Research Article

Evaluation of bio-tolerance of the ethyl acetate fraction from *Lophira lanceolata* (Ochnaceae) leaves in rats.

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ABSTRACT

The effect of repeated administration of ethyl acetate fraction of Lophira lanceolata (LLFEA), once daily for 28 days on the hematological parameters and some function indices of rat heart and liver were investigated to assess the safety use of this herbal plant by population. Twenty-four male and female white albino rats were randomly grouped into 8 (MC: male control group; ML: male low dose group; MM: male medium dose group; MH: male high dose group; FC: female control group; FL: female low dose group; FM: female medium dose group; and FH: female high dose group) with 3 rats each. MC and FC served as the control and were administered distilled water once daily for 28 days while ML and FL 250; MM and FM 500; MH and FH 1000 mg/kg body weight (b.w.) of Lophira lanceolata extract. The effects of this extract were carried out on the body weight, the ratio organs-body weight, the hematological and biochemical parameters. LLFEA did not affect the body weight of the rats but create an inflammation. Lymphocytes, monocytes, mean corpuscular hemoglobin concentration and eosinophilis were significantly affected ($P<0.05$). There was an increase ($P<0.01$) in the concentration of aspartate aminotransferase in rats after 28 days feeding. The results indicated that LLFEA is not totally safe regarding its effects on the rats' heart, kidney and liver.

Key words: *Lophira lanceolata*, haematological parameters, biochemical parameters, Albino rats

1. INTRODUCTION

Lophira lanceolata is a tree of the wooded savannah. It often grows gregariously on fallow land at the edge of forests. It is found out from Senegal to Cameroon and Sudan and also in Côte d'Ivoire where the Baoulé (an ethny in the center of Côte d'Ivoire) calls it « n'goinyassoua » in reference of oil made from the seeds [1]. It is a tree of 8 to 10 m tall, straight or twisted, with leaves alternate, clustered at the end of short straight branches, glabrous, bright and blade oblong-lanceolate. The bark surface is corky grey [2]. The young leaves are red. Its fruits develop between February and March [3].This plant is used in traditional medicine to treat several illnesses. The decoction of the fresh leaves is administered orally against headaches, dysentery, diarrhoea, cough, abdominal pains and cardiovascular diseases. It is also used on skin to cure wounds [2]. The infusion of young leaves of the plants is used taken orally for the treatment of fever [4]. Phytochemical Screening of *Lophira lanceolata* leaves and seeds revealed the presence of compounds such as flavonoids, anthraquinones, phenols, saponins, and tannins [5,6].In addition, some secondary metabolites were isolated from the leaves and the stem bark of this medicinal plant [7,8,9,10,11]. *L. lanceolata* has a range of pharmacological effects wherein some of them are extremely beneficial, such as antioxidant, antimalarial, anti-hypertensive effect, anti-bacterial, antiviral activity, sexual enhancement properties [12,13,14,15]. But beyond the efficacy of herbal remedies, there is always a serious concern for the safety. Some researchers have earlier reported the safety of an aqueous stem bark extract of *Lophira lanceolata* in Sprague dawley rats [16].

The aim of this research was to determine the effects of ethyl acetate fractions of *Lophira lanceolata* on hematological and biochemical parameters of some organs (heart, liver and kidney) in albinos' rats.

2. MATERIALS AND METHODS

2.1 Material

2.1.1 Plant material

Fresh leaves of *Lophira lanceolata* Tiegh. Ex Keay (Ochnaceae) were collected locally from the savanna region of Bouake (7°44'N; 5°04'W) in central Côte d'Ivoire in July 2013. It is a tree of 8 to 10 m tall, straight or twisted, with alternate, clustered at the end of short straight branches, glabrous, bright and blade oblong-lanceolate. The bark surface is corky grey [2]. It fruits between February and April and it has tough reddish elongated seeds [3].

Plant identification of the leaves was done by Professor Aké-Assi Laurent at the National floristic center of University of Felix Houphouet Boigny, Cocody- Abidjan, Côte d'Ivoire, where a voucher specimen was deposited (*Lophira lanceolata* Tiegh. ex Keay n° 9397, December 1966, Côte d'Ivoire national herbarium). Fresh plant materials were washed in tap water, and dried away from the sun for 2 weeks. They were later homogenized to fine powder and stored in airtight bottles until ready for use.

