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ORIGINAL ARTICLE

Acute Toxicity of *Oroxylum indicum* Fruit Extracts in Rats

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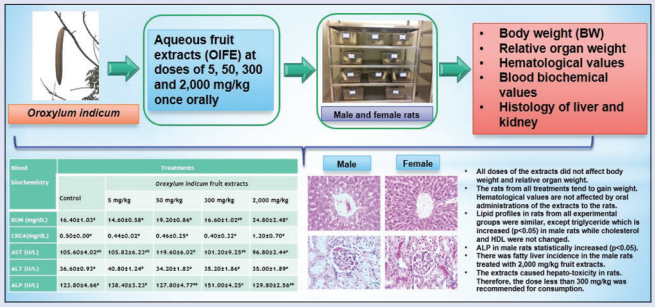
ABSTRACT

Background: The fruit parts of *Oroxylum indicum* have been used as local vegetables and folklore medicine among Southeast Asian people including Thailand. There is no report on their safety evaluation. **Objectives:** The present study was aimed to evaluate the acute toxicity of *O. indicum* fruit extracts in male and female rats. **Materials and Methods:** The acute toxicity study was performed according to OECD guideline. The male and female Wistar rats were once and orally administered with the extracts at doses of 5, 50, 300, and 2000 mg/kg. The acute toxicity symptoms and mortality rates were observed within 24 h after administrations and until 14 days of the experiments. Body weight was measured in weeks 0, 1, and 2. At the end of the experiment, internal organ weights were measured. Hematological values, blood biochemistry values, and histology of liver and kidney were also examined. **Results:** All doses of the extracts did not affect body weight and relative organ weight. The rats from all treatments tend to gain weight. Hematological values are not affected by oral administrations of the extracts to the rats. Lipid profiles in rats from all experimental groups were similar, except triglyceride which is increased ($P < 0.05$) in male rats while cholesterol and high-density lipoprotein were not changed. Blood biochemical values in rats from all experimental groups were similar, but alkaline phosphatase in male rats statistically increased ($P < 0.05$). In addition, the inflammation was not found in liver tissue. While the histology study found that there was fatty liver incidence in the male rats treated with 2000 mg/kg fruit extracts. No change in histopathology of kidney in rats treated with the extracts was found. **Conclusion:** These findings indicate that *O. indicum* fruit extracts caused hepatotoxicity in rats. Therefore, the dose less than 2000 mg/kg was recommended for consumption.

Key words: Acute toxicity, blood biochemistry values, fruit extracts, hematological values, histology of liver and kidney, *Oroxylum indicum*, rats

SUMMARY

- All doses of *O. indicum* fruit extracts did not cause any mortality and toxicity sign in the controls and treated male and female rats. The extracts did not affect body weight, relative organ weight and hematological values. However, triglyceride and ALP increased in male rats treated with the extracts. In additions, there were fat droplets in liver tissues of male rats treated with 2,000 mg/kg extracts. These findings suggest that *O. indicum* fruit extracts at dose of 2,000 mg/kg caused hepatotoxicity in rats



Abbreviations used: SEM: Standard error of mean; WBC: White blood cell; RBC: Red blood cell; HGB: Hemoglobin; HCT: Hematocrit; MCA: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; PLT: Platelet; LYMPH: Lymphocyte; MONO: Monocyte; BASO: Basophil

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INTRODUCTION

Oroxylum indicum (Family: Bignoniaceae) is a local plant and commonly found in the southeastern Asian continent including Thailand. All parts of this plant are used in medicine and food ingredients. Young fruits of this plant are bitter but edible and taste better after cooking and are commonly consumed in Thailand and Malaysia as a traditional vegetable. Young leaves and fruits are boiled and eaten with salted fish in Vietnam. The fruit is grilled and the outer skin remove and the inner parts are sliced and eaten with salted fish.[1]

