بسم الله الرحمن الرحيم

The role of scorpion antivenom in abolishing the histopathological changes in some parenchymatous organs of the rat associated with scorpion envenoming syndrome

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Abstract

BACKGROUND:. Scorpions are arthropods belonging to class arachnida. The value of antivenom was never questioned following snake bites, but opinions differ in case of scorpion stings. **OBJECTIVES:** To investigate the effectiveness of scorpion antivenom in preventing or abolishing the histopathological changes occurring in the parenchymatous organs following experimental scorpion envenoming. **METHODS:** Forty five male Albino rats were divided into nine groups, five animals each: Group 1 was control; Groups 2, 3, 4 and 5 were subcutaneously injected with the LD_{50} (35µg) of scorpion venom then sacrificed after 1, 3, 7 and 10 days of injection respectively. Groups 6, 7, 8 and 9 were subcutaneously injected by the LD_{50} followed by IV injection of scorpion antivenom after 30 min of envenoming, then sacrificed after 1, 3, 7 and 10 days of administration respectively. Kidney, liver, lung and heart were evaluated for the histopathological changes in all examined groups. **RESULTS:** Groups 2, 3, 4 and 5 showed many histopathological changes in most examined organs. The renal corpuscles and renal tubules suffered from severe cellular degeneration.The liver revealed manifestations of both degeneration and apoptosis.The lungs, showed severe cellular infiltration in the interalveolar septa and congestion of the blood capillaries with extravasation of RBCs. The cardiac muscles showed no apparent morphological changes. All the previous changes were less marked in groups 6, 7, 8 and 9. **CONCLUSION:** Scorpion antivenom was found to be effective in abolishing some of the various histopathological changes occurring in the parenchymatous organs following scorpion envenoming.

Key words : ***scorpion,*** **envenoming**, ***histopathological, parenchymatous***, ***antivenom,***

Introduction

Scorpions are arthropods in the class of arachnids . They are more closely related to spiders , ticks and mites . They are of wide geographical distribution particularly in tropical and subtropical areas of the world (Bawaskar and Bawaskar , 1998) .
They are distinguished from insects by having two body segments instead of three and by having eight legs as compared to six . The characteristic, long , segmented abdomen terminating in a curved tail with its stinging apparatus and the set of claw like pincers are the closely identifiable features of the scorpion .
Scorpions vary in size from 1-20 cm in length, out of 1500 scorpion species, 50 are dangerous to humans (Allen, 1992).The species responsible for severe human envenoming belongs to the Buthidae family . The Buthid Scorpion Leiurus quinquestriatus is found throughout Egypt , Israel , Jordon and Saudi Arabia (Lucas and Meier , 1995) . It is one of the commonest and most dangerous species in these areas . Injection of just 17 mg of its venom into an average sized human adult results in a less than 50% chance of survival . Severe envenoming may develop rapidly with progression after taking only 5 to 30 minutes . Severe systemic complications such as heart failure, pulmonary edema, convulsions and severe histopathological changes including degeneration of cardiac fibres, focal necrosis, interstitial edema and haemorrhage worsen the prognosis (Omran and Abdel-Rahman , 1992 and Omran and Mcvean , 2000) .
Venoms contain small molecular weight peptides capable of causing cell function impairement by interfering with ion channel permeability of excitable cell membranes Scorpion venoms consist of a mixture of many pharmacologically active proteins , and they have higher toxin contents than their snake counterparts . Most scorpion toxins contain four disulphide bridge , the location of which is quite different from that found in snake toxins . these differences may in part explain the diverse modes of neurotoxic action of venoms from these species (Gordon et al ., 1998 and Anderson and Greenberg , 2001) . Deaths due to scorpion sting are common in developed and developing countries (Ismail , 1995) . The value of antivenom was never questioned following snake bites , but opinions differ in the case of scorpion stings . Most investigators consider antivenom the only specific treatment for scorpion stings (Rezende et al ., 1995 and Amaral and Rezende , 1997) . Others however , question the effectiveness of antivenom in preventing and abolishing the manifestations associated with scorpion envenoming syndrome (Gueron and Ilia , 1996) . All standard medical textbooks carry very little informations about the pathophysiological mechanism/s responsible for death due to venomous scorpion stings . Consequently the current therapeutic approach remain highly unsatisfactory (Murthy and Abbas Zare , 2002) .The aim of the present work was to study the histopathological changes occurring in the parenchymatous organs (kidney, liver , lung and heart) following experimental scorpion envenomation and to investigate the role of scorpion antivenom in abolishing or reversing these changes.

Materials and Methods

The experimental protocol was approved by the Institutional Animal Care and Use Committee of the Sohag University, Faculty of Medicine, Sohag, Egypt.
Rats and maintenance: Three –month old Albino rats were obtained from Assuit University Animal Facility, Faculty of Medicine, Assuit University, Assuit, Egypt. They were housed in Animal Facility at Faculty of medicine, Sohag University, Sohag, Egypt, All rats were given ad libitum access to Taklad rodent chow diet and water from sanitized

bottle fitted with stopper and sipper tubes. These conditions were adopted following other groups (Hussein, et al. 2005).

Preparation of the scorpion venom

· Lyophilized crude venom of scorpion Leiurus quinquestriatus was purchased from Alam El-Zawahef office , Abo-Rawash , Embaba, Egypt . Before commencement of the experiment,the crude venom was dissolved in distilled water and left over night to achieve complete dissolution, then filtered .The injected dose was the LD_{50} (35 µg/g) of scorpion venom calculated according to the LD_{50} (0.25µg / g) of mice (***Paget and Barnes, 1964***) . Experimental envenomation was carried out by a subcutaneous injection of freshly prepared scorpion venom .

Preparation of the scorpion anti-venom

Anti–scorpion serum (polyvalent) ampoules were purchased from the Egyptian organization for biological products and vaccines, Cairo . One ampoule of anti–scorpion serum (polyvalent) was added to 100 ml of distilled water and each rat was injected with 0.05 µL calculated according to the dose of adult human (one ampoule)(***Paget and Barnes 1964***), then injected i.v. (Krifi et al ., 2005).

Rats and envenomation : After a 7-days acclimatization period, a randomized block design based on the animal body weights, was used to divide rats into nine different groups. nine separate experiments were executed using a total of 45 rats. Each experiment had 5 rats in each of the following groups: group 1, control; groups 2,3,4 and 5 injected subcutaneously with the LD_{50} (35 µg/g) of scorpion L quinquestriatus venom Groups 6,7,8 and 9 injected subcutaneously with the LD_{50} (35 µg/g of scorpion L quinquestriatus venom and after 30 minutes. of venom injection,they were injected i.v. with scorpion antivenom .

Animal sacrification and histopathological examination of the parenchymatous organs : Groups 2 and 6, 3 and 7 ,4 and 8and 5 and 9 were sacrificed by cervical dislocation after 1,3,7 and 10 days respectively. The kidney,liver ,lung and heart were removed from rats of the experimental groups in addition to the control group(group 1). Tissue samples were pinned out on paraffin blocks, and floated upside down in 10% buffered formalin overnight, dehydrated, and embedded in paraffin. Sections of 4 µm were cut with a Leica sliding microtome (RM 2035 , Germany), and slides were stained with Haematoxylin and Eosin.. Sections were evaluated in blinded fashion using Olympus BH2 microscope. Some of the examined sections were photographed.

