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SCORPIOM VENOM USES AGAINST CANCER

Scorpions

Scorpions are the oldest arthropod representatives and were the first ones to conquer the Earth (Álvarez, N. y cols. 1993). Presently the number of known species is 1500. Of these, Cuba homes 32 species and subspecies, which is considered a large **endemism,** given that among such known forms, 29 are exclusive to our country (Armas, ÑF. 1974).

Six out of the seven living phyla, live in America, and two of them are represented in our fauna: ***Dipocentridae y Buthidae.*** The latter and most highly evolved for the order, includes the most dangerous as well as highest medical significant species,. (Armas, L. F.,1974). Of the two, only ***Buthidae*** is harmful to humans.

The ***Buthidae*** phylla includes 8 genus: *Alayctyus; Anantaris; Centruroides; Isometrus; Microtityus; Tityopsis; Tityus* y *Rhopalurus* (*R. garridoi; R. princeps; R. junceus*).

Scorpion *R. junceus* reaches 55-100 mm in adulthood, is brown-yellowish has a black interocular triangle, blackish caudal segments, peptines with 16-21 teeth and pedipalp fingers with 8 rows of movable supernumerary granules and the basal lobule is more developed in males.

General traits of scorpion venom

Scorpion sting poisoning is a common problem in tropical and subtropical countries. The severity of this poisoning and the high mortality rate among victims has driven research on the subject to identify the nature of this venom's toxic components. (Campos y cols., 1980).

According to Zlotkin (1972) scorpion venoms registered as dangerous are those with toxic potency fluctuating between 0.3-1.0 mg/Kg. Variability of the toxic effect depends on: origins of lab. animals on which the venom is tested, administration route, method of venom extraction and treatment, geographical origin of tested animals, and statistics methods applied.

In terms of scorpion venom, toxins are those components with higher responsibility for the toxic effect on the sting on humans. There is a clear specificity for these toxins according to the species. Therefore, they can be specific for mammals, insects or crustaceans. Chemical evidences (Miranda, F. y cols., 1960, 1961) allow to assert that lethal and paralyzing action of scorpion venom from the Buthidae phyla, is caused by low molecular weight contents and its basic nature, showing different pharmacological activity based their high affinity and selectivity to bond with specific marker-sites which are ionic channels in excitable cell membranes with influence on specific cell functions (Müller, 1993; Adams y Swason, 1996). Recent investigations research showed a much more extensive range of action in scorpion neurotoxins, not only because they are specific sodium and potassium markers, but because they show signs of activity by their selective bonding to chloride channels as expressed in malign cells, a very important basis for its use and assessment in cancer therapy. (Soroceanu y cols., 1998).

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In addition, the evidence confirms the presence in the venom, of some elements in some way linked to its (the venom) toxicity (calcium, sodium, zinc, silice, magnesium, o, manganese, nickel, potassium and phosphorus). The toxicity of the venom is related to the higher proportion of these minerals, which allows to speculate about the role played by the disbalance of elements in venom toxicity.

Scorpion venom as antitumoral agent

Though limited, products from animal sources are climbing to a significant rank among suggested research lines directives aimed to develop effective treatment for cancer. (Einat y cols.,1995). In several animal species materials with antitumoral activity have been extracted in a preliminary manner. Such species are represented in the following Phyla: Porifera, Coelenterata, Bryozoa, Echinodermata, Mollusca, Cordata, Arthropoda (Harry, B. y Woud, Jr., 1971). Within the frame of the search for pharmacologically active products, for a long time, toxins have been particularly marked as bearers of activity. (Cotte y cols.,1972). Interesting results from studies on *Crotalus durissus terrificus* snake venom reported over 80% tumoral mass reduction in patients under treatment. (Costa, L. A., y cols. 1998).

In regards with antitumoral action in scorpion venom, DeBin y cols. in 1993 showed that venom from scorpion *Leiurius quinquestriatus*, Buthidae phyla, contains a small basic peptide, namely, Chlorotoxin suggested to play an important role in gliomal growth control , as the lack of chloride currents may cause changes in cellular shape and volume thus impeding their migration to periphereal tissues (Sontheimer y cols., 1999).

Backgrounds of the use of scorpion venom as an agent against tumors in Cuba.

The use of scorpion for therapeutic purposes has been known in Cuba since the beginnings of last Century, when a so called “scorpion oil” was dispensed as useful in counteracting retention of urine, as showed in the Matanzas Pharmaceutical Museum (Armas, L.F.., 1974). Additional information, give credit to scorpion alcohol extract analgesic properties in rheumatic and muscular pain, but isn’t until early 1980’s that a research team from the School of Medical Sciences in Guantanamo starts working with venom from *Rhopalurus junceus*, scorpion, an endemic species of the *Buthidae* phyla (Armas, L.F..,1974) with the purpose of showing its anti-tumor effects, as it was being used by local population to treat tumors in lesser animals.

In January 1994, was reported the realization of preliminary experimental studies on mice, dogs and humans, according to which, once scorpion toxin was administered, natural or transplanted tumors in dogs and albino mice either disappeared or reduced their size. (Erlich tumors, adenocarcinomes and malign neoplastics with diverse localizations).

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Studies performed on humans, resulted in life-quality improvement, overriding adverse medical prognosis and complete response to the disease in a group of patients, indicating that scorpion *R. junceus* venom bears, among others, analgesic and anti-inflammatory properties, stimulates body immunity and acts over a wide variety of tumors; over 2,000 persons have experienced encouraging results when treated with scorpion *R. junceus* venom.

