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Research Article

Acute toxicity on the ethanolic fruit extracts of *Morinda* sp. in Wistar albino rats

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ABSTRACT

The different maturity stages of ethanolic fruit extracts of *Morinda citrifolia* and *Morinda tinctoria* were evaluated for its acute toxicity effect on Wistar albino rats. The extracts were administered orally at the doses of 100, 200, 500, 1000 and 2000 mg/kg body weight in sighting study and observed for 14 days. Based on this observation, the highest dose 2000 mg/kg body weight was chosen for the acute toxicity study. Wistar rats were separated into seven and four groups of three animals each for *M. citrifolia* and *M. tinctoria* respectively. All the rats were observed for signs of toxicity for 14 days. During experimental period, rats were observed for any changes in body weight, food and water intake. On the 15th day, all the rats were sacrificed. Internal organs were excised and weighed. Hematological and biochemical parameters were analyzed. The results revealed that there was no indication of toxicity, behavioral or physiological changes. Also the extract did not made any considerable alterations in food and water intake in rats throughout the experimental time. The biochemical and hematological results of the groups were not considerably different. Overall, our study confirmed that an oral administration of *M. citrifolia* and *M. tinctoria* extracts at the dose of 2000 mg/kg body weight does not cause any toxicity in rats. The data of the toxicity studies could increase the assurance in its safety to human.

Keywords: Acute toxicity; Maturity stages; *Morinda citrifolia*; *Morinda tinctoria*; Sighting study

INTRODUCTION

Herbal medicine, also known as phytomedicine has a great importance in prevention and treatment of different ailments since ancient time (Usman et al., 2012). The use of herbal medicines can be recognized to their supposed efficacy and the fact that they are an economical resource of medicals (Ogbonnia et al., 2010). On the other hand herbal preparations implicit to be safe and may have contaminants such as pathogenic microbes, heavy metals, and aflatoxins due to the manner they prepared. Many of the medicinal preparations have been reported to be non-toxic and several others were found to be toxic (Albert et al., 2011). The purpose of toxicity testing is to provide enough record to make assessment relating to the toxicology properties of chemicals and commercial products and to choose whether the drug or chemicals will be harmless or not.

Morinda citrifolia L. popularly known as Noni or Indian mulberry is an evergreen small tree bearing flowers and fruits throughout the year. Noni belongs to the Rubiaceae family and has been used in the Polynesian folk medicine for over 2000 years (Ying et al., 2002). Noni fruit juice is in high demand in alternative medicine for different kinds of illness such as diabetes, high blood pressure, arthritis, menstrual difficulties and heart disease. Recently this plant has been the center of attention for several studies because of its nutraceutical properties (Zin et al., 2006). The components isolated from Noni include scopoletin, octoanoic acid, potassium, vitamin C, terpenoides, alkaloids, anthroquinones, sitosterol, β-carotene, vitamin A, flavone glycosides and linoeic acid (Wang Mian et al., 2002).

Morinda tinctoria Roxb also known as Nuna, belongs to the family of Rubiaceae. It is considered as an important folklore medicine. There is a greater demand for fruit extract of *Morinda* species in treatment for different kinds of illness such as cancer, arthritis, gastric ulcer and other heart disease (Sivaraman and Muralidharan, 2010). The ashes of *M. tinctoria* leaves are also reported to act as biosorbents in controlling ammonia pollution in waste waters (Suneetha and Ravindhranath, 2012). The major components have been identified in the Nuna plant, which includes octoanicacid, potassium, vitamin C, terpenoids, scopoletin, flavones, glycosides, linoleic acid, anthraquinones, morindone, rubiadin and alizarin (Duduku et al., 2007).

The present study was designed to investigate the acute toxicity effects of ethanolic fruit extracts of *M. citrifolia* and *M. tinctoria* at different stages of maturity.

