

## **Assessment of Sub chronic Toxicity of *Sonchus cornutus* in Rats**

### **ABSTRACT**

**Aim:** To assess the sub chronic toxicity of the aqueous extract of *Sonchus cornutus* in Wistar albino rats.

**Methodology:** The aqueous extract of *Sonchus cornutus* whole plant was administered orally to rats in group 2, 3 and 4 at a dose of 50, 500 and 2000 mg/ kg, respectively for four weeks whereas, group 1 was kept as a control. The animals were observed daily for clinical signs and mortality. Weekly, the weights of the animals were recorded, and blood samples were collected for haematological and biochemical analysis. Specimens of Liver and kidney were kept in 10% formalin for histopathology.

**Results:** The results revealed that all the animals in the four groups survived, and no mortality was recorded. The highest percentage of weight gain was recorded in the control group. The extract had no adverse effects on haematology, biochemistry and histology of rats at doses of 50 and 500 mg/ kg. But dose 2000 mg/kg proved to have significant alteration in White blood cells (WBCs), Red blood cells (RBCs), Haemoglobin (Hb) and Packed cell volume (PCV). In addition, total protein, albumin, urea, creatinine, Alanin Transaminase (ALT), Asparate Transaminase (AST) were significantly ( $P < 0.05$ ) changed. These findings correlated with the histopathological changes on liver and kidney.

**Conclusion:** The highest dose of *S. cornutus* aqueous extract (2000 mg/kg) was not fatal, but may have some toxic effects on liver and kidney.

## 22 1. INTRODUCTION

23 Medicinal plants are often assumed to be efficient and safe; however there are some reports on poisoning  
24 consecutive to plant based-medicine administration [1]. Thus, interest is accorded to toxic effects of plant  
25 extracts.

26 Many plants contain chemical constituents which are used for different medical purposes. However, over  
27 dosage of plant products containing medical compounds may cause toxic effects when introduced into  
28 the body [2]. The toxic phytochemicals produced by plants include alkaloids, sulphur, phenol, tannin,  
29 proteins and enzyme inhibitors [3]. Toxins have direct and indirect mechanisms of actions on the most  
30 frequently induced organs (liver, kidney, brain, lung, intestine and others). The mechanisms of actions  
31 include direct and indirect damage of tissue, effect on function and genetic defect [4].

32 *Sonchus cornutus* has been used traditionally as a remedy to treat many diseases beside the biological  
33 activities. *Sonchus* was used as herbicide [5]. *Sonchus asper* methanolic extract had protective effect  
34 against CCl<sub>4</sub> induced kidney damage in rat [6]. Additionally, it possessed antioxidant activity and used for  
35 treatment of liver and kidney disorders [7]. The plant was used in folk medicine for treatment of hormonal  
36 disturbance and oxidative stress [8]. The aqueous methanolic extract of *S. asper* administered to rats at  
37 doses of 250, 500 and 1000 mg/kg exerted considerable antihypertensive activity [9].

38 Although extensive works have been conducted on this herb, no conspicuous information on toxicity is  
39 available so far. Therefore, attention has been directed towards toxicity of the plant. *Sonchus cornutus*  
40 aqueous extract showed partial cytotoxicity at concentrations of 5000 and 10000 µg/ ml [10]. However,  
41 little was made available for other species such as *S.arvensis*, *S.oleraceus* and *S.transcaspicus*. Two  
42 eudesmanolides isolated from *S.transcaspicus* whole plant showed *in vitro* cytotoxicity against cultured  
43 human cell lines [11] .Likewise, *S.oleraceus* was mild toxic as it may contain large quantities of nitrates  
44 [12].

45 In Sudan, *S. cornutus* was assessed for antitheilerial activity [10]; food consumption, and traditionally for  
46 treatment of malaria, hypertension and hyperglycemia [13].On the other hand, *S.oleraceous* was  
47 investigated for antimalarial and antimicrobial activities [14], and against malaria vectors [15].

48 The objective of plant toxicity testing is to elucidate the toxic effects of the plant. The toxicity of *Sonchus*  
49 *cornutus* extract is necessary since this has not been previously done in depth.