2.2.1.2 Preparation of extract and administration

Three hundred grams (300g) of air-dried powder was weighed and mixed with Methanol 80% (3 L) using a rotary shaker (Orbit Lab-line, Ill, USA) at 200 rpm for 24 hours at room temperature(25±3ºC). The mixtures were pooled and filtered on cotton wool. The residue was re-extracted twice for 6 hours. The filtrates were pooled and filtered two times on cotton wool and once on Whatman (n°1) filter paper. The methanol was

evaporated at 50º C using a rotary evaporator (Buchi Rotavapor, Model R-210) and freeze dried using a freeze dryer (Super Modul YO 230, USA) to obtain a powder. The powder was weighed and labeled as LL^{CE} and stored at 4 ° C in airtight bottles until ready to use.

Twenty grams (20g) of LL^{CE} was dissolved in 500 ml of distilled water. The mixture was further fractionated successively by using following solvents: petroleum ether, dichloromethane, ethyl acetate and saturated butan-1-ol**.** Solvents were evaporated using a rotary evaporator (Buchi Rotavapor, R-210) at 100 rpm. The dry extracts were weighed, labeled and stored at 4 ° C in airtight bottles until ready to use.

Water solution was prepared from LL^{FEA} and was administered orally by gavages to animals using a metal oropharyngeal cannula.

2.2 Animals and maintenance

Twenty-four (24) male and female adult albinos rats, 7 weeks age were purchased from the animal house of the department of microbiology, University of Ghana. On the starting day, the rats were allocated in four male groups and four female groups of 3 rats each. Animals were house in cages with stainless steel grid covers and sterilized wood shaving as bedding material in a controlled environment (Temperature 25ºC, relative humidity 60 ±10% and light at 12h light/dark cycles). A commercial feed and tap water was provided *ad libitum*. About 7 days of acclimation, the rats were 8 weeks old. At the start of treatment, feed and drinking water were available *ad libitum* except the overnight fasting to administer the extract and necropsy. Health conditions were observed daily. The control groups received distilled water while the treatment groups were treated with LL^{FEA} at 250, 500 and 1000mg/kg b.w.by day for 28 days successively. The body weight of rats was measured weekly. The equipment, including handling and sacrificing of the animals were in accordance the guideline of **OECD** [17]. At the termination of experiment, all rats were subjected to haematology, blood chemistry and organs weighing. The protocol was approved by the departmental protocol and review committee.

2.3 Experimental technique

The rats were observed once daily for abnormal clinical signs. Body weights were recorded on days 0, 7, 14, 21, 28. On the days 28, in each group, animals were anesthetised with ether. The cardiac puncture method was used to collect blood from the animals. From the same animal, 3 ml of blood was collected and draw in K_3-EDTA tube for haematology and other 3 ml was collected and draw into tube containing Gel and Clot activator for biochemical analysis. Routine haematology and clinical chemistry were conducted on all animals at the end of exposure period. Plasma was prepared by centrifugation (4000 rpm for 5 minutes) using a centrifuge (Powerspin™ LX, Unico). Count in the blood was determined with an auto haematology analyser (Sysmex XT 2000i, Japan). Plasma concentrations of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Albumin, Alkaline phosphatase (ALP), Total Bilirubin, Direct Bilirubin, Gamma glutamyltranferase (GGT) and Total Protein were determined using a clinical chemistry analyser (Hospitex Mega, 2000). Organ-to-body weights were calculated from the absolute organ weights and the terminal body weight of the rats.

Following sacrifice a thorough necropsy was performed in all animal and the organs were weight after dissection: Heart, Liver, Kidney, Lung and Spleen.

2.4 Statistic analysis

Statistical analysis was undertaken with GraphPad Prism *V5.01* software (Washington, USA). Groups of data were compared one-way analysis of variance (ANOVA). Due to the small population size, the non-parametric Dunnett test was performed to compare assess difference between the control group and the other groups. Differences were considered statistically significant at $p< 0.05$.

3. RESULTS

3.1Abnormal clinical signs and body weight

All rats survived and were clinically safe until the end of the experiment before the dissection sacrification and showed normal growth and appeared healthy through the study. The changes of body weight were not significantly different ($p>0.05$) in either male or female rats or between treatment and control groups (Table1).