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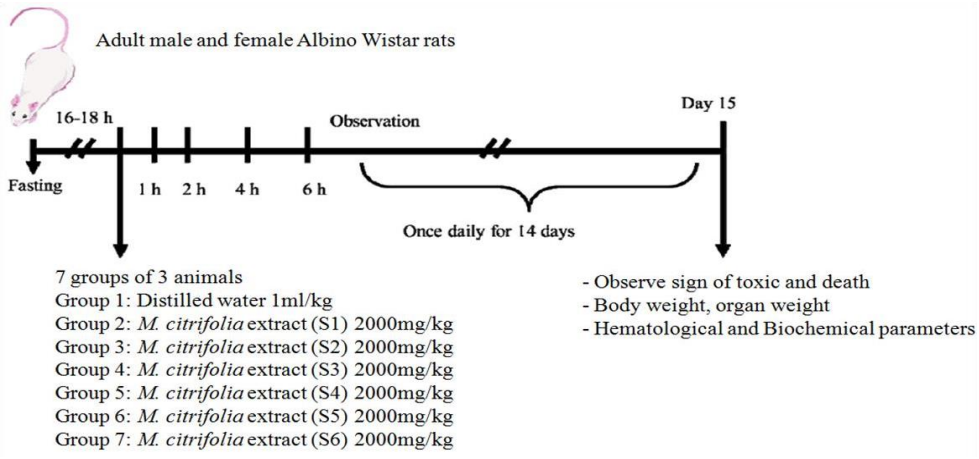

Figure 1: Scheme for acute toxicity test of M. citrifolia L. fruit extracts at different maturity stages

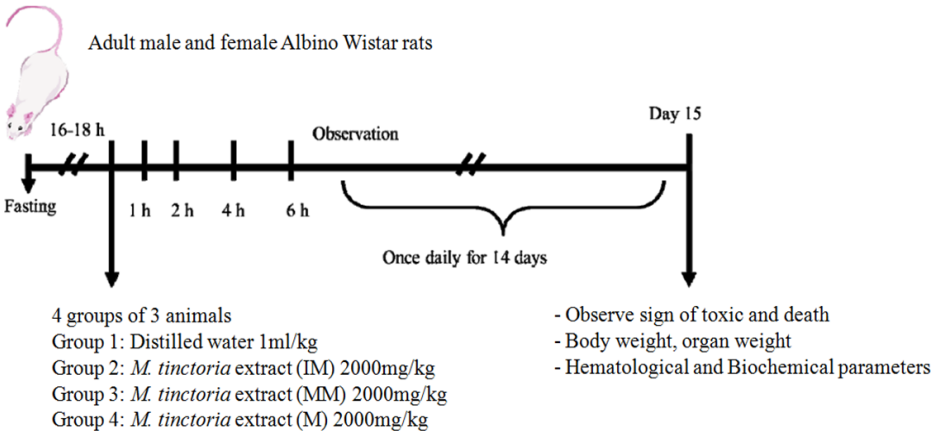

Figure 2: Scheme for acute toxicity test of M. tinctoria Roxb fruit extracts at different maturity stages

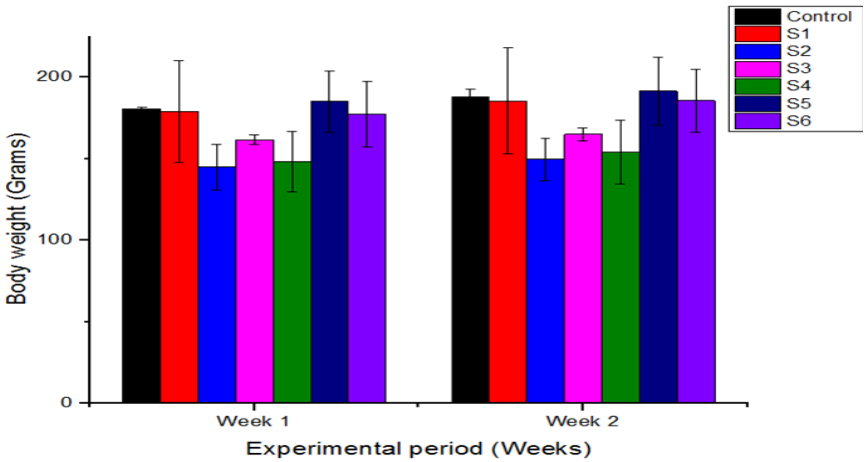

Figure 3: Body weights of rats after 14 days of acute toxicity study of ethanolic extract of M.citrifolia Linn

MATERIALS AND METHODS

Collection of fruits

Six levels of Noni fruit developmental stages were identified (S1: Three weeks after fruit set; S2: Six weeks after fruit set; S3: Nine weeks after fruit set; S4: Twelve weeks after fruit set; S5: Fifteen weeks after fruit set; S6: Over ripe stage) and used for present analysis (Ponnuswami et al., 2012). Noni fruits at different maturity stages were procured from National Research Centre for Noni Research (NRCN), Noni cultivation farm (Salavakkam, Kanchipuram District, Tamil Nadu, India).

