

The acute effects of scorpion (*Leiurus quinquestriatus*) venom on some clinicalpathological parameters in Guinea pigs

Muhammad M. A. Salman

Zoology department, Faculty of Science, South Valley University, Qena, Egypt
salman2_2000@yahoo.com

Abstract: Scorpions are venomous arthropods of the Arachnida class and are considered relatives of spiders, ticks and mites. The venom of *Leiurus quinquestriatus* is responsible for a number of deaths of infants, children and adults in tropical and subtropical countries. There have been few studies on the clinical and biochemical effects of *Leiurus quinquestriatus* venom. Therefore, the present study was performed to assess the toxicity of *Leiurus quinquestriatus* crude venom and its effects on the biochemical parameters in serum of Guinea pigs (*Cavia porcellus*). Adult male Guinea pigs (600 ± 30 g body weight) were divided into three groups (15 each). In the control group, Guinea pigs were interaperitoneally injected with 50 µL saline solution. The second and third groups were injected intraperitoneally with 0.1 mg/kg body weight and 0.2 mg/kg body weight of crude venom, respectively. The crude venom was diluted in 50µL saline solution. Blood samples were taken after 1, 2 and 4 hours. Serum biochemical parameters, the levels of total proteins albumin, globulin, urea, creatinine, uric acid, glucose, cholesterol and triglycerides were measured. Serum levels of glucose, cholesterol, creatinine, urea and uric acid increased significantly in envenomed animals within 1, 2 and 4 hrs. post-injection, compared to controls. The levels of total serum protein, albumin globulin and triglycerides were significantly decreased within 1, 2 and 4 hrs. post-injection. Hence, it can be conclude that, *Leiurus quinquestriatus* crude venom caused alterations in the investigated biochemical arameters.

[Muhammad M. A. Salman. **The acute effects of scorpion (*Leiurus quinquestriatus*) venom on some clinicalpathological parameters in Guinea pigs**. Journal of American Science 2011; 7(9):794-801]. (ISSN: 1545-1003). <http://www.americanscience.org>.

Keywords: Scorpion venom, *Leiurus quinquestriatus*, biochemical parameters, clinical pathology and Guinea pigs (*Cavia porcellus*).

1. Introduction

Scorpions are arachnids of wide geographical distribution particularly in tropical and subtropical areas of the world. Scorpion venoms contain small molecular weight peptides capable of causing cell function impairment by interfering with ion channel permeability of excitable cell membranes (Gordon *et al.*, 1998 and Anderson and Greenberg, 2001). The species most responsible for severe human envenoming belongs to the Buthidae family. The Buthid scorpion *Leiurus quinquestriatus* is found throughout Egypt, Syria, Jordan, and Saudi Arabia (Lucas and Meier, 1995). Severe envenoming progresses rapidly after the first symptom and often takes from 5 to 30 minutes. Severe systemic complications such as heart failure, pulmonary edema, convulsions and severe degenerative changes of cardiac fibers worsen the prognosis (Omran *et al.*, 1992; Omran and Abd-El-Rahman, 1992 and 1994; Fatani *et al.*, 1998; Tarasiuk *et al.*, 1998 and Omran and Mcvean, 2000). Scorpion venoms have been reported to increase acetylcholine release from nerve cells *in vitro* (Diniz and Torres, 1968 and Gomez and Farrell, 1985). The venom-induced hypertension has been ascribed to the activation of the sympathetic nervous system and increased

release of catecholamines from adrenal medulla (Moss *et al.*, 1974). The venom-induced bradycardia has been postulated to be at least in part due to vagal stimulation (Freire-Maia and Diniz, 1970; Ismail *et al.*, 1976; Gueron and Ovsyshcher, 1987; Ismail *et al.*, 1990 and 1992; Ismail, 1994 and 1995 and Gueron, *et al.*, 1998). The present study was designed to investigate the effects of the scorpion (*Leiurus quinquestriatus*) crude venom on some serum clinico-pathological parameters of Guinea pigs over various periods.

2. Material and Methods:

The scorpions were gathered from Qena governorate of Egypt. The scorpions *Leiurus quinquestriatus* were kept in boxes at the Department of Zoology, Faculty of Science, South Valley University, Qena, Egypt. Crude venom was obtained by using specific device inducing electrical shocks (6 volts) at the articular membrane of the telson, then lyophilized and stored in a desiccator at 4 °C in the dark and reconstituted in saline solution prior to use as milked venom. LD₅₀ of crude venom was determined as described by Meier and Theakston (1986). The LD₅₀ of venom was 0.3 mg/kg b. w. of Guinea pigs.

Study design:

Forty five of adult male Guinea pigs (*Cavia porcellus*) weighing (600 ± 30 g) were used. Guinea pigs were obtained from the Animal House Facility of Egyptian Organization for biological products and Vaccines (VACSERA), Helwan, Cairo, Egypt. Animals were housed in standard condition and fed with standard diet and water *ad libitum*. The Guinea pigs were divided randomly into three groups as follows:

Group1: Fifteen animals were given intraperitoneal (i.p.) injection of 50 μ L physiological saline (0.9 % NaCl) and served as control.

