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Effects of Different Doses of *Cerastes cerastes* Crude Venom on Biochemical Parameters in Serum of Guinea pigs at different times

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ABSTRACT: In the present work we studied the effects of *Cerastes cerastes* (Cc) crude venom on serum biochemical parameters of Guinea pigs (*Cavia porcellus*). 30 males Guinea pigs weighing 300 ± 30 g. were divided into three groups (10 each). In the control group the Guinea pigs were injected interaperitoneally (i.p) with 100 µL saline solutions. The second group was i. p. injected with 0.2 µgm/g. b.w. of crude venom in 100 µL saline solutions. The third group was i.p. injected with 0.4 µgm/g. b.w. of crude venom in 100 µL saline solution. The results indicated that, after injection of the single dose of Cc crude venom, induced a significant decrease in total serum protein, albumin, globulin and uric acid within 12 and 24 hr. On contrary, levels of serum glucose, cholesterol, triglycerides, urea, creatinine, alanine amino transferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were elevated in serum of envenomated Guinea pigs after 12 and 24 hours post-injection of Cc crude venom. In addition, Cc crude venom caused hepatic and renal dysfunction in envenomated Guinea pigs. These disturbances remained for at least 24 hr after envenomation, regardless of the used dose.

Keywords: Envenomation, *Cerastes cerastes*, crude venom, biochemical parameters, different doses and Guinea pigs (*Cavia porcellus*).

INTRODUCTION

There are approximately 420 venomous species of snakes living on the earth (Lewis and Gutmann, 2004). It is worthy to mention that, intra-specific venom disparity takes place among individual snakes, due to seasonal variation, diet, habitat, age, and sexual dimorphism Venom variability occurs at a number of ambits including inter-and intra-species variations (Tan and Ponnudurai, 1990 and Sasa, 1999). Additionally, venom components may be altered by the geographical location and habitat of the snake (Zingali *et al.,* 1993; Sasa, 1999 and Salazar *et al.,* 2007). Furthermore, zoological distribution and environmental condition could influence the overall biological behavior of snake venoms of the same species (Hassan *et al.,* 1980 and Warrell, 1997).

The desert horned vipers (*C. cerastes* and *C. gasperettii)* are the most familiar snakes of the great deserts of North Africa and the Middle East (Gasperetti, 1988 and Schneemann *et al.,* 2004). Viper snakes are widely distributed snakes in Africa (Marsh *et al.,* 1997 a and b). Viper *C. cerastes* is commonly known as desert-horned or Egyptian sand Viper (Soslau *et al.,* 1988 and Chippaux *et al.,* 1991). It is a poisonous snake and as its name implies, inhabits the sandy deserts of Egypt (Zimmerman *et al.,* 1981). Several studies have been made on the metabolic, cardiovascular and hematological effects of viper venoms on man and animals (Tilbury *et al.,* 1987; Soslau *et al.,* 1988; Abu-Sinna *et al.,* 1993; Abdul-Nabi *et al.,* 1997; Fahim, 1998 and Al-Jammaz *et al.,* 1999). In contrast, there is a paucity of information on the effects of the viper *C. cerastes* crude venom on biochemical parameters of Guinea pigs. Schneemann *et al.* (2004) reported that there is a small literature on envenoming by desert horned vipers. So, the present study is planned to investigate the effects of two different doses of the *C. cerastes* crude venom on the biochemical parameters in serum of Guinea pigs.

MATERIAL AND METHODS

Crude venom was obtained from the viper *C. cerastes* kept in a serpentarium at the Department of Zoology, Faculty of Science, and South Valley University. The snakes were collected from the Qena region of Egypt. Venom was milked, lyophilized, stored in a desiccator at 4ºC in the dark and reconstituted in saline solution prior to use.

A. Determination of LD_{50} dose

The approximate median lethal dose (LD_{50}) of the crude venom was calculated according to the method described by Meier and Theakston (1986).

B. Experimental animals

Thirty male Guinea pigs (*Cavia porcellus*) weighing 300 ±30 g. were used. Guinea pigs were obtained from the Animal House Facility of the Egyptian Organization for Biological Products and Vaccines (VACSERA), Helwan, Cairo, Egypt. Animals were housed in standard condition and fed with normal diet and water ad libitum.

The experimental procedures, animal care and research ethics has been approved by the scientific committee at the Faculty of Science, South Valley University. The Guinea pigs were divided randomly into three groups as the following:

Group 1: Ten animals were injected interaperitoneally (i.p.) with 100 µL physiological saline (0.9 % Na Cl) and served as a control.

Group 2: Ten animals were i.p. injected of a single low dose of Cc crude venom in 100 µL saline solution containing 0.66 mg/kg body weight.

Group 3: Ten animals were i.p. a single high dose of Cc crude venom in 100 µL saline solution according to Salman (2009; 2010 and 2011).

