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Acute Toxicity Study Of Ethanolic Extract Of S*olanum sanitwongsei* Craib Fruits on Mice

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Abstract: Solanum sanitwongsei fruits are used as tradisional medicine like antidiabetic, antihypertensive, antiherpes and antiHIV. The aim of the study was to evaluate the oral acute toxicity of ethanolic extract of S.sanitwongsei Craib fruits on male and female swiss albino mice. Ethanolic extract of S.sanitwongsei fruits was administered orally for the first 24 hours at various dose levels 0.5, 5, 50, 500 and 1000 mg/kg bw to determine the toxicity effect. The treatment groups were compared to the normal control. LD50 was determine using Reed and Munich Method. The highest dose administered (1000mg/kg bw) did not produce mortality or changes in general behaviour of the test animals. The result showed that the oral administration of S.sanitwongsei ethanol fruits extract did not produce any significant toxic effect in mice.
Key word : *Solanum sanitwongsei,* acute toxicity, $LD_{50.}$

Introduction

Solanum sanitwongsei (Inggir-inggir) is a member of *Solanaceae* family, which is known as terung siam. This plant is grown in Southeast Asia like Thailand, Indonesia, Fillipina and Malaysia. The plant has bitter fruits and has been used in the tradisional medicine such as diabetic, cough, diuretic and hypertensive like People in Buntu Bayu Villange, Pematang Siantar, Indonesia. However, there are few scientific literatures to support this. Previous investigation on the chemical constituens of S.sanitwongsei have found glycoside that effective as antiherpes and antiHIV [1,2,3]

Plants or drugs must be ensured to be safe before they could be used as medicines. A key stage in ensuring the safety of drugs is to conduct toxicity tests in appropriate animal models, and acute toxicity studies are just one of toxicity tests that are used[4]. In this study, acute toxicity of ethanolic extract of S.sanitwongsei fruit was investigated because of limited information available on its toxicity, despite the widespread use of this medicinal plant.

Experimental

Plant Collection

Solanum sanitwongsei was collected from Buntu Kayu Village, Siantar City, Indonesia. The plant was idenfied in Indonesia Institute of Science, Research Center for Biology, Bogor, Indonesia.

Extraction of Plant

The dried plant material was grinded to a coarse powdered form, and was kept for maceration with distilled ethanol for 5 days, The extract was filtered through in vacuum evaporator.

Animals

Sixty swiss albino mice (20-30g) were purchased from Pharmacology Laboratory of University of Sumatera Utara, Medan, Indonesia. They were housed in polypropylene cages in a controlled room temperature 25^{o}C. The animals were maintained with standard pellet diet. The animals were acclimatized to laboratory condition for two weeks before experiment. All studies were carried out using 10 mice in each group consisting of five male mice and five female mice.

Acute toxicity Study

The acute toxicity study was conducted in accordance with Reed and Munch Method. The treated group received the extract orally in a singel dose with varied doses (0.5, 5, 50, 500, 1000 mg/ kg b.w). Control group animals treated with 0.5% cmc-Na served as control. They were continuously observed first 4 hours and followed by 14 days after the administration to detect any changes in autonomic or behavioral responses, catalepsy, defecation, urination and salivation. Any mortality during the experimentation period of 14 days was also recorded. The percentage in mortality in each group was noted. The animals that died within 14-day period were subjected to necropsy. All of the mice were sacrificed on day 15 after the administration, and then the vital organs including liver, heart and kidneys were grossly examined. The analysis of LD50 was evaluated using the Reed and Munich Method [5].

Statistical Analysis

The results are expressed as the mean±SD for each group. Statistical differences were evaluated using a one way analysis of variance (ANOVA) followed by Post Hoct Test. Results were considered to be statistically significan at $p<0,05$.

Results and Discussion

The oral administration of S. sanitwongsei fruits extract in doses ranging from 0.5 mg/kg bw to 1000 mg/kg bw did not produce significant changes in behavioral responses, catalepsy, defecation, urination and salivation effects in male and female mice (data not shown). These effects were observed during the experimental period (5,10,15, 30, 60, 120, 180, 240 minutes after the oral route). During the 14 days after the oral administration, there were no deaths in both male and female groups (Table 1).

The median lethal dose (LD50) obtained from the Reed Munich method but it can not be determined because there were no death in the treated groups. The result showed that S.sanitwongsei fruits extract is save for oral administration.

Table 1. Number of Mice Death

Dose (mg/kg bw)	Number of death	Number of live
0	0/0	5/5
0.5	0/0	5/5
5	0/0	5/5
50	0/0	5/5
500	0/0	5/5
1000	0/0	5/5

Macroscopy examination was done by observasing the change of color, shape and consistency of the organ (liver, kidney, and heart). It showed changes in color, shape and consistency of liver in group 50, 500 and 1000 mg/kg bw compared to control (Table 2).