Group 2: Fifteen animals received single i.p. injections of a sublethal dose (low dose; 0.1mg/kg body weight) of scorpions; *Leiurus quinquestriatus* crude venom in 50 μ L saline solutions.

Group 3: Fifteen animals received single i.p. injections of a sublethal dose (high dose; 0.2 mg/kg body weight) of scorpions; *Leiurus quinquestriatus* crude venom in 50 μ L saline solutions.

Five animals of each group (1, 2 and 3) were sacrificed at 1, 2 and 4 hours post-injection of crude venom, respectively.

Serum analysis:

Blood was collected from each animal into plain centrifuge tubes and left at the room temperature to clot. After one hour, serum was separated by centrifugation at 3000 g for 30 min (**Dacie and Lewis, 1975**). The sera were collected in aliquots in labeled-Epindorff's tubes and stored at -20 °C until used. The concentration of total protein, albumin, urea, creatinine, uric acid, glucose, cholesterol and triglycerides were analyzed. The Kits used were purchased from Spinreact (S. A. Ctra. Santa Coloma, Spain). All other chemicals used were of analytical reagent grade. Glucose determination was carried out according to the method of **Trinder (1969)**. Determination of total serum protein was estimated according to **Peters (1968)** method. Serum albumin was determined according to the method described by **Doumas et al. (1971, 1972)**. Serum globulin was obtained from the difference between the total protein and serum albumin. The cholesterol was determined by enzymatic method as described by **Richmond (1973)**, while triglycerides were determined by the enzymatic colorimetric method as described by **Young (1990)**. Creatinine was determined by a kinetic method described by **Hare (1950)**, while determination of urea was according to the enzymatic method of **Patton and Crouch (1977)**. Serum uric acid was determined by a quantitative method of **Young (1990)**.

Statistical analysis:

Data were analyzed statistically using SPSS Software and presented as means and standard error (Mean \pm S.E.). Parameters of groups 2 and 3 were compared with control group. Results were considered significant when p value was lower than 0.05.

3. Results:**1-Effect of crude venom injection on the biochemical parameters****Effects on the levels of serum total proteins, albumin and globulin:**

Administration of 0.1 mg/kg and 0.2 mg/kg body weight crude venom (groups2,3), respectively, led to a significant decrease ($p < 0.05$) in serum total protein at the 1st, 2nd and 4th hours after injection. The decreases of serum total proteins (group2) were 18%, 21.68% and 32.20% after 1, 2 and 4 hours post-injection, respectively. In group3, the decreases of serum total proteins were 25% ($P < 0.05$), 30.92% ($P < 0.01$) and 34.24% ($P < 0.01$) after 1, 2 and 4 hours post-injection, respectively as compared with those of control animals (Table 1). The decreases of serum albumin in (group2) were 13.76% ($P < 0.05$), 25.50% ($P < 0.05$) and 41.39 % ($P < 0.01$) after 1, 2 and 4 hours post-injection, respectively. In group3 the decreases of serum albumin were 20.11% ($P < 0.05$), 33.52% ($P < 0.01$) and 44.44% ($P < 0.01$) after 1, 2 and 4 hours post-injection, respectively, as compared with those of control animals (Table1). The decreases of serum globulin in (group2) were 25% ($P < 0.05$), 16.26% ($P < 0.05$) and 17.83 % ($P < 0.05$) after 1, 2 and 4 hours post-injection, respectively. While, in group3 the decreases of serum globulin were 31.75% ($P < 0.01$), 27.24% ($P < 0.01$) and 18.26% ($P < 0.05$) after 1, 2 and 4 hours post-injection, respectively, as compared with those of control Guinea pigs (Table1).

Effects on the levels of the serum creatinine, urea and uric acid:

Both of the injected groups showed an increase in serum urea, uric acid and creatinine levels, as compared with concurrent control. Serum creatinine, uric acid and urea levels were significantly increased at 1, 2 and 4 hours after injection of crude venom in group3. The increases of serum creatinine were highly significant ($P < 0.001$) after 1, 2 and 4 hours post-injection. However, in (group2) the increases were 36.36% ($P < 0.05$), 125% ($P < 0.01$) and 118.6% ($P < 0.01$) after 1, 2 and 4 post-injection, respectively. The increases of serum urea was highly significant ($P < 0.001$) after 1, 2 and 4 hours post-injection (in group 3) as compared with those of control group. While, the concentration of serum urea levels were lower in group2 than in group3. However, the levels

of serum urea lower significantly ($p < 0.05$) increased after 1, 2 and 4 hours post-injection (Table 2). The increase of uric acid after one hour post-injection in group2 was not significant. However, the increases of uric acid were significant increase ($p < 0.05$) after 2 and 4 hours post-injection. In group3, the levels of serum uric acid were significantly increased, ($p < 0.05$), ($p < 0.05$) and ($p < 0.01$) after 1, 2 and 4 hours post-injection, respectively as compared with those of control animals.