## 50 **2. MATERIALS AND METHODS**

### 51 **2.1 PLANT COLLECTION**

52 *Sonchus cornutus* Hochst. ex. Oliv. and Hiern, is locally known as Moleita or Molat. The whole plant was  
53 collected from the banks of the Blue Nile River, South of Khartoum state. The plant was identified and  
54 authenticated by a botanist at the Medicinal and Aromatic Plants Research Institute, Khartoum, Sudan.  
55 The voucher specimen has been deposited in the herbarium museum of the Institute. The plant air- dried  
56 in the shade, coarsely powdered and kept in polythene bags at room temperature.

### 57 **2.2 ANIMALS**

58 Clinically normal, twenty four male Wistar albino rats, 4- 5 weeks of age, weighing (113- 118 g) were  
59 brought from the Medicinal and Aromatic Plants Research Institute, Khartoum, Sudan. The animals were  
60 kept in metal cages to adapt for one week prior to the start of the experiment. The rats were fed with a  
61 standard diet which is manufactured commercially for poultry (Layers) and vegetables. Feed and water  
62 were provided *ad libitum*. All principles involving the animals were conducted with strict adherence to  
63 standard guidelines of laboratory procedures.

### 64 **2.3 PREPARATION OF PLANT EXTRACT**

65 The plant extract was prepared as described previously [16]. Hot distilled water (500 ml) was added to  
66 100 g of the coarsely powdered plant and left to cool down with continuous stirring at room temperature.  
67 The extract was filtered through Whatman No. 1 filter paper and then transferred to the freeze- drier  
68 (Trivac, U.S.A.). The yield percentage of the aqueous extract of *S. cornutus* (w/w) was 15.4%.

69 The required weight of the extract for each group was calculated according to the dose, dissolved in 6 ml  
70 of distilled water. The volume of the extract administered orally to each animal based on the body weight.

71

## 72 **2.4 EXPERIMENTAL DESIGNS**

73 Twenty four male Wistar albino rats were divided into four groups, each of 6 rats. Group 1, 2 and 3 were  
74 used for evaluation of sub chronic toxicity, and group 1 was kept as a control. The extract was given at  
75 one of the fixed dose level (50, 500 and 2000 mg/kg).

### 76 **2.4.1 Screening of the aqueous extract of *Sonchus cornutus* for toxicity**

77 The aqueous extract of the plant was administered orally to rats in group 2, 3 and 4 at doses of 50, 500  
78 and 2000 mg/ kg/ day, respectively for four weeks whereas, group 1 was kept as a control.

79 Clinical signs of toxicity and mortality were observed daily. The weights of the rats were recorded at the  
80 day of dosing, at weekly intervals thereafter, and at the time of death or when the animals were sacrificed.

## 81 **2.5 BLOOD COLLECTION FOR HAEMATOLOGICAL AND BIOCHEMICAL ANALYSIS**

82 Blood samples were collected weekly-starting from week zero (Control) - from the orbital sinus of rat's eye  
83 - in Ethylene Diamine Tetra acetic acid (EDTA) and plain vacutainers, for hematological and biochemical  
84 tests, respectively. Sysmex Haematology System KN-21N/Germany and Sysmex Biochemistry System /  
85 Germany) instrument were used for analysis. The procedures were carried out as described in the  
86 manual of the automated machines.

## 87 **2.6 PATHOLOGICAL EXAMINATION**

88 Rats in group 1, 2, 3 and 4 were sacrificed at the end of the experiment. Specimens of normal and  
89 abnormal liver and kidney were fixed in 10% neutral buffered formalin and processed for histopathological  
90 examination.

## 91 **2.7 STATISTICAL ANALYSIS**

92 The data collected during the study were analyzed using the computer program SPSS version 20. The  
93 statistical analysis was done using One Way ANOVA, followed by Duncan multiple comparison test. The  
94 data are expressed as mean  $\pm$ SD. The results with  $P < 0.05$  were considered significant.

### 95 3. RESULTS

#### 96 3.1 EFFECT OF THE EXTRACT ON MORTALITY AN BODY WEIGHT

97 There was no mortality recorded even at the highest dose (2000 mg/kg) after oral administration of the  
98 extract.

99 The effect of the extract on body weights of rats was summarized (Table 1). The extract significantly  
100 ( $P<0.05$ ) increased the body weight of rats at doses of 50, 500 mg/kg. However, the lowest weight gain  
101 was recorded at dose 2000 mg/kg.