Table 2. Macroscopic assays of mice' liver, kidney and heart

Group	Dose (mg/kg bw)	Color	Shape	Consistency
Control	-	Red brown	Smooth	Elastic
I	0.5	Red brown	Smooth	Elastic
II	5	Red brown	Smooth	Elastic
III	50	Pale	Not Smooth	Non elastic
IV	500	Pale	Not Smooth	Non elastic
V	1000	Pale	Not Smooth	Non elastic

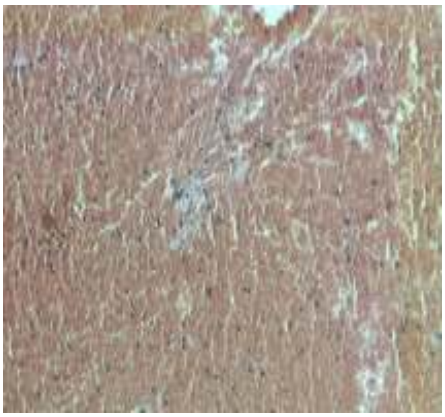
Histopathological examination revealed normal architecture and no significant adverse effects observed on the liver, kidney, and heart in group control, 0.5, 5 mg /kg bw, meanwhile there were hepatocyte damage in group 50, 500 and 1000 mg/kg bw like degeneration of hydropic and necrosis (Table 3).

Table 3 Histopathological examination of liver

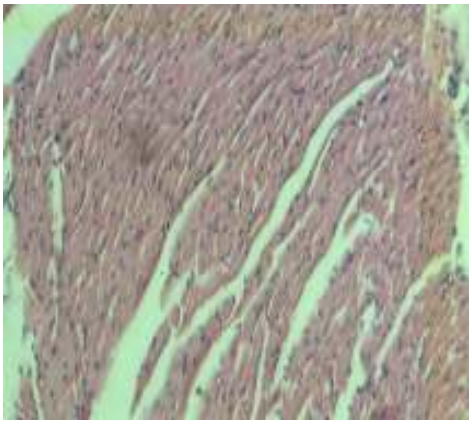
Dose (mg/kg bw)	Hepatocyte damage	
	Degeneration of hidropyc	Necrosis
0	Normal	Normal
0,5	Normal	Normal
5	Normal	Normal
50	Damage	Damage
500	Damage	Damage
1000	Damage	Damage

The data shows that the change in color of the organ to be one of the parameters of toxic effect on the organ . It can be caused by sensitivity of an organ or higher levels of the chemical and its metabolites in organ[6] .

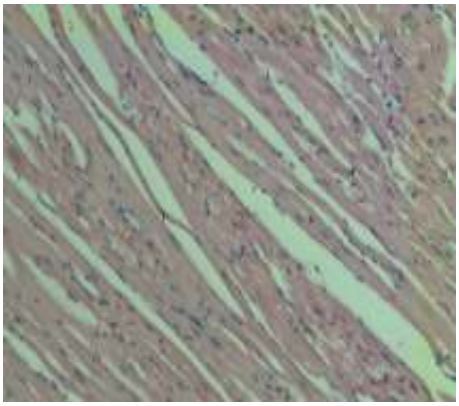
Figure 1. Histological examination of heart.