Effects on the levels of serum glucose, triglycerides and cholesterol:

Administration of 0.1mg/gk and 0.2 mg/kg body weight of crude venom (group2 and group3), respectively, led to an increase in the serum glucose level at 1, 2 and 4 hours post-injection. The levels of serum glucose (group2) were 84.55% ($P < 0.01$), 30.27% ($P < 0.05$) and 27.62% ($P < 0.05$) after 1, 2 and 4 hours post-injection, respectively. The levels of serum glucose were 156.37% ($P < 0.001$), 84.66 % ($P < 0.01$) and 80.74% ($P < 0.01$) after 1, 2 and 4 hours post-injection, respectively, (in group 3) as compared with those of control Guinea pigs (Table 3). Also, the levels of serum cholesterol (group2) were 52.63% ($P < 0.05$), 31.36% ($P < 0.05$) and 49.32% ($P < 0.01$) after 1, 2 and 4 hours, respectively. In group 3 the increases of serum cholesterol were 95.83% ($P < 0.01$), 58.75 % ($P < 0.01$) and 61.56% ($P < 0.01$) after 1, 2 and 4 hours, respectively as compared with those of control Guinea pigs (Table 3). However, the levels of triglycerides were significantly decreased at 1, 2 and 4 hours post-injection in group2 and group3 as compared with those of control group (Table 3). The decreases of serum triglycerides (group2) were 19.54% ($P < 0.05$), 17.36% ($P < 0.05$) and 13.17% ($P < 0.05$) after 1, 2 and 4 hours, respectively. The decreases in group 3 of serum triglycerides were 30.53% ($P < 0.05$), 34.94 % ($P < 0.05$) and 28.74% ($P < 0.05$) after 1, 2 and 4 hours, respectively as compared with those of control group (Table 3)

2- Effect of doses of scorpion crude venom on the biochemical parameters:

The levels of serum total protein, albumin, globulin and triglycerides were significant decrease post-injection with high dose (0.2 mg/kg b. w.) or low dose (0.1 mg/kg b. w.) as compared with those of control animals. However, the levels of serum total protein, albumin, globulin and triglycerides of high dose were lower than those of the low dose as compared with those of control animals. On the other hand, the levels of the serum creatinine, urea and uric acid, glucose and cholesterol were significantly

increased post-injection with high dose (0.2 mg/kg b. w.) or low dose (0.1 mg/kg b. w.) as compared with those of control animals. However, these increases in group3 were higher than group2 as compared with those of control animals. However, these increases were higher in group3 than group2.

3-Effect of duration post-injection of scorpion crude venom on the biochemical parameters

As indicated in table (1 and 3) the levels of serum total protein, albumin, globulin and triglycerides were significantly decreased post-injection with high dose (0.2 mg/kg b. w.) or low dose (0.1 mg/kg b. w.) as compared with those of control animals. These levels were still significantly decreased at 4 hours post-injection when compared with those of the control group. Moreover, values were significantly lower in group 3 than those of group 2 after 1, 2 and 4 hours post-injection. The reduction of these parameters was time-dependant and the decreases were descending. On the other hand, injection of crude venom with high dose (0.2 mg/kg b. w.) or low dose (0.1 mg/kg b. w.) lead to a time-dependent rise in serum creatinine, urea and uric acid, glucose and cholesterol levels that became significant after 1, 2 and 4 hours post-injection onwards. Moreover, values were significantly higher in group 3 than group 2 after 1, 2 and 4 hours post-injection (Tables 2 and 3). **4. Discussion:**

Scorpion venoms consist of a mixture of many pharmacologically active proteins (Tu, 1977). Venoms of scorpion (including *Leiurus quinquestriatus*) contain small molecular weight peptides capable of causing cell function impairment by interfering with ion channel permeability of excitable cell membranes (Omran and Abd-El-Rahman, 1992; Gordon et al., 1998 and Anderson and Greenberg, 2001). The venom from *Leiurus quinquestriatus* contains the vaso-active peptide bradykinin (Fatini et al., 1992 and Ismail et al., 1992). Bradykinin-potentiating peptides were isolated from *Leiurus quinquestriatus* and *Buthus occitanus* scorpion venom (Nassar et al., 1989 and Salman, 1995, 2002, 2008 and 2009). These peptides play a role in ischaemia, acute myocardial infarction, pancreatitis, burns, trauma, shock states, secondary hemorrhage and endotoxin shock (Hashimoto et al., 1978; Bhoola et al., 1992 and Briner et al., 1993). In the present study, serum total protein, albumin and globulin were decreased after i. p. injection of crude venom of *Leiurus quinquestriatus* (Table 1).

Table (1): The effects of intraperitoneal injection of scorpion (*Leiurus quinquestriatus*) crude venom on the levels of serum total proteins (mg/dl), albumin (mg/dl) and globulin (mg/dl) in Guinea pigs after the 1st, 2nd and 4th hours post-injection. 5 animals were used in each group.