Five animals of each group (1, 2 and 3) were sacrificed at 12 and 24 hours, after injection of crude venom (Al-Jammaz *et al.*, 1999)

Serum analysis: The animals were sacrificed and blood was collected from each animal into plain centrifuge tubes, left for one hr. at room temperature to clotting. Serum was separated by centrifugation at 3000 g for 30 min. and analyzed, for the concentration of total protein, albumin, globulin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), urea, creatinine, uric acid, glucose, cholesterol and triglycerides determination. Kits 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 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 and 1972). Serum globulin was obtained from the difference between the total serum protein and serum albumin. Cholesterol was determined by enzymatic method as described by Richmond (1973), while triglycerides were determined by the enzymatic colorimetric method as described by Young (1972). Creatinine was determined by 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 quantitative determination method of Fossati *et al.*, (1980). The principle of determination of transaminases (ALT and AST) activities was based on the methods of Reitman and Frankel (1957), while determination of alkalin (ALP) activities was done according to the enzymatic method of El-Aaser and El-Merzabani (1975).

C. Statistical analysis

Data were statistically analyzed using SPSS Software and presented as means and standard error (Mean ± S.E.). Parameters of groups 2 and 3 were compared to control group using one way analysis of variance test. Results were considered significant when p value was lower than 0.05.

RESULTS

A. Lethality test:

Results indicated that the approximate (LD_{50}) of the venom is equal to 0.66 mg/kg (0.66 µg/g) body weight (Fig. 1).

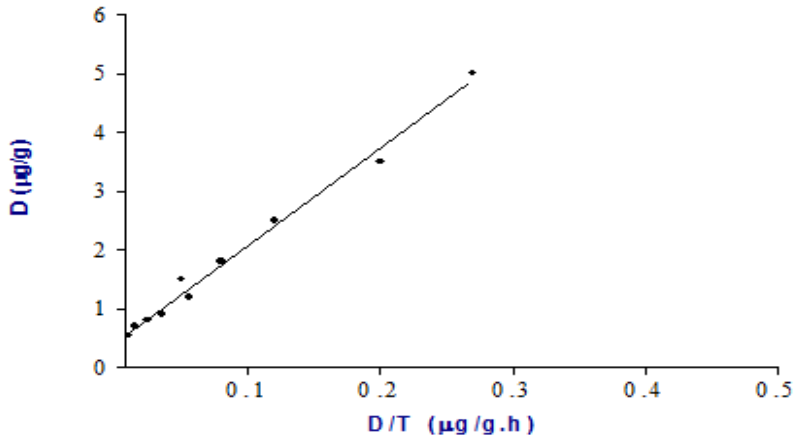

Fig. 1. Twenty four hours dose mortality curve of male Guinea pigs administrated different doses of *C. cerastes* venom by i.p. injection.

The LD_{50} of venom was found to be 0.66 mg/kg (0.66 µg/g) of Guinea pigs.

1. Effects of two different doses of viper *C. cerastes* crude venom on the levels of serum total protein, albumin and globulin.

A) Total protein content in serum: In group 3, the Administration of single dose crude venom 0.4 µgm/g body weight led to decrease the level of serum total protein at the 12th and 24th hours after venom injection. These decreases were 21.57 % (P<0.05) and 28.46 % (P<0.01) at the 12th and 24th hours, respectively. However, in group 2 the injection 0.2 µgm/g of crude venom body weight (group 2), serum total protein level insignificant decreased (1.96%) after 12 hours, but it was significant decrease 20.53% (p<0.05) at the 24th hours as compared with those of control animals.

B) Serum albumin content: In gruop3 serum albumin level significantly decreased, the decreases were significant 13.04% (p<0.05) at the 12th and 23.75% (p<0.01) at the 24th hours post-injection. Meanwhile, serum albumin level in group2 decreased at 12th, the decrease was insignificant (-2.32%) while at the 24th the decrease of serum albumin was significant 12.02% (p<0.05) as compared with those of control (Table, 1).

C) Serum globulin content: In group 3, serum globulin levels significantly reduced (p<0.01) the decreases were 30.82% and 33.55% at the 12th and 24th hours respectively in envenomed Guinea pig. However, in group2 there was insignificant decrease at the 12th (-1.57% (but, this decrease was statistically significant decrease 29.90% (p<0.01) at 24th, post-injection as compared with those of control (Table, 1).

2. Effects of two different doses of crude venom injected (i.p.) on the levels of creatinine, urea and uric acid.

A) Serum creatinine content: Both groups 2 and 3 showed an increase in serum creatinine at the 12th and 24th hours, post-injection as compared with those controls. In group2 statistically significant increases were 22.22% (p<0.05) and 75.51% (p<0.01) after 12th and 24th hours, respectively. In group3 the increases were 77.78% (p<0.01) and 165.31% (p<0.001) after 12th and 24th hours, respectively post-injection as compared with those controls (Table, 2).

B) Serum urea: Statistically significant changes in serum urea levels were found increase both in groups 2 and 3. Serum urea levels increased at the 12th and 24th hours as compared with those of control. The increases in group2 were 51.26% (p<0.01) and112.43% (p<0.001) after 12th and 24th hours, respectively. Also, the increases in group3 were 86.16% (p<0.01) and141.12% (p<0.001) after 12th and 24th hours, respectively after injection as compared with those of control Guinea pigs (Table, 2).