#### 102 3.2 EFFECT OF THE EXTRACT ON HAEMATOLOGICAL AND BIOCHEMICAL

##### 103 PARAMETERS

104 The plant extract altered the haematology and biochemistry of rats in group 4 only. The haematological  
105 parameters in blood of rats administered orally aqueous extract of *S. cornutus* at different doses were  
106 presented (Table 2). WBCs, RBCs, Hb and PCV were not affected in group 2 and 3, but significantly  
107 changed in group 4.

108 The toxicological effects of the extract on the biochemical parameters were summarized (Table 3). Oral  
109 administration of the aqueous extract at doses of 50 mg/ kg (group 2) and 500 mg/ kg (group 3) had no  
110 effect. However, a dose of 2000 mg/ kg (group 4) was significantly ( $P< 0.05$ ) altered all the parameters  
111 except ALP.

#### 112 3.6 HISTOPATHOLOGICAL CHANGES

113 Necropsy of rats in group 1, 2 and 3 showed normal livers and kidneys. Histopathological changes in  
114 livers and kidneys of rats occurred in group 4. The liver characterized by necrosis of liver cells,  
115 dissociation of hepatocytes with degeneration of cytoplasm, dilatation of sinusoid, and inflammation of  
116 cells (mononuclear cells) (Fig. 1 B) compared with the control (Fig. 1 A). The kidney revealed dilated and  
117 segmented glomerular tuft, necrosis of tubular epithelial cells (Fig. 2 B) using (Fig. 2 A) as a control.

118 **4. DISCUSSION**

119 The aqueous extract of *S.cornutus* at dose 2000 mg/kg caused haematological, biochemical and  
120 histopathological changes. However, the aqueous extract of *S.oleraceous* had low toxicity against  
121 *Artemia salina* at 5117.2 ppm [17]. The variation in the result may be due to the difference in the plant  
122 species, the solvents used, and phytochemical compounds of the plant. Due to the bio- active properties  
123 of plants from Asteraceae family, *S.oleraceus* was mild toxic as it may contain large quantities of nitrates.  
124 Hence toxicity of *S.cornutus* could be to nitrates or other compounds [18].The result was interpreted with  
125 other plant Species, because there was no information about *S. cornutus* toxicity found.

126 In the current study, the increase in the percentage of body weight gain indicated that the extract of *S.*  
127 *cornutus* did not have general toxic effects and influence on animal food intake at doses of 50 and 500  
128 mg/ kg. However, the lowest body weight gain at dose of 2000 mg/kg confirmed abnormality or toxicity  
129 which influenced food consumption and metabolism.

130 On the other hand, changes on haematological as well as biochemical parameters are biomarkers of  
131 abnormalities and/or toxicities in the body. This means that the doses of 50 and 500 mg/kg had no toxic  
132 effects on both parameters as well as the histological. The combined effects of physiological and  
133 chemical factors in the metabolism system of animals could lead to increase in WBCs [19]. This  
134 information support the present result exhibited increase in number of WBCs in group 4, associated with  
135 inflammation seen in histopathological investigation. The alteration in RBCs and Hb may be due to  
136 defective haematopoiesis inhibited erythropoiesis or increase in destruction of red blood cells [20. 21].

137 The clinical biochemical parameters are indicators of liver and kidney function [22]. Decrease of serum  
138 total protein and albumin could be indicative of impaired liver excretory and synthetic function. Primary  
139 and secondary hepatic disease can cause elevation of both ALT and AST [23]. Elevated transaminases  
140 are suggestive of liver necrosis [24]. On the other hand, urea and creatinine were determined to diagnose  
141 the function of kidney [25]. The elevation in the level of serum renal function parameters in rats was  
142 associated to renal dysfunction and metabolic disturbances [26, 27].

143 The safety of the extract at doses of 50 and 500 mg/kg was confirmed by previous findings which  
144 exhibited that in sub chronic toxicity test of ethyl acetate extract of *S.arvensis* leaves at doses of 100, 400  
145 and 1000 mg/ kg had no toxic effects on body weight, haematological and biochemical parameters, and  
146 histological changes [28].