Nuna fruits at different maturity stages (immature, midmature and mature) were collected from Thanjavur, Tamil Nadu, India.

Preparation of fruit extracts

Different maturity stages of Noni and Nuna fruits were washed with tap water followed by washing with distilled water. The fruits were peeled and the core was

Table 1: Food consumption and water intake of animals treated with M. citrifolia fruit extract during experimental period

		Food consumption (g)		Water intake (ml)	
Groups	Dose(mg/kg body weight)	Week 1	Week 2	Week 1	Week 2
Control	-----	93.52±2.45	87.7±0.77	105.5±2.50	108±2.00
S1	2000	87.52±2.04	92.92±0.97	167.75±4.75	168.75±0.75
S2	2000	85.68 ±2.30	92.69±0.36	180.5±2.50	180.5±7.50
S3	2000	91.73±1.28	88.34±0.59	148±2.00	146.5±11.5
S4	2000	93.1±1.90	92.04±0.61	158.5±3.50	157.5±2.50
S5	2000	89.32±1.23	88.09±0.83	165±3.00	163±3.00
S6	2000	92.45±0.97	91.56±0.77	122±2.00	121.5±3.50

Values are expressed as mean ± standard deviation (n=3).

Table 2: Food consumption and water intake of animals treated with M. tinctoria fruit extracts

		Food consumption (g)		Water intake (ml)	
Groups	Dose(mg/kg body weight)	Week 1	Week 2	Week 1	Week 2
Control	-----	92.99±0.98	93.09±1.91	162.5±7.50	161±3.00
Immature	2000	88.43±2.04	91.70±0.86	150.00±10.00	145.50±9.50
Midmature	2000	87.50±1.07	87.99±0.98	150.00±5.00	142.50±7.50
Mature	2000	88.99±0.56	84.45±1.02	239.00±17.03	220.05±5.01

Values are expressed as mean ± standard deviation (n=3).

Table 3: Effect of different maturity stages of ethanolic extract of Noni fruits on serum biochemical parameters of rats

Treatment	Control	S1	S2	S3	S4	S5	S6
Dose (mg/kg. B.W)	--	2000	2000	2000	2000	2000	2000
Glucose (mg/dL)	55.6±0.2	53.3±0.6	55.2±1.1	51.1±0.3	53.3±0.8	56±0.4	50.4±0.0
Urea (mmol/L)	5.4±0.5	6±0.1	7.3±0.9	6.8±0.4	7±0.0	7.3±0.7	6.7±0.3
Creatinine (mg/ml)	1.8±0.0	2.4±0.4	2±0.0	1.8±0.1	2±0.2	2.6±0.5	2.8±1.2
Cholesterol (mg/dL)	61.3±0.9	55.6±0.2	60.6±0.6	65.5±0.3	70.3±0.0	65.6±0.7	70.8±0.4
Total protein (g/dL)	7.9±0.3	7.9±0.1	7.1±0.4	7.6±0.1	7.8±0.2	7.5±0.4	7.2±0.6
Albumin (g/dL)	4.1±0.8	4.7±0.3	3.3±0.6	4.5±0.5	3.6±0.8	4.5±0.0	4.3±0.2
Globulin (g/dL)	2.85±0.4	3.1±0.2	1.8±0.1	2.2±0.2	2.2±0.6	1.9±0.3	1.9±0.4
AST (U/ml)	49±0.7	42±1.3	47.2±0.9	48.5±0	40.1±0.3	48±0.6	45±0.8
ALT (U/ml)	29.61±0.59	28.80±1.20	29.15±0.45	28.95±1.25	26.25±1.25	25.95±2.75	29.90±0.30
ALP (U)	115.4±0.4	120.7±0.7	127.9±0.0	128.5±0.1	118.4±0.3	121.3±0.9	110.6±0.4

cut into small pieces and kept for shade drying and the dried fruit was then finely powdered using a mixer.

Dried powder of fruits was then macerated with ethanol in 1:10 (W/V) ratios. The contents were kept as such in room temperature for 48 hour with constant stirring at regular gap. After that the contents were filtered through Whatmann No.1 filter paper. Then filtrates were concentrated in hot air oven at 40°C and were stored at 4°C and used for further analysis. Working concentrations of the extract were made in distilled water before use in the experiments.