C) Serum uric acid content: The levels of serum uric acid in (groups 1 and 2) decreased at the 12th and 24th hours in envenomed Guinea pigs. Statically significant difference was observed in group2 at the 12th and 24th hours 18.75% (P<0.05) and 35.29% (P<0.01), respectively. The decreases in group3 were 37.5% (P<0.05) and 50% (P<0.01) after 12th and 24th hours, respectively pos-injection as compared with those of control (Table, 2).

3. Effects of two different doses of crude venom injected (i.p.) on the levels of serum glucose, cholesterol and triglycerides.

A) The levels of serum glucose: Serum glucose levels increased at the 12th and 24th hours, post-injection in groups 2 and 3 compared with those of controls. Statistically significant changes in serum glucose levels were found in group2 significant increase at the 12th (21.63 %) and (18.97%) at 24th hours (P<0.05). However, in group3 the increases were significantly at the 12th (42.57%) and (47.36%) 24th hours, (P<0.01) as compared with those of control.

B) The levels of serum cholesterol: The venom effects on serum cholesterol levels led to increase after 12th and 24th hours post-injection in group2. The statistically of these increases were (187.8%; P<0.001 and 191.3%; P<0.001) respectively as compared with those of control. Meanwhile, in group3 serum cholesterol changes were highly significant 171.51% (P<0.001) and 186.4% (P<0.001) after 12 and 24 hours, respectively as compared with those of control (Table, 3).

C) The levels of serum triglycerides: The injection of crude venom 0.2 µgm/g. body weight (group2) and 0.4 µgm/g. body weight (group3) led to increases in serum triglycerides levels at the 12th and 24th hours after injection. These increases of group2 was 173.3% (P<0.001) at 12th and 173.3 % (P<0.001) at 24th hours post-injection. The increases in serum triglycerides of group3 were 197% (P<0.001) and 192% (P<0.001) at 12th and 24th hours post-injection, respectively, when compared to those of control (Table, 3).

4. Effects of (i.p) injection of different doses of viper *C. cerastes* crude venom on the levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP):

A) serum alanine aminotransferase (ALT): The injection of crude venom 0.2 µgm/g. body weight (group 2) and 0.4 µgm/g. body weight (group 3) led to increases in serum alanine aminotransferase (ALT) levels at the 12th and 24th hours after injection. These increases of group 2 were 92.63% (P<0.01) and 72.31% (P<0.01) at 12th and 24th hours, respectively after injection and the increases of group3 were 140.75% (P<0.001) and 127.77% (P<0.001) at 12th and 24th hours, respectively post-injection as compared with those of control guinea pigs (Table, 4).

B) Serum aspartate aminotransferase (AST): The injection of crude venom 0.2 µgm/g. body weight (group2) and 0.4 µgm/g. body weight (group3) led to increases in serum aspartate aminotransferase (AST) levels at the 12th and 24th hours after injection. These increases of group2 were 28.29% (P<0.05) and 22.93% (P<0.05) at 12th and 24th hours, respectively and the increases of group3 were 37.12% (P<0.05) and 31.60% (P<0.05) at 12th and 24th hours, respectively post-injection as compared with those of control (Table, 4).

Table 1: The effects of the different (i.p) injected doses of viper *C. cerastes* crude venom on the levels of serum total proteins (mg/dl), albumin (mg/dl) and globulin (mg/dl) in Guinea pigs at the 12 and 24 hours after crude venom injection.

Time	Parameters	Experimental groups and doses		
		Group1 (Control)	**Group2 (0.2µgm/g.)**	**Group3 (0. 4µgm/g.)**
12 hours post-injection crude venom	**Total protein**			
	Means ± S.E. (mg/dl)	6.63±0.43	6.5±0.33	5.2±0.32
	Change%		-1.96%	-21.57%
	P-value		N.S.	P<0.05
	Albumin			
	Means ± S.E. (mg/dl)	3.45±0.41	3.37±0.32	3.00±0.23
	Change%		-2.32%	-13.04%
	P-value		N.S.	P<0.05
	Globulin			
	Means ± S.E. (mg/dl)	3.18±0.34	3.13±0.31	2.2±0.23
	Change%		-1.57%	-30.82%
	P-value		N.S.	P<0.01
24 hours post-injection crude venom	**Total protein**			
	Means ± S.E. (mg/dl)	6.43±0.42	5.11±0.34	4.6±0.34
	Change%		-20.53%	-28.46%
	P-value		P<0.05	P<0.01
	Albumin			
	Means ± S.E. (mg/dl)	3.41±0.24	3.00±0.21	2.6±0.22
	Change%		-12.02%	-23.75%
	P-value		P<0.05	P<0.01
	Globulin			
	Means ± S.E. (mg/dl)	3.01±0.121	2.11±0.111	2.00±0.211
	Change%		-29.90%	-33.55%
	P-value		P<0.01	P<0.01

N = 5 animals were used in each group, **P** = significantly different from the control, **NS** =Insignificant different from the control.

C) Serum alkaline phosphatase (ALP): The injection of crude venom 0.2 µgm/g. body weight (group2) and 0.4 µgm/g. body weight (group3) led to increases in serum alkaline phosphatase (ALP) levels at the 12th and 24th hours after injection.