The phytochemical screenings suggest that *O. indicum* crude extracts contain a flavonoid so-called chrysin (5,7-dihydroxyflavone).[1] The fruit extracts from this plant contained the high total phenolic and flavonoid contents, and a flavonoid was identified as baicalein by thin-layer chromatographic analysis.[2] However, baicalein was found to be the major compound in *O. indicum* seed extract followed by baicalein and chrysin, respectively.[3]

The studies on biological and pharmacological properties of this plant revealed that *O. indicum* fruit has an *in vitro* antioxidant effect with antibacterial potential on clinically pathologic bacteria.[2] Baicalein showed high *in vitro* antibacterial effect.[3] The fruits showed the anti-helminthic and stomachic stimulation activities.[4] Total flavonoid derived from the seed extracts of *O. indicum* inhibits tumor growth by inducing apoptosis through PI3k/Akt/PTEN signaling pathway.[5] The stem bark extracts from *O. indicum* have anti-inflammatory, antiulcer,

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antidiabetic, and antidyslipidemic potentials but have no ameliorative on liver enzyme.[6] In addition, stem bark extracts have strong antioxidant capacity and potential to inhibit BSA glycation and α-glucosidase activity. They also improved insulin sensitivity in mature 3T3-L1 adipocytes. *In vivo* effects of stem bark extracts on STZ-induced type II diabetic rats normalized the antioxidant status with lowering of total cholesterol and high-density lipoprotein (HDL) levels and restoration of glycated *hemoglobin* (Hb).[7] The stem bark of *O. indicum* also exhibited a high level of antioxidant capacity by inhibiting lipid-peroxidation.[8] The root bark extracts of this plant exhibit the protective effect against acute colitis by antioxidant, anti-lipoperoxidative activities, or the reduction of nitric oxide generation.[9] Acute toxicity study of ethanol leaf extracts of this plant in mice revealed that *O. indicum* ethanol extracts up to 5000 mg/kg do not cause any acute toxicity in mice.[10]

Although the fruit parts of *O. indicum* have been locally used as food and folk remedy ingredients in southeastern part of Asia, the safety evaluation has not been intensively examined. Therefore, the present study was aimed to evaluate the acute toxicity of *O. indicum* fruit extracts in male and female rats.

MATERIALS AND METHODS

Plant materials

The fruit parts of *O. indicum* were collected from the local cultivation area in Mahasarakham province, Thailand. They are authenticated at the Department of Biology, Faculty of Science, Mahasarakham University, Thailand. Voucher specimens were deposited at the herbarium of the Faculty of Science, Mahasarakham University, Thailand.

Plant extract preparations

The fruits (pots) were rinsed with clean tap water to remove dirt. They were then cut into small pieces and dried in hot air oven at 60°C for 48 h. The dried fruits of these plants were then ground into fine powder using an electrical grinder. They were macerated in the solvent (95% ethanol) for 7 days with the proportion of fruit powder and solvent of 1:4. The crude extracts were filtered by filter paper Whatman No. 1. The extracts were then evaporated to remove the solvent by rotary evaporator. The crude extracts were lyophilized by freeze dryer. The fruit extracts were kept at 4°C for further *in vivo* study.

Animal model

The acute toxicity study was performed according to OECD 420 guideline. The male and female Wistar rats with weight of 150–200 g were used in this study. They were purchased and housed at the animal house (Animal Biosafety Level 3; ABSL3) in the Northeastern Laboratory Animal Center, Khon Kaen University, Khon Kaen, Thailand. The animal protocol was approved by Animal Ethics Committee, Khon Kaen University, Thailand. Approval number is KKU 61/62.

Experimental design

According to OECD guidelines for acute toxicity study, the Wistar rats were divided into 10 groups; male 5 groups and female 5 groups. Group 1 was the control. Group 2 was normal rats received 5 mg/kg extracts. Group 3 was normal rats received 50 mg/kg extracts. Group 4 was normal rats received 300 mg/kg extracts. Group 5 was normal rats received 2000 mg/kg extracts.