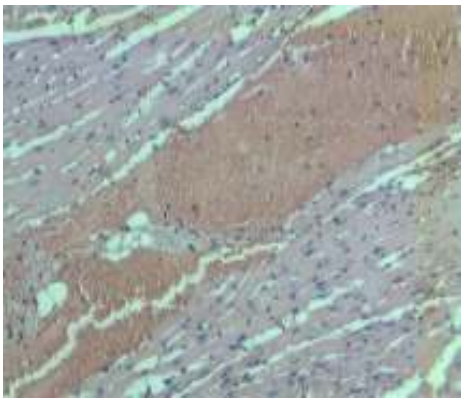
Control



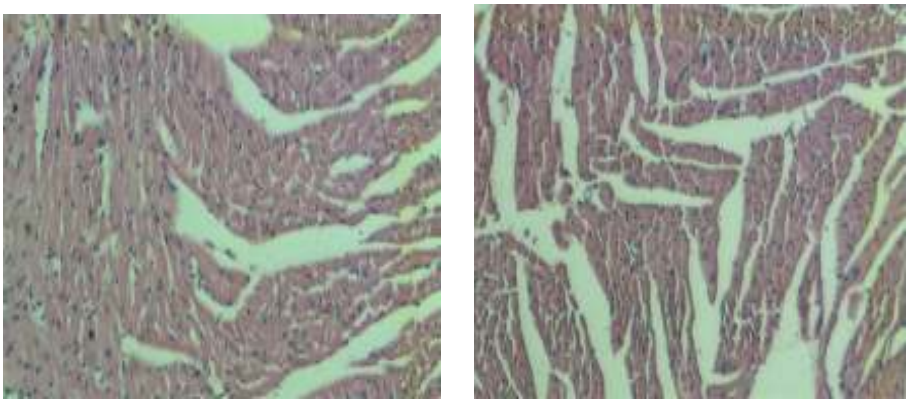
Group I



Group II

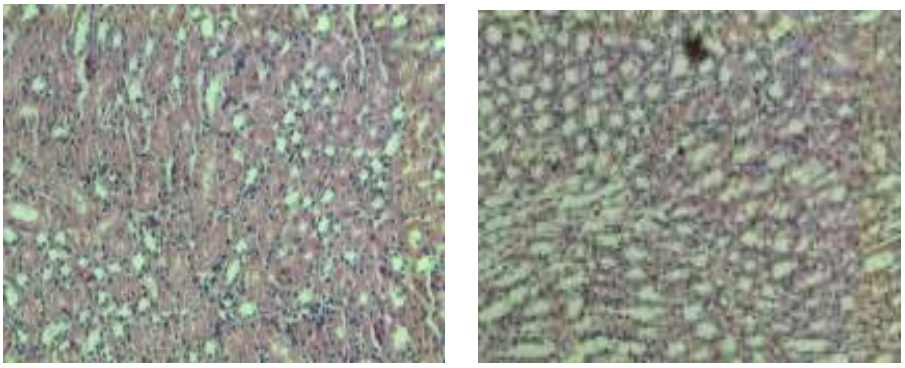


Group III

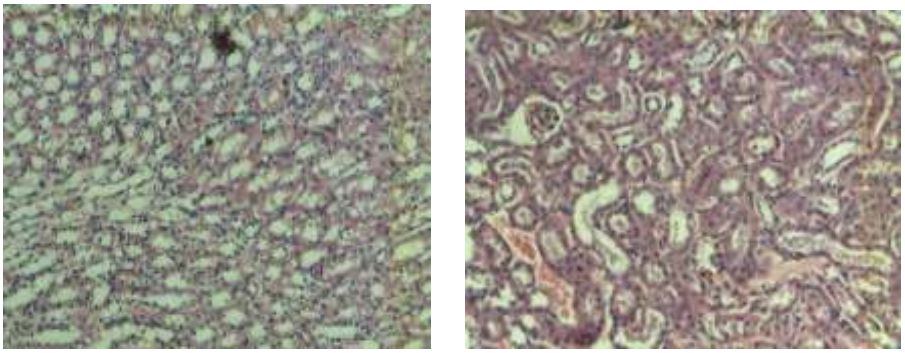


Group IV **Group V**

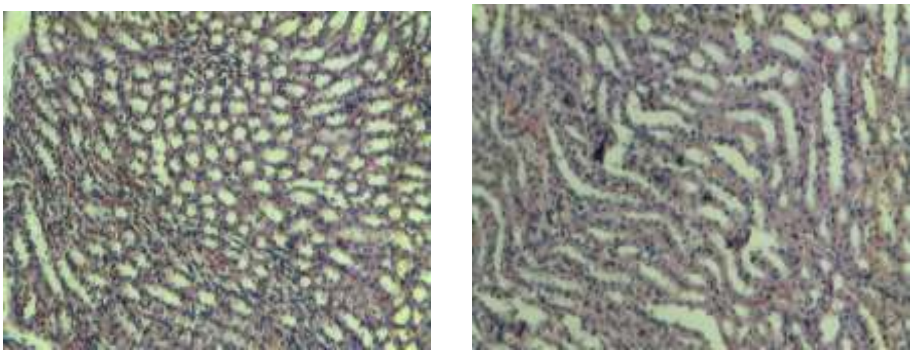
Figure 1. Histological examination of heart.



