https://dx.doi.org/10.4314/jpb.v14i2.12
Vol. 14 no. 2, pp. 187-196 (September 2017)
http://ajol.info/index.php/jpb

Journal of
PHARMACY AND BIORESOURCES

Acute and subacute toxicity study of ethanol extract of *Ficus sycomorus* L. (Moraceae) leaf and *Faidherbia albida* (Fabaceae) stem bark

Samuel Y. Timothy[1*], Hayatu I. Galadima[2], Olufunke A. Sodipo[3], Hamza H. Milagawanda[4]

[1]Department of Pharmacology and Toxicology, Faculty of Pharmacy; [3]Department of Clinical Pharmacology and Therapeutics, College of Medical Sciences; [4]Department of Pharmaceutical Chemistry, Faculty of Pharmacy; University of Maiduguri, Maiduguri. Nigeria.
[2]Department of Medicinal Chemistry and Quality Control, National Institute for Pharmaceutical Research and Development, Idu, Abuja. Nigeria.

Received 28th July 2017; Accepted 27th August 2017

Abstract
Traditionally in northern Nigeria, different parts of *Ficus sycomorus* (FS) and *Faidherbia albida* (FA) plants are commonly used to manage diverse medical ailments including diabetes and epilepsy. This study was undertaken to ascertain the acute and sub-acute toxicity of ethanol extracts of FS leaves and FA stem bark in Wistar albino rats. The fresh leaves of FS and the stem bark of FA were collected, prepared and extracted using 95% ethanol. The sub-acute toxicity test was carried out using ten groups of five rats each: control group, four doses of ethanol leaf extract of FS, four doses of ethanol stem bark extract of FA and combination of FS and FA extract. The extracts were administered orally on daily basis for 28 days. At the end of the study, all animals were sacrificed at which the blood samples were collected for biochemical and haematological analysis respectively. The results of acute toxicity study showed the extracts were relatively less toxic. Sub-acute administration of the combined extract of FS and FA did not significantly affect haematological, renal and hepatic functions. However, there was a dose dependent decrease in the renal function. Bark extract of FA significantly increased the levels of ASAT, ALAT, TB and CB ($p<0.05$) at the doses of 250 and 500mg/kg. The combined extract of FS and FA was found to be relatively safe on hematological parameters and did not alter the hepatic and renal functions. Thus, justifies the traditional use of these plants combination for managing diseases in northern Nigeria.

Keywords: *Ficus sycomorus*; *Faidherbia albida*; Ethanol extract; Acute toxicity; Sub-acute toxicity

INTRODUCTION

Plants contain many biologically active components which have potentials for development as medicinal agents, most of which were found to be safe and affordable by the common man [1]. According to the World Health Organization (WHO), such species of plants are used worldwide in the treatment of diverse medical ailments and substantial number of them showed effective activities [2]. It is for this reason that the WHO recommended the appropriate use of medicinal herbs by patients as well as physicians, and be included in the drug policies of member States [3]. Typical examples of such plants are *Ficus sycomorus* and *Faidherbia albida*, which are used traditionally in the management of diseases

[*] Corresponding author. *E-mail*: satiye2002@gmail.com *Tel*: +234 (0) 8034955545
ISSN 0189-8442

including pains, infections, diabetes and epilepsy. Ethno medical and medical survey conducted have revealed that *Ficus sycomorus* and *Faidherbia albida* plants have potent antioxidant, antidiabetic, anti-pyretic, anti-inflammatory and anti-diarrheal effects as well as for coughs, throat infections, chest pains and to aid child birth [4-9]. Preliminary phytochemical studies of *Ficus sycomorus* and *Faidherbia albida* plants revealed the presence of flavonoids, saponins, alkaloid, glycoside, carbohydrate, anthraquinones, triterpenoids, steroids, phlobatannins and tannins [10-12]. Traditionally, these two plants are often used alone or in combination for the management of diseases in most part of northern Nigeria. However, the safety profile of such plants combination is yet to be evaluated scientifically. Therefore, this study was embarked upon in order to evaluate the acute and subacute toxicity of these plants.

EXPERIMENTAL

Plant collection and identification. The leaves and stem-bark of *Ficus sycomorus* and *Faidherbia albida* respectively were freshly collected from their natural habitat around Dalori primary school area, opposite University of Maiduguri, Borno State, in March 2016 based on folklore report from a renowned traditional medical practitioner (Consultant herbalist Faculty of Pharmacy University of Maiduguri) on the therapeutic potential of the plants. An acknowledged authority in taxonomy identified the plants in the Department of Medicinal Plant Research and Traditional Medicine, National Institute for Pharmaceutical Research and Development (NIPRD) Idu-Abuja, and a voucher specimen numbers were assigned as NIPRD/H/6830 and NIPRD/H/6831 for *Ficus sycomorus* leaf and *Faidherbia albida* stem bark respectively. The plant samples were deposited at the institute herbarium for future studies and reference.