Male and female rats were once orally administered with the distilled water and the fruit extracts of *O. indicum*. The acute toxicity symptoms and mortality rates were observed within 24 h after administrations and further 14 days of the experiments. Body weight was measured in weeks 0, 1, and 2. At the end of the study, the rats were sacrificed by isoflurane inhalation. The blood samples were immediately collected from cardiac puncture for hematological and biochemical investigations.

The hematological parameters including red blood cell (RBC), white blood cell (WBC), platelets, hematocrit and Hb and biochemical parameters including blood urea nitrogen (BUN), creatinine, alkaline phosphatase (ALP), and lipid profiles were determined by automatic blood chemical analyzer (BT 200 Plus, Germany).

The internal organs including liver, kidney, heart, lung, and spleen were removed for relative organ weight calculation. They were weighed by digital balance and calculated the relative organ weight using the following formula:

Relative organ weight (%) = organ weight (g)/body weight (g) ×100

For histological investigation, liver and kidney tissues were fixed in 10% neutral formalin. The tissues were washed with normal saline and immediately fixed in 10% formalin for 72 h and the fixative was changed daily. The tissues were then dehydrated by the series of alcohols and xylene in the tissue processor machine. The dehydrated tissues were cut in small pieces and place in cassettes. The tissues were embedded in paraffin and cut with the thickness of 5–7 μm using rotary microtome. The ribbon liked tissues were placed in warm water bath to remove paraffin. The tissues were fixed on microscope slide and stained with hematoxylin and eosin. The histopathology of these tissues was examined under the light microscope.[11]

Statistical analysis

The values of all parameters except histological study were expressed in form of mean ± standard error of mean. Comparison of means was analyzed by one-way ANOVA. Statistical analysis was carried out using SPSS software version 23 (IBM Corp., Armonk, New York, USA).

RESULTS

The results revealed that all doses of the extracts did not cause any mortality and toxicity sign in the controls and treated male [Table 1] and female rats [Table 2]. The behavioral changes including reluctance to move, abnormal movement, loss of appetite, and loss weight as well as mortality were not found [Tables 1 and 2].

Body weight and relative organ weight

The results revealed that all doses of the extracts did not cause mortality or toxicity signs in rats. All doses of the extracts did not affect body weight and relative organ weight. The rats from all treatments tend to gain weight [Tables 3 and 4]. Moreover, the relative organ weight of liver, kidney, heart, lung, and spleen in rats treated with the extracts at doses of 5, 50, 300, and 2000 mg/kg was not statistically different in comparison to those of the controls [Tables 5 and 6].

Hematological values

The fruit extracts from *O. indicum* did not produce any signs of toxicity on hematological parameters [Tables 7 and 8]. The RBC and WBC counts, platelet counts, Hb, and hematocrit values were similar among the controls and the rats treated with the extracts at doses of 5, 50, 300, and 2000 mg/kg.

Lipid profiles

The lipid profiles including total cholesterol, triglyceride, and HDL cholesterol were in the normal range and they were similar among all experimental groups [Tables 9 and 10]. These results suggested that the extracts did not affect the lipid profiles in rats. However, the results revealed that lipid profiles in rats from all experimental groups were similar, except triglyceride which is increased ($P < 0.05$) in male rats while cholesterol and HDL were not changed.

Table 1: Toxicity signs of male rats treated once and orally with *Oroxylum indicum* fruit extracts for 14 days

Treatment	Behavioral change				Mortality
	Reluctance to move	Abnormal movement	Loss of appetite	Loss weight	
Control	x	x	x	x	x
OIFE 5 mg/kg	x	x	x	x	x
OIFE 50 mg/kg	x	x	x	x	x
OIFE 300 mg/kg	x	x	x	x	x
OIFE 2000 mg/kg	x	x	x	x	x

X: Not found; OIFE: *Oroxylum indicum* fruit extracts

Table 2: Toxicity signs of female rats treated once and orally with *Oroxylum indicum* fruit extracts 14 days