Treatment (mg/kg b.w.)	Days				
	0	7	14	21	28
Sex			**Male weight (g)**		
Control	120 ± 0.0	127 ± 1.15	137 ± 2.73	149 ± 3.38	157 ± 3.33
250	120 ± 0.0	127 ± 0.88	138 ± 1.53	149 ± 0.57	160 ± 0.0
500	120 ± 0.0	129 ± 2.03	141 ± 3.84	150 ± 5.21	160 ± 5.77
1000	120 ± 0.0	126 ± 0.88	133 ± 1.2	146 ± 4.04	153. ± 3.33
			Female weight (g)		
Control	120 ± 0.0	127 ± 1.15	137 ± 2.08	146 ± 2.91	153 ± 3.33
250	120 ± 0.0	127 ± 1.15	136 ± 2.03	142 ± 3.28	150 ± 5.77
500	120 ± 0.0	126 ± 0.88	135 ± 1.15	145 ± 2.33	153 ± 3.33
1000	120 ± 0.0	125 ± 0.88	135 ± 2.33	141 ± 2.52	147. ± 3.33

Table 1: Weekly body weight of albino rats treat with ethyl acetate fraction of *Lophira lanceolata* Values are mean ± SEM (n=3/sex/dose).

3.2 Relative organs-body weight

There was no significantly difference (p> 0.05) between relative organ weight/body weights in LL^{FEA} groups compared to controls. However, the higher dose (1000 mg/kg bw) of the extract induced a significant increase (p<0.05) of the weight of the female heart(0.33 ± 0.02 to 0.43 ± 0.01%) and the male Left kidney (0.33 ± 0.01 to 0.38 ±0.01%) (Table 2).

Treatment (mg/kg b.w.)	Heart	Liver	Kidney R	Kidney L	Lung	Spleen
Sex	**Male organs-to-body weight (%)**					
Control	0.37 ± 0.01	2.51 ± 0.1	0.32 ± 0.0	0.33 ± 0.01	0.66 ± 0.03	0.19 ± 0.0
250	0.39 ± 0.02	2.74 ± 0.17	0.31 ± 0.0	0.31 ± 0.0	0.91 ± 0.11	0.2 ± 0.1
500	0.32 ± 0.02	2.64 ± 0.06	0.3 ± 0.02	0.3 ± 0.0	0.87 ± 0.08	0.35 ± 0.1
1000	0.35 ± 0.0	2.5 ± 0.03	0.35 ± 0.01	0.38 ±0.01*	0.69 ± 0.0	0.2 ± 0.0
Sex	**Female organs-to-body weight (%)**					
Control	0.33 ± 0.02	2.41 ± 0.12	0.3 ± 0.01	0.3 ± 0.0	0.78 ± 0.05	0.23 ± 0.2
250	0.37 ± 0.01	2.9 ± 0.19	0.32 ± 0.02	0.32 ± 0.0	0.8 ± 0.09	0.24 ± 0.1
500	0.33 ± 0.01	2.76 ± 0.28	0.33 ± 0.01	0.32 ± 0.01	0.82 ± 0.03	0.22 ± 0.1
1000	0.43 ± 0.01*	2.81 ± 0.07	0.32 ± 0.01	0.32 ± 0.03	1.03 ± 0.15	0.24 ± 0.1

Table 2: Organ-to-body weight ratios from rats fed with LL^{FEA} for 28 days. Mean organ-to-body weight in g/100 g (± SEM) of albino rats weight (n=3/sex/dose). P < 0.05 sstatistically different with control group (ANOVA).