Preparation and extraction of plant materials. The fresh leaves of *Ficus sycomorus* and the stem bark of *Faidherbia albida* were collected, washed and air-dried at room temperature for about three weeks. They were then cut into small pieces and homogenized into powder by use of a mechanical mill. One thousand grams (1000 g) of the finely powdered samples of *Ficus sycomorus* leaves and the stem bark of *Faidherbia albida* were defatted with petroleum ether, after which they were subjected to maceration with 95% ethanol. One litre of ethanol was poured into the sample separately and both samples were kept for 24 hours and then filtered. The residues of the two samples were soaked in another 1000 ml of ethanol and were kept for another 24 hours. This procedure was repeated for three (3) consecutive days, after which a brown syrupy mass of filtrates were obtained and were finally dried at low temperature under reduced pressure in a rotary evaporator. A crude residue of 37.6 g and 45.2 g for *Ficus sycomorus* leaves *and Faidherbia albida* stem bark were obtained with a yield of 3.76% and 4.52 % respectively. A stock solution of all extracts and standard drug used were prepared by taking a known quantity of extract and dissolved in water for injection BP. Freshly prepared stock solution of reference standard drugs and test extracts were then tightly covered and refrigerated.

Animal experiments. Male and female albino rats weighing between 150 g and 250 g were obtained from the animal house, Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Maiduguri and University of Maiduguri Teaching Hospital respectively. The rats were acclimatized for 7 days under standard environmental conditions of temperature, relative humidity and dark/light cycle before the commencement of the study. They were kept in a clean cages embedded with sawdust and fed with vital feed growers (pelletized).

Water was constantly supplied to the rats in a clean drinking bottle. The weights of the rats were also determined using a beam balance and were randomized into different groups for the study.

Acute toxicity study. The acute toxicity study was performed based on the modified method described by Lorke [13] according to the Organization for Economic Co-operation and Development (OECD) guideline 420 for testing chemicals. Healthy animals of both sexes were randomly sampled and fasted overnight before the administration of the ethanol leaf extract of *Ficus sycomorus* and *Faidherbia albida* stem bark at different dose levels per body weight for both phase one (10, 100, 1000 and 2000 mg/kg) and two (2900, 3500 and 5000 mg/kg) for intraperitoneal and oral routes. After administration of the extracts, the rats were observed for mortality within 24 hours. The dose that killed 50% of the rats (LD_{50}) was determined after phase two.

Sub-acute toxicity study. The sub-acute toxicity test was performed following the protocol described by the OECD guideline 408 for testing chemicals. Rats of both sexes were randomly assigned into ten groups of five rats each: control group, four doses of ethanol leaf extract of *Ficus sycomorus* (62.5, 125, 250 and 500 mg/kg), four doses of ethanol stem bark extract of *Faidherbia albida* (62.5, 125, 250 and 500 mg/kg) and combination of FS and FA plants extracts (500mg/kg). The extracts were administered orally on daily basis for 28 days at a single dose of 62.5, 125, 250, 500 mg/kg and a combined dose of 500 mg/kg for the two extracts (250 mg of FS + 250 mg of FA). The control group received only distilled water at a dose of 2ml/kg. The extracts were freshly prepared with vehicle on daily basis. The rats were weighed and visual observations for mortality, behavioral pattern (salivation, fur, lethargy and sleep), changes in physical appearance and sign of illness. At the end of the study, all animals were sacrificed. Blood samples were collected in plain and EDTA-containing tubes for biochemical and haematological analyses respectively. The organs were excised, weighed and examined macroscopically.

Organ weight: After 28 days of extract administration, all the rats were sacrificed after which their organs, which include liver, kidney, lung and spleen, were removed and weighed on a Metler balance.

Haematological analysis: Five millilitres (5 ml) of blood was obtained from the animals after 28 days of extracts administration through humane killing (sacrifice) without haemostasis and was used for determining the levels of haemoglobin, packed cell volume, red blood cells, white blood cells, platelets, MCV, MCH and MCHC according to the standard methods of Jain [14] and Odutola [15].

Chemical pathological analysis: Liver function test (LFT) and renal function test (RFT) were performed on each study rat after 28 days of extracts administration. Five millilitres (5 ml) of blood was acquired aseptically from the sacrificed rat without haemostasis and used for the analysis. Total bilirubin, conjugated bilirubin, total protein, albumin, alkaline phosphatase (ALP), aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT) were used to assess the effect of extracts on liver function. Similarly, the effect of these extracts on the kidney was assessed by measuring (assaying) levels of bicarbonate (HCO_3^-), chloride (Cl^-), potassium (K^+), sodium (Na^+), urea and creatinine based on the standard procedures outlined by Reitman and Frankel [16], Klein *et al* [17], Schmidt and Schmidt [18], Babson [19] and Babson *et al* [20].