These increases of group2 were 45.56% (P<0.01) and 39.67% (P<0.05) at 12th and 24th hours, respectively and the increases of group3 were 58.46 % (P<0.01) and 44.69% (P<0.01) at 12th and 24th hours, respectively post-injection as compared with those of control guinea pigs (Table, 4).

Table 2: The effects of the different (i.p) injected doses of viper *C. cerastes* crude venom on the levels of serum creatinine (mg/dl), urea (mg/dl) and uric acid (mg/dl) in Guinea pigs at the 12 and 24 hours after crude venom injection.

Time	Parameters	Experimental groups and doses		
		Group1 (Control)	**Group2 (0.2µgm/g.)**	**Group3 (0. 4µgm/g.)**
12 hours post-injection crude venom	**Creatinine**			
	Means ± S.E. (mg/dl)	0.45 ±. 060	0.55 ±0. 04	0.8 ±0. 05
	Change%		%22.22+	77.78 %+
	P-value		P< 0.05	P<0.01
	Urea			
	Means ± S.E. (mg/dl)	35.33 ± 2.6	53.44 ± 3.7	65.77 ± 2.4
	Change%		% 51.26+	86.16%+
	P-value		P< 0.01	P< 0.01
	Uric acid			
	Means ± S.E. (mg/dl)	1.6± 0.06	1.3 ± 0.08	1.0± 0.03
	Change%		-18.75%	-37.5%
	P-value		P< 0.05	P< 0.05
24 hours post-injection crude venom	**Creatinine**			
	Means ± S.E. (mg/dl)	0.49 ±0. 07	0.86 ±0.04	1.3 ±0. 08
	Change%		75.51+	165.31+
	P-value		P< 0.01	P< 0.001
	Urea			
	Means ± S.E. (mg/dl)	40.22 ± 3.3	85.44 ± 2.4	96.98 ± 3.8
	Change%		112.43+	141.12+
	P-value		P< 0.001	P< 0.001
	Uric acid			
	Means ± S.E. (mg/dl)	1.7± 0.07	1.1 ± 0.08	0.85± 0.04
	Change%		35.29%-	- 50%
	P-value		P< 0.05	P< 0.01

N = 5 animals were used in each group,
P = significantly different from the control,
NS = Insignificant different from the control.

Table 3: The effects of the different (i.p) injected doses of viper *C. cerastes* crude venom on the levels of serum glucose (mg/dl), cholesterol (mg/dl), and triglycerides (mg/dl) in Guinea pigs at the 12 and 24 hours after crude venom injection.

Time	Parameters	Experimental groups and doses		
		Group1 (Control)	**Group2 (0.2µgm/g.)**	**Group3 (0. 4µgm/g.)**
12 hours post-injection crude venom	**Glucose**			
	Means ± S.E. (mg/dl)	95.0±5.31	115.55±6.11	135.44±7.22
	Change%		+ 21.63 %	42.57%+
	P-value		P<0.05	P<0.01
	Cholesterol			
	Means ± S.E. (mg/dl)	83.00±5.33	55.88±3.14 1	42.36±8.131
	Change%		%+187.8	+ 171.51
	P-value		P<0.001	P<0.001
	Triglycerides			
	Means ± S.E. (mg/dl)	87.89±8.11	57.44±8.141	52.31±4.211
	Change%		%+ 172.3	173.3%+
	P-value		P<0.001	P<0.001
24 hours post-injection crude venom	**Glucose**			
	Means ± S.E. (mg/dl)	98.6±5.41	117.30±6.34	145.30±4.11
	Change%		18.97%+	47.36%+
	P-value		P<0.05	P<0.01
	Cholesterol			
	Means ± S. E. (mg/dl)	86.0±6.41	64.50±5.521	60.32±5.241
	Change%		+ %191.3	+ %186.4
	P-value		P<0.001	P<0.001
	Triglycerides			
	Means ± S.E. (mg/dl)	82.42±5.11	162.34±6.42	58.22±7.111
	Change%		197%+	%+ 192
	P-value		P<0.001	P<0.001

N = 5 animals were used in each group.
P = significantly different from the control.
NS =Insignificant different from the control.

Table 4: The effects of (i.p) injection of different doses of viper *C. cerastes* crude venom on the levels of serum alanine aminotransferase (ALT; U/L), aspartate aminotransferase (AST; U/L) and alkaline phosphatase (ALP; U/L) in male Guinea pigs at 12 and 24 hours after injection.