## 147 **5. CONCLUSION**

148 The results revealed that the aqueous extract of *Sonchus cornutus* at doses of 50 and 500 mg/ kg was  
149 safety, but dose 2000 mg/ kg may have hepatorenal toxicity. Further work is needed for determination of  
150 LD<sub>50</sub> and LD<sub>99</sub>. Phytochemical analysis and mechanism of actions are recommended to define the toxic  
151 compounds that may exist.

## 152 **CONSENT**

153 It is not applicable.

## 154 **ETHICAL APPROVAL**

155 All authors hereby declare that “Principles of laboratory animal care” (NIH Publication No. 85-23, revised  
156 1985) were followed, as well as national laws were applicable. The protocol used in this study for the use  
157 of laboratory animals was approved by the Ethical Approval No EA /0019/ 2018, The Sudan Veterinary  
158 Council, Ministry of Cabinet, Republic of The Sudan.

## 159 **REFERENCES**

- 160 1. Fennel CW, Lindsey KL, McGaw LJ, Sprag SG, Stafford GI, et al. Assessing African medicinal plants  
161 for efficacy and toxicology. J Ethnopharm. 2004; 94: 205- 217.
- 162 2. Farah HF, Elamin TH, El Hussein AM, Khalid HE. Assessment of antittheilerial activity of *Kigelia*  
163 *africana* fruits against *Theileria lestoquardi*. Eur J Med Plants. 2015; 5 (1): 101-108. ISSN:  
164 2231-2927.

- 165 3 Maiga A, Diallo D, Fane S, Sango K, Paulsen BS, Cisse B. A survey of toxic plants on the market in the  
166 district of Bamako, Mali: Traditional knowledge compared with literature search of modern  
167 pharmacology and toxicology. J Ethnopharm. 2005; 96: 183-193.
- 168 4. Chandra SJ, Sandhya S, Vinod KR, David B, Sudhakar K, chaitanga R, Plant toxins harmful effects.  
169 Hygeia J Drugs Med. 2012; 4 (1): 70—90. Available: [www.hygeiajournal.com](http://www.hygeiajournal.com)
- 170 5. Braun M, Burgstaller H, Hamdoun AM, Walter H. *Sonchany.us CGermornutus*, Asteraceae, Common  
171 Weeds of Central Sudan. Vier-Türme-verlag, Benedict Press, Münster schwarzach, Germany,  
172 Weinketsheim: Merggraph; 1991..
- 173 6. Khan RA, Khan MR, Sahreen S, Bokhari J. Prevention of CCl<sub>4</sub> induced nephrotoxicity with *Sonchus*  
174 *asper* in rat. Food Chem Toxicol. 2010; 48 Suppl 8-9: 2469- 2476
- 175 7. Khan MR, Badar I, Siddiquah A. Prevention of hepato-renal toxicity with *Sonchus asper* in gentamicin  
176 treated rats. Complement Altern Med. 2011; 11: 113. [http://www.biomedcentral.com/1472-](http://www.biomedcentral.com/1472-6882/11/113)  
177 [6882/11/113](http://www.biomedcentral.com/1472-6882/11/113).
- 178 8. Khan RA. Protective effects of *Sonchus asper* (L.) Hill, (Asteraceae) against CCl<sub>4</sub> induced oxidative  
179 stress in the thyroid tissue of rats. BMC Complement Altern Med. 2012; 12: 181-188.  
180 <http://www.biomedcentral.com/1972-6882/12/181>
- 181 9. Mustaq MN, Akhtar MS, Alamgeer, Ahmad T, Khan HU, Maheen S, Tabassum N et al. Evaluation of  
182 antihypertensive activity of *Sonchus asper* L. in rats. Acta pol phar. 2016; 73 (2): 425- 431.  
183 PMID: 27180435 [ Indexed for MEDLINE].
- 184 10. Farah HM, Elamin TH, Khalid HE, Elhussein AM. Evaluation of *in vitro* antitheilerial activity of *Sonchus*  
185 *cornutus* aqueous extract. Topcls J Herb Med. 2013; 2 (5): 90- 94.
- 186 .
- 187 11. Han Y, Zhang G, Gav K, Jia Z. Natural product chemistry. Newsesquiterpens from *S.transpicus*.  
188 Planta Med. 2005; 543-547
- 189 12. Leonard DB. Plants and food. *Sonchus oleraceus*. Med at your Feet. (2007).