Time	Parameter		Experimental and doses of S. venom		
			Group1(Control) (0.9 NaCl)	Group 2 (0.1mg/kg.)	Group3 (0.2 mg/kg)
One hours post-injection	Total protein	Mean ± S.E	6.00± 0.37	4.89 ± 0.11 - 18.5 % P<0.05	4.5 ± 0.27 - 25% P<0.05
		Change %			
		P – value			
Albumin	Mean ± S.E	3.48±0.21	3.00 ± 0.10 - 13.79% P<0.05	2.78 ± 0.14 - 20.11% P<0.05	
	Change %				
	P – value				
Globulin	Mean ± S.E	2.52 ± 0.11	1.89 ± 0.21 - 25% P<0.05	1.72 ± 0.13 - 31.75 % P<0.01	
	Change %				
	P – value				
Two hours post-injection	Total protein	Mean ± S.E	5.95 ± 0.11	4.66±0.12 -21.68% P<0.05	4.11 ± 0.12 - 30.92 % P<0.01
		Change %			
		P – value			
Albumin	Mean ± S.E	3.49 ± 0.14	2.60 ± 0.11 - 25.50 % P<0.05	2.32 ± 0.14 - 33.52% P<0.01	
	Change %				
	P – value				
Globulin	Mean ± S.E	2.46 ± 0.21	2.06 ± 0.21 - 16.26% P<0.05	1.79 ± 0.11 - 27.24% P<0.01	
	Change %				
	P – value				
Four hours post-injection	Total protein	Mean ± S.E	5.90 ± 0.31	4.00±0.17 -32.20% P<0.01	3.88 ± 0.14 - 34.24% P<0.01
		Change %			
		P – value			
Albumin	Mean ± S.E	3.60 ± 0.21	2.11 ± 0.14 - 41.39 % P<0.01	2.00 ± 0.13 - 44.44% P<0.01	
	Change %				
	P – value				
Globulin	Mean ± S.E	2.30± 0.11	1.89 ± 0.21 - 17.83% P<0.05	1.88 ± 0.23 - 18.26% P<0.05	
	Change %				
	P – value				

Table (2): The effects of intraperitoneal injection of scorpion (*Leiurus quinquestriatus*) crude venom on the levels of serum creatinine (mg/dl), urea (mg/dl) and uric acid (mg/dl) in Guinea pigs after the 1st, 2nd and 4th hours post-injection. 5 animals were used in each group

Time	Parameter		Experimental and doses of S. venom		
			(0.9 NaCl)	Group 2 (0.1mg/kg.)	Group3 (0.2 mg/kg.)
One hour post-injection	Creatinine	Mean ± S.E	0.44 ± 0.04	0.6 ± 0.04 +36.36% P<0.05	0.90 ± 0.05 104.55 %+ P<0.001
		Change %			
		P – value			
Urea	Mean ± S.E	33.60 ± 4.7	59.2 ± 3.5 +76.19 % P<0.01	85.60 ± 7.30 154.76 %+ P<0.001	
	Change %				
	P – value				
Uric acid	Mean ± S.E	1.6± 0.05	1.7 ± 0.01 + 6.25% NS	1.8± 0.03 +12.5 % P<0.05	
	Change %				
	P – value				
Two hours post-injection	Creatinine	Mean ± S.E	0.40 ± 0.07	0.90 ± 0.05 +125 % P<0.01	1.2 ± 0.08 +200% P<0.001
		Change %			
		P – value			
Urea	Mean ± S.E	44.11 ± 3.3	99.33 ± 2.3 +125.19 % P<0.01	102.33 ± 3.8 +131.99 % P<0.001	
	Change %				
	P – value				
Uric acid	Mean ± S.E	1.48± 0.06	1.95 ± 0.06 +31.76 % P<0.05	1.99± 0.09 +34.46 % P<0.05	
	Change %				
	P – value				
Four hours post-injection	Creatinine	Mean ± S.E	0.43± 2.2	0.94 ± 0.03 118.60 %+ P<0.01	1.4 ± 0.07 +225.58 % P<0.001
		Change %			
		P – value			
Urea	Mean ± S.E	43.44 ± 3.34	89.50 ± 3.66 +106.03 % P<0.01	111.22 ± 3.40 +156.03 % P<0.001	
	Change %				
	P – value				
Uric acid	Mean ± S.E	1.45± 0.02	1.90± 0.02 +31.03% P<0.05	2.7± 0.04 86.21 %+ P<0.01	
	Change %				
	P – value				

Table (3): The Effects of intraperitoneal injection of scorpion (*Leiurus quinquestriatus*) crude venom on the levels of serum glucose (mg/dl), triglycerides (mg/dl) and cholesterol (mg/dl) in Guinea pigs after the 1st, 2nd and 4th hours post-injection. 5 animals were used in each group.