Treatment	Behavioral change				Mortality
	Reluctance to move	Abnormal movement	Loss of appetite	Loss weight	
Control	x	x	x	x	x
OIFE 5 mg/kg	x	x	x	x	x
OIFE 50 mg/kg	x	x	x	x	x
OIFE 300 mg/kg	x	x	x	x	x
OIFE 2000 mg/kg	x	x	x	x	x

X: Not found; OIFE: *Oroxylum indicum* fruit extracts

Table 3: Effects of *Oroxylum indicum* fruit extracts on body weight increasing in control and treated male rats during 14 days of the experiments

Treatments	Increasing body weight (%) (mean±SEM)	
	Week 1	Week 2
Control	57.22±1.63	37.68±1.77
OIFE 5 mg/kg	60.56±4.18	31.25±1.45
OIFE 50 mg/kg	56.20±1.70	29.09±4.09
OIFE 300 mg/kg	59.06±3.39	35.95±3.67
OIFE 2000 mg/kg	55.13±3.21	31.42±4.37

OIFE: *Oroxylum indicum* fruit extracts; SEM: Standard error of mean

Table 4: Effects of *Oroxylum indicum* fruit extracts on body weight increasing in control and treated female rats during 14 days of the experiments

Treatments	Increasing body weight (%), mean±SEM	
	Week 1	Week 2
Control	42.22±18.05	5.13±1.28
OIFE 5 mg/kg	15.31±10.84	7.57±1.92
OIFE 50 mg/kg	27.41±1.31	11.33±1.73
OIFE 300 mg/kg	27.84±13.10	11.33±1.73
OIFE 2000 mg/kg	33.57±9.14	5.27±0.82

OIFE: *Oroxylum indicum* fruit extracts; SEM: Standard error of mean

Blood biochemistry

The liver function parameters including serum aspartate aminotransferase (AST), serum alanine aminotransferase, and ALP and the kidney function parameters including BUN and creatinine in the controls and rats treated with the extracts at doses of 5, 50, 300, and 2000 mg/kg were examined. Blood biochemical values in rats from all experimental groups were similar [Tables 11 and 12], but ALP in male rats statistically increased ($P < 0.05$) [Table 11]. These findings indicate that *O. indicum* fruit extracts caused hepatotoxicity in rats. Therefore, the dose < 300 mg/kg was recommended for consumption.

Histopathological investigations

The study on histopathology of liver and kidney of rats treated with fruit extracts from *O. indicum* at doses of 5, 50, 300, and 2000 mg/kg revealed that the extracts did not cause any lesions in liver and kidney tissues of the rats.

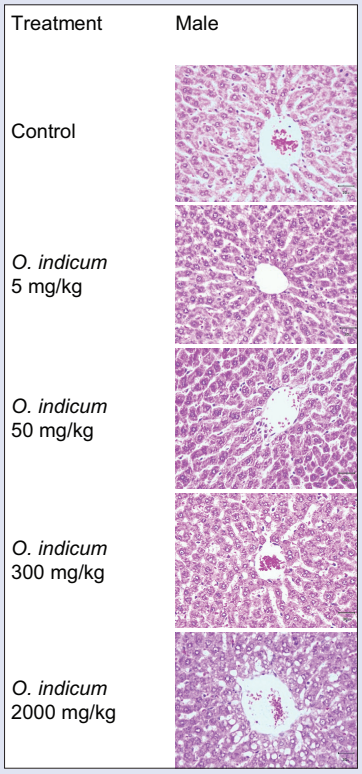

Figure 1: Histopathological illustration of liver in the controls and male rats treated with *Oroxylum indicum* fruit extracts at doses of 5, 50, 300, and 2000 mg/kg for 14 days (magnification = ×40)

No change in histopathology of liver in female rats treated with the extracts was found. It was found that hepatocytes are polygonal in shape with single columnar cell (hepatic cord). Central vein was covered by simple squamous epithelium called sinusoid. In addition, the inflammation was not found in liver tissue [Figure 1]. While the histology study found that there was fatty liver incidence in the male rats treated with 2000 mg/kg fruit extracts [Figure 2]. The results demonstrated that fruit extracts from *O. indicum* at dose of 2000 mg/kg caused hepatotoxicity in male