- 190 13. Fashir GA, Abdalla NI, Fangama IM. Assessment the consumption of *Sonchus cornutus* (Hochst) in  
191 Khartoum State, Sudan. Intern J Curr Microbiol Appl Sci. 2015; 4 (6): 833-839. ISSN: 2319-7706.  
192 <http://www.ijcmas>
- 193 14. Adam FAH. Phytochemical, antimalarial and antimicrobial activity of some medicinal plants. M.Sc.  
194 Thesis, University of Khartoum, Sudan; 2002.
- 195 15. Elimam AMA. Larvicidal, ovicidal, oviposition deterrence and emergence inhibition activity of selected  
196 Sudanese plants against *Anopheles arabiensis* and *Culex quinquefasciatus*. Ph.D.Thesis,  
197 University of Khartoum, Sudan; 2008.
- 198 16. Harborne JB.editor. Phytochemical Methods. 2<sup>nd</sup> ed, Chapman and Hall Ltd., London. 1984.
- 199 17. Lima JM, Silva CA, Rosa MB, Santos JB, Oliveria TG, Silva MB. Phytochemical prospective of  
200 *Sonchus oleraceus* and its toxicity to *Artemia salina*. Planta Daninha. 2009; 27 (1): 7-11.
- 201 18. Wegiera M, Smolarz HD, Jeduch M, korczak M, Kopron K. Cytotoxic effect of some medicinal plants  
202 from Asteraceae family on J-45.01 leukemic cell lines. Pilot study. Acta Pol pharm. Drug Res.  
203 69 (2): 263-268.
- 204 19. Nyarko AK, Okine LKN, Wedzi RK, Addo PA, Ofosuhne M. Sub chronic toxicity of the antidiabetic  
205 herbal preparation ADD 199 in the rat: Absence of organ toxicity and modulation of cytochrome  
206 P450. J Ethnopharm. 2015; 97 (2): 319-325. <http://hdl.handle.net/123456789/3231>.
- 207 20. Keinänen M, Kunutila S, Bloomfield CD, Elonen E, de la Chapelle A. The proportion of mitosis in  
208 different cell line changes during short-term culture of normal human bone marrow. Blood. 1986;  
209 67: 1244-1243.
- 210 21. Selmanoglu G, Barlas N, Songür S, Kockaya EA. Carbendazim induced haematological , biochemical  
211 and histopathological changes to the liver and kidney of male rats. Hum Exp Toxicol. 2001; 20:  
212 625-630.
- 213 22. Crook M A. Clinical chemistry and metabolic medicine, 7<sup>th</sup> ed. London: Hodder Arnold; 2006.
- 214 23. Cheesbrough M. Medical laboratory manual for tropical countries. Microbiology Tropical Health  
215 Technology/ Butterworth Scientific Publications, Boston; 1991 <http://www.isorjournals.org>

- 216 24. Wuruchekke, AU, Anthony AG, Obiolah W. Biochemical effects on liver and kidney of rats  
217 administered aqueous extract of *Xemenia Americana*. African J Biotech. 2008; 7: 2777-2780.
- 218 25. Sharma A, Hirluukar N B, Wadel P, Das P. Influence of hyperglycemia on renal function parameter in  
219 patients with Diabetes Mellitus. Int J Pharmaceut Biol Arch. 2011; 2 Suppl 2: 734- 739.
- 220 26. Bayramoglu G, Senturk H, Bayramonglu A, Uyanoglu M, Colka S, Ozmen A, et al. Carvacrol partially  
221 reserves symptoms of diabetes in STZ- induced diabetic rats. Cytotech. 2014; 66: 215- 217.
- 222 27. Madinov IV, Balabadkin MI, Markov DS, Markov TN, Main causes of hyperureamia in diabetes  
223 mellitus. Terk Arkh. 2000; 55-58
- 224 28. Nurianti Y, Henandriani R, Sukandar EY, Anggadiredja K. Acute and subchronic oral toxicity studies  
225 of ethylacetate extract of *Sonchus arvensis* L. leaves. Int J Pharm and Pharmaceut Sci. 2014;  
226 65 (5): 343-347.
- 227 .
- 228
- 229
- 230

231 **Table 1. Percentage of weight gain of rats given aqueous extract of *Sonchus cornutus***