Control **Group I**

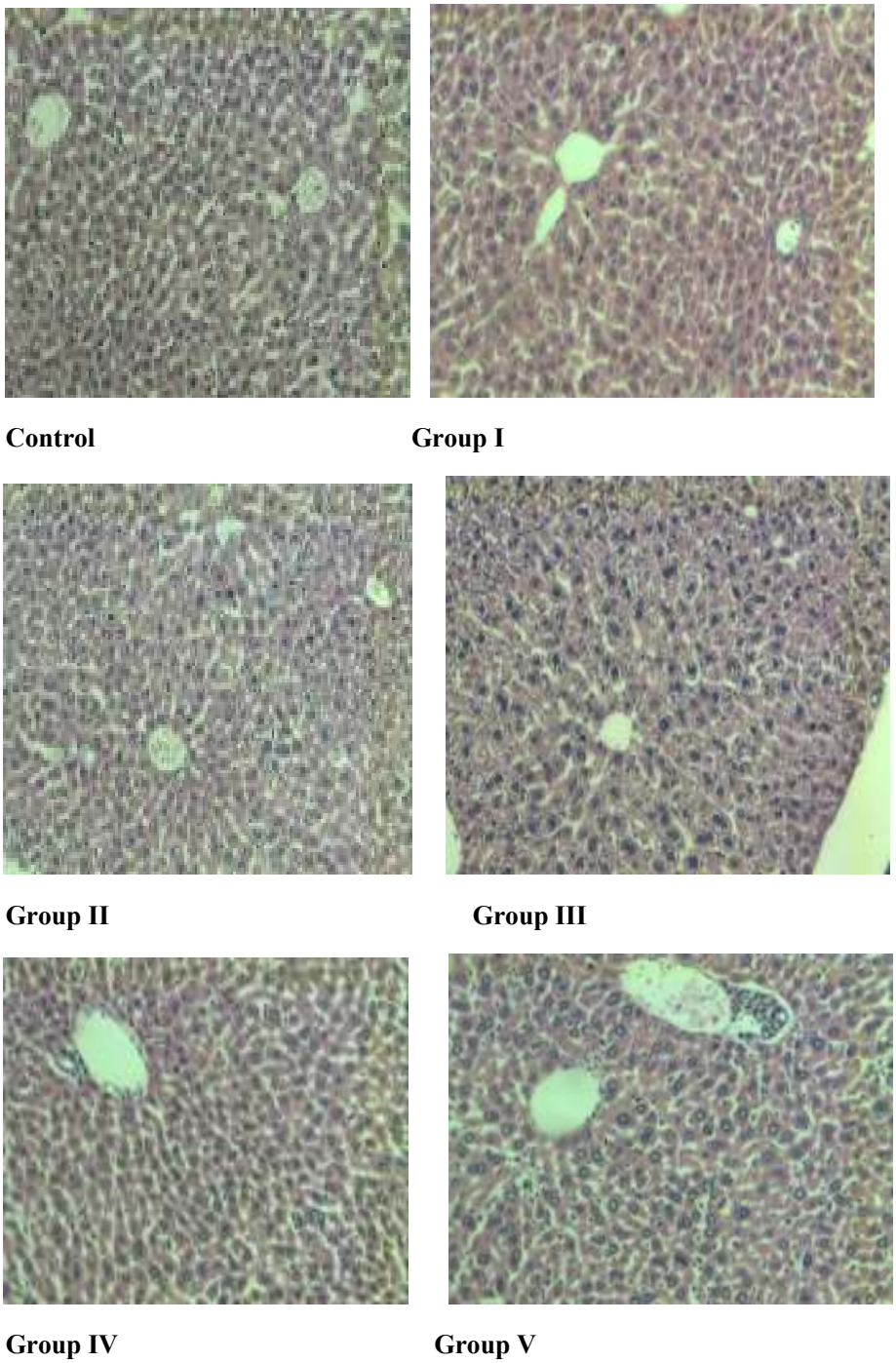


Group II **Group III**



Group IV **Group V**

Figure 2. Histological examination of kidney.



Control **Group I**

Group II **Group III**

Group IV **Group V**

Figure 3. Histological examination of liver.

The microscopic structures of the heart (Figure 1) shows differences between the control and test groups. The microscopic examination revealed that, all the heart from the extract treated mice show an alteration in cell structure. Based on the microscopic structures of the kidneys (Figure 2) showed unnoticeable differences between the control and test groups (0.5 and 5 mg / kg bw). Renal tubular damage that has occurred many open tubules at doses of 50 , 500 and 1000 mg / kg bw. There was degeneration of hydropic and necrosis observed in liver (Figure 3).

Previous study demonstrated the presence of phytochemicals like flavonoids, alkaloids, steroids, glycoside, saponin and tanin in the extract. These metabolites are generally used in various pharmaceutical and cosmetic preparations. For any therapeutic and cosmetic application, compounds of the plant or its extracts used must be practically non-toxic[7,8].

It conclude that a singel oral dose of 0.5, 5, 50, 500 and 1000 mg/kg bw of ethanolic extract of S.sanitwongsei fruits are unable to induce acute toxic effects. It indicates that S.sanitwongsei is practically non-toxic for oral administration. Further studies are warranted for determining chronic toxic symptoms.

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