Time	Parameters	Experimental groups and doses		
		Group1 (Control)	**Group2 (0.2µgm/g.)**	**Group3 (0. 4µgm/g.)**
12 hours post-injection crude venom	**Alanine aminotransferase (ALT)**			
	Means ± S.E. **(U/L)**	62.53 ±5.31	120.45±7.21	150.54±6.54
	Change%		92.63 %+	140.75%+
	P-value		P<0.01	P<0.001
	Aspartate aminotransferase (AST)			
	Means ± S.E. **(U/L)**	112.41±5.22	144.21±4.14	154.14 ±6.72
	Change%		28.29%+	37.12%+
	P-value		P<0.05	P<0.05
	Alkaline phosphatase (ALP)			
	Means ± S.E. **(U/L)**	170.66±7.12	248.42±8.66	270.42±5.21
	Change%		45.56%+	+ 58.46 %
	P-value		P<0.01	P<0.01
24 hours post-injection crude venom	**Alanine aminotransferase (ALT)**			
	Means ± S.E. **(U/L)**	65.32±4.44	112.55±7.8.22	148.78±6.42
	Change%		72.31%+	127.77%+
	P-value		P<0.01	P<0.001
	Aspartate aminotransferase (AST)			
	Means ± S. E. **(U/L)**	115.41±7.25	141.87±8.70	151.88±7.54
	Change%		22.93%+	31.60%+
	P-value		P<0.05	P<0.05
	Alkaline phosphatase (ALP)			
	Means ± S.E. **(U/L)**	177.47±7.14	247.87±7.57	256.78±6.69
	Change%		39.67%+	44. 69 %+
	P-value		P<0.05	P<0.01

N = 5 animals were used in each group.
P = Significantly different from the control.
NS =Insignificant different from the control.

DISCUSSION

In the present study, results indicated that, the approximate (LD_{50}) of the venom is equal to 0.66 mg/kg body weight. Several investigators reported that, venom components may be altered by the geographical location and habitat of the snake (Zingali *et al*., 1993; Sasa, 1999 and Salazar *et al.,* 2007). Furthermore, It variability occurs at a number of ambits including inter- and intra-species variations (Sasa, 1999). Therefore, the difference in LD_{50} attributed to either the species or the environment.

The major functions of protein are maintenance of the intravascular osmotic pressure, maintenance of the blood pressure and fluids in the circulation. They also carry out transport and storage function for several minerals, growth factors and hormones (West, 1985; Marinova *et al.,* 1991 and Guyton and Hall, 2000). However, low total protein can result from protein loss, as it occurs in hemorrhage, glomerulonephritis, nephrosis and chronic liver disease (Al-Jammaz, 1995 and Al-Sadoon and Fahim, 2012). The present study revealed that, the injection of crude venom of viper *C. cerastes* causes a reduction in serum total proteins, albumin, globulin and uric acid in envenomated Guinea pigs. Several investigators reported that, the reduction in serum total proteins, albumin, globulin and uric acid in envenomated rats and Guinea pig were in laboratory animals injected with viper snake venoms (Abdul-Nabi *et al*., 1997; Fahim 1998; Al-Jammaz *et al*., 1998, 1999). The reduced levels of these serum constituents could be due to disturbances in renal functions as well as haemorrhages in some internal organs. In fact, the increasing in vascular permeability and haemorrhages in vital organs due to the toxic action of various snake venoms were described by (Al-Sadoon, 1991; Meier and Stocker 1991; March *et al*., 1997 a and b; Al-Sadoon and Fahim, 2012). It worthy to mention that, several studies have been made on the metabolic, cardiovascular and hematological effects of viper venoms on man and experimental animals (Tilbury *et al*., 1987**;** Soslau *et al*., 1988**;** Abu-Sinna *et al*., 1993; Abdel-Nabi *et al.*, 1997 and Fahim, 1998), and found that, various venoms viper cause alterations of rat and Guinea pig metabolism (Al-Jammaz *et al*., 1998, 1999; Salman 2009). Additionally, Tilbury *et al*., (1987) reported that, acute renal failure characterized by vascular lesions and tubular necrosis in the renal cortex following various snake bites. In the present study, the rise in serum urea and creatinine levels indicates impairment of renal function. Similar observations were reported in rats following administration of various viper venoms (Abdel-Nabi, 1993; Rahmy *et al*., 1995; Omran *et al*., 1997; Abdel-Nabi *et al*., 1997 and Schneemann *et al*., 2004). Such increased vascular permeability, together with, renal damage would further aggravate the accompanying hypoproteinemia and hypoalbuminaemia. Furthermore, the rise in serum urea and creatinine associated with the reduction of serum uric acid level observed, in the present study, supports the proposed impairment of renal function. Similar observations were reported following various viper envenomation of rats (Sant and Purandare, 1972; Rahmy *et al*., 1995; Abdel-Nabi *et al*., 1997 and Omran *et al.*, 1997).

In the present study, snake venoms caused an increase in serum glucose level in the envenomated animals. Snake venoms were found to produce hyperglyceamia in rats and mice (Mohamed *et al*., 1980 and 1981; Abdel-Nabi *et al*., 1997; Fahim, 1998 and Al-Jammaz *et al*., 1999; Pung *et al.,* 2005 and Sleat *et al*., 2006). The levels of serum glucose were significantly increase after 12 and 24 hours in the envenomated Guinea pigs. The increases in serum glucose levels could be attributed to the effects of the venom on glycogen metabolism in the hepatocytes, muscle fibers and medullary catecholamines that stimulate glycogenolysis and gluconeogenesis in those tissues (Ohhira *et al*., 1991, Abdel-Nabi *et al*., 1997 and March *et al*., 1997 a and b).