Table 5: Effects of *Oroxylum indicum* fruit extracts on relative organ weight in control and treated male rats during 14 days of the experiments

Relative organ weight (%), mean±SEM	Treatments				
	Control	OIFE 5 mg/kg	OIFE 50 mg/kg	OIFE 300 mg/kg	OIFE 2000 mg/kg
Liver	3.41±0.08	3.35±0.09	3.59±0.20	3.61±0.21	3.63±0.18
Kidney	0.85±0.03	0.91±0.06	0.84±0.03	0.87±0.04	0.90±0.06
Heart	0.45±0.01	0.45±0.01	0.47±0.02	0.46±0.03	0.47±0.02
Lung	0.24±0.01	0.24±0.01	0.28±0.01	0.27±0.03	0.25±0.02
Spleen	0.66±0.06	0.80±0.06	0.88±0.08	0.96±0.06	0.86±0.10

OIFE: *Oroxylum indicum* fruit extracts; SEM: Standard error of mean

Table 6: Effects of *Oroxylum indicum* fruit extracts on relative organ weight in control and treated female rats during 14 days of the experiments

Relative organ weight (%), mean±SEM	Treatments				
	Control	OIFE 5 mg/kg	OIFE 50 mg/kg	OIFE 300 mg/kg	OIFE 2000 mg/kg
Liver	3.13±0.16	3.36±0.08	3.45±0.09	3.57±0.07	3.45±0.09
Kidney	0.72±0.01	0.75±0.01	0.75±0.01	0.73±0.01	0.74±0.02
Heart	0.34±0.02	0.41±0.02	0.35±0.01	0.36±0.05	0.34±0.01
Lung	0.24±0.01	0.26±0.01	0.27±0.02	0.25±0.01	0.24±0.01
Spleen	0.76±0.02	0.74±0.01	0.74±0.01	0.75±0.00	0.73±0.01

OIFE: *Oroxylum indicum* fruit extracts; SEM: Standard error of mean

Table 7: Effects of *Oroxylum indicum* fruit extracts on hematological values in control and treated male rats during 14 days of the experiments

Hematological values, mean±SEM	Treatments				
	Control	*Oroxylum indicum*			
		5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
WBC (10^3/µl)	4.51±0.07	4.67±0.56	3.98±0.37	4.96±0.15	4.97±0.30
RBC (10^3/µl)	8.02±0.08	7.94±0.05	7.22±0.23	7.66±0.24	7.90±0.07
HGB (g/dL)	14.48±0.16	14.64±0.07	13.84±0.29	14.20±0.35	14.70±0.18
HCT (%)	43.52±0.39	44.24±0.28	43.74±0.50	43.84±0.56	44.56±0.69
MCV (fL)	53.68±0.24	55.30±0.16	56.58±1.53	57.60±0.88	55.36±1.18
MCH (pg)	17.72±0.10	18.50±0.07	18.60±0.17	18.64±0.19	18.02±0.34
MCHC (g/dL)	33.02±0.12	33.30±0.09	32.20±0.45	32.64±0.23	33.54±0.24
PLT (10^3/µl)	1080.00±4.48	939.20±5.15	990.20±2.13	1068.80±1.48	1180.20±1.46
LYMPH (10^3/µl)	3.92±0.08	3.84±0.48	3.41±0.37	4.21±0.14	4.66±0.21
MONO (10^3/µl)	0.13±0.01	0.16±0.02	0.11±0.02	0.18±0.02	0.12±0.02
BASO (10^3/µl)	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00

SEM: Standard error of mean; WBC: White blood cell; RBC: Red blood cell; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration, PLT: Platelet; LYMPH: Lymphocyte; MONO: Monocyte; BASO: Basophil

Table 8: Effects of *Oroxylum indicum* fruit extracts on hematological values in control and treated female rats during 14 days of the experiments