Experimental animals

Albino rats of both sexes procured from G.S.A. Animal Farm, Mayiladuthurai, Tamil Nadu were used for the study. The rats were maintained over husk bedding in polypropylene cages at an ambient temperature of 25°C±1°C with a 12:12h light/dark cycle in the central animal house facility of the institution. The rats were fed throughout the experimental period with balanced commercial pellet diet and water *ad libitum*. Animals were acclimatized for at least one week before using them for the experiments. The principles of animal

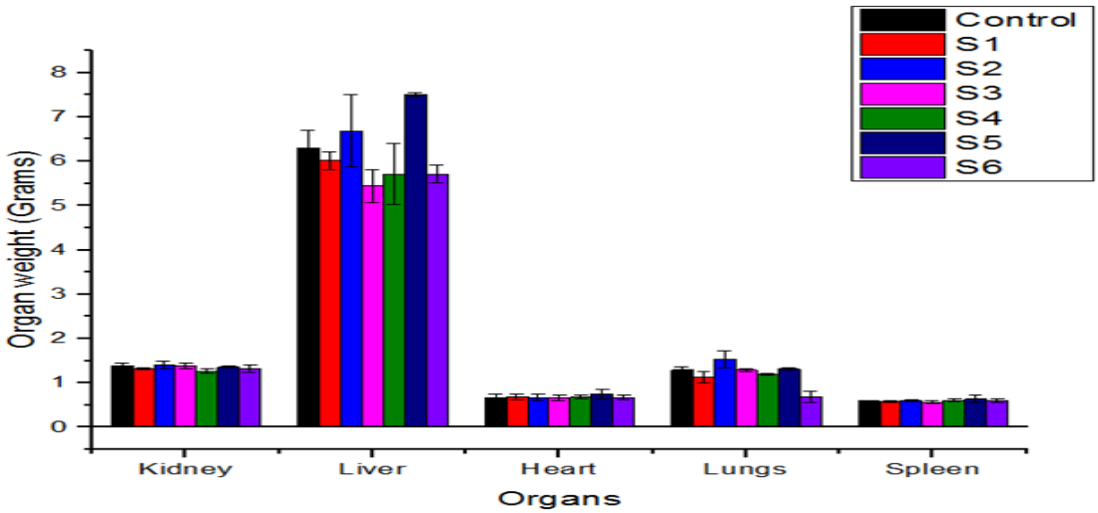

Figure 4: Absolute organ weight of rats treated with different maturity stages of M. citrifolia fruit extracts

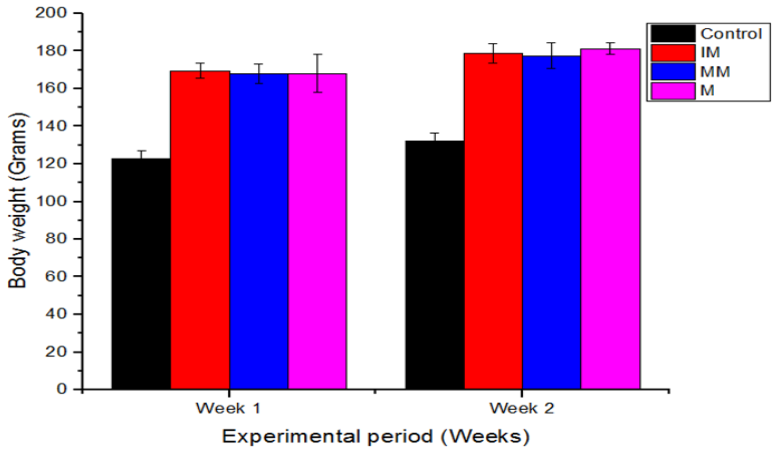

Figure 5: Body weights of rats after 14 days of acute toxicity study of ethanolic extract of M.tinctoria

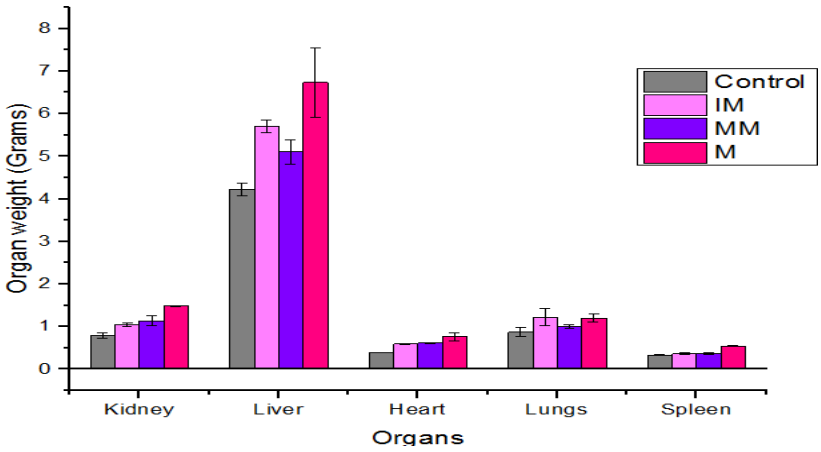

Figure 6: Absolute organ weight of rats treated with different maturity stages of M. tinctoria fruit extracts

care laboratory were followed, whereas the Institutional Animal Ethics Committee approved the use of animals and the study design (Approval No. PRIST/IAEC/Project MB 01-2012-2013).