Time	Parameter		Experimental and doses of S. venom		
			Group1(Control) (0.9 NaCl)	Group 2 (0.1mg/kg.)	Group3 (0.2 mg/kg.)
One hour post-injection	Glucose	Mean ± S.E Change % P – value	97.70±6.33	180.31±7.44 84.55 %+ P<0.01	250.47±8.88 156.37 %+ P<0.001
	Cholesterol	Mean ± S.E Change % P – value	88.00±7.3	134.31±4.44 +52.63 % P<0.05	172.33±6.22 +95.83% P<0.01
	Triglycerides	Mean ± S.E Change % P – value	87.00±3.43	70.00±3.42 -19.54 % P<0.05	60.44±7.24 -30.53 % P<0.05
Two hours post-injection	Glucose	Mean ± S.E Change % P – value	97.8±6.41	127.4±7.43 +30.27 % P<0.05	180.60±6.22 +84.66 % P<0.01
	Cholesterol	Mean ± S.E Change % P – value	88.00±7.11	115.6±6.25 +31.36 % P<0.05	139.70±7.24 +58.75 % P<0.01
	Triglycerides	Mean ± S.E Change % P – value	85.22±6.21	70.43±4.24 - 17.36 % P<0.05	55.44±4.21 - 34.94 % P<0.05
Four hours post-injection	Glucose	Mean ± S.E Change % P – value	94.50±4.32	120.60±7.24 +27.62 % P<0.05	170.80±5.37 +80.74 % P<0.01
	Cholesterol	Mean ± S.E Change % P – value	80.90±5.33	120.8±7.31 + 49.32 % P<0.05	130.70±5.44 +61.56 % P<0.01
	Triglycerides	Mean ± S.E Change % P – value	83.50 ±6.11	72.50±3.14 - 13.17 % P<0.05	59.50±3.78 -28.74 % P<0.05

The reduced levels of these serum constituents are considered to be due to disturbances in renal functions as well as haemorrhages in some internal organs such as liver, kidney, lung and heart (Amaral *et al.*, 1994; Amaral and Rezende, 1997 and Mohamed *et al.*, 2007). Furthermore, the increase in vascular permeability and haemorrhages in vital organs are due to the toxic action of various scorpions venoms including *Leiurus quinquestriatus* (Omran and Abd-El-Rahman, 1992; Fatini *et al.*, 1998; Mirakabadi *et al.*, 2006 and Ozkan *et al.*, 2008). Additionally, as the liver is the main source of plasma albumin, the decrease in plasma albumin is mainly due to the diminishing of its synthesis in hepatic cells. Also, the decrease in plasma is due to accompanied losses of large amounts of albumin into the urine and gastrointestinal tract due to damaged kidney and intestinal mucosa (West, 1985 and Sofer *et al.*, 1997). It worthy to mention, that Omran (2003) reported that *Leiurus quinquestriatus* venom kills cells by different mechanisms, and its cytotoxic effects were dose and time dependant. In addition, the venom was found to induce both necrotic and apoptotic changes. Consequently, the renal corpuscles and renal tubules suffered from severe cellular degeneration (Mohamed *et al.*, 2007). Significant increases in uric acid, urea and creatinine were observed (Table 2) in groups 2

and 3 injected I.P. with crude venom of *Leiurus quinquestriatus*. The uric acid, urea and creatinine are the final products of protein metabolism, and their concentration would increase in renal failure. Renal failure and decrease of glomerular filtration may be related to severe cardiovascular perturbation (Omran and Abd-El-Rahman, 1992 and Mohamed *et al.*, 2007). Additionally, acute renal failure has been reported to occur after scorpion sting (Radmanesh, 1990; Patel *et al.*, 1992; Farasiuk *et al.*, 1998 and Sofer *et al.*, 2009)

Determination of blood sugar levels in the serum of Guinea pigs showed a highly significant increase compared with the levels of the control group (Table 3). These changes were observed in experimental animals injected with crude venom of scorpions of the Buthidae family (Zare *et al.*, 1994 and 2006). Clinical manifestations of scorpion envenomation appeared to be secondary to the activation of both sympathetic and parasympathetic autonomic nervous system (Gueron *et al.*, 1992; Ismail *et al.*, 1992 and Murthy and Zare, 1998). Such manifestations reveal that scorpion envenomation causes an autonomic storm (Ismail and Abd-El-Salam, 1987; Murthy *et al.*, 1990 and Mazzeffi *et al.*, 2002). In the present study, significant hyperglycemia was noticed after *Leiurus quinquestriatus* venom administration, which is quite