Results

Histopathological examination of the kidney tissue :

The kidney of the control group (group 1) was formed of cortex and medulla . The cortex was mostly occupied by renal corpuscles and the surrounding proximal and distal tubules . The renal corpuscle was formed of renal glomeruli surrounded by Bowman`s capsule. The proximal tubules were lined by cuboidal cells with deeply acidophilic cytoplasm and rounded vesicular basal nuclei .The apical cell membranes were provided with brush borders . The distal tubules exhibited wide lumen and were lined with low cuboidal cells . (Fig.1) .

In group 2, the renal corpuscles appeared swollen with marked glomerular congestion. The capsular spaces were markedly wide. Most of the podocytes and mesangial cells had

dark nuclei. The proximal and distal tubular cells appeared degenerated with destructed upper borders .There was congestion in the peritubular capillaries (Fig 2, a).
In groups 3,4and 5 some glomeruli appeared slightly swollen with relatively wide capsular space. These glomeruli appeared as highly acidophillic amalgamated mass with markedly pyknotic nuclei. The apical brush borders of most of the tubular cells were destructed. Some of the tubular cells appeared binucleated (Fig 2, b). Other glomeruli appeared highly swollen with completely degenerated glomeruli that appeared as reminants of cells scattered through the capsule (Fig 2, c).
In groups 6 and 7 the renal corpuscle appeared swollen with marked congestion of the renal glomeruli. The tubular cells appeared having destructed upper borders, wide lumens and some cells showed vacuolated cytoplasm and peritubular congestion (Fig 3, a).

In groups 8 and 9 most of the glomeruli had more or less normal appearance. Some renal tubules appeared having wide lumens with acidophillic material (Fig 3, b). Other tubules appeared more or less normal but in some cases, groups of adjacent tubules appeared with wide lumens and lined with completely flattened cells (Fig 3, c).

Histopathological examination of the liver tissue :

The parenchyma of the control liver was formed of ill-defined classic lobules which were characterized by the presence of a central vein in the central and peripheral six portal areas . Plates of hepatocytes radiated from the centre to the periphery and were separated by blood sinusoids. The hepatocytes were large polyhedral cells . Their cytoplasm were slightly acidophilic with basophilic patches . Each cell had one or two rounded and vesicular nuclei . (Fig. 4) .
In groups 2 and 3 the hepatocytes were markedly degenerated. They appeared having nuclei, slightly dark-stained with irregular outlines. The cytoplasm appeared rarified and vacuolated (Fig 5, a).
In groups 4 and 5 in addition to these changes, manifestations of apoptosis were observed in the form of skrunked cells and dark, small nuclei with irregular outlines (Fig 5, b).
In group 5, there were marked congestion in the blood sinusoids. The cytoplasm of some cells appeared vacuolated (Fig 5,c).
In groups 7,8 and 9 the vacuoles were rarely seen. The blood sinusoids appeared more or less normal (Fig 5, d).

Histopathological examination of the lung tissue :

The lung of the control animals were formed of the intrapulmonary bronchial trees and the alveoli . The latters were lined with simple squamous epithelium and separated by interalveolar septae which contained numerous capillaries (Fig. 6) .

In groups 2 and 3 the interalveolar septae appeared markely infiltrated with different types of inflammatory cells. The alveoli appeared narrow and some of them appeared collapsed (Fig. 7, a).
In groups 4 and 5 the cellular infiltration in the interalveolar septae was less marked. There was marked congestion in the septal capillaries. Some of them appeared ruptured and numerous extravasated RBCs were observed both within the septae and inside the alveoli. The alveolar lumens were wide and contained extravasated RBCs as well as numerous alveolar macrophages (Fig. 7, b).

In group 6 there was marked cellular infiltration within the interalveolar septae and sometimes inside the alveolar lumen. Most of these cells were eosinophils and macrophages to a less extent (Fig. 7, c).
In groups 7,8 and 9 the cellular infiltration was less marked. Most of the cells were macrophages. There was moderate congestion in the septal capillaries (Fig. 7,d).

Histopathological examination of the heart tissue :

The cardiac muscles of the control animals appeared as short branching cells run in different directions with minimal amounts of loose connective tissue in between . The fibres showed cross striations and each fiber contained one central rod-shaped or oval nucleus (Fig .8).
The cardiac muscles of all treated groups showed no significant changes and they were similar to the control one (Fig . 9 and 10).

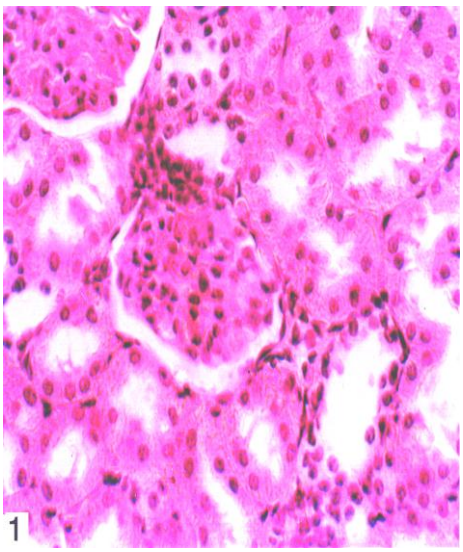
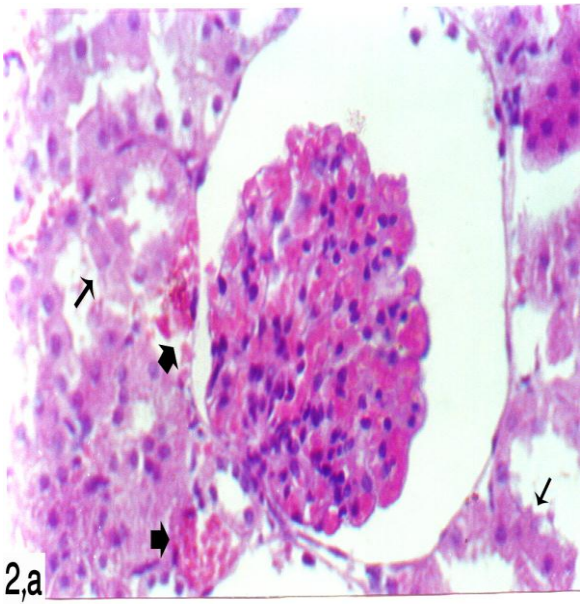


Fig .(1) : A photomicrograph of the control rat`s kidney section showing the renal corpuscle surrounded by the kidney tubules . Note the the brush border of the apices of the tubular cells . (H&E; x400)



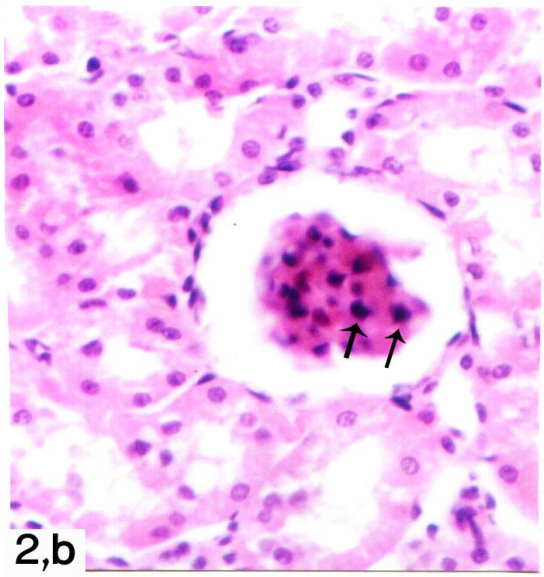


Fig. 2,a : A photomicrograph of kidney section of the rat from groups 2. The renal corpuscle is swollen and the glomeruli are congested. Note the destructed upper border of most of the tubular cells (arrows) and the peritubular congestion (arrow heads).
(H&E ; x400).