Study design and selection of doses

Acute oral toxicity test was carried out according to the Organization for Economic Cooperation and Development (OECD) guidelines for testing of chemicals number 420 (OECD, 2001). The study was initiated with a sighting study aimed to find out the dose for the acute toxicity study. The sighting study consist of Wistar albino rats dosed in a stepwise method using the graded doses of 100, 200, 500, 1000, 2000 mg/kg body weight. All the rats were monitored and observed once daily for the next 14 days. The sighting study revealed that

Table 4: Effect of different maturity stages of ethanolic extract of Noni fruits on liver biochemical parameters of rats

Treatment	Control	S1	S2	S3	S4	S5	S6
Dose (mg/kg. B.W)	--	2000	2000	2000	2000	2000	2000
Glucose (mg/dL)	60.5±0.4	54±0.7	51.8±0.2	52.8±0.9	60.7±0.3	57.1±0.0	59.4±0.6
Cholesterol (mg/dL)	45±1.2	45.5±0.6	55.5±0.1	47.3±0.3	51±0.7	48.4±0.4	45.6±0.2
Total protein (g/dL)	7.1±0.4	7.9±0.1	7.4±0.6	7.7±0.9	6.1±0.1	6.3±0.5	7.1±0.8
Albumin (g/dL)	4.1±0.1	4.5±0.4	3.9±0.6	4.6±0.8	4.4±0.5	4.8±0.2	4.5±0.7
Globulin (g/dL)	2±0.3	2.4±0.2	1.3±0.0	2.3±0.2	1.3±0.4	2.4±0.3	2.6±0.1
AST (U/ml)	23.6±1.9	18.9±0.2	21.4±0.4	15.5±0.0	18.6±0.5	20.7±0.3	21.5±0.0
ALT (U/ml)	18.5±0	20.1±0.9	20.5±0.4	20.7±1.2	19±0.0	16.5±0.2	17.5±0.1
ALP (U)	99.6±0.2	101±0.4	86±0.7	104.5±0.1	100.7±0.3	99.1±0.0	100.7±0.5

Values are expressed as mean ± standard deviation (n=3).

Table 5: Effect of different maturity stages of ethanolic extract of M. tinctoria fruits on serum biochemical parameters of rats

Treatment	Control	IM	MM	M
Dose (mg/kg. B.W)	--	2000	2000	2000
Glucose (mg/dL)	57.95±2.45	62±3.50	57.50±2.0	52.2±1.1
Urea (mmol/L)	67.8±2.30	63±2.50	72±1.50	74±1.50
Creatinine (mg/ml)	1.85±0.05	2.3±0.10	1.85±0.05	2.1±0.10
Cholesterol (mg/dL)	50.55±1.65	67±1.50	56.95±1.55	51±.0.5
Total protein (g/dL)	7.4±0.20	7.5±0.10	7.4±0.10	7.2±0.10
Albumin (g/dL)	4.95±0.05	6.35±0.35	4.7±0.30	5.45±0.45
Globulin (g/dL)	2.95±0.25	3.20±0.20	4.01±0.20	3.70±0.70
AST (U/ml)	46.85±1.35	46.30±0.80	46.25±1.15	46.25±0.95
ALT (U/ml)	24.85±3.75	27.55±1.85	25.45±1.15	22.26±0.76
ALP (U)	125.15±1.75	124.70±0.40	125.90±1.40	125.65±1.75

Values are expressed as mean ± standard deviation (n=3).