compatible to the results of other studies (EL-Asmar *et al.*, 1974; Murthy *et al.*, 1986; Omran *et al.*, 1992 and Zare *et al.*, 1994). The proposed mechanism of this effect included peripheral and central stimulation of the adrenergic system activation of β -receptors with catecholamine and serotonin secretion; blockage of insulin secretion and insulin resistance (Gueron *et al.*, 1992 and Zare *et al.*, 1994). Additionally, the scorpion venom from *Leiurus quinquestriatus* activates Na^+ channels on the chromaffin cells inducing catecholamine secretion (Ito *et al.*, 1981). In this study, blood glucose was found to be higher after one, two and four hours of venom injection (Table 3). These results confirmed the previous findings (Ismail and Abd-El-Salam, 1987 and Radha *et al.*, 1992 and 1994). The inhibition of insulin release and the stimulation of glucagon secretion by toxin from *Leiurus quinquestriatus* scorpion venom in rat pancreatic islets had been previously reported (Johanson *et al.*, 1975). Johanson *et al.* (1975) and Johanson and Ensink (1976) have suggested that norepinephrine release from sympathetic nerve endings is probably much greater when stimulated by scorpion venom toxin than by physiologic stimulation. Furthermore, they added, that the strong release of glucagon caused by scorpion venom is due to the release of norepinephrine from the adrenergic nerve terminals of the pancreas. The scorpion venom may be a more effective stimulus to glucagon secretion than norepinephrine reaching the pancreas through the general circulation. The increase in serum cholesterol levels in envenomated Guinea pig observed in the present study (Table 3) could be due to the hepatocytes damage rendering them unable to phosphorylate the increased amounts of fatty acids, therefore leading to fatty liver and alternation of cell membranes of tissues (EL-Asmar *et al.*, 1979). The level of triglycerides was decreased after crude venom injection (Table 3). Some reports notify that the free fatty acids level increases significantly after scorpion venom administration. The present results also confirmed the previous reports (Radha and Medh, 1986 and Radha, *et al.*, 1992). Stimulatory effect of catecholamines on the breaking down of triglycerides has been confirmed *in vivo* and *in vitro* (Fatani *et al.*, 1998). Hence, according to obtained the results, the scorpion (*Leiurus quinquestriatus*) venom caused an acute dose- and time-dependent alterations in the clinic-pathological parameters. These changes in biochemical chemistry parameters are most probably related to the toxic effect of the venom on the target organs.

Corresponding author

Muhammad M. A. Salman

Zoology department, Faculty of Science, South Valley

University, Qena, Egypt

salman2_2000@yahoo.com

References:

- Amaral CFS, Barbosa AJA, Leite VHR, Tauri WL and Rezend NA. (1994). Scorpion sting-induced pulmonary oedema: evidence of increased alveolocapillary membrane permeability. *Toxicon*; 32: 999 -1003.
- Amaral CFS and Rezende NA. (1997). Both cardiogenic and non-cardiogenic factors are involved in the pathogenesis of pulmonary oedema after scorpion envenoming. *Toxicon*; 35: 997- 998.
- Anderson PA and Greenberg RM. (2001). Phylogeny of ion channels: clues to structure and function. *Comp. Biochem. Physiol B*; 129: 17- 28.
- Bhoola KD, Figueroa C and Worthy K. Bioregulation of kinins : kallikreins, kininogen kininases. *Pharmacol Rev* 1992; 44: 1- 80.
- Briner VA, Tsai P and Schrier RW(1993). Bradykinin potential for vascular constriction in the presence of endothelial injury. *Am J Physiol.*; 264: F322 - F327.
- Dacie JV and Lewis SM. (1975). Practical haematology 5th edition. The English Language Book Society and Churchill Livingstone..
- Diniz CR and Torres JM. (1968). Release of an acetylcholine-like substance from Guinea pig ileum by scorpion venom. *Toxicon.*; 5: 277 - 281.
- Doumas BT, Watson WA and Biggs HG(1971). Determination of serum albumin. Standard methods. *Clin Chem.*; 7: 87- 96.
- Doumas BT, Biggs HG, Arends RL and Pinto PCV(1972). Determination of serum albumin. Standard methods. *Clin Chem.*; 7: 175 - 188.
- EL-Asmar MF, Soliman SF, Ismail M and Osman OH(1974). Glycemic effect of venom from the scorpion *Buthus minax* (L.Koch). *Toxicon.*; 12: 249 - 251.
- EL-Asmar MF, Farag RM, Shoukry S and EL-Shimi IR(1979). Effects of scorpion *Leivrus quinquestriatus* H&E venom on lipid metabolism. *Toxicon.*; 17: 279 - 283.
- Fatani AJ, Furman BL and Zeitlin IJ(1998). The involvement of plasma kinins in the cardiovascular effects of *Leiurus quinquestriatus* scorpion venom in anaesthetised rabbits. *Toxicon*; 36 : 523 – 536.
- Freire-Maia L and Diniz CR(1970). Pharmacological action of a purified scorpion toxin in the rat. *Toxicon.*; 8: 132 (abstract).
- Gomez MV and Farrell, N(1985). The effect of *Tityus* toxin and ruthenium red on the release of acetylcholine from slices of cortex of rat brain. *Neuropharmacology*; 24:1103 - 1107.
- Gordon D, Savarin P, Gurevitz M, and Zinn-justin S(1998). Functional anatomy of scorpion toxins affecting sodium channels. *J Toxicol Toxin Rev.*;