Fig. 2,b: A photomicrograph of kidney section of the rat from group 4. The renal glomeruli appear as acidophillic amalgamated mass with scattered pyknotic nuclei (arrows).(H&E; x400).

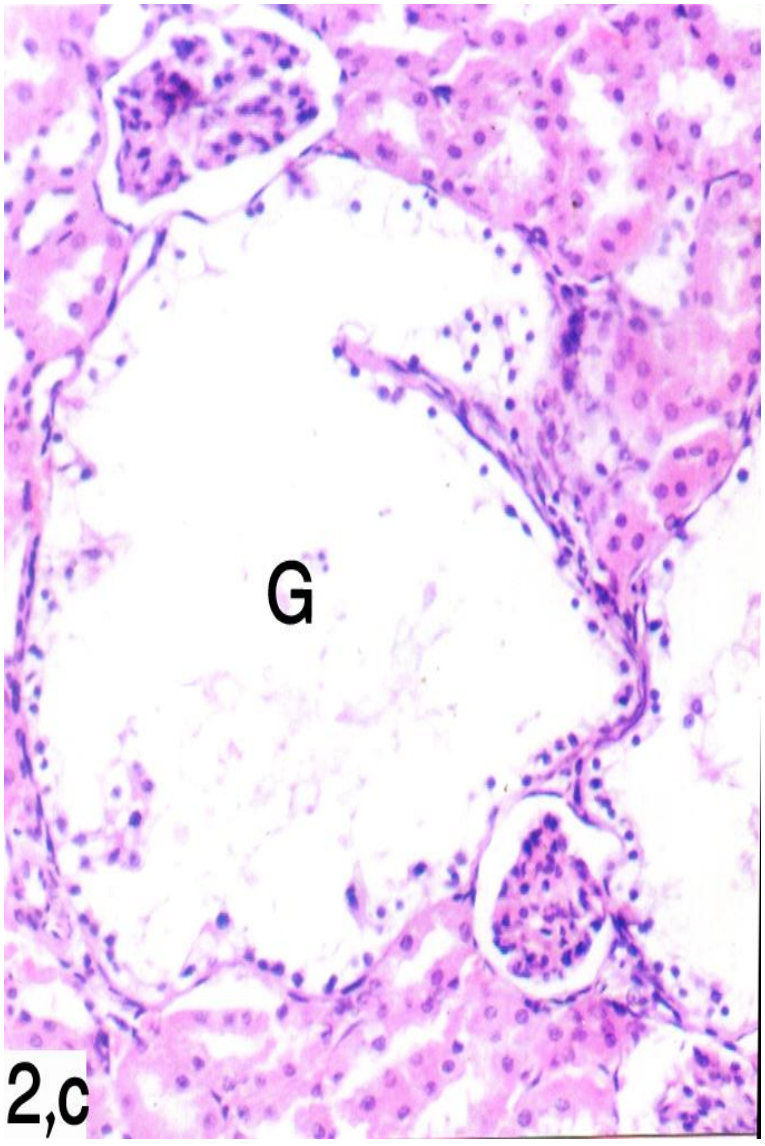


Fig. 2,c : A photomicrograph of kidney section of the rat from group 4. The renal corpuscle is highly swollen with completely dgenerated glomeruli (G).
(H&E; x200).

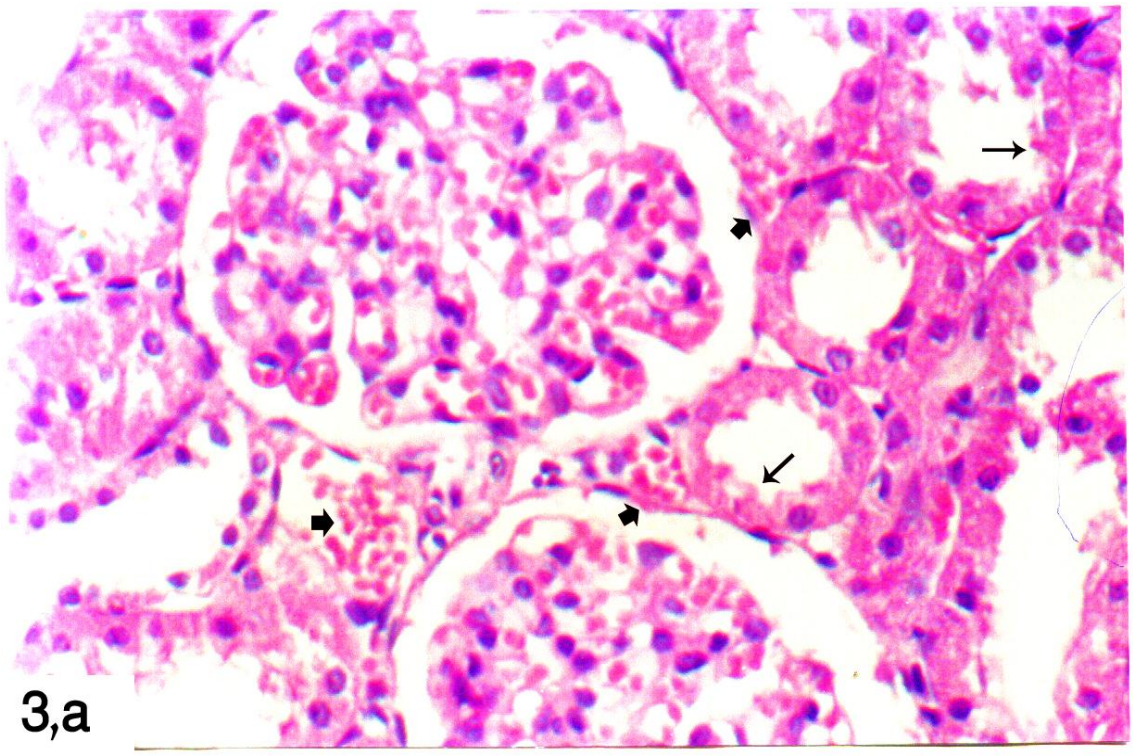
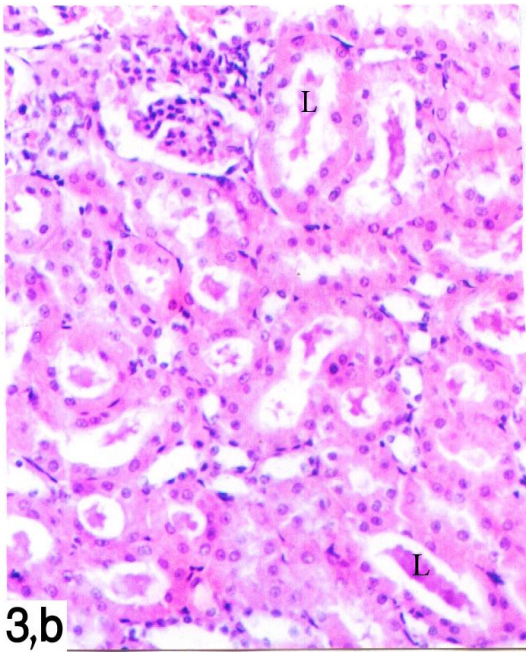


Fig. 3,a : A photomicrograph of kidney section of rat from group 6. The renal corpuscles appear swollen with glomerular congestion. Some tubular cells have destructed upper borders (arrows) and peritubular congestion (arrow heads) . (H&E; x400).