Table 6: Effect of different maturity stages of ethanolic extract of M. tinctoria fruits on liver biochemical parameters of rats

Treatment	Control	IM	MM	M
Dose (mg/kg. B.W)	_	2000	2000	2000
Glucose (mg/dL)	58.85±3.35	53±2.50	60.35±0.25	60.85±1.35
Cholesterol (mg/dL)	53.45±2.95	51.25±0.95	55.45±5.05	59.30±0.80
Total protein (g/dL)	7.6±0.6	7.1±0.4	7.1±0.2	7.15±0.1
Albumin (g/dL)	4.85±0.15	3.95±0.55	5.40±0.25	5.25±0.25
Globulin (g/dL)	2.6±0.6	2.75±0.2	3.3±0.6	3.7±0.2
AST (U/ml)	47.35±1.25	46.66±1.64	48.25±1.05	46.55±1.05
ALT (U/ml)	17.45±0.05	29.90±0.20	19.35±0.75	18.85±0.35
ALP (U)	81.70±1.20	109.55±4.85	90.35±1.85	80.65±0.15

Values are expressed as mean ± standard deviation (n=3).

rats orally administered with the dose of 100, 200, 500, 1000, 2000 mg/kg body weight were survived. Based on this observation, the highest dose 2000 mg/kg body weight was selected for the acute toxicity study.

Acute toxicity study

For the study, Albino Wistar rats were divided into seven groups of three animals each. The ethanolic fruit extracts of *M. citrifolia* at different maturity stages were suspended in distilled water. This solution was administered orally in a single dose of 2000 mg/kg body weight. The control group received an equal volume of distilled water as vehicle (Figure 1).

Wistar albino rats were divided into four groups of three animals each. The ethanolic fruit extracts of *M. tinctoria* at different maturity stages were suspended in distilled water. This solution was administered orally in a single dose of 2000 mg/kg body weight. The control group received an equal volume of distilled water as vehicle (Figure 2).

Collection of blood samples

Table 7: Effect of different maturity stages of ethanolic extract of Noni fruits on hematological indices of Wistar albino rats

Treatment	Dose (mg/kg. B.W)	Hemoglobin (g/dL)	RBC (10^6/mm^3)	WBC (Cells/ mm^3)	MCV (fl)	MCH (pg)	MCHC (g/dl)	Platelets (lakhs/mm^3)
Control	_	12.05±0.2	7.05±0.2	760.5±0.7	72.1±0.1	31.3±0.4	27.2±0.2	1.75±0
S1	2000	12.05±0.5	7.75±0.8	640.4±0.5	70.7±0.9	28.5±0.7	25±0.7	1.5±0.3
S2	2000	15.15±0.3	7.28±0.9	680.2±0.2	71±0.0	31.4±0.5	27.6±0.8	2.3±0.9
S3	2000	14.45±0.7	6.96±0.5	580.4±0.6	80.2±0.3	35.1±0.1	30.4±0.6	2±0.1
S4	2000	11.95±0.4	7.01±0.1	590±0.2	77.5±0.7	34.6±0.9	33±0.5	2.3±0.4
S5	2000	13.9±0.3	7.35±0.1	700.2±0.3	72.2±0.2	31±0.0	26.9±1.3	2.3±0.7
S6	2000	15.05±0.7	9.14±0.5	720.1±0.1	75.4±0.5	33.2±0.3	28.1±0.2	1.9±0.9

Values are expressed as mean ± standard deviation (n=3).

Table 8: Effect of different maturity stages of ethanolic extract of M. tinctoria fruits on hematological indices of Wistar albino rats

Treatment	Dose (mg/kg. B.W)	Hemoglobin (g/dL)	RBC (10^6/mm^3)	WBC (Cells/ mm^3)	MCV (fl)	MCH (pg)	MCHC (g/dl)	Platelets (lakhs/mm^3)
Control	_	11.9±0.3	6.98±0.67	895±5.0	78±2.0	32±2.0	26±1.0	2.05±0.05
IM	2000	12.15±0.25	6.31±0.08	840±1.0	92.5±2.5	35.5±0.5	32.5±2.5	2.05±0.05
MM	2000	12.75±0.95	6.97±0.16	855±5.0	91±1.0	31±1.0	28.5±6.5	1.65±0.15
M	2000	14.95±0.25	9.10±0.63	905±5.0	77.5±2.5	35±2.0	28.5±3.5	1.8±0.10

Values are expressed as mean ± standard deviation (n=3).