Group No.	Dose (mg/kg)	Mean weight of rats per week (g)					Weight gain (g)	Weight gain (%)
		W0	W1	W2	W3	W4		
1	0	114.52±1.05	124.00±0.63*	133.17±1.47*	142.17±1.72*	153.67 ±2.16*	39.17	34.22
2	50	115.17±0.75	124.17±0.75*	133.20±1.37 *	142.67±0.82*	152.33 ±0.82*	37.17	32.32
3	500	116.83±0.98	125.67±0.52*	134.87±0.52*	144.33±0.52*	154.00±0.00*	37.16	31.82
4	2000	115.33±0.52	122.83±0.75*	129.80±0.84*	136.50±1.05*	136.50±0.00*	21.17	18.36

232 *The data presented as Mean ± SD, \*P < 0.05 is significantly different from the control, n= 6. W (Week).*

233

234

235

236

237

238

239

240 **Table 2. Hematological changes on the blood of rats given aqueous extract of *Sonchus cornutus***

Group No.	Week No.	Dose (mg/kg)	WBCs ( $\times 10^3/\text{mm}^3$ )	RBCs ( $\times 10^6/\text{mm}^3$ )	Hb (g/dl)	PCV (%)
1	0	0	5.90 $\pm$ 0.14	6.32 $\pm$ 0.08	11.68 $\pm$ 0.19	37.50 $\pm$ 0.40
	1		5.90 $\pm$ 0.09	6.35 $\pm$ 1.05	11.72 $\pm$ 0.21	37.53 $\pm$ 0.39
	2		5.92 $\pm$ 0.80	6.35 $\pm$ 0.08	11.72 $\pm$ 0.21	37.55 $\pm$ 0.39
	3		5.93 $\pm$ 0.10	6.38 $\pm$ 0.08	11.73 $\pm$ 0.15	37.57 $\pm$ 0.42
	4		5.91 $\pm$ 0.15	6.37 $\pm$ 0.08	11.73 $\pm$ 0.15	37.57 $\pm$ 0.43
2	0	50	6.78 $\pm$ 0.12	6.72 $\pm$ 0.10	11.80 $\pm$ 0.10	37.65 $\pm$ 0.19
	1		6.78 $\pm$ 0.12	6.72 $\pm$ 0.10	11.82 $\pm$ 0.10	37.65 $\pm$ 0.19
	2		6.82 $\pm$ 0.08	6.70 $\pm$ 0.10	11.82 $\pm$ 0.10	37.68 $\pm$ 0.17
	3		6.78 $\pm$ 0.12	6.65 $\pm$ 0.10	11.80 $\pm$ 0.10	37.73 $\pm$ 0.16
	4		6.78 $\pm$ 0.12	6.70 $\pm$ 0.13	11.80 $\pm$ 0.10	37.73 $\pm$ 0.16
3	0	500	6.32 $\pm$ 0.75	6.90 $\pm$ 0.06	11.93 $\pm$ 0.12	37.72 $\pm$ 0.15
	1		6.35 $\pm$ 0.10	6.90 $\pm$ 0.06	11.93 $\pm$ 0.12	37.72 $\pm$ 0.15
	2		6.35 $\pm$ 0.08	6.90 $\pm$ 0.06	11.90 $\pm$ 0.09	37.73 $\pm$ 0.14
	3		6.38 $\pm$ 0.08	6.83 $\pm$ 0.08	11.88 $\pm$ 0.10	37.75 $\pm$ 0.10
	4		6.37 $\pm$ 0.08	6.82 $\pm$ 0.10	11.90 $\pm$ 0.09	37.72 $\pm$ 0.15
4	0	2000	6.68 $\pm$ 0.10	6.97 $\pm$ 0.12	11.98 $\pm$ 0.08	37.97 $\pm$ 0.16
	1		8.62 $\pm$ 0.08*	5.45 $\pm$ 0.10*	9.73 $\pm$ 0.31*	37.78 $\pm$ 0.28*
	2		8.93 $\pm$ 0.08*	5.00 $\pm$ 0.14*	9.62 $\pm$ 0.23*	35.70 $\pm$ 0.33*
	3		8.97 $\pm$ 0.04*	4.02 $\pm$ 0.17*	8.82 $\pm$ 0.23*	35.57 $\pm$ 0.37*
	4		8.92 $\pm$ 0.00	4.00 $\pm$ 0.10*	8.82 $\pm$ 0.34*	35.54 $\pm$ 0.38