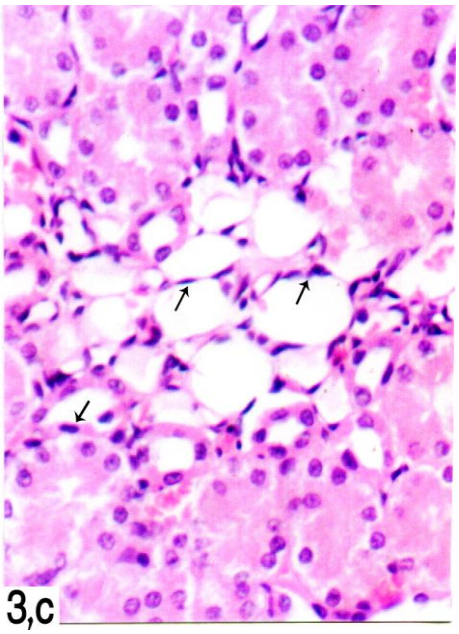


Fig. 3,b : A photomicrograph of kidney section of the rat from group 8. The renal corpuscle has normal appearance. Some tubules has destructed upper borders, wide lumens with acidophillic material (L). (H&E; x200).

Fig. 3, c: A photomicrograph of kidney section of the rat from group 8. Most of the tubules have normal appearance. A group of tubules appear having completely flattened cells (arrows). (H&E; x400).

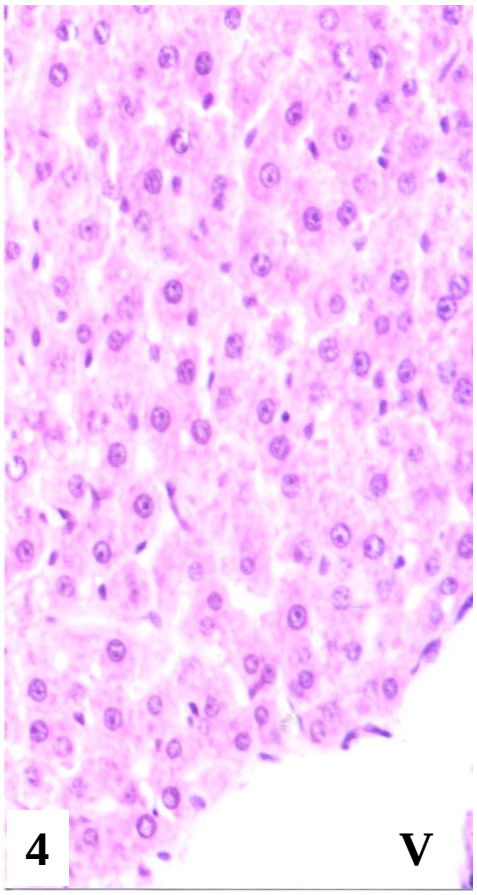
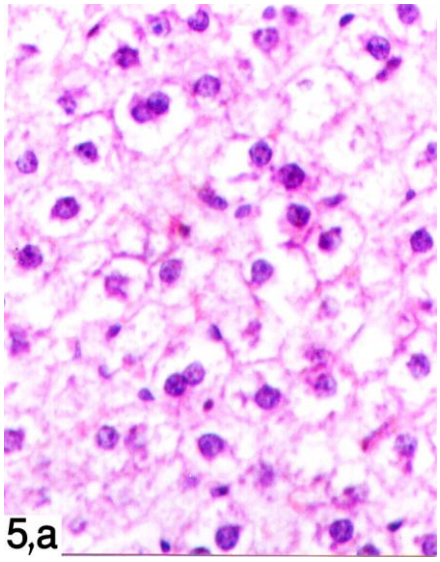


Fig . (4) : A photomicrograph of liver section of the rat from control group showing the hepatic plates radiate from the central vein (V). (H&E; x400)



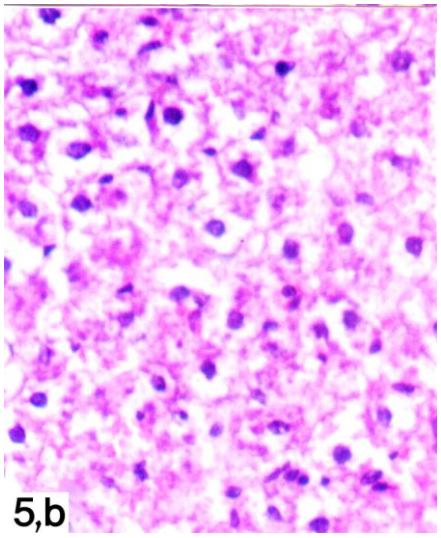
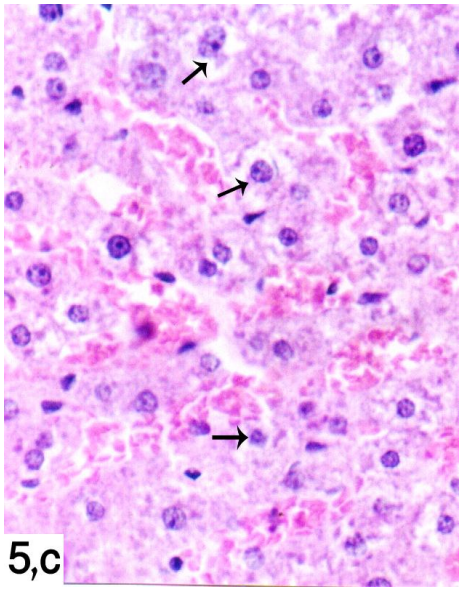


Fig. 5,a : A photomicrograph of liver section of the rat from groups 2. The cytoplasm of most of the cells is rarified and vacuolated. (H&E; x400).

Fig. 5, b : A photomicrograph of the liver section of the rat from group 4. Most of the cells are shrunken with dark-stained small nuclei and vaculated cytoplasm (H&E; x400).



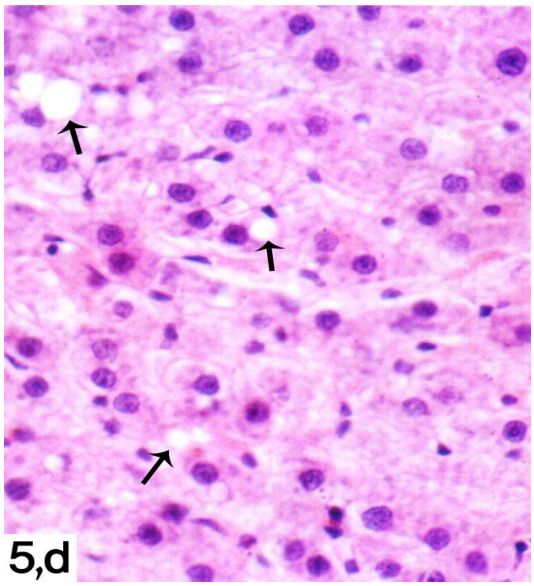


Fig.5,c : A photomicrograph of liver section of the rat from group 6. The blood sinusoids are markely congested. Some cells show vacuolated cytoplasm (arrows) . (H&E ;x400).