Hematological values, mean±SEM	Treatments				
	Control	*Oroxylum indicum*			
		5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
WBC (10^3/µl)	2.59±0.16	2.67±0.12	2.63±0.09	3.78±0.20	5.16±0.31
RBC (10^3/µl)	8.07±0.12	7.71±0.11	7.69±0.09	7.98±0.10	8.15±0.04
HGB (g/dL)	14.78±0.19	14.60±0.14	14.72±0.24	14.58±0.09	15.20±0.07
HCT (%)	42.16±0.22	43.20±0.34	43.98±0.72	43.70±0.18	45.56±0.27
MCV (fL)	53.26±0.27	54.20±0.18	54.96±0.47	54.90±0.47	55.70±0.19
MCH (pg)	18.00±0.12	18.98±0.26	18.22±0.20	18.42±0.19	18.54±0.08
MCHC (g/dL)	33.90±0.17	33.92±0.28	33.50±0.18	33.70±0.09	32.82±0.31
PLT (10^3/µl)	1058.40±7.05	899.60±16.19	874.00±7.96	1097.40±3.70	1118.4±34.08
LYMPH (10^3/µl)	1.93±0.01	2.80±0.20	2.50±0.09	3.61±0.05	5.17±0.18
MONO (10^3/µl)	0.10±0.03	0.07±0.02	0.08±0.02	0.10±0.01	0.15±0.01
BASO (10^3/µl)	0.00±0.00	0.00±0.00	0.01±0.00	0.00±0.00	0.00±0.00

SEM: Standard error of mean; WCA: White blood cell; RBC: Red blood cell; HGB: Hemoglobin; HCT: Hematocrit; MCA: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; PLT: Platelet; LYMPH: Lymphocyte; MONO: Monocyte; BASO: Basophil

Wistar rats. Therefore, the dose <2000 mg/kg was recommended for consumption.

The results revealed that all doses of the extracts did not cause mortality or toxicity signs in rats. No change in histopathology of kidney in rats treated with the extracts was found [Figures 3 and 4]. It was found that the glomerulus of the kidney cells has a rounded bulbous cup-shaped area of the nephron in mature male rats, and the parietal epithelium of Bowman's capsule is shaped as a square cuboidal [Figure 3]. In

Table 9: Effects of *Oroxylum indicum* fruit extracts on lipid profiles in control and treated male rats during 14 days of the experiments

Lipid profiles	Treatments				
	Control	*Oroxylum indicum*			
		5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
Cholesterol (mg/dL)	36.20±1.93[a]	37.80±3.89[a]	38.20±0.97a	33.80±0.37[a]	37.00±2.12[a]
Triglyceride (mg/dL)	85.00±20.27[a]	142.00±21.39[ab]	199.80±19.29b	185.40±33.34[b]	112.00±6.14[a]
HDL (mg/dL)	20.00±0.71[ab]	18.60±1.36[ab]	21.20±0.58[b]	18.20±0.66[a]	19.80±0.58[ab]

[a, b]Different superscripts in the same row indicate statistical significance (P<0.05). HDL: High density lipoprotein

Table 10: Effects of *Oroxylum indicum* fruit extracts on lipid profiles in control and treated male rats during 14 days of the experiments

Lipid profiles	Treatments				
	Control	*Oroxylum indicum*			
		5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
Cholesterol (mg/dL)	24.80±2.44[a]	38.40±1.20[c]	28.20±0.58[ab]	29.60±1.36[b]	31.60±0.51[b]
Triglyceride (mg/dL)	46.60±6.47[a]	44.00±2.55[a]	48.00±10.21[a]	104.4±27.65[b]	40.00±3.79[a]
HDL (mg/dL)	15.20±1.59[a]	19.40±0.25[b]	15.60±0.51[a]	16.20±0.97[a]	16.60±0.40[a]

[a, b, c]Different superscripts in the same row indicate statistical significance (P<0.05). HDL: High density lipoprotein