The present study has revealed significantly increased in serum cholesterol and triglycerides levels in envenomated Guinea pigs following viper *C. cerastes* injection after 12 and 24 hrs. (Table 3). The observed in serum cholesterol and triglycerides indicated that plasma lipids are possible targets for the *C. cerastes* venom. Phospholipase A_2 hydrolyzes phospholipids, mainly hosphatidylethanolamine, liberating polyunsaturated triglycerides (El-Hakim *et al*., 2008). The increases in serum cholesterol and triglycerides levels in envenomated Guinea pig could be due to the hepatocytes damage rendering them unable to phosphorylate the increasing amounts of fatty acids, hence leading to fatty liver and alteration of cell membranes of tissues (El-Asmar *et al*., 1979; Al-Sadoon and Fahim, 2012 and Al-Sadoon *et al*., 2013). Several investigators who reported that, the increases in serum cholesterol and triglycerides levels envenomated rats and Guinea pig were in laboratory animals injected with viper snake venoms (Abdel-Nabi *et al*., 1997 and Al-Jammaz, 2002, Salman, 2009). They reported that, the snake venom might have mobilized level lipids from adipose and other tissues. Lipolytic enzymes could have split tissue lipid with the liberation of free fatty acids (Abdel-Nabi *et al*., 1997; Al-Jammaz, 2002 and Tohamy *et al*., 214).

Measurement of the serum enzyme activities are important in assessment of vital organs, and crude snake venoms have been shown to affect the activities of several serum enzymes (Mohamed *et al*., 1980; Al-Jammaz *et al*., 1992; Abdel-Nabi *et al*., 1997 and Fahim, 1998). Those enzyme activities fluctuate following the damage to liver, myocardial and skeletal muscles (Mohamed *et al*., 1981). In the present study, the rise in the activities of ALT, ALP and AST indicate the damage of liver, heart and other organs brought about by the venom. Such findings are in agreement with previous reports on venoms of other snake species such as *Echis carinatus*, viper *B. arietans*, *Walterinessia aegyptia*, *Echis coloratusis*, *Cerastes cerastes gasperetti*, *Naja haje* (Abdel-Nabi *et al.*, 1997; Fahim, 1998; Al-Sadoon and Fahim, 2012 and Al-Quraishy, *et al*., 2014)

In conclusion, the measurements of biochemical parameters following viper *C. cerastes* crude venom injection, clearly demonstrate the disturbances of vital organs, especially liver, kidney and muscles. Such these disturbances are remaining for 24 hr after envenomation of Guinea pigs at least, regardless the using dose.

REFERENCES

Abu-Sinna G, AL-Zahaby AS, Abd EL-Aal A, Abd-EL-Baset, Soliman NA (1993). The Effect of the viper *Cerastes cerastes cerastes* venom and venom fractions on carbohydrate metabolism**.** *Toxicon,* **31**(6): 791- 801.

Abdel-Nabi IM (1993). Effect of crude *Cerastes cerastes* venom and fraction B clinical biochemical parameters of white rat .*J. Egypt Ger. S. Zool*. **10**(A): 315-326.

Abdel-Nabi IM, Raafat A, El-Shamy HI (1997). Biological effects of intraperitoneal injection of rats with the venom of the snake *Echis carinatus. Egypt. J. Zool.* **29**: 195-205.

El-Hakim AE, Walaa H, Salama E, Mahdi M , Wahby AF (2008). Assessment of the Phospholipase A_2 Patterns of Some Egyptian Snakes Venoms. *Bull. Nrc.* **33**: 181-191.

Al-Jammaz, I. (1995): Effects of the venom of *Walterinnesia aegyptia* and *Echis coloratus* on solute levels in the plasma of albino rats. J. King. Saud Univ.7, *Science.* (1): 63-69.

Al-Jammaz I (2002). Effects of envenomation by *Creastes* vipera crude venomon plasma and tissue metabolites of rats. *Kawait, J. Eng.* **29**(1): 111-119.

Al-jammaz I, Al-Sadoon MK, Attia MA, Fahim A (1992). Effects of *Walterinessia aegyptia* venom on serum, tissue metabolites and some enzyme activities in male albino rats.1- Enzyme activities. *Ain Shams Sci. Bull.* **30**: 207-222.

Al-Jammaz I, Al-Ayed MI, Al-Yahya H (1998). Effect of acute envenomation with LD_{50} of *B. arietans,* Ain. Shams. *Sci. Bull.* **36**: 207-222.

Al-Jammaz I, Al-Sadoon MK, Fahim A (1999). Effect of LD_{50} dose of *Echis coloratus* venom on serum and tissue metabolites and some enzyme of male albino rats. J. King Saud. Univ., **11**, *Science.* (2): 61-68.

Al-Quraishy S, Dkhill MA, and Abdel Moneim AE (2014). Hepatotoxicity and oxidative stress induced by *Naja haje* crude venom. *J. Venom Anim Toxins Incl Trop Dis.* **20**(1): 42-52.

Al-Sadoon, MK (1991). Metabolic rate-temperature curves of the horned viper, *Cerastes cerastes gasperetti*, the moila snake, Malpolon moilensis, and the adder, *Vipera berus. Comparative Biochemistry and Physiology a Comparative Physiology*. **99A**: 119-122.