Fig. 5,d : A photomicrograph of liver section of the rat from group 8. Few cells show cytoplasmic vacuoles (arrows) . (H&E ;x400).

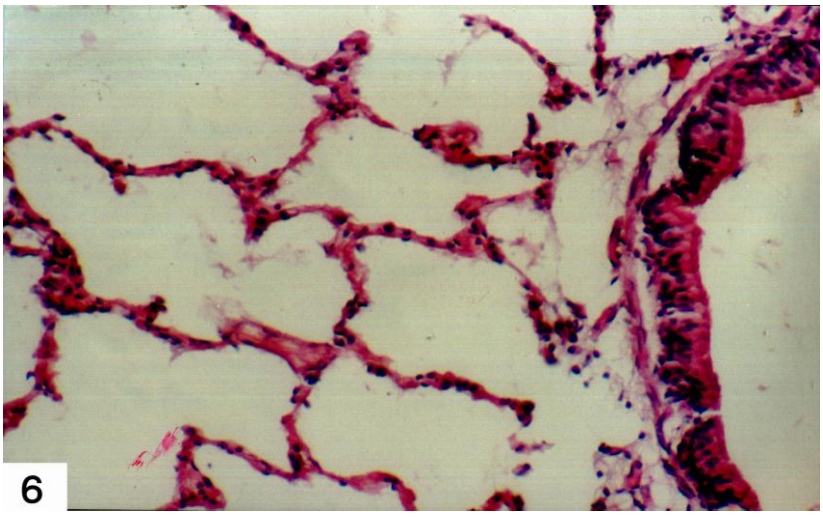
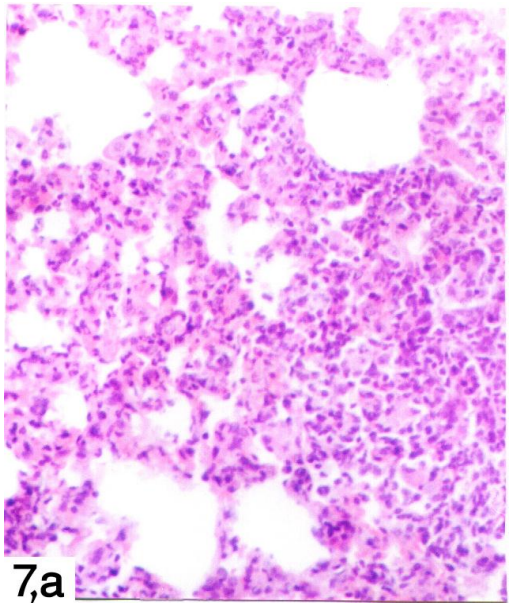


Fig . (6) : A photomicrograph of lung section of the rat from control group showing a part from a bronchial trees and the alveoli (H&E; x400).



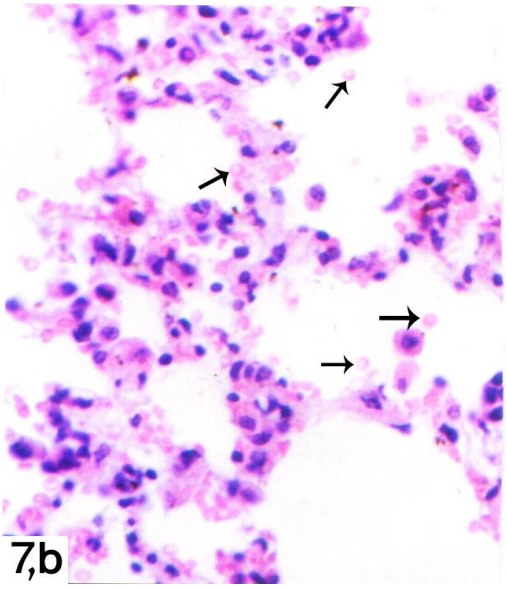
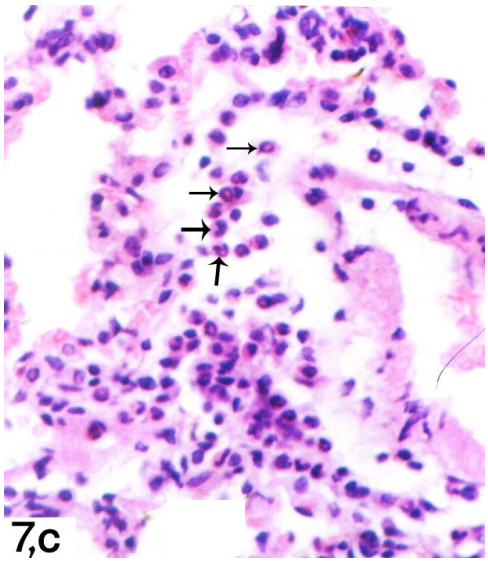


Fig.7,a : A photomicrograph of lung section of the rat from group 2. Showing marked cellular infiltration in the interalveolar septae. The alveolar lumens appeare narrow and some of them are collapsed (arrows). (H&E; x200).

Fig. 7,b : A photomicrograph of lung section of the rat from group 5 . showing numerous RBCs extravasated within the interalveolar septae and sometimes inside the alveoli (arrows). (H&E; x400).



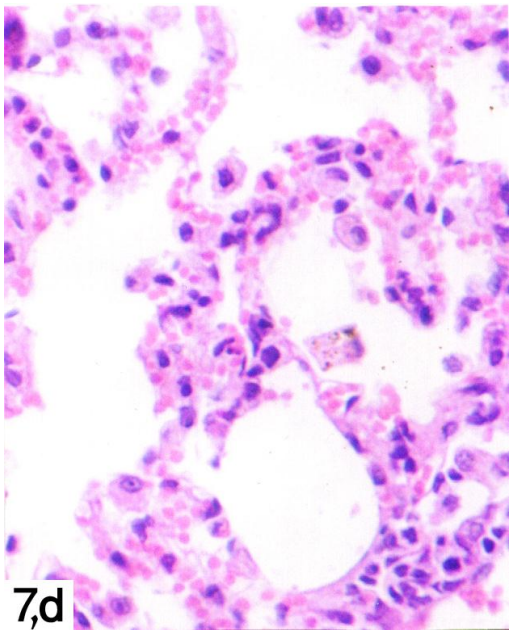


Fig.7,c : A photomicrograph of lung section of the rat from group 6 showing numerous eosinophils within the interalveolar septae and inside the alveolar lumens (arrows).(H& E x 400).

Fig.7,d : A photomicrograph of lung section of the rat from group 8 showing moderate congestion of septal capillaries but the nuclei are more or less normal. (H&E; x400).