241 *The data presented as Mean  $\pm$  SD, \*P < 0.05 is significantly different from the control, n=6*

242

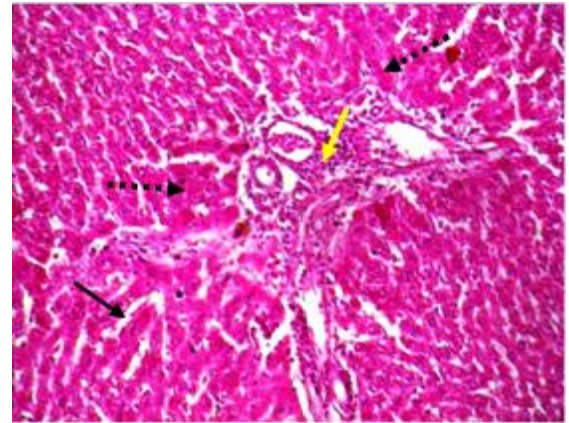
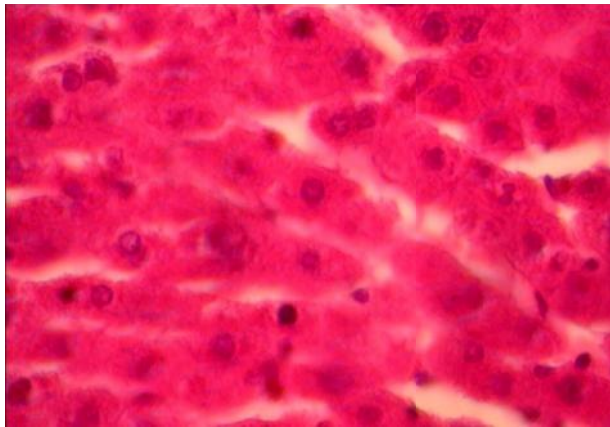
243

245 **Table 3. Biochemical changes on blood of rats after administration of aqueous extract of *Sonchus cornutus***

Group No.	Week No.	Dose	Total Protein (g/dl)	Albumin (g/dl)	Urea (mg/dl)	Creatinine (mg/dl)	ALT ( IU/L )	AST ( IU/L)	ALP ( IU/ L)
1	0	0	6.35± 0.20	3.53 ± 0.16	14.67± .26	0.53 ± 0.05	13.00±0.89	18.33±0.82	53.00±1.41
	1		6.39 ± 0.18	3.55 ± 0.31	14.68± 0.23	0.53 ± 0.05	13.05±0.90	18.33±0.82	53.00±1.41
	2		6.46 ± 0.19	3.65 ± 0.26	14.68± 0.32	0.53 ± 0.05	13.05±0.90	18.42 ± 0.83	53.00±1.67
	3		6.47± 0.25	3.73 ± 0.23	14.70 ± 0.28	0.58 ± 0.04	13.08±0.94	18.42±0.83	53.17±1.17
	4		6.67 ± 0.16	3.80 ± 0.17	14.70± 0.26	0.53 ± 0.05	13.08±0.92	18.43±0.80	53.17±1.17
2	0	50	6.67 ± 0.16	3.67 ± 0.12	14.75± 0.19	0.50 ± 0.09	13.50±0.55	18.95±0.19	54.00±0.63
	1		6.67 ± 0.16	3.67 ± 0.12	14.75 ± 0.19	0.50 ± 0.09	13.50±0.55	18.95±0.19	54.00 ± 0.63
	2		6.67 ± 0.16	3.68 ± 0.13	14.75 ± 0.19	0.52 ± 0.08	13.53±0.52	18.97 ± 0.19	54.00±0.63
	3		6.69 ± 0.16	3.70 ± 0.13	14.77 ± 0.21	0.52 ± 0.08	13.50±0.55	18.97±0.19	54.33±0.52
	4		6.69 ± 0.16	3.70 ± 0.13	14.75 ± 0.19	0.50 ± 0.09	13.50±0.55	18.97±0.19	54.33±0.52
3	0	500	6.88 ± 0.10	3.80 ± 0.14	14.87 ± 0.05	0.50 ± 0.00	13.75±0.19	18.77±0.21	53.83±0.75
	1		6.88 ± 0.10	3.80 ± 0.14	14.87 ± 0.05	0.52 ± 0.04	13.75±0.19	18.77±0.21	53.83±0.75
	2		6.90± 0.11	3.82 ± 0.16	14.87 ± 0.05	0.52 ± 0.04	13.80±0.18	18.78±0.17	53.83 ± 0.75
	3		6.90 ± 0.11	3.82 ± 0.16	14.88 ± 0.04	0.50 ± 0.00	13.80±0.18	18.78±0.17	54.00±0.63
	4		6.90 ± 0.11	3.83± 0.19	14.88 ± 0.04	0.50± 0.00	13.78±0.17	18.80±0.19	54.00±0.63
4	0	2000	6.50 ± 0.14	3.95 ± 0.19	14.90 ± 0.13	0.50 ± 0.06	13.83±0.10	18.85±0.19	53.50±0.55
	1		5.10 ± 0.14*	3.07 ± 0.08*	18.48±0.31*	0.70 ± 0.09*	15.87±0.27*	21.10±0.39*	53.50 ± 0.55
	2		4.00 ± 0.06*	2.02 ± 0.04*	19.33±0.38*	0.72 ± 0.08*	16.37±0.28*	21.80±0.43*	53.67±0.52
	3		3.43 ± 0.14*	2.00 ± 0.00*	19.92±0.37*	0.73 ± 0.08*	17.27±0.31*	22.37±0.30*	53.67±0.52
	4		3.43 ± 0.00*	2.01± 0.06	19.90± .35*	0.71± 0.07*	17.27±0.31*	22.36±0.38*	53.67±0.53