- 17:131-59.
- Gueron M, Llia R and Sofer S(1992). The cardiovascular system after scorpion envenomation: A review. *J Toxicol Clin Toxicol.*; 30P: 245-258.
- Gueron M and Ovsyshcher I(1987). What is the treatment for the cardiovascular manifestations of scorpion envenomation? *Toxicon*; 25: 121-124.
- Hashimoto K., Hamamoto H, Honda Y, Hirose M, Honda Y, Hirose M, Furukawa S, Kimura E(1978). Changes in components of kinin system and hemodynamics in acute myocardial infraction. *Am Heart J.*; 49: 275 - 281.
- Hare RS. (1950). Endogenous creatinine in serum and urine. *Pro Soc Exp Biol Med.*; 147-148.
- Ismail M. (1994). The treatment of the scorpion envenoming syndrome: the Saudi experience with serotherapy. *Toxicon*; 32: 1019-1026
- Ismail M(1995). The scorpion envenoming syndrome. *Toxicon*; 33: 825-858.
- Ismail M, Abd-El-Salam MA(1987). Are the toxicological effects of scorpion envenomation related to tissue venom concentration? *Toxicon*; 26: 233-239.
- Ismail M, Abd-El-Salam MA and Morad AM(1990). Do changes in body temperature following envenomation by the scorpion *Leiurus quinquestriatus* influence the course of toxicity? *Toxicon*; 28:1265-1284.
- Ismail M, Fatani AJY and Dabees TT(1992). Experimental treatment protocols for scorpion envenomation: a review of common therapies and an effect of kallikreinkin inhibitors. *Toxicon*; 30: 1257 - 1279.
- Ismail M, Osman OH, Ptkovic D(1976). Electrocardiographic studies with scorpion (*Buthus minax*, I. Koch) venom. *Toxicon.*, 14: 79 - 83.
- Ito S, Nakazato Y and Ohga A(1981). Further evidence for the involvement of Na⁺ channels in the release of adrenal catecholamine: the effect of scorpion venom and grayanotoxinI. *Br J Pharmacol.*; 72: 61-67
- Johnson DG and Ensinnck JW(1976). Stimulation of glucagon secretion by scorpion toxin in the perfused rat pancreas. *Diabetis*; 25: 645 - 649.
- Johnson DG, Henry DP, Moss Y, Williams RH(1975). Inhibition of insulin release by scorpion toxin in the pancreatic islets. *Diabetes*; 25: 198-201.
- Lucas SM, Meier J(1995). Biology and distribution of scorpions of medical importance. In: MAYR E. Animal species and evolution. Massachusetts: Harvard University Press; 205-219.
- Mazzfi DE, Davila CA, Davila DF, Donis JH, Bellabarba GA, Villarreal V and Barboza JS (2002). Sympathetic nervous system activation, antivenin administration and cardiovascular manifestation of scorpion envenomation. *Toxicon.*; 40:1339-1346.
- Meier J, Theakston RDQ(1986). Approximate LD₅₀ Determinations of snake venoms using eight to ten experimental animals. *Toxicon*; 24: 395-401.
- Mirakabadi AZ, Jalali A, Jahromi AE, Vatanpur H and Akbary A(2006). Biochemical changes and manifestations of envenomation produced 75 by *odonthobuthus doriae* venom in rabbits. *Venom Anim Toxins incl Trop Dis.*; 12: 67-77.
- Mohamed SA, Hilal MA, Abdel-Maaboud RM and Abu-Dief EE(2007). Histopathological changes parenchymatous organs of the rat due to scorpion envenoming and the role of the antivenin in abolishing these in some changes. *Egyptian Journal of Natural Toxins.* 4: 45-68.
- Moss J, Thoa NB and Kopin IJ(1974). On the mechanism of scorpion toxin-induced release of norepinephrine from peripheral adrenergic neurons. *J Pharmacol Exp Ther.*; 19: 39-48.
- Murthy KRK, Billimoria FR, Khopkar M and Dave KN(1986). Acute hyperglycemia and hyperkalaemia in acute myocarditis produced by scorpion (*Buthus tamulus*) venom injection in dogs. *Indian Heart J.*; 38: 71-74.
- Murthy KRK, Vakil AE and Yeolekar KE(1990). Insulin administration reverses the metabolic and electrocardiographic changes in acute myocarditis induced by Indian red scorpion (*Buthus tamulus*) venom in experimental dogs. *Indian Heart J.*; 42: 35-42.
- Murthy KRK and Zare MA(1998). Effect of Indian red scorpion (*Mesobuthus tamulus concanesis*, Pocock) venom on thyroxine and triiodothyronine in experimental acute myocarditis and its reversal by specific antivenom. *Indian J Exp Biol.*; 36: 16-21.
- Nassar AY, Abu-Sinna G and Abu-Amra S(1989). Isolated fractions from toxins of Egyptian scorpions and cobra, activated smooth muscle contraction and glomerular filtration. *Toxicon*; 27: 57(abstract).
- Omran MAA(2003). Cytotoxic and apoptotic effects of scorpion *Leiurus quinquestriatus* venom on 293T and C2C12 eukaryotic cell lines. *J Venom Anim Toxins incl Trop Dis.*; 9: 255-267
- Omran MA and Abd-El-Rahman MS(1992). Effect of scorpion *Leiurus quinquestriatus (H and E)* venom on the clinical chemistry parameters of the rat. *Toxicol Lett.*; 61: 99-109.
- Omran MA and Abd-El-Rahman MS(1994). Effect of scorpion venom on *in vitro* rat blood glutathione levels and erythrocyte osmotic fragility. *J NatToxins*; 3: 69-78.
- Omran MA, Abd-El-Rahman MS and Nabil ZI(1992). The role of atropine and propranolol in mitigating the toxic effects of scorpion venom on rat