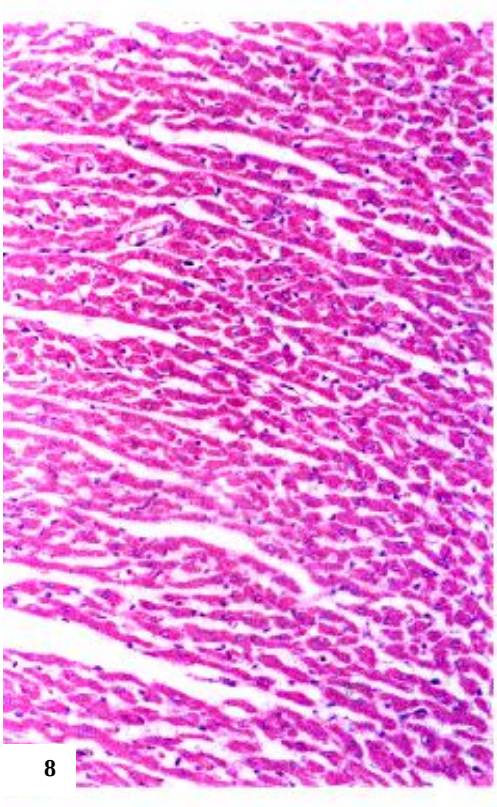


Fig . (8) : A photomicrograph of the cardiac muscles of the rat from control group showing the fibres run in different directions . (H&E; x400)

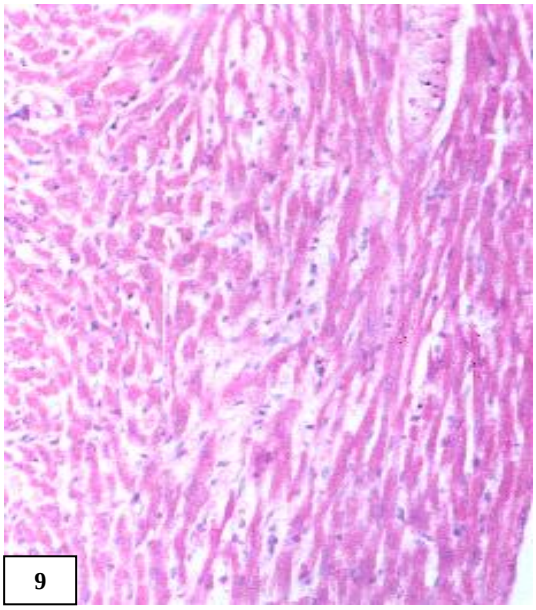


Fig . (9) : A photomicrograph of the cardiac muscles of the rat of group 4 showing the fibres more or less similar to the control . (H&E; x400)

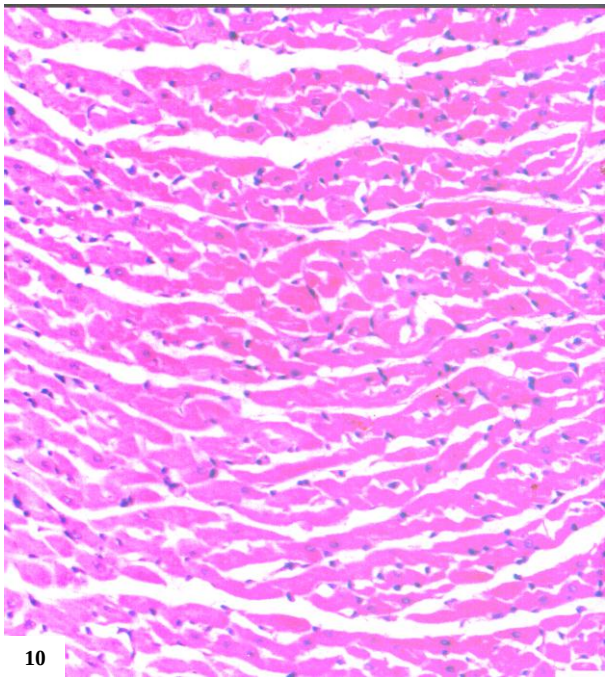


Fig . (10) : A photomicrograph of the cardiac muscles of the rat of group 8 showing the fibers more or less similar to the control . (H&E; x400)

Discussion

A high incidence of scorpion stings leading to a very high mortality in children and adults is reported (Yugandhar et al ., 1999) . All venomous scorpion species reported to cause death in humans all over the world belong to the Buthidae family (Tikedar and Bastawade , 1983) .

Signs and symptoms following stings by dangerous scorpions from different parts of the world are remarkably similar (Murthy and Abbas Zare , 1998) .

In the present work , the studied organs , kidney, liver, and lung of the rat showed marked histopathological changes following experimental scorpion envenomation but the heart showed no significant changes.The specific dose of scorpion venom (LD_{50}) was selected as it provides suitable time for studying the histopathological changes associated with scorpion envenomation .

The kidney tissue showed after one day, marked congestion of the glomeruli with widening of the Bowman`s capsule and degeneration of the kidney tubules . These degenerative changes increased in severity at the 3^{rd} and the 7^{th} days till they reached its maximum level at the 10^{th} day where some of the glomeruli showed apoptotic changes in addition to necrotic changes with hyaline cast inside the kidney tubules which indicate damage of the basement membrane . These results were fully in agreement with the results obtained by Omran (2003), where L quinquestriatus venom was found to induce both necrotic and apoptotic changes .But the apoptotic changes in that study occurred earlier than the necrotic changes and these results were unexpected to occur .Clinically, Chadha and Leviav (1979) reported that scorpion envenoming causes severe hemolysis and secondary renal failure .In the present study it was found that the kidney cells were severely affected than other cells . Omran (2003) reported that L quinquestriatus venom has a greater selectivity for primary human embryonic kidney cells than for the other types of tested cell lines . Also , this effect might be mediated through specific unknown receptor(s) located on the plasma membrane or in the cytosol , affecting the cell signaling system leading to cell death . This postulation is in part in agreement with the reports of Bruses et al . (1993) , who mentioned the possibility that some toxins must bind to a specific receptor in the membrane before they can exert their action . If such a toxin receptor is extensively present on certain membranes such as kidney cells , this could explain the high selectivity of scorpion toxins for these cells . Murugesans et al. (1999) studied the biodistribution of labeled scorpion venom after intravenous injection . They found that within 5 minutes of adminstration the level of venom in the kidney (13%) was higher than in the liver (10%) . The labeled venom was excreted through renal and hepatobiliary pathways .

In the present work, the effect of scorpion venom on the liver cells was studied**.**The hepatocytes after one and three days of venom injection showed marked degeneration . In addition to these changes , at the 7^{th}& 10^{th}days manifestations of apoptosis were observed . These results were in agreement with the results reported by Balasubramaniam and Murthy (1984) who found that scorpion sting causes rise in liver enzymes and necrosis of liver were seen at autopsy of some cases . Also, Biswal et al. (1999) reported that scorpion envenoming causes increased liver transaminases, hyperbilirubinemia, intrahepatic hemorrhage and liver necrosis .

Murthy and Abbas Zare (2002) explained that scorpion envenoming is a condition of fuel energy deficits and inability to utilize the existing metabolic substrates so causing multi-system organ failure .

The lung tissue after one and three days of venom injection showed marked infiltration of the interalveolar space with different types of inflammatory cells and some of the alveoli appeared collapsed . After 7 and 10 days of venom injection, the septal capillaries showed marked congestion . Some of them ruptured and numerous extra-vasated RBCs were observed . These results were in agreement with the results of the previous work of D`Suze et al . (1999) where it was found that some species of scorpion cause abundant microthrombi in rabbit lungs . These clotting alterations are fundamental to produce lung injury and increase alveolocapillary membrane permeability .