Statistical analysis. The results were expressed as mean ± standard error of the mean (SEM) and analyzed with Graph pad Instat software using pooled Student's t-test.

A $p<0.05$, $p<0.01$ and $p<0.001$ were considered significant, highly significant and extremely significant respectively.

RESULTS

Acute toxicity study of ethanol extracts of *Ficus sycomorus* leaves and *Faidherbia albida* stem bark. The acute toxicity of ethanol extracts of *Ficus sycomorus* leaves and *Faidherbia albida* stem bark in albino rats at doses of 10, 100, 1000 and 2000 mg/kg intraperitoneally, resulted in the death among the rats that received 2000 mg/kg in both the plant extracts. In the second phase in which doses of 1200, 1400 and 1800 mg/kg intraperitoneally leads to the death of the rats that received 1800 mg/kg at which the LD_{50} was calculated to be 1587.5 mg/kg for both the plant extracts (Table 1). The LD_{50} of ethanol extracts of *Ficus sycomorus* leaves and *Faidherbia albida* stem bark at doses of 10, 100, 1000 and 2000 mg/kg orally, did not cause death among the albino rats after phase 1 of acute toxicity study. In the second phase, doses of 2900, 3500 and 5000 mg/kg were administered but no mortality was observed. Therefore, the LD_{50} of ethanol extracts of the two plants after oral route was found to be greater than 5000mg/kg (Table 1).

The effects of ethanol extracts of *Ficus sycomorus* leaves and *Faidherbia albida* stem-bark on organs weight of Wistar albino rats for 28 days. The effects of ethanol stem bark extract of *Faidherbia albida* on the weight of the liver of Wistar albino rats that were treated for 28 days showed a significant decrease ($p<0.05$) at 500 mg/kg when compared with control group. Ethanol extracts of *Ficus sycomorus* leaves and *Faidherbia albida* stem-bark did not affected the weights of lungs, kidneys and spleen of Wistar albino rats after 28 days of administration when compared with the control group ($p>0.05$) (Table 2).

Effect of ethanol leaf extracts of *Ficus sycomorus* and stem-bark of *Faidherbia albida* on hematological parameter in Wistar albino rats for 28 days. The ethanol leaf extract of *Ficus sycomorus* and stem-bark extract of *Faidherbia albida* at different dose levels showed no statistical significant difference in the levels of Hb, MCV, MCH, MCHC when compared with the control ($p>0.05$). However, 500 mg/kg of ethanol leaf extract of *Ficus sycomorus* showed a statistical significant difference in the levels of PCV and Platelets ($p<0.05$). Similarly, 250 mg/kg stem-bark extract of *Faidherbia albida* showed a statistical significant decrease in the levels of platelets ($p<0.05$) when compared with control group. Furthermore, it was observed that 500mg/kg of ethanol extract of stem-bark of *Faidherbia albida* was able to decrease significantly the level of RBC, WBC and Platelets ($p<0.01$) (Table 3).

Effect of ethanol leaf extracts of *Ficus sycomorus* and stem-bark of *Faidherbia albida* on liver function in Wistar albino rats for 28 days. Moderate doses (250 mg/kg) of ethanol leaf extract of *Ficus sycomorus* after 28 days of administration showed a significant increase in the levels of alkaline phosphatase (ALP) and alanine aminotransferase (ALAT) when compared with control group ($p<0.05$). A significant increase in the level of total bilurubin was also observed due to 500 mg/kg of FS plant extract ($p<0.05$) after sub-acute therapy. Sub-acute toxicity study of the ethanol leaf extract of *Ficus sycomorus* in Wistar albino rats did not affected the levels of aspartate aminotransferase (ASAT), total protein (TP), albumin (ALB) and conjugated bilirubin (CB) ($p>0.05$). The ethanol stem bark extract of *Faidherbia albida* after 28 days of administration did not alter the levels of ALP, TP and albumin ($p>0.05$) when compared with control. However, there was a significant increase in the levels of ASAT ($p<0.01$), ALAT ($p<0.01$), TP ($p<0.05$) and CB

($p<0.01$) after 28 days of administration of 250 and 500 mg/kg of the stem bark extract of FA. Combined extract of Ficus and Faidherbia administration did not affect serum biochemical parameters assessing liver function in the present study.