246 *The data expressed as Mean ± SD, \*P < 0.05 is significantly different from the control, n = 6*

248



252

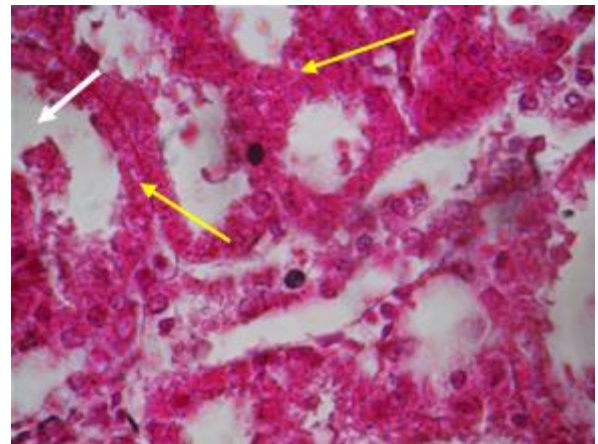
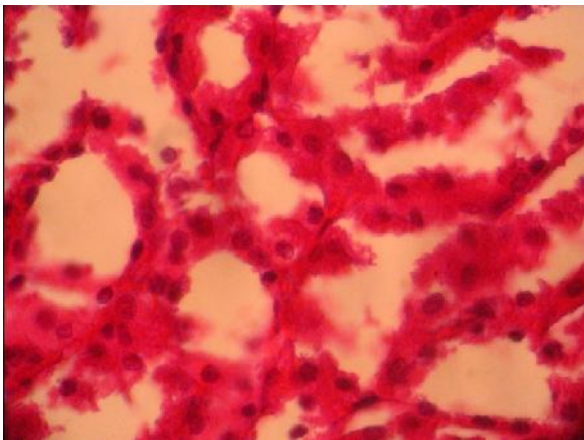
A

B

253 **Fig. 1.** Section of rat liver: (A) Normal control (group 1). (B) After given aqueous extract of  
 254 *Sonchus cornutus* at a dose of 2000 mg/ kg (group 4) showed necrosis of liver cells (black  
 255 dotted arrows), dissociation of hepatocytes with degeneration of cytoplasm, dilatation of  
 256 sinusoid, (black arrow), inflammatory cells (mononuclear cells) (yellow arrow), H&E ( $\times 10$ )

257

258



259

A

B

261 **Fig.2.** Section of rat kidney: (A) Normal control (group 1). (B) After dosing of 2000 mg/ kg aqueous  
 262 extract of *Sonchus cornutus* (group 4) dilated and segmented glomerular tuft (white arrow);  
 263 necrosis of tubular epithelial cells (yellow arrow), H&E ( $\times 40$ )