Also Murthy and Abbas Zare (2001) suggested that scorpion venom causes an autonomic storm leading to massive release of counter-regulatory hormones , such as catecholamines, angiotensin 11 , glucagons , cortisol , thyroxine , and changes in insulin secretion resulting in hematologic and osmotic fragility changes of erythrocytes . In the present work, the effect of scorpion venom on the heart was studied . It was fond that examination of the heart tissue by light microscope, no significant histopathological changes were detected . On the other hand, many studies reported the cardiac manifestations of scorpion envenoming . Vik Harald and Ole (1981) found that scorpion envenoming predisposes to arrhythmias and heart failure . These effects returned to the increased amounts of circulating FFA resulting in increased oxygen consumption which aggravates ischemic injury to the myocardium . Murthy and Anita (1986) added that scorpion envenoming causes hyperglycemia, hyperkalemia and accumulation of fatty acids and free radicals . All these metabolic disturbances produce injurious effect on the myocardium . So further studies are recommended to be applied especialy for the cardiac muscles . In the present work it was found that , the cytotoxic effect of scorpion venom increased with time . These results were in accordance with the results reported by Omran (2003) who found that Leiurus quinquestriatus venom kills cells by different mechanisms , and its cytotoxic effects were dose and time dependant . In the present work, the effect of scorpion antivenom (SAV) on the histopathological changes occurring in the kidney , liver , lung and heart tissues following scorpion envenomation was studied . SAV was injected intravenously to induce an immediate , complete and durable neutralization of the toxins , as well as their rapid redistribution from the peripheric compartment to the vascular one (Krifi et al ., 2005) . In the present study it was found that the histopathological changes which occured in the kidney , liver and lung tissues of the animals received SAV were markedly decreased . And by the end of 10^{th} day most of the cells became normal . It is important to realize that huge ranges in toxicity are present between different species . So the usefulness of SAV varies between countries . Doctors from Brazil , Mexico and Saudi Arabia reported its benefit (Freire-Maia et al ., 1994 and El Amin et al ., 1994) . On the other hand Belghith et al ., (1999) reported that systemic adminstration of scorpion antivenom did not alter the clinical course of scorpion sting . Antivenom in the US and other parts of the world is harvested from animals . Since antivenom contains foreign antigens and the risk of serum sickness is always present . So antivenom is not routinely used in most US centres and is only available in the state of Arizona .Its use in that state is reversed for only serious envenomations (Sofer et al ., 1994) . In Saudi Arabia evaluation of antivenom use was designed , utilizing 18 centres and examining more than 24,000 cases it strongly supports the use of antivenom . The overall mortality rate was reduced from 4-6.8% to less than 0.05%when antivenom was employed (Ismail , 1995) .

Murthy and Abbas Zare (2001) designed a study about the effect of scorpion venom on the hematologic and osmotic fragility changes of erythrocytes and the effect of SAV on them in experimental envenomatiom . A rise in the plasma hemoglobin (Hb), mean corpuscular hemoglobin concentration (MCHC), packed cell volume (PCV) and increased osmotic fragility of erythrocytes was found . Adminstration of SAV effectively

neutralized , prevented , and reversed scorpion venom toxicity and related osmotic fragility of erythrocytes .In another study made by the same authers in 2002, who found that scorpion antivenom reversed the metabolic , electrocardiographic , and hormonal disturbances caused by scorpion envenomation .The results of the present study were in harmony with the previously reported findings that scorpion venom induced marked histopathological changes in the kidney , liver and lung tissues . Administration of SAV abolished these changes . So the effect of antivenom in preventing or abolishing the various clinical manifestations of human scorpion envenoming is evident .

Conclusions

In the present study, the venom of Scorpion Leiurus quinquestriatus was found to induce marked histopathological changes in the kidney , liver and lung tissues. These changes increased with time . No significant changes were detected in the heart tissue. Scorpion antivenom was found to be effective in abolishing some of the various histopathological changes occurring in the parenchymatous organs following scorpion envenoming.

Recommendations

- More studies about increasing the dose of SAV and the rapidity of its injection is recommended.
- Further histopathological studies, e.g. electron microscopic or immunohistochemical studies are recommended to be applied specially for the cardiac muscles .

References

Allen, C. (1992) : Arachnids envenomations . Emerg. Med. Clin. North. Am.,10 : 269-298.

Amaral, C.F.S. and Rezende,N.A. (1997): Both cardiogenic and non-cardiogenic factors are involved in the pathogenesis of pulmonary oedema after scorpion envenoming. Toxicon, 35: 997-998.

Anderson, P.A.V. and Greenberg,R.M. (2001): Phylogeny of ion channels: clues to structure and function. Comp. Biochem. Physiol. B., 129: 17 – 28.

Balasubramaniam, P. and Murthy, K.R.K . (1984) : Liver glycogen depletion in acute myocarditis produced by scorpion venom (Buthus tamulus) . Indian Heart J ., 36 : 101 – 104 .

Bawaskar, H.S. and Bawaskar, P.H. (1998): Scorpion sting. J. Assoc. Physicians India (JAPI), 46: 388-392.

Belghith, M .; Boussarsar, M .; Haguiga, H .and Abroug, F . (1999) : Efficacy of serotherapy in scorpion sting : A matched pair study . J. Toxicol. Clin. Toxicol ., 37 : 51 – 57 .

Biswal, N.;**Charan, M.V.; Betsy, M.; Nalini, P.; Srinivasan, S.and Mahadevan, S. (1999)** *:Management of scorpion envenomation . Pediatrics Today, 2 : 420-426 .*

Bruses ,J.l.; Capaso, J.; Katz, E. and Pilar, G. (1993) : Specific in vitro biological activity of snake venom myotoxins. J. Neurochem., 60: 1030-1042.

***Chadha,* J.S. and Leviav, A. (1979) :** Hemolysis, renal failure and local necrosis following scorpion sting . JAMA, 241-1038 .

D`Suze, G .; Comellas, A .; Pesce, L .; Sevci, K.C . and Sanchez-de-leon, R. (1999) : Tityus discrepans venom produces a respiratory distress syndrome in rabbits through an indirect mechanism . Toxicon , 37 : 173 – 180 .

El-Amin, E.O .; Sultan, O.M .; Al-Magamci, M.S . and Elidrissy, A . (1994) : Serotherapy in the management of scorpion sting in children in Saudi Arabia . Ann.Trop. Pediatr., 14 : 21 – 24 .

Freire-maia, L .; Campos, J.A . and Amaralk, C.F . (1994) : Approaches to the treatment of scorpion envenoming . Toxicon , 32 : 1009 – 1014 .

Gordon, D.; Savarin, P.; Gurevitz, M. and Zinn-Justin, S. (1998): Functional anatomy of scorpion toxins affecting sodium channels. J. Toxicol. Toxin Rev., 17: 131-159.

Gueron, M.and Ilia, R. (1996): Non-cardiogenic pulmonary oedema after scorpion envenomation: a true entity? Toxicon, 34: 393-395.

Hussein, M. R.; Abu-Dief, E. E.; El-Hady, H. A.; Mahmoud, S. S.and Salah, E. M. (2005) : Quantitative comparison of infected schistosomiasis Mansoni and haematobium : Animal model analysis of the granuloma cell population . J. Egypt. Soc. Parasitol., 35(2):467-476.

Ismail, M. (***1993):*** Serotherapy of the scorpion envenoming syndrome is irrationally convicted without trial. Toxicon, 31: 1077-1087.