Effect of ethanol leaf extracts of *Ficus sycomorus* and stem-bark of *Faidherbia albida* on renal function in Wistar albino rats for 28 days. *Ficus sycomorus* leaf extract did not alter the level of Na^+ among the albino rats after 28 days of treatment except the highest tested dose of 500 mg/kg that significantly increased the level of Na^+ ($p<0.05$). *Ficus sycomorus* leaf extract at 250 and 500 mg/kg significantly increased the levels of potassium when compared with the control ($p<0.05$). There was no statistical significant difference in the levels of Na^+ and K^+ due to the stem-bark extract of *Faidherbia albida* at the tested doses. The level of chloride ion significantly increased due to ethanol leaf extracts of *Ficus sycomorus* and stem-bark of *Faidherbia albida* in Wistar albino rats treated for 28 days. At 500 mg/kg dose of both plant extracts, there is a statistical significant difference in the serum biochemical level of bicarbonate ($p<0.05$) when compared with control. *Ficus sycomorus* leaf extract at 250 and 500 mg/kg significantly increased the level of urea among the studied rats when compared with the control ($p<0.05$), whereas only 500 mg/kg of the stem-bark of *Faidherbia albida* was able to increase the level of urea among the rats ($p<0.05$). The *Ficus sycomorus* and *Faidherbia albida* ethanol extracts have produced a significant increase in the level of creatinine at all the tested doses when compared with control ($p<0.05$) (Table 5).

Table 1: Acute toxicity study of ethanol extracts of *Ficus sycomorus* (L.) leaves and *Faidherbia albida* stem bark in albino rats

Phases	Intraperitoneal route		Oral route	
	Ficus sycomorus leaf extract	*Faidherbia albida* stem bark extract	*Ficus sycomorus* leaf extract	*Faidherbia albida* stem bark extract
Phase 1	10 mg/kg	10 mg/kg	10 mg/kg	10 mg/kg
	100 mg/kg	100 mg/kg	100 mg/kg	100 mg/kg
	1000 mg/kg	1000 mg/kg	1000 mg/kg	1000 mg/kg
	2000 mg/kg*	2000 mg/kg*	2000 mg/kg	2000 mg/kg
Phase 2	1200 mg/kg	1200 mg/kg	2900 mg/kg	2900 mg/kg
	1400 mg/kg	1400 mg/kg	3500 mg/kg	3500 mg/kg
	1800 mg/kg*	1800 mg/kg*	5000 mg/kg	5000 mg/kg
LD_{50}	1587.5 mg/kg	1587.5 mg/kg	>5000 mg/kg	>5000 mg/kg

*= Death

Table 2: Effect of ethanol leaf extract of *Ficus sycomorus* and stem-bark extract of *Faidherbia albida* on organs weight in Wistar albino rats for 28 days

Group & Dose (mg/kg)	Organ weight (g) (Mean±SEM)			
	Liver	*Lungs*	*Kidneys*	*Spleen*
Control	3.46±0.19	1.50±0.07	0.96±0.11	0.48±0.04
FS 62.5	3.64±0.13	1.42±0.09	0.76±0.05	0.60±0.04
FS 125	3.48±0.22	1.46±0.22	0.88±0.07	0.50±0.07
FS 250	3.32±0.26	1.38±0.15	0.86±0.11	0.58±0.07
FS 500	3.26±0.19	1.32±0.08	0.80±0.14	0.56±0.08
FA 62.5	3.42±0.37	1.38±0.20	0.84±0.12	0.62±0.07
FA 125	3.10±0.15	1.30±0.25	0.82±0.07	0.54±0.07
FA 250	3.26±0.27	1.38±0.14	0.72±0.08	0.40±0.03
FA 500	2.82±0.15*	1.28±0.12	0.74±0.10	0.46±0.09
FS/FA 500	3.68±0.25	1.40±0.07	0.94±0.07	0.42±0.04

FS = *Ficus sycomorus*, FA = *Faidherbia albida*, n = 5, Student's t- test, * = p<0.05 (significant)

Table 3: Effect of ethanol leaf extracts of *Ficus sycomorus* and stem-bark of *Faidherbia albida* on hematological parameters in Wistar albino rats for 28 days

Dose & Group (mg/kg)	Hematological parameter (Mean±SEM)							
	Hb (g/dl)	PCV	RBC ($x10^{10}$/L)	MCV	MCH	MCHC	WBC ($x10^9$/L)	Platelets ($x10^9$/L)
Control	15.22±1.60	0.50±0.04	248.00±12.04	204.46±19.71	6.28±0.87	31.21±3.80	7.62±0.35	526.00±26.62
FS 62.5	14.42±1.15	0.53±0.04	254.80±12.89	210.67±22.38	5.77±0.65	27.48±1.66	7.32±0.65	519.60±16.75
FS 125	14.50±1.42	0.52±0.05	233.80±9.75	222.02±17.34	6.24±0.65	28.34±2.74	6.92±0.49	564.00±32.96
FS 250	16.48±0.94	0.60±0.06	269.60±10.30	224.00±22.78	6.14±0.39	27.98±1.98	7.84±0.74	564.60±35.27
FS 500	17.88±0.56	0.69±0.04*	285.60±23.11	247.92±25.17	6.53±0.84	26.26±1.51	8.40±0.40	605.40±15.13*
FA 62.5	13.76±0.86	0.52±0.06	235.20±9.99	223.60±30.02	5.90±0.47	28.32±4.67	6.40±0.63	469.20±29.76
FA 125	14.64±0.72	0.50±0.04	232.20±13.95	218.88±17.18	6.38±0.43	30.17±3.74	6.90±0.65	446.20±29.54
FA 250	11.84±0.99	0.49±0.04	217.80±16.61	229.55±23.97	5.69±0.87	24.83±2.78	6.38±0.52	394.60±28.28*
FA 500	11.18±0.72	0.42±0.03	197.60±5.80**	213.01±20.71	5.68±0.40	27.71±3.57	5.72±0.41**	365.00±24.60**
FS/FA 500	15.52±1.00	0.53±0.75	245.20±15.29	212.68±20.42	6.37±0.40	31.06±3.30	7.02±0.51	545.20±37.88