- electrocardiogram. *Toxicol Lett.*; 61: 175-184.
- Omran MA and Mcvean A(2000). Intraspecific variation in scorpion *Leiurus quinquestriatus* venom collected from Egypt (Sinai and Aswan deserts). *J Toxicol Toxin Rev.*; 19: 247-264.
- Ozkan O, Bakir F and Adiguzel S(2008). Effects of *Androctonus crassicauda* (Olivier, 1807) (scorpions: Buthidae) venom on rat metabolism. *J Venom AnimToxins incl Trop Dis.*; 1:45 -57.
- Patel BG, Bhattand MI and Dave KC(1992). Toxic effects of scorpion venom (*Buthus tamulus*) in rabbits and guinea pigs. *Indian J Pharmacol.*; 24: 212-5.
- Patton CJ and Crouch SR. (1977): Spectrophotometric and kinetics investigation of the Berthelot reaction for determination of ammonia, *Anal Chem.*, 49: 464-469.
- Peters Jr(1968). Proposals for standardization of total protein assays. *Clin Chem.*;14: 1147- 1159.
- Radha KMK and Hase NK(1994). Scorpion envenoming and the role of insulin. *Toxicon*; 32:1041-1044.
- Radha KMK and Medh JD(1986). Increase in serum free fatty acids, phospholipids and reduction in total cholesterol in acute myocarditis produced by scorpion (*Buthus tamulus*) venom. *Indian Heart J.*; 38: 369-372.
- Radha KMK, Kankonkar RC, Zare AM, Malathi A, Balasubramaniam P, Yeolekar ME(1992). Reversal of metabolic and electrocardiographic changes by scorpion antivenin administration in experimental myocarditis induced by Indian red scorpion (*Buthidae family*) venom. *Recent Adv. Toxinol, Res.*; 2: 70-83.
- Radmanesh M (1990). Clinical study of *Hemiscorpion lepturus* in Iran. *J Trop Med Hyg.*; 93: 327.
- Richmond W (1973). Preparation of properties of the cholesterol oxidase from *naecordia* sp. And its application of the enzymatic assay of total cholesterol in serum. *Clin Chem.*; 19: 1350-1356.
- Salman MMA(1995). Effect of a bradykinin potentiating factor isolated from scorpion venom, *Buthus occitanus* on burnt skin of Guinea pig in comparison with other drugs. M. Sc. Thesis, Faculty of Science, Ain Shams University.
- Salman MMA(2002). Serological, hematological and biochemical studies on bradykinin Potentiating factor isolated from scorpion venom. D. Ph. Thesis, Faculty of Science, Ain Shams University.
- Salman MMA(2008). Effect of a bradykinin potentiating factor isolated from scorpion venom on red blood cells indices in alloxan-induced diabetic guinea pigs. 3rd international conference on natural toxins, Cairo-Egypt, 16-18 December, 2008.
- Salman MMA(2009). Effect of a single dose of a bradykinin potentiating factor isolated from scorpion venom (*Buthuthus occitanus*) on total protein and albumin in serum of irradiated growing male Guinea pigs. *Egypt Acad J biolog Sci.*; 1: 33-43.
- Sofer S, Cohen R, Shapir Y, Chen L, Colon A and Scharf SM(1997). Scorpion venom leads to gastrointestinal ischemia despite increased oxygen delivery in pigs. *Crit Care Med.*; 25: 834-40.
- Sofer S, Bawaskar HS and Gueron M(2009). Antivenom for children with neurotoxicity from scorpion stings. *Engl J Med.*; 361: 631-632.
- Tarasiuk A, Khvatskinn S, Sofer S(1998). Effects of antivenom serotherapy on hemodynamic pathophysiology in dogs injected with of *Leiurus quinquestriatus* scorpion venom. *Toxicon*; 36: 963-971.
- Trinder P(1969). Enzymatic determination of glucose. *Ann Clin Biochem.*; 6- 24.
- Tu, AT(1977). In venoms: Chemistry and Molecular. Biology Wiley New York pp. 1977; 132- 134.
- West JB(1985). Blood and the plasma proteins: Function and composition of blood In: Best and Taylors physiological basis of medical practice.; 11th ed. Williams and Wilkins, Baltimore, pp. 334-340.
- Young DS(1990). Effects of Drugs on Clinical Laboratory Test. Third Edition.; 3: 19-25.
- Zare MA, Murthy KRK and Haghazari L(1994). Scorpion venom poisoning in experimental animals. *Arch. Inst. Razi*; 44/45: 67-72.
- Zare MA, Jalali A, Jahromi EA, Vatanpur H and Akbary A(2006). Biochemical changes and mani-festation of envenomation produced by *Odonthobuthus doriae* venom in rabbits. *J Venom AnimToxins incl Trop Dis.*; 12: 67-77.

8/9/2011