Observations of toxic symptoms were made and recorded 1, 2, 4, 6 and 24h after administration of the extract. The number of animals that stay alive were noted after 24h and then maintained for the further 14 days with daily observations. Visual observations included such as. Skin changes, mobility, aggressiveness, and sensitivity to sound and pain. During the experimental period animals were weighed, food and water intake were monitored. At the end of the experiment, all the animals were fasted overnight prior to the blood collection by cardiac puncture technique (Beeton et al., 2007). After blood collection animals were sacrificed and internal organs such as liver, lungs, heart, kidney and spleen were excised and weighed. The pathological observations of these tissues were performed on gross. The blood samples were collected freshly in the dry EDTA tubes. Blood was allowed to coagulate before the centrifuge to separate the serum. This serum was examined for biochemical parameters. The liver was cut out, rinsed, in ice-normal solution followed by 0.1M Tris-HCL (pH 7.5), blotted, dried and weighed. The 20% (w/v) liver homogenates was prepared in 0.1M Tris-HCL buffer and the supernatant was used for biochemical analysis. Lung, kidney, heart and spleen were removed, washed in 0.9% of NaCl and weighed.

Biochemical and hematological parameters

Standard diagnostic kits (Agappe) were used for the determination of biochemical parameters. Blood samples was collected in the EDTA tubes were centrifuged at 3000 rpm for 10 minutes to separate the serum. This serum was used to investigate the liver enzyme functions through biochemical parameters such as aspartate aminotransferease (AST), alanine aminotransferease (ALT), alkaline phosphatase (ALP), creatinine and total protein, albumin, globulin, glucose, urea and cholesterol.

Liver homogenates were examined for biochemical parameters such as, aspartate aminotransferease (AST), alanine aminotransferease (ALT), alkaline phosphatase (ALP), total protein, albumin, globulin, glucose, and cholesterol.

The blood for hematological assay was immediately analyzed using a hematological analyzer. The parameters measured were hemoglobin, red blood cell (RBC), white blood cell (WBC), mean corpuscular value (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and platelets.

RESULTS AND DISCUSSION

Acute toxicity study

The oral administration of ethanolic extract of Noni fruits at different maturity stages did not cause mortality during 24 h and 14 day observation, and there was no indication of toxicity, behavioral or physiological changes. Also the extract did not made any alterations in food and water intake in either the male or female rats throughout the experimental period (Table 1). Assessment of the extracts on body weight and organs of experimental animals is a vital test in toxicity evaluation. The alteration in overall body weight or organ weight is a sign of damage in normal functioning of the organs (Amresh et al., 2008). Both the control and treated groups of rats showed increase in body weight (Figure 3) and organs (Figure 4) over the course of the

two weeks treatment. The observed increase in the body weight may be endorsed to the nutritive components in the plant (Ezeonwumelu et al., 2011). The growth response effect could be as a result of food and water intake. The results of the in vivo acute toxicity study indicated that the LD50 of the extract of Noni fruits at different maturity stages is more than 2000 mg/kg. Thus, it is evident that oral administration of Noni fruit at a dose of 2000 mg/kg is nontoxic to the system, consistent with earlier reports (Mancebo et al., 2002; Chearskul et al., 2004; West et al., 2006).

In the present study, an acute toxicity study of ethanolic extract of Nuna fruits at different maturity stages has been performed. A single administration of extracts by the oral route up to a dose of 2000 mg/kg body weight did not produce mortality, any signs of toxicity or changes in general behavior or other physiological activities when compared with control group. Likewise, the body weight and internal organ weight of treated rats were somewhat similar to that of the control group. The results of the present study revealed that Nuna fruit extracts has no acute oral toxicity.

Generally, the reduction in body weight (Figure 5) gain and internal organ weights (Figure 6) is a simple index of toxicity exposure to toxic substances (Teo et al., 2002). In acute toxicity study, rats treated with 2000 mg/kg doses of ethanol extract of Nuna had a progressive weight in body. The increase in the weight was not different from control group. This may indicate the development in the nutritional state of the animal. The extract did not appear to affect the body weight of the rats and caused no changes in their food and water consumption (Table. 2). Consumption of food and water exhibited normal metabolism in the animals (Mukinda and Syce, 2007). And this denotes that single oral dose of extract does not retard the growth of rats.

Biochemical parameters

Assessment of liver and kidney function is very important in toxicity evaluation of plant extracts as they both are essential for the continued existence of organism. AST and ALT activities are commonly measured to monitor liver damage. A mild or elevated activity of AST indicates liver injury or myocardial infarction and the ratio of the AST/ALT may be used for disease diagnosis (Feldman and Zinkl, 2000; Crook, 2006). An AST/ALT ratio greater than 1 suggests myocardial infarction, while ratio less than 1 may be due to the discharge of ALT from the affected liver (Sacher and Mepherson, 1991). Whereas, if the ratio more than 2 indicates alcoholic hepatitis or cirrhosis (Varadarasou et al., 2010). In the present study, Noni fruit extracts did not bring on any damage to the liver or kidney as revealed by the results of clinical biochemistry analysis (Table 3 and 4). The lack of alterations in the indicators of liver damage such as AST, ALT, ALP, total protein and albumin in both serum and liver homogenates suggests that administration of ethanolic extract of Noni fruits does not affect hepatocyte function in the animals.