FS = *Ficus sycomorus*, FA = *Faidherbia albida*, n = 5, Student's t- test, * = p<0.05 (significant), ** = p<0.01 (highly significant)

Table 4: Effect of ethanol leaf extract of *Ficus sycomorus* and stem-bark extract of *Faidherbia albida* on liver function in Wistar albino rats for 28 days

Dose & Group (mg/kg)	Serum Biochemical Parameter (Mean ± SEM)						
	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	TP (g/L)	ALB (g/L)	TB (µmol/L)	CB (µmol/L)
Control	254.00±6.37	57.40±2.91	23.60±2.20	43.00±2.53	25.40±2.14	12.60±1.50	2.08±0.19
FS62.5	228.40±15.53	55.00±4.55	23.40±1.99	45.40±1.75	26.40±1.81	13.40±1.63	1.96±0.32
FS125	253.20±13.04	60.80±5.20	25.40±2.80	42.80±2.96	25.60±2.42	12.40±1.72	2.14±0.14
FS250	284.60±9.92*	54.00±2.30	31.80±1.53*	45.20±2.18	24.00±1.70	15.60±0.93	2.26±0.28
FS500	298.40±24.97	64.00±5.03	32.20±3.48	45.00±2.26	27.80±1.88	18.40±0.93*	2.28±0.29
FA62.5	225.40±14.58	49.40±5.61	25.00±2.35	43.60±4.42	23.20±2.27	13.20±1.24	2.30±0.27
FA125	273.00±27.27	61.40±5.28	35.40±2.27**	49.20±4.21	28.80±3.22	15.00±1.48	2.54±0.17
FA250	307.60±24.56	73.00±3.30**	44.00±2.51***	43.40±2.80	29.40±2.98	19.20±1.85*	2.96±0.32*
FA500	316.40±28.12	77.80±3.95**	45.20±3.68**	51.60±4.07	30.80±3.68	20.80±2.65*	3.16±0.16**
FS/FA500	280.20±16.65	56.20±3.37	25.00±2.35	40.60±1.54	29.80±1.39	12.80±1.07	2.10±0.14

FS = *Ficus sycomorus*, FA = *Faidherbia albida*, n = 5, Student's t- test, * = p<0.05 (significant), ** = p<0.01 (highly significant), *** = p<0.001 (extremely significant)

Table 5: Effect of ethanol leaf extract of *Ficus sycomorus* and stem-bark extract of *Faidherbia albida* on renal function in Wistar albino rats for 28 days

Dose & Group (mg/kg)	Serum Biochemical Parameter (Mean±SEM) (mmol/L)					
	Na^+	K^+	Cl^-	HCO_3^-	Urea	Cr
Control	131.20±10.73	5.42±0.50	89.00±6.23	20.40±1.03	5.70±0.45	96.60±4.60
FS 62.5	136.40±7.55	5.46±0.62	97.80±6.84	20.60±2.29	6.10±0.57	113.80±4.91*
FS 125	142.40±10.08	6.76±0.50	113.20±4.31*	23.40±1.69	6.58±0.46	128.00±3.96**
FS 250	153.00±8.05	7.16±0.42*	120.60±5.95**	24.80±1.93	7.18±0.34*	131.80±6.53**
FS 500	161.80±4.62*	7.30±0.28*	123.40±4.57**	25.00±1.52*	7.40±0.24*	136.20±3.76***
FA 62.5	139.00±7.84	5.76±0.32	109.60±3.08*	21.20±1.16	6.46±0.28	116.20±4.04*
FA 125	147.40±6.86	5.72±0.56	116.80±6.01*	23.20±1.02	6.66±0.37	122.00±5.52**
FA 250	150.60±4.73	5.74±0.43	123.80±6.72*	24.20±1.66	6.70±0.25	124.60±8.23*
FA 500	156.00±10.97	6.10±0.53	131.60±6.80**	26.40±1.96*	7.18±0.19*	147.00±3.63***
FS/FA 500	142.40±12.23	5.82±0.73	90.20±4.51	19.80±2.01	6.50±0.49	108.40±7.19