Al-Sadoon and Fahim (2012): Possible recovery from an acute envenomation in male rats with LD_{50} of *Echis coloratus* crude venom: I-Aseven days hematological follow-up study. *Saudi. J. Biol. Sci.* **19**: 221–227.

Al-Sadoon MK, Abdel Moneim AE, Diab MS, and Amira A, Bauomy AA(2013). Hepatic and renal tissue damages induced by *Cerastes cerastes gasperetti* crude venom. *Life Science J.* **10**(4):191-197.

Chippaux JP, Williams V, White J (1991). Snake venom variability: methods of study, results and interpretation. Toxicon. (29)11: 1279-1303.

Doumas BT, Biggs HG, Arends R.L., Pinto P.C.V. (1972). Determination of serum albumin. Standard methods. *Clin. Chem*. **7**: 175-188.

Doumas BT, Watson WA, Biggs H.G. (1971). Determination of serum albumin.Standard methods. *Clin. Chem.***7**: 87-96.

El-Aaser A.A., El-Merzabani M.M. (1975). Simultaneous determination of 5 nucleotidase and alkaline phosphatase activities in serum. *Z. Klin. Chem. Klin. Biochem.***13**: 453-459.

EL-Asmar M.F., Farag R.M., Shoukry S., EL-Shimi I.R. (1979). Effect of scorpion *Leivrus quinquestriatus* H & E venom on lipid metabolism *Toxicon.* **17**: 279 - 283.

Fahim A (1998). Biological effects of the viper *B. arietans,* crude venom on albino rats. *Egypt. J. Zool.* **30**: 35-54.

Fong IW (2003). Infections and the Cardiovascular System: New Perspectives. Emerging Infectious Diseases of the 21st Century. Springer Comp. Bourton on the Water, GLO, UK, pp. 95–96.

Fossati P, Prencipe L, Berti G (1980). Use of 3, 5 dichloro-2-hydroxybenezen-esufonic acid/4-aminophenzone chromogenic system in direct enzymatic assay of uric acid in serum and urine. *Clin chem*. **26**: 227-230.

Gasperetti J (1988). Snakes of Arabia. *Fauna of Saudi Arabia*. **9**: 169–450.

Guyton AC, Hall JE (2000). The microcirculation and the lymphocytic system: capillary fluid exchange, interstitial fluid and lymph flow.In: Medical physiology 10th ed. (Guyton, A. C. and Hall, J. E., eds), chapter No. 16, pp 162-174. W. B. Saunders co., NY.

Hare RS (1950). Endogenous creatinine in serum and urine. *Pro. Soc. Exp. Biol. Med*. 147 -148.

Hassan F., El-Hawary M.F., Gazawi A., Anis A., Wanas S. (1980). Biochemical properties of Egyptian *Cerastes* venoms in relation to geographic distribution. *Zeitschrift* fur *Ernahrungs wissenschaft*. **19**: 259–265.

Lewis, R. L. and Gutmann, L. (2004): Snake venoms and the neuromuscular junction. *Semin Neurol.*, **24**(2):175-179.

Marinova T.S., Georgieva T.R., Pantev T. (1991). Proteins synthesis changes in peripheral blood leukocytes following *in vivo* and *in vitro* irradiation mammalian spermatogonia. *Rentgen. Radiolog.* **30**(1): 63 – 66.

Marsh NA, Fyffe TL, Bennett EA (1997a). Isolation and partial characterization of a prothrombin-activating enzyme from the venom of the Australian rough-scaled snake (*Tropidechis carinatus*). *Toxicon.* **35**(4): 563-571.

Marsh N, Gattullo D, Pagliaro P, Losano G (1997b). The *Gaboon viper*, and *Bitis gabonica*: hemorrhagic, metabolic, cardiovascular and clinical effects of the venom. *Lif. Sci.* **61**(8): 763-769.

Meier J, Theakston RDQ (1986). Approximate LD_{50} Determinations of snake venoms using eight to ten experimental animals. *Toxicon.* **24**(4): 395-401.

Meier J, Stocker K (1991): Effect of snake venoms on homeostasis. *Toxicology,* **21**(3): 171-1820.

Mohamed AH, Foaud S, Abbas F, Abd-El-Aal A, Abd-El-Baset A, Abbas N, Zahran F (1980). Metabolic studies of the Egyptian and allied African snake venoms. *Toxicon.* **18**: 381 – 383.

Mohamed AH, Fouad S, El-Assar AM, Salem A, Abdel Aal A, Amr Hassan Zahran F. and Abbas, N. (1981). Effects of several snake venoms on serum and tissue transaminase, alkaline phosphatase and lactate dehydrogenase. *Toxicon*, **19**: 605-609.

Ohhira M, Gasa S, Makita A, Sekiya C, Namiki M (1991). Elevated carbohydrate phosphotransferase activity in human hepatoma and phosphorylation of cathepsin D. *Br. J. Cancer*. **63**: 905 –908.

Omran MA, Abdel-Nabi IM, El-Naggar MH (1997) Serum biochemical and hormonal parameters as biomarkers for the toxic effects of Egyptian cobra (*Naja haje*) envenmation. *J. Nat. Toxins.* **6**: 69-83.