Parameters	Treatment (mg/kg b w)			
	Control	250	500	1000
WBC (×10^9/L)	6.6 ± 0.25	7.25 ± 2.19	6.73 ± 0.52	7.1 ± 0.51
RBC (×10^{12}/L)	8.35 ± 0.5	8.44 ± 0.18	8.88 ± 0.12	8.57 ± 0.11
Hb (g/dL)	14.5 ± 0.83	14.5 ± 0.26	14.9 ± 0.31	14.7 ± 0.33
Hematocrit (%)	41.0 ± 3.19	41.1 ± 0.75	42.3 ± 0.4	42.0 ± 1.33
MCV (fL)	79.0 ± 0.91	78.7 ± 0.18	77.7 ± 0.2	79.0 ± 1.31
MCH (pg)	27.4 ± 0.2	27.2 ± 0.08	26.8 ± 0.17	27.2 ± 0.32
MCHC (g/dL)	35.4 ± 0.8	35.3 ± 0.05	35.1 ± 0.04	35.1 ± 0.31
Platelet(×10^9/L)	447.0 ±241	742 ± 168	762 ± 68.1	804 ± 143
Neutrophilis(×10^9/L)	2.08 ± 0.36	1.54 ± 0.23	1.29 ± 0.35	1.34 ± 0.14
Lymphocytes(×10^9/L)	4.53 ± 0.24	7.57 ± 0.68**	5.16 ± 0.32	4.94 ± 0.3
Monocytes(×10^9/L)	0.24 ± 0.09	0.25 ± 0.17	0.31 ± 0.12	0.91 ± 0.29 *
Eosinophilis(×10^9/L)	1.39 ± 0.09	1.38 ± 0.1	1.39 ± 0.07	1.54 ± 0.14
Basophilis(×10^9/L)	0.01 ± 0.1	0.01 ± 0.0	0.02 ± 0.0	0.01 ± 0.0

Table 3: Effects of LL^{FEA} on the hematological parameters of male albinos' rats. **WBC**: white blood cell; **RBC**: red blood cell; **Hb**: hemoglobin; **MCV**: mean corpuscular volume; **MCH**: mean corpuscular hemoglobin **MCHC**: mean corpuscular hemoglobin concentration. Values are mean ± SEM (n=3/sex/dose); *P < 0.05 and **P < 0.01 statistically different with control groups (ANOVA).

Parameters	Treatment (mg/kg b w)

	Control	250	500	1000
WBC (×10⁹/L)	4.44 ± 2.95	3.67 ± 0.99	6.39 ± 0.67	9.78 ± 1.76
RBC (×10¹²/L)	5.73 ± 2.37	7.86 ± 0.26	7.66 ± 0.29	8.38 ± 0.22
Hb (g/dL)	13.4 ± 1.03	13.7 ± 0.47	13.8 ± 0.24	15.1 ±0.31
Hematocrit (%)	39.3±2.64	41.8 ± 1.2	40.4 ± 0.72	43.1 ± 0.57
MCV (fL)	82.5 ± 1.63	83.2 ± 0.72	82.8 ± 1.27	81.5 ± 0.75
MCH (pg)	28.0 ± 0.46	27.4 ± 0.26	28.0 ± 0.4	28.1 ± 0.12
MCHC (g/dL)	34.2 ± 0.2	32.7 ± 0.18 *	34.0 ± 0.06	35.1 ± 0.3
Platelet (×10⁹/L)	518.0 ± 207	411.0 ± 53.9	770.0 ± 60.8	740.0 ±57.9
Neutrophilis (×10⁹/L)	2.02 ± 0.28	0.94 ± 0.21	1.38 ± 0.03	1.66 ± 0.12
Lymphocytes(×10⁹/L)	3.51 ± 2.47	2.58 ± 0.84	4.54 ± 0.64	4.07 ± 0.13
Monocytes(×10⁹/L)	0.1 ± 0.08	0.27 ± 0.05	0.26 ± 0.03	0.37 ± 0.06 *
Eosinophilis(×10⁹/L)	1.13 ± 0.06	1.19 ± 0.05	1.2± 0.01	1.37 ± 0.07 *
Basophilis(×10⁹/L)	0.006 ± 0.003	0.013 ± 0.003	0.006 ± 0.0	0.013 ± 0.003

Table 4: Effects of LL^{FEA} on the hematological parameters of female albinos' rats. **WBC**: white blood cell; **RBC**: red blood cell; **Hb**: hemoglobin; **MCV**: mean corpuscular volume; **MCH**: mean corpuscular hemoglobin **MCHC**: mean corpuscular hemoglobin concentration. Values are mean ± SEM (n=3/sex/dose); **P* < 0.05 statistically different with control groups (ANOVA).