FS = *Ficus sycomorus*, FA = *Faidherbia albida*, n = 5, Student's t- test, * = $p<0.05$ (significant), ** = $p<0.01$ (highly significant), *** = $p<0.001$ (extremely significant)

DISCUSSION

Ficus sycomorus and *Faidherbia albida* have been used for long period of time as traditional medicine to counter hyperglycemia and various disorders in northern Nigeria. However, scientific studies to evaluate their safety and possible mode of action are still lacking. In the present study, the oral and intraperitoneal lethal dose (LD_{50}) of greater than 5000 mg/kg and 1587.5 mg/kg respectively for both plant extracts indicate that they are relatively safe. Several literature reports agree with the report of the present study in which the plants extracts were found to be relatively less toxic [21,22]. However, Sandabe and his colleagues [4] reported a slight toxicity of *Ficus sycomorus* leaves of 720 mg/kg intraperitoneally. The plant extracts of *Ficus sycomorus* and *Faidherbia albida* are therefore safe especially when used orally and this could justify the potential of these plants by most communities in the traditional management of diverse medical ailments in northern Nigeria.

The organ weight changes with respect to the body weight in the present study serve as a sensitive indication of the general health status of animal. There was no statistical significant difference between the weights of the liver, lungs, kidneys and spleen due to the extracts of *Ficus sycomorus* leaves and *Faidherbia albida* stem-bark at tested dose levels with that of the control group. Therefore, this is an indication that both plants extracts are relatively safe for short and moderate term uses especially in chronic ailments such as diabetes mellitus. However, the significant decrease in the weight of the liver by 500 mg/kg of the ethanol stem bark extract of *Faidherbia albida* observed in this study may be an indication that treatment with the plant extract at this dose level may have adversely affected this organ. This is in agreement with the report of Konan *et al* [23] in which a decrease in organ weight has been linked to the disintegration of cytoplasmic material and necrotic changes.

The haemoglobin, hemotocrit and erythrocytes profile of ethanol leaf extract of *Ficus sycomorus* treated groups, which was statistically comparable with the control group, eliminates the occurrence of anaemia or adverse effects on normal RBC and Hb functions. This agrees with the report of Odutola [15] in which determination of the concentration of RBC in the blood could help detect the presence or absence of anaemia. Rudorfer and his colleagues [24] also reported that anaemia occurs when the Hb, PCV and RBCs count falls below the normal range. The significant increase in the level of platelets due to 500 mg/kg of ethanol leaf extract of *Ficus sycomorus* observed in this study may suggest that the extract may enhance blood coagulation [15]. Leucocytes (WBC) are mediators of immunity and largely contribute to immunoprotection against inflammation [25]. The levels of these cells were within normal levels in this study showing that administration of the ethanol leaf extract of *Ficus sycomorus* did not elicit inflammatory changes in these groups. The ethanol bark extract of *Faidherbia albida* in the present study affected the haematological parameters especially erythrocytes, leucocytes and thrombocytes much more than the ethanol leaf extract of *Ficus sycomorus*. The significant decrease in the levels of RBC, WBCs and platelets by 500 mg/kg of ethanol extract of *Faidherbia albida* ($p<0.05$) observed in this study indicates an anaemic and immunosuppressant causing potential. This is consistent with the report of Adedapo *et al* [26] in which some plants are known to cause destruction of red blood cells leading to anaemia. The significant decreased in the

level of platelets due to 250 and 500 mg/kg of ethanol bark extract *Faidherbia albida* observed in this study may suggest that the extract may have potential in causing clotting disorder as previously reported by Odutola [15]. The plants extracts combination therapy (FS/FA) in this study was observed to be relatively safe on all the hematological parameters studied. To the best of our knowledge, the safety profile of this combination therapy of these plants has not been reported elsewhere. This is an advantage in the use of cocktail of plant extracts in managing diseases by most communities in Northern Nigeria.

The serum levels of ALP,ASAT, ALAT, TP, ALB, TB and conjugated bilirubin which reflect the state of hepatic function [23] in *Ficus sycomorus* extract were not significantly altered at the tested doses used in this study, this is an indication that the extract did not affect normal hepatic function. However, the extract at 250 mg/kg has shown a significant increase in the levels of ALP and ALAT respectively. Similarly, the extract at 500 mg/kg dose has resulted in increased level of total bilirubin. The ethanol stem bark of *Faidherbia albida* extract at 250 and 500 mg/kg have shown a significant elevation in the levels of ASAT, ALAT, total bilirubin and conjugated bilirubin. Similarly, there was a significant increase in the level of ALAT at 125 mg/kg dose of ethanol stem bark of *Faidherbia albida* extract. Thus, an elevated ALAT as observed in this study is a sensitive clinical index of acute hepatocellular injury [15]. Similarly, the significant increase in the levels of ALP is an indication of tissue damage such as intestine, kidney, liver, bones, platelet and white blood cells. The elevated levels of both total and conjugated bilirubin is a clinical indication hemolysis of red blood cell and liver damage. Several herbal remedies have been reported to cause liver dysfunction especially when used subchronically: *Teucrium chamaedrys*, *Larrea divaricata*, *Scutellaria laterifolia* and *Valeriana officinalis* [27]. *Zizyphus jujuba, Bupleurum falcatum, Herba jinqianca*o and *Fructus abri* are herbal remedies with claims of beneficial effects on the liver [27].