Patton CJ, Crouch SR (1977). Spectrophotometeric and kinetics investigation of the Berthelot reaction for determination of ammonia, *Anal. Chem.* **49**: pp. 464– 469.

Pung YF, Wong PT, Kumar PP, Hodgson WC, Kini RM (2005). Ohanin, a novel protein from king cobra venom, induces hypolocomotion and hyperalgesia in mice. *J. Biol. Chem.* **280**: 13137 –13147.

Peters T.Jr (1968). Proposals for standardization of total protein assays. *Clin. Chem.* **14**(12): 1147-1159.

Rahmy TR, Ramadan RA, Farid TM, EL-Asmar MF (1995). Renal lesions induced by cobra envenomation .*J. Egypt. Ger. Soc. Zool.* **17**(C): 251-271.

Reitman S, Frankel SA (1957). A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminases. *Am. J. Clin. Path.* **28**: 56-65.

Richmond W (1973). Preparation of properties of the cholesterol oxidase from *Nacordia sp*. and its application of the enzymatic assay of total cholesterol in serum. *Clin. Chem.***19**: 1350-1356.

Sant SM, Purandare NM (1972). Autopsy Study of Cases of Snake Bite with Special Reference to Renal Lesions. *J. Postgrad. Med.,* **18**: 181-188.

Salazar AM, Rodriguez-Acosta A, Girón ME, Aguilar I, Guerrero B (2007). Comparative analysis of the clotting and fibrinolytic activities of the snake venom (*Bothrops atrox*) from different geographical areas in Venezuela. *Hromb. Res*. (1): 5-104.

Salman MMA (2009). Physiological effects of envenomation by two different doses of the viper *Echis coloratusis* crude venom on biochemical parameters in serum of Guinea pigs at different times. *Egypt. Acad .J. biolog. Sci*. **1**(1): 21-31.

Salman MMA (2010). Biochemical studies on the effects of the crude venom of the scorpion *Buthus occitanus* on the serum of Guinea pig. *Egyptian Journal of Natural Toxins*. **7**(1,2): 86-102.

Salman MMA (2011): The acute effects of scorpion (*Leiurus quinquestriatus*) venom on some clinical pathological parameters in Guinea pigs. *Journal of American Science.* **7**(9): 794-801.

Sasa, M. (1999): Diet and snake venom evolution: can local selection alone explain intra-specific venom variation?. *Toxicon.* **37**(2): 249-252.

Sleat DE, Wang Y, Sohar I, Lackland H, Li Y, Li H, Zheng H, Lobel P (2006): Identification and validation of mannose 6-phosphate glycoproteins in human plasma reveals a wide range of lysosomal and non-lysosomal proteins. *Mol. Cell. Proteomics.* **5**: 1942 –1956.

Soslau G, El-Asmar MF, Parker J (1988). *Cerastes cerastes* (Egyptian sand viper) venom induced platelet aggregation as compared to other agonist. *Biochem. Biophys. Res. Commun.* **150**(3): pp. 909 – 916.

Schneemann M, Cathomas R, Laidlaw ST, El Nahas AM, Theakston RD, Warrell DA (2004). Life-threatening envenoming by the Saharan horned viper (*Cerastes cerastes*) causing micro-angiopathic haemolysis, coagulopathy and acute renal failure. *Clinical cases and review.* **97**(11): 717-727.

Tan NH, Ponnudurai G (1990). A comparative study of the biological properties of venoms from snakes of the genus *vipera* (True adders). *Comp. Biochem. Physiol.* **96**(B): 683- 688.

Tohamy AA, Mohamed AF, Abdel Moneim AE, Diab MSM (2014). Biological effects of *Naja haje* crude venom on the hepatic and renal tissues of mice. *J. of King Saud University Science.* **26**(3): 205–212.

Tilbury RC, Madkour MM, Saltissi D., Suleiman M. (1987). Acute renal failure following the bite of Burton`s Carpet *Viper Echis coloratus Gunther* in Saudi Arabia: Case report review. *Saudi. Med. J.* **8**: 87-95.

Trinder P (1969): Enzymatic determination of glucose. *Ann. Clin. Biochem.* 6- 24.

Warrell DA (1997). Geographical and intraspecies variation in the clinical manifestations of envenoming by snakes. Symp. *Zool. Soc. London*. **70**: 189 –203.

West JB (1985). Blood and the plasma proteins: Function and composition of blood. In: Best and Taylor's physiological basis of medical practice. 11th edt. Williams and Wilkins, Baltimore. pp. 334-340.

Young DS, Thomas DW, Friedman RB, Pestaner L.C. (1972). Effects of drugs on clinical laboratory tests. *Clin. Chem.*, **8**(10): 1041-303.

Zimmerman J, Mann G, Kaplan HY, Sagher U. (1981). Envenoming by Cerastes vipera report of two cases. *Trans. R. Soc. Trop. Med. Hyg.* **75**(5): 702-705.

Zingali RB, Jandrot-Perrus M, Guillin MC, Bon C. (1993). Bothrojaracin, a new thrombin inhibitor isolated from *Bothrops jararaca* venom: characterization and mechanism of thrombin inhibition. *Biochemist.* **32**(40): 10794- 10802.