parameters	Treatment (mg/kg b w)			
	Control	250	500	1000
AST (U/L)	29.3 ±5.8	54.3± 18.5	77.3 ± 25.8	101.0 ± 7.37**
ALT(U/L)	54.3 ± 10.4	87.0 ± 5.13	88.0 ± 3.84	86.0 ± 16.6
Albumin(g/L)	45.1 ± 0.11	47.0 ± 0.56	45.9 ± 2.15	43.0 ± 0.61
ALP (U/L)	381.0 ± 79.2	514.0 ± 47.4	548.0 ± 114	518.0 ± 77.5
T- Bil.(µmol/l)	2.17 ± 0.06	2.37 ± 0.49	2.2 ± 0.2	1.53 ± 0.26
D- Bil. (µmol/l)	1.6 ± 0.19	4.76 ± 3.23	1.8 ± 0.18	0.96 ± 0.45
GGT (U/L)	3.0 ± 1.15	6.0 ± 2.31	2.0 ± 2	2.0 ± 0.57
Total Protein(g/L)	63.8 ± 0.72	70.5 ± 2.49	71.0 ± 5.37	62.8 ± 1.75
Cholesterol(mmol/L)	2.18 ± 0.02	1.91± 0.12	1.98 ± 0.08	2.18 ± 0.14
HDL - C(mmol/L)	0.677 ± 0.01	0.623 ± 0.0	0.623 ± 0.01	0.607 ± 0.05
LDL - C (mmol/L)	1.35 ± 0.02	1.06 ± 0.1	1.21 ± 0.09	1.35 ± 0.11
Triglycerides (µmol/L)	0.307 ± 0.01	0.513 ± 0.09	0.32 ± 0.02	0.503 ± 0.23
Coronary risk (Cholesterol/HDL)	3.22 ± 0.08	3.06 ± 0.16	3.19 ± 0.19	3.61 ± 0.14
Creatinin(µmol/L)	59.2 ± 5.38	60.2 ± 4.2	53.5 ± 2.52	52.5 ± 2.45

Table 5: Effects of LL^{FEA} on the biochemical parameters of male albino rats. **AST**: Aspartate aminotransferase, **ALT**: Alanine aminotransferase, **ALP**: Alkaline phosphatase, **T-Bil**: Total Bilirubin, **D-Bil**: Direct Bilirubin, **GGT:** Gamma glutamyltransferase, **HDL-C**: High density lipoprotein, **LDL-C:** Low density lipoprotein. Values are mean ± SEM (n=3/sex/dose). ** $P < 0.01$ statistically different with control groups (ANOVA).

Parameters	Treatment (mg/kg b w)			
	Control	250	500	1000

AST (U/L)	13.0 ± 5	15.0 ± 2.08	16.7 ± 2.85	47.3 ± 2.91**
ALT(U/L)	86.7 ± 6.69	99.7 ± 18.2	77.0 ± 1.73	79.0 ± 3.06
Albumin(g/L)	43.9 ± 0.78	44.3 ± 1.68	46.3 ± 0.12	46.2 ± 1.93
ALP (U/L)	364.0 ± 49.7	336.0 ± 35	371.0 ± 28.3	378.0 ± 60.1
T - Bil. (µmol/l)	2.3 ± 0.52	1.93 ± 0.66	1.6 ± 0.11	1.9 ± 0.58
D-Bil.(µmol/l)	1.52 ± 0.42	9.74 ± 5.83	2.42 ± 0.35	2.86 ± 1.08
GGT(U/L)	2.67 ± 1.2	7.67 ± 3.53	5.67 ± 0.06	2.0 ± 1.53
Total Protein(g/L)	68.6 ± 1.8	70.6 ± 1.71	69.8 ± 2	70.7 ± 4
Cholesterol(mmol/L)	1.66 ± 0.23	1.72 ± 0.23	1.64 ± 0.09	1.92 ±0.05
HDL – C (mmol/L)	0.667 ± 0.1	0.52 ± 0.12	0.527 ± 0.09	0.593 ± 0.10
LDL – C (mmol/L)	0.65 ± 0.11	0.83 ± 0.13	0.743 ± 0.05	0.923 ± 0.08
Triglycerides (µmol/L)	0.617 ±0.07	0.807 ± 0.02	0.663 ± 0.14	0.693 ± 0.18
Coronary risk (Cholesterol/HDL)	2.51 ± 0.13	3.48 ± 0.45	3.24 ± 0.37	2.84 ± 0.1
Creatinin (µmol/L)	62.1 ± 11.6	64 ± 2.72	52.6 ± 2.81	51.3 ± 6.32

Table 6: Effects of LL^{FEA} on the biochemical parameters of female albino rats. **AST:** Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **ALP:** Alkaline phosphatase, **T–Bil:** Total bilirubin, **D–Bil:** Direct bilirubin, **GGT:** Gamma glutamyltransferase, **HDL-C:** High density lipoprotein, **LDL-C**: Low density lipoprotein.Values are mean ± SEM (n=3/sex/dose).**$P < 0.01$ statistically different with control groups (ANOVA).