Hypernatremia observed in this study due to 500 mg/kg of ethanol leaf extract of *Ficus sycomorus* may signify either sodium increase or dehydration. This agrees with the report of Odutola [15] in which sodium retention was reported as loss of free water as in diabetic insipidus or loss of hypotonic fluid as in gastroenteritis or excess sodium intake. The significant increase in the level of potassium ion due to 250 and 500 mg/kg of FS extract which was found to be dose dependent indicates acute renal failure or excessive cellular breakdown [15]. Therefore, the use of this extract within this dose range has to be with caution in order to avoid toxicity. The stem bark extract of Faidherbia albida did not alter the levels of Na^+ and K^+ at the tested doses when compared with untreated control group. On the other hand, hyperchloremia, which was observed in both plants' extracts in this study, was found to be dose independent has no real diagnostic significance. It can only be useful in validating or cross-checking the level of sodium ion, because both chloride and sodium ion correlates its other and are excreted via renal route. The level of bicarbonate that was found to be significantly higher than the untreated group due to the highest tested doses of the two plant extracts (500 mg/kg) may not seem to pose any serious medical problems. However, pH changes needs to be monitored to avoid metabolic alkalosis that may have medical consequences. The serum creatinine and urea levels which are indicators of renal function were found to increase significantly higher than the control group for both plant extracts ($p<0.05$). This indicates that the plants may relatively affect the kidney function. Creatinine, which is a major component of muscle and a waste product that

usually is released from muscle to plasma and exclusively excreted by the kidney by glomerular filtration, is often used as indicator of renal function. Increased creatinine levels do not appear unless significant renal impairment exist [15,28]. However, it was observed in this present study that the combination plant therapy did not affected any of the serum biochemical parameters used in assessing renal function. Therefore, the use of this plants extract as a monotherapeutic agent based on this study should be with caution to avoid kidney damage. More scientific study, such as chronic toxicity study, needs to be carried out in order to verify the present finding.

Conclusion. The acute toxicity study of ethanol extracts of *Ficus sycomorus* leaves and *Faidherbia albida* stem-bark have shown to be relatively less toxic. The combined ethanol plants extract of FS and FA did not significantly affected the hematological parameters or hepatic and renal functions. Therefore, the traditional use of these plants in combination for managing diverse ailments in northern Nigeria is hereby justified.

Acknowledgement. The authors are highly grateful to the staff of Pharmacology and Toxicology, Faculty of Pharmacy, University of Maiduguri, Haematology and Chemical Pathology, University of Maiduguri Teaching Hospital, Maiduguri, Nigeria for their technical assistance and support.

REFERENCES

1. Gilani, A.H., Molla, N., Alta-ur-Rahman, I., Shah, B.H. (1992). Role of natural products in modern medicine. *Journal of Pharma. Med*. 2: 111-118.

2. Rajasekar, A., Anandkumar, B., Maruthamuthu, S., Ting, Y. and Rahman, P.K. (2010). Characterization of corrosive bacterial consortia isolated from petroleum product transporting pipelines. *Journal of Applied Microbiology and Biotechnology*, 85(4): 1175-1188.

3. WHO. (2002). "WHO Traditional Medicine Strategy 2002-2005, Geneva"

4. Sandabe, U., Onyeyili, P., Chibuzo, G. (2006). Phytochemical screening and effect of aqueous extract of *Ficus sycomorus* L. (Moraceae) stembark on muscular activity in laboratory animals. *J. Ethnopharmacol*., 104: 283–285.

5. Tijani, A.Y., Uguru, M.O. Salawu, O.A. (2008). Antipyretic, anti-inflammatory & antidiarrhoeal properties of *Faidherbia albida* in rat. *Africa Journal of Biotechnology*, **7**(6): 696-700.

6. Adoum, O. A., Nenge, H. P., Bashir, C. (2012). The steroidal component and hypoglycaemic effect of stem bark extract of *Mitragyna inermis* (wild) o. kundze (Rubiaceae) in alloxan induced diabetic Wistar rats. *IJABPT*, 3(2): 169-174.

7. Wurochekke, A.S., Mahmoud, S.J. and Zailani, H.A. (2013). Antimicrobial activity of stem bark of *Faidherbia albida*. *British Journal of Pharmaceutical Research*, 3(4): 786-794.

