group. This is partly due to reduced food intake with the animals appearing to be dull. On the other hand, it depicts a level of toxicity exerted by the extract on the animals which interfered with their normal weight gain.

There was bleeding from the eyes, hair losing, and aggressive behavior towards one another. Similarly, acute administration of aqueous extract of *Ficus Lyrala* in the dose of 200mg/kg showed change in behavior as reported by (Sayeed, 2010). These results suggest that the extract has direct effect on the central nervous system (CNS).

Effect of the extract on hematological parameters

Effects was observed on the white blood cells, red blood cells, hemoglobin and packed cell volume, showing values below normal.

Table 1, displays the result of the effect of the extract of *platyphylla* on the red blood cells (RBC). From the table, a significant reduction in the red blood cells was observed. The reduction was as a result of the effect of the extract; with group C showing the lowest value, followed by group B and A. The reduction is in the order of their concentrations

Table 2, shows the effects of the extract on the white blood cells (WBC). The effects vary between the groups, the variance being a function of concentration of the extract administered to the rats. Hence, the rats in group C have the lowest WBC volume with highest concentration of extract. The reduction in white blood cells and lymphocytes was glaring when compared to the control group. The reduction is possibly caused by the presence of steroids in the extract as reported by (Gillard, *et al.*, 2000 and Chinenye, 2011). Decrease in white blood cells leads to less immune system. Sex steroids have been reported to reduce immune system (Gillard *et al.*,

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Prof. A.S. Hossein [Saskatchewan]

2000) Animals in this condition are prone to attacks by any foreign bodies like bacteria, virus, fungi etc resulting in diseased condition.

Table 3, shows the effects of the extract on the packed cell volume (PCV). The effect of the extract has led to the reduction in the volume of PCV. Group 1 with lower concentration, showed little reduction compared to groups B and C with higher concentrations of the extracts. The reduction in the packed cell volume could be due to the presence of saponins which is known to reduce PCV as reported by (Oyeyemi, s*et al., 2015*)

Table 4 shows the effect of the extract on hemoglobin. From the result it was observed that there was reduction in the hemoglobin values in all the three groups compared to the control group. Group C shows the lowest value followed by group B and group A. The reduction is inversely proportional to the concentration of the extract. The purpose for the estimation of hemoglobin is to determine the oxygencarrying capacity of blood. The drop in the value consequently will result in anemic and leukemic conditions due to decreased red blood cells.

Effects on the hispathological parameter

Histopathological studies showed that the extract has adverse effects on the lungs, central cortex and on the intestines but there were no effects on kidneys and liver.

Animals in group A treated orally with 1% extract (figure 1), showed that there was hemorrhage, congestion, oedema and bronchopneumonia found in the lungs.

Animal in group B treated orally with 2% extract (figure 2) showed that there was hemorrhage, congestion, oedema, neuronal necrosis (focal) with gliosis characterized by aggregate cells were found on the central cortex (brain).

Animals in group C treated orally with 3% extract (figure 3) showed that there was sub-acute L, enteritis characterized by L. sub mucosal (family lymphocytes) infiltration of leucocytes L, increased number of globule cells, epithelial necrosis and villus atrophy in the intestine.

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Animals in group D showed none of the effects above, this confirms that the effects observed in the three groups above is a function of the extract administered.

Conclusion

The results of the investigation conducted on stem-bark of *Ficus platyphylla* Del. using albino rats, revealed that the extract is toxic. However this does not underscore its medicinal status on the fact that several research works had unveiled the efficacy of the plant extracts in the treatment of mental disorder and other ailments, but this work suggest that its application should be with caution.

Recommendations.

The potency and application of the extract of *F. platyphylla* in traditional medicine has been scientifically established. However the implications of over dosage has clearly been revealed by this work. It is therefore recommended that the extract should be administered in a moderate or mild dose, because excessive dosage could cause reduction in the levels of white blood cells, red blood cells, packed cell volume and hemoglobin and could also induce degenerative changes in the lung, brain and the intestine which may result to death. More work should be done on isolation and structural elucidation to establish the structures of the phyto-components of the extracts of *F. platyphylla* which are responsible for its medicinal property.

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