The secretory ability of the liver was considered by assessing changes in albumin, and globulin concentrations (Guyton and Hall, 2000). Reduction in total protein, albumin and globulin are indications of diminished synthetic function of the liver or may be because of the impaired hepatocellular function. Low serum albumin content may suggest infection or continuous loss of albumin (Yakubu et al., 2003). Thus, insignificant modifications in total protein, albumin and globulin in the treated and control group further recommends that the extract does not impair hepatocellular or secretory functions of the liver at the tested dose. Still, this should be further confirmed in the sub chronic toxicity studies.

Kidney function was evaluated by means of urea, serum creatinine concentrations. Increased serum creatinine is a fine indicator of compromised kidney functions. In the present study, serum creatinine, and urea were not affected by extract treatment. These results suggest that the extract does not alter the kidney function.

The ethanolic extracts of Nuna fruits at different maturity stages did not induce any damage to kidney and liver as examined by clinical blood chemistry (Table 5 and 6). ALT and AST are two liver enzymes that are associated to the hepatic damage. Although both are common liver enzymes, because of their higher concentrations in hepatocytes only ALT is remarkably specific for liver function since AST is mostly present in myocardium, brain and kidneys (Sacher and Mepherson, 1991). The liver releases ALT and an elevation in plasma concentration is an indicator of liver damage (Crook, 2006). In this study, no notable changes was found in these enzymes indicates that the extract had no deleterious effect on liver function.

Kidney is a sensitive organ, whose function is known to be affected by various factors such as drugs including phytochemicals of plant origin that ultimately lead to renal failure. Assessment of possible renal damage due to ethanolic extracts of Nuna was made by assaying serum urea and creatinine levels. Results showed no alteration in urea and creatinine levels due to administration of extract. Moreover, there was no effect on the levels of AST and ALT which is considered to be sensitive indicators of hepatocellular damage and within limits may be offering a quantitative evaluation of the degree of damage to the liver (Crook, 2006). It is reasonable to deduce, therefore the Nuna fruit extracts did not induce any damage to liver and kidney. It is apparent form the results of the clinical blood chemistry analysis of serum and liver homogenates, most of the biochemical parameter were not altered in treated groups by the extract. The lack of alterations in the levels of ALT, AST, ALP, glucose and creatinine which are good indicators of liver and kidney functions sug-

gests that acute oral administration of extract neither altered hepatocytes and kidneys of rats nor the normal metabolism of animals.

Hematological parameters

Investigation of hematological parameter is most needed for toxicity assessment as changes in hematological indices have a higher predictive value for human toxicity (Saidu et al., 2007). In the present study, administration of ethanolic fruit extracts of Noni did not cause any alterations in hematological profile (Table.7). The results illustrated no deleterious effects on blood cell count and hemoglobin content and the extracts may contain biologically active compounds that can boost the immune system (Al-Habori et al., 2002). The effect of extracts on RBC, Hemoglobin, WBC, MCV, MCH, MCHC, and platelets denotes that extract does not affect erythropoiesis, morphology, or osmotic fragility of the red blood cells. Thus by supports that Noni fruit extracts had no toxic effect on blood system.

The hematopoietic system is very sensitive to toxic compounds and serves as an important index of physiological and pathological status in both human and animals (Adeneye et al., 2006). The hematological status after the oral administration of the ethanol extracts of Nuna fruits was also assessed (Table 8). No changes were observed in the hematological parameters between the control and treatment groups. In general the results showed that values for hemoglobin and WBC were slightly increased in mature fruits of Nuna compared with control. However, the values detected are within the normal range (Johnson-Delaney, 1996). This indicates the non toxic nature of Nuna fruit extracts at different maturity stages.

CONCLUSION

It was concluded that the acute toxicity study of Noni and Nuna fruit extracts at 2000 mg/kg BW administered orally to Wistar albino rats did not caused any death or acute adverse effect on the clinical observation and mortality to the treated rats. The outcome of the present investigation gives fundamental information to make use of these spices and the essential measures to be initiated before carry out pre-clinical trial of these crude drugs in the future.

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