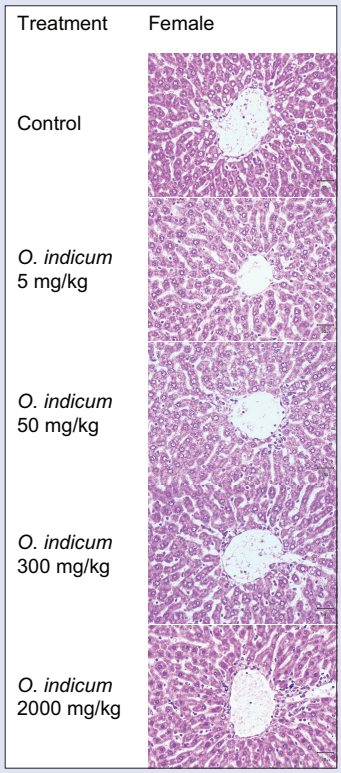

Figure 2: Histopathological illustration of liver in the controls and female rats treated with *Oroxylum indicum* fruit extracts at doses of 5, 50, 300, and 2000 mg/kg for 14 days (magnification = ×40)

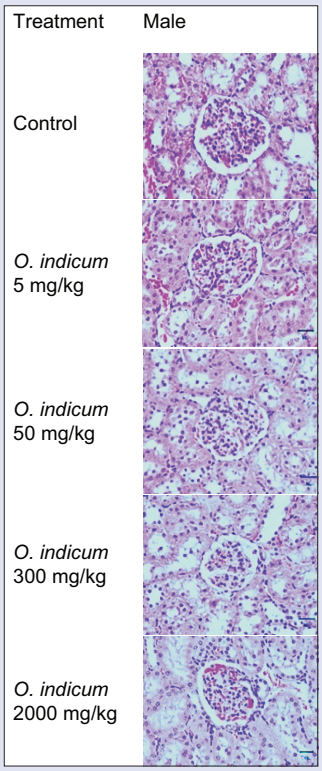

Figure 3: Histopathological illustration of kidney in the controls and male rats treated with *Oroxylum indicum* fruit extracts at doses of 5, 50, 300, and 2000 mg/kg for 14 days (magnification = ×40)

female rats, the parietal epithelium of Bowman's capsule is generally flattened [Figure 4]. The findings indicate that all doses of *O. indicum* extracts do not have any effect on kidney histopathology, suggesting that the extracts from this plant do not exhibit the toxicity on rat's kidney.

DISCUSSION

The fruit (pod) of *O. indicum* has been used as food ingredients and local vegetable among Asian people. The outer part of this fruit tastes bitter because of some phytochemicals such as alkaloids. Consumption of bitter vegetable may cause toxicity in liver and kidney. Therefore, the present study aimed to study the acute toxicity of these extracts in male and female rats to clarify the safety of utilization of the fruit (pod) of *O. indicum* as food or medical products.

In the present study, it was found that all doses of the extract did not affect or exhibit the acute toxicity in male and female rats. However, there are some notifications on liver histopathology. There are a few fat droplets found in the liver tissues of male rats treated with the extracts

Table 11: Effects of *Oroxylum indicum* fruit extracts on blood biochemistry values in control and treated male rats during 14 days of the experiments

Blood biochemistry	Treatments				
	Control	*Oroxylum indicum*			
		5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
BUN (mg/dL)	16.40±1.03[a]	14.60±0.58[a]	19.20±0.86[b]	16.60±1.02[ab]	24.80±2.48[c]
Creatinine (mg/dL)	0.50±0.00[a]	0.44±0.02[a]	0.46±0.25[a]	0.40±0.32[a]	1.20±0.70[a]
AST (U/L)	105.60±4.02[ab]	105.82±6.23[ab]	119.60±6.02[b]	101.20±9.25[ab]	96.80±2.44[a]
ALT (U/L)	36.60±0.93[a]	40.80±1.24[b]	34.20±1.83[a]	35.20±1.86[a]	35.00±1.89[a]
ALP (U/L)	123.80±4.66[a]	138.40±3.23[b]	127.80±4.77[ab]	151.00±4.25[c]	129.80±2.56[ab]