8. Alhaji, U.I., Samuel, N.U., Aminu, M., Chidi, A.V., Umar, Z.U., Umar, U.A. and Adewale, B.M. (2014). *In vitro* antitrypanosomal activity, antioxidant property and phytochemical constituents of aqueous extracts of nine Nigerian medicinal plants. *Asian Pacific Journal Tropical Disease*, 4: 348-355.

9. Kashimawo, A.J., Kolawole, J.A. and Kemelayefa, J.O. (2017). Antidiabetic activity of the stem bark extract and fraction of *Faidherbia albida* Del (Mimosaceae) in murine model. IOSR *Journal of Pharmacy and Biological Sciences (IOSR-JPBS)* 12(4): 26-30.

10. Pithayanukul, P., Nithtanakool, S., Bavovada, R. (2009). Hepatoprotective potential of extracts from seeds of *Areca catechu* and nutgalls of Quercus infectoria. *Molecules*, 14(12): 4987-5000.

11. Elekofehinti, O.O., Adanlawa, I.G., Komolafe, K., Ejelonu, O.C. (2012). Saponins from *Solanum anguiri* fruits exhibit antioxidant potential in Wistar rats. *Annals of Biol Res*, 3(7): 3212-17.

12. Sheikh, K.A., Ruqaiya, N.S.A, and Mohammed, A.H. (2015). Total flavonoids content and antimicrobial activity of crude extract from leaves of *Ficus sycomorus* native to sultanate of Oman. *African Journal of Biotechnology*, 8: 6004-6006.

13. Lorke, D.A (1983). A new approach to practical acute toxicity testing. *Arch of Toxicol.* 45: 275-7.

14. Jain, N.C. (1986). Schalm Veterinary haematology. 4th ed, Lea & Febiger, Philadelphia, pp23-34.

15. Odutola, A. A. (1992). Rapid explanation of routine clinical laboratory tests. Desktop publishing, Zaria, 1st edition, pp41-56.

16. Reitman, S., Frankel, S.A. (1957). A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminases. *Am J Clinical Pathology*, 28(1): 56-63.

17. Klein, B., Read, P.A., Babson, L.A. (1960). In vitro determination of alkaline phosphatase in serum or plasma. *Clinical Chemistry*, 6: 269-275.

18. Schmidt, E., Schmidt, F.W. (1963). In vitro determination of aspartate aminotransferase and alanine aminotransferase. *Journal of Clinical Enzymology and Biology*, 3: 1-5.

19. Babson, L.A. (1965). In vitro determination of alkaline phosphatase in serum or plasma. *Clinical Chemistry*, 11: 789-793.

20. Babson, L.A., Greeley, S.J., Coleman, C.M., Phillips, G.D. (1966). In vitro determination of alkaline phosphatase in serum or plasma. *Clinical Chemistry*, 12: 482-490.

21. Tijani, A.Y., Uguru, M.O., Salawu, O.A., Abubakar, A., Onyekwelu, N.O., Akingbasote, J.A. (2009). Effect of *Faidherbia albida* on some biochemical parameters of rats infected with *Trypanosoma brucei brucei. Afr. J. Pharm. Pharmacol*., 3(1): 26-30.

22. Bello, O.M., Zack, A.M. and Adikwu, J.G. (2013). Comparative studies of phytochemical screening of *Ficus sycomorus* Linn stem bark extract and *Pilostigma thonningii* root extract. *Asian Journal of plant Science Research*, 3(6): 69-73.

23. Konan, N.A., Bacchia, E.M., Lincopan, N., Varelac, S.D., Varandac, E.A. (2007). Acute, subacute toxicity and genotoxic effects of a hydroethanolic extract of the cashew. *Journal of Ethnopharmacology*. 110: 30-38.

24. Rudorfer, M.V., Lane, E.A., Chang, W.H. (1984). Desipramine pharmacokinetics in Chinese and caucasian volunteers. *Br J. Clin Pharmacol*, 17, 1984, 433-440.

25. Tripathy, S., Pradhan, D., Anjana, M. (2010). Anti-inflammatory and antiarthritic potential of *Ammania baccifera* Linn. *International Journal of Pharma Bio Science*, 1: 23-45.

26. Adedapo, A.A, Abatan, M.O., Olorunsogo, O.O. (2004). Toxic effects of some plant in the genus Euphorbia on haematological and biochemical parameters in rats. *Vet. Archive*, 74(1): 33-63.

27. Timothy, S.Y., Helga, B.I., Bomai, H.I., Musa, A.H. (2015). Acute and subchronic toxicity study of the aqueous and ethanolic extracts of *Mitragyna inermis* bark in albino rats. *International Journal of Pharmacology and Toxicology*, 5(1): 24-32.

28. Tietz, N.W. (1994). Serum albumin determination. Fundamentals of clinical chemistry with clinical correlation. Balliere Tindall, London, UK, pp23-34.