Ismail, M. (***1995):*** The scorpion envenoming syndrome. Toxicon, 33: 825-858.

Krifi, MN.; Savin, S.; Debray, M.; Bon, C. El Ayeb, M. and Choumet, V. (2005) : Pharmacokinetic studies of scorpion venom before and after antivenom immunotherapy. Toxicon. 45(2):187-198.

Lucas, S.M. and Meier, J. (1995): Biology and distribution of scorpions of medical importance. In; Mayr, E. Animal species and evolution. Massachusetts: Harvard University Press. 205-219.

Mahadevan, S. (2000): Scorpion sting. Indian Pediatrics, 37: 504-551.

Murthy' K. R. K. ***(1982):*** Investigations of cardiac sarcolemmal ATPase activity in rabbits with acute myocarditis produced by scorpion (Buthus tamulus) venom. Jpn. Heart J., 23: 835-842 .

Murthy' K. R. K. and Abbas Zare' M. (1998) : Effect of Indian red scorpion (Mesobuthus tamulus concanesis, Pocock) venom on thyroxine and triiodothyronine in experimental acute myocarditis and its reversal by species specific antivenom. Indian J. Exp. Biol., 36: 16-21.

Murthy' K .R.K. and Abbas Zare ,M. (2001) : The use of antivenom reverses haematological and osmotic fragility changes of erythrocytes caused by Indian red scorpion . Mesobuthus tamulus concanesis, Pocock in experimental envenoming . J. Venom. Anim. Toxins, 7, 113- 138.

Murthy' K. R.K. and Abbas Zare ,M. (2002 ***) :*** Scorpion antivenom reverses metabolic, electrocardiographic, and hormonal disturbances caused by the indian red scorpion Mesobuthus tamulus concanesis, Pocock envenomation J. Venom. Anim. Toxins, vol.8 no.1: 30-48.

Murthy' K. R.K.; Abbas Zare ,M. ***and Haghnazari, L. (2003):*** Investigations on the role of insulin and scorpion antivenom in scorpion envenoming syndrome. J. Venom. Anim. Toxins, 9: 202-238.

Murthy' K. R.K and Anita, A.G. (1986) : Reduced insulin secretions in acute myocarditis produced by scorpion (Buthus tamulus) venom injection in rabbits . Indian Heart J., 38 : 467-471.

Murthy' K. R.K.*; Zolfagharian, H.; Medh, J.d.; Kkudalkar, J.Á.; Yeolekar, M.E.; Pandit,.P.; Khopkar, M.; DaveK, N. and Billimoria, F.R. (1988):* Disseminated intravascular coagulation and disturbances in carbohydrate and fat metabolism in acute myocarditis produced by Indian red scorpion (Buthus tamulus) venom. Indian J. Med. Res., 87: 318-325.

Murugesan, S. Radha, K.M.; Noronha, O.P.D. and Samuel, A.M*. *(1999): Tc 99m -scorpion venom: labeling, biodistribution and scintiimaging. J. Venom. Anim. Toxins, 5: 46-55.

Omran, M.A.A. (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 (2): 255-267.

Omran, M.A.A. and Abdel-Rahman, M.S. (1992): Effect of Leiurus quinquestriatus (H&E) venom on the clinical chemistry parameters of the rat. Toxicol . Lett., 61: 99-109.

Omran, M.A.A. 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.

Paget,G.E. and Barnes, J.M. (1964): Evaluation of drug activities: Pharmacometrics, (Eds. Laurence and Acharach), vol. 1, Academic Press, New York, 85.

Rezende, N.A.D.; Dias, M.B.; Campolina, D.; Chavezolortegui, C.; Diniz, C.and Amaral, C.F.S. (1995): Efficacy of antivenom therapy for neutralizing venom antigen in patients stung by Tityus serrulatus scorpion Am. J. Trop. Med. Hyg., 52: 277-280.

Sofer, M .; Shahak, E .and Gueron, M . (1994) : Scorpion envenoming and antivenom therapy . J Pediatr ; 124 : 973 - 978 .

Tikedar, B.K.and Bastawade, D.B. (1983): The fauna of India. Scorpions, Scorpionida, Arachnida. Calcutta: Zoological survey of India, Government of India, 3: 1-671.

T U AT.(1977) : Venoms: chemistry and molecular biology. New York: Wiley. P.560

Vik Harald, M.O. and Ole, D.M. (1981): Influence of free fatty acids on myocardial oxygen consumption and ischemic injury. Am. J. Cardiol., 48: 361-367.

Yugandhar, B. Murthy' K. R. K. ***and Sattar, S.A. (1999):*** Insulin administration in severe scorpion envenoming. J. Venom. Anim. Toxins, 5: 200-219.

الملخص العربى

دور مضاد سم العقرب فى تقليل التغيرات الهستوباثولوجيه التى تحدث فى الاعضاء الحشوية للفأر و المصاحبة للدغ العقرب

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تعتبر العقارب من المفصليات و التى تنتمى للعنكبوتيات . فى حالات لدغ العقرب اختلفت الاراء كثيرا فى تقدير مدى اهمية مضاد سم العقرب فىالعلاج . و لكن فى علاج حالات لدغ الثعبان لم يحدث اى اختلاف فى الرأى فى تقدير اهميه مضاد سم الثعبان فىالعلاج.
الهدف من هذه الدراسة هو تقدير ما اذا كان مضاد سم العقرب له دور في منع او تقليل التغيرات الهستوباثولوجيه المصاحبة للدغ العقرب في الاعضاء الحشوية للفأر.
و فد اجريت هذه الدراسه على ٤٥ فأرأبيض ذكر . تم تقسيمهم الى ٩ مجموعات في كل مجموعة ٥ فئران . المجموعة الاولى هى المجموعة الضابطة تم حقنها بماء مقطر . اما المجموعات ٢، ٣، ٤، ٥ فتم حقنهم تحت الجلد بالجرعة المميتة للنصف (٣٥ ميكروجرام) من سم العقرب . تم ذبح فئران كل من المجموعة٢، ٣، ٤، ٥ بعد ١، ٣، ٧، ١٠ ايام على التوالى . اما المجموعات ٦، ٧، ٨، ٩ فتم حقنهم في الوريد بمضاد سم العفرب بعد ٣٠ دقيقة من حقن سم العقرب . تم ذبح فئران كل من المجموعات ٦، ٧، ٨، ٩ بعد ١، ٣، ٧، ١٠ ايام على التوالى . تم فحص انسجة كل من الكلى و الكبد و الرئة و القلب لكل المجموعات التي خضعت للدراسة . و قد اسفرت النتائج عن حدوث العديد من التغيرات الهستوباثولوجيه المصاحبة للدغ العقرب فىكل من انسجة الكلى و الكبد و الرئة فى المجموعات ٢، ٣، ٤، ٥ . و لكن لم تسفر النتائج عن حدوث تغيرات هستوباثولوجيه ذات أهمية واضحة في انسجة القلب . و بفحص كل من المجموعات ٦، ٧، ٨، ٩ وجد ان التغيرات الهستوباثولوجيه المصاحبة للدغ العقرب قد قلت بدرجة ملحوظة .من هنا يتضح ان مضاد سم العقرب له دور في تقليل التغيرات الهستوباثولوجيه المصاحبة للدغ العقرب في الاعضاء الحشوية.