LITERATURA CONSULTADA

1. Adams, M. E. and Swanson, G. (1996) TINS Neurotoxins supplement, 1-37.
2. Álvarez, N.; Rivera, F.; Bello, J. (1993). Algunos aspectos farmacológicos del extracto crudo de un escorpión cubano. *Trabajo de Diploma. Facultad de Biología, Universidad de la Habana.*
3. Armas, L.F. (1974) Poeyana. Escorpiones del Archipiélago Cubano. Nueva Especie de Rhopalurus (Scorpionida: Buthidae).
4. Balozet, L. (1971). Scorpionism in the old world. In Venomous animals and their venoms. Bücherd, W.; Buckley, E. Eds. Vol 3, 349. New York-London. Academic Press.
5. Bougis, P. E.; Rochat§, H.; Smith, L. A. (1989). Precursors of *Androctonus australia* scorpion neurotoxins. *J. Biol. Chem. 264(32), 19259-19265.*
6. Campos, J. A., Silva, O. A., Lopez, M. and Freire-Maria, L. (1980). Signs, symptoms and treatment of severe scorpion sting in children. In: Natural Toxins (Eaker, D. and Wodstrom, T.) p.61. Oxrford: Pergamon Press.
7. Carbone, E., Wanke, E., Prestipino, G., Possani, L.D. and Maelicke, A. (1982) Selective blockage of voltage-dependent K^+ channels by a novel scorpion toxin. *Nature 296, 90-91.*
8. Catterall, W. A. (1980) Neurotoxins that act on voltage-sensitive sodium channels, in excitable membranes. Annu. Rev. Pharmacol. *Toxicol. 20, 15-43.*
9. Costa, L. A.; Miles, H.; Araujo, C. E.; González, S.; Villarubia, V. G. (1998). Tumor regression of advanced carcinomas following intra- and/or peri-tumoral inoculation with VRCTC-310 in humans: preliminary report of two cases. *Immunopharmacology and immunotoxicology, 20 (1), 15-25.*
10. Cotte, C. A., Essenfeld-Yahr, E. Calvo, L. A. (1972). Effects of crotal and bothrop venoms on normal and malignant cell cultivated in vitro. *Toxicon 10, (2): 157-161.*
11. DeBin, J. A., Strichartz, G. R. (1991). Chloride Channel Inhibition by the Venom of the Scorpion *Leiurus Quinquestriatus*. *Toxicon 11,(9):1403-1408.*
12. Einat, M., et. al. (1995). Potent antileukemia activity of the novel agents norsegoline and pibezine. *Clinical Cancer Res. 1, (8): 823-829.*
13. García, M. L., Galvez, A., García-Calvo, M., Frank King,V., Vazquez, J. and Kaczorowski, G. J. (1991) Use of toxins to study potassium channels. *J. Bioenerg. Biomembr. 23, 615-646.*
14. Gragg, G. M., Newman, D. J., Weis, R. B (1997). Coral reef, forest and thermal vents: the worldwide exploration of nature for novel antitumor agents. *Seminars in Oncology, 24: 156-163.*
15. Harry, B.; Woud, Jr. (1971). Selection of agents for the tumor screem. *Cancer chemotherapy Reports 2, 9-21.*

16. Kirsh, G. E., Skattebol, A., Possani, L. D.band Brown, A. M. (1989) Modification of Na channel gating by an alfa scorpion toxin from Tityus serrulatus. *J. Gen. Physiol. 93, 67-83.*
17. Martin-Eauclaire, M-F.; Søgoard, M.; Ramos, C.; Cestele, S.; Bougis, P.E.; Svenson, B. (1994). Production of active insect-specific scorpion neurotoxin in yeast. *Eur. J. Biochem. 223, 637-645.*
18. Miranda, F.; Rochat, H.; Lissitzky, S. (1960). Sur la nuerotoxine du venin de scorpions. 1. Purification a partir du venin de devx especes de scorpions nord-africains. *Bull. Soc. Chim. Biol. (Paris), 42, 379-391.*
19. Miranda, F.; Lissitzky, S. (1961). Scorpamins the toxin proteins of scorpion venoms. *Nature (London), 190, 443-444.*
20. Muller, G. J. (1993) Scorpionism in South Africa, a report of 42 serious scorpion envenenomations. *S. Afr. Med. J. 83, 405-411.*
21. Serraino, M and Thompson, L. U. (1992) Flaxseed Supplementation and Early Markers of Colon Carcinogenesis. *Cancer Letters 63, pp159-165*.
22. Sontheimer, H.; Soroceanu, L.; Manning, T.J. Jr. (1999). Modulation of glioma cell migration and invasion using Cl(-) and K(+) ion channel blockers. *J Neurosci Jul 15;19(14):5942-54*
23. Soroceanu, L.; Gillespie, Y.; Khazaeli, M.B.; Sontheimer, H. (1998). Use of chlorotoxin for targeting of primary brain tumors. *Cancer Res Nov 1;58(21):4871-9.*
24. Stahnke, H. L. (1963). Variables in venom research. *Biosystems, 34, 64-71*.
25. Zlotkin, E.; Lebovitz, N.; Shulov, A. (1972). Toxic effects of the venom of the scorpion *Scorpiomaunus palmatus* (Scorpionadae). *Riv. Parassit., 33, 237-243.*