3.3 Haematological and biochemical Effects of LL^{FEA}

Haematological parameters are presented in Table 3 (males) and Table 4 (females). Most of them did not show any statistically significant (p> 0.05) between rats fed with LL^{FEA} and controls. However male rats' lymphocytes and monocytes increased significantly (p<0.05), respectively at the dose of 250 and 1000mg/kg b.w., when compared to controls. For female rats, mean corpuscular hemoglobin concentration (MCHC) decreased significantly (p<0.05), from 34.2 ± 0.2 to 32.7 ± 0.18 at the dose 250 mg/kg b.w. but monocytes and eosinophilis was significantly increased (p<0.05) at the high dose.

All clinical chemistry values showed no statistically significant changes in LL^{FEA} groups compared to controls (Table 5 and Table 6). Except for aspartate aminotransferase which was significantly increased (p<0.05) in both sexes at the dose 1000 mg/kg b.w.

3. DISCUSSION

The various hematological and biochemical parameters investigated in this study are useful indices of evaluating the toxicity of plant extract in animals [18, 19]. Assessment of hematological parameters can be used to determine the extent of deleterious effect of extracts on the blood of an animal. Such analysis is relevant to risk evaluation as changes in the hematological system have higher predictive value for human toxicity, when the data are translated from animal studies [20]. The non-significant effect of the extract on the RBC may be an indication that the balance between the rate of production and destruction of the blood corpuscles was not altered. MCHC, MCH and MCV relates to individual red blood cells while Hb, RBC and Hematocrit are associated with the total population of red blood cells. Therefore, the absence of significant effect of the extract, in both sexes, on RBC, Hb, Hematocrit, MCV and MCH could mean that neither the incorporation of hemoglobin into red blood cells nor the morphology and osmotic fragility of the red blood cells was altered [21]. The decreased MCHC, in female rats at 250 mg/kg b.w., by the extract further suggest selective toxicity of the extract. The non- significant decrease in the neutrophils by the extract could possibly suggest that LL^{FEA} doesn't lose the ability of the blood component to the phagocytosis. Lymphocytes are the main effector cells of the immune system [22]. The increase in the lymphocytes of male rats and female rats' eosiniphilis, in this study, may affect the effectors cells of the immune system. Since monocytes have been shown to increase in cases of infection, the increase in monocytes at 1000 mg/kg b.w. of LL^{FEA} observed in this study could be as result of selective and dose specific effect of the extract on the immune system of the animals. The biochemical indices

monitored in the serum can be used as 'markers'of the liver and heart for assessing the functional capacities of these organs [23]. The absence of significant effect on the plasma concentrations of Alanine aminotransferase (ALT),Alkaline phosphatase (ALP), Total bilirubin (T–Bil), Direct bilirubin (D–Bil), Gamma glutamyltransferase (GGT), High density lipoprotein (HDL–C), Low density lipoprotein (LDL–C) Albumin, Total protein, Cholesterol, Triglycerides and Creatinine of the animals suggest that the secretory ability and normal functioning of the heart and the liver were unaffected. However, the non-significant increase of ALT and the significant increase of AST in the plasma show selectivity toxicity on the heart. According to two researchers, an increase in organ-body weight ratio is an indication of inflammation while a decrease may be due to cell constriction [24]. The increase in the female rats' heart and male rats' left kidney-body weight ratio observed with the extract at 1000 mg/kg body weight may be due to increase in functional ability of these organs. The absence of significant effect on the liver, the lung and spleen-body weight ratios of the animals is an indication that the extract did not adversely affected the size of these organs in relation to the weight of the animals.

5. CONCLUSION

Our study has shown that the ethyl acetate fraction of *Lophira lanceolata* leaves is not completely safe for oral remedies. Because, it can induce a toxic effect on the liver and the dysfunctional of defense system of the body through disturbance of the monocytes count in high concentrations. However, it should be used at the lower concentrations of 1000 mg/kg bw and with care.

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