[a, b, c]Different superscripts in the same row indicate statistical significance (P<0.05). BUN: Blood urea nitrogen; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase

Table 12: Effects of *Oroxylum indicum* fruit extracts on blood biochemistry values in control and treated female rats during 14 days of the experiments

Blood biochemistry	Treatments				
	Control	*Oroxylum indicum*			
		5 mg/kg	50 mg/kg	300 mg/kg	2000 mg/kg
BUN (mg/dL)	20.80±0.58[a]	14.20±1.28[bc]	14.00±0.71[b]	16.60±0.51[c]	15.60±0.68[bc]
Creatinine (mg/dL)	0.44±0.04[a]	0.38±0.09[a]	0.40±0.03[a]	0.44±0.02[a]	0.44±0.02[a]
AST (U/L)	93.00±4.69[a]	110.40±11.58[a]	96.00±7.09[a]	102.80±10.81[a]	115.60±4.25[a]
ALT (U/L)	30.00±0.84[ab]	30.00±0.89[ab]	26.60±0.68[a]	30.40±1.91[b]	29.20±0.66[ab]
ALP (U/L)	44.40±4.23[a]	64.80±7.75[b]	61.40±5.50[ab]	51.20±8.35[ab]	47.20±10.99[a]

[a, b, c]Different superscripts in the same row indicate statistical significance (P<0.05). BUN: Blood urea nitrogen; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase

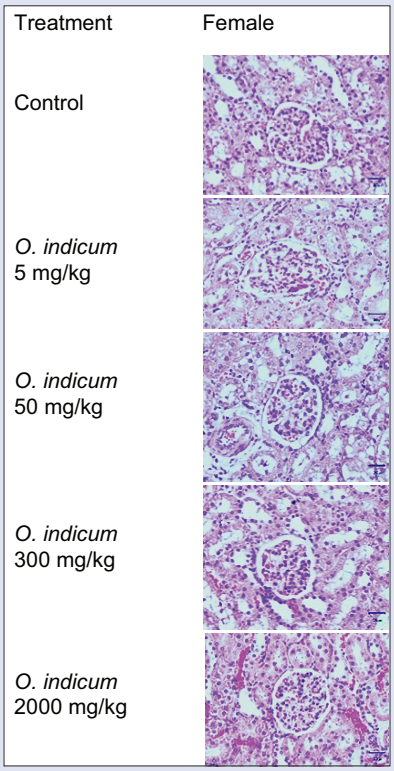

Figure 4: Histopathological illustration of kidney in the controls and female rats treated with *Oroxylum indicum* fruit extracts at doses of 5, 50, 300, and 2000 mg/kg for 14 days (magnification = ×40)

at dose of 2000 mg kg. Interestingly, the fat droplets are not found in the liver tissues of female rats. Moreover, the extracts did not have any effect on histology of kidney suggesting that the extracts are no toxicity or in very mild level of toxicity in rat models. The results of the present study are comparable to the study by Reduan *et al*. in which single and oral administration of ethanol leaf extracts of *O. indicum* at dose of 1000, 2000, and 5000 mg/kg to mice does not cause mortality and behavioral changes. No changes in body weight, relative organ weight, hematology, serum biochemistry, as well as histopathology of liver and kidney were found.[10]

These findings are in accordance with the phytochemical screenings suggesting that the fruit extracts from this plant contained the high total phenolic and flavonoid contents that exhibit antioxidant activities.[2,8] In addition, Harminder and Chaudhary found that the fruit extracts from this plant exhibit the anti-helminthic and stomachic stimulation activities.[4] Therefore, the extracts should not contain any toxic substances. However, consumption of fruit parts of this plant in high dose may cause the toxicity in liver.

CONCLUSION

These findings indicate that *O. indicum* fruit extracts caused fatty liver in male rats. Therefore, the dose <2000 mg/kg was recommended for consumption.

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Conflicts of interest

There are no conflicts of interest.

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