Scorpion Anti-Venom Activity of Botanicals: A Pharmacological Approach

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Abstract: Scorpion bite is considered as one of the common and dangerous phenomenon throughout the world. The clinical manifestations include pulmonary edema, myocardial damage, intracerebral haemorrhage, brachial plexopathy, renal failure etc. which sometimes leads to mortality. The common antivenin therapy includes anti-scorpion venom serum or prazosin. In the vast rural areas of the third world countries phytotherapy is considered as an alternative system of medicine and scorpion sting is treated with the help of medicinal botanicals. As the safety and efficacy are considered as important aspects of anti venin therapy, conventional treatment can be supported by the herbal remedy. The present review compiles a number of medicinal plants pharmacologically evaluated in vitro and/or in vivo for scorpion antivenin properties. Considering the aspects like cost effectiveness, availability, lesser side effects and development of drug resistance, plant based antivenin therapy may be considered as a possible remedy against scorpion envenomation.

Key words: Scorpion sting, anti-scorpion venom serum, envenomation, antivenin, myocarditis

INTRODUCTION

Scorpions are widely distributed throughout the world (Uwonggul et al., 2005). Around 700 people/year die in Mexico due to scorpion bite (Calderon-Aranda et al., 1993). Scorpion antivenin serotherapy, considered as the most popular treatment in scorpion sting, has been questioned for effectiveness in clinical trials, especially in cases of severe envenomations (Abroug et al., 1999; Belghith et al., 1999). Although human death due to scorpion sting is not a very common phenomenon, severe pain and inflammatory reactions are common associated symptoms (Uwonggul et al., 2005). Traditional use of medicinal plants are popular in the treatment of various diseases such as gastrointestinal disorders (Dey and De, 2012a), snakebite (Dey and De, 2011a, 2012b), ailments of mother and child (Dey and De, 2011b) and livestock (Dey and De, 2010) etc. Medicinal plants are reported for antibacterial (Dey et al., 2011, Mukherjee et al., 2012), antifungal (Dey and De, 2011c), anti mycobacterial (Dey and De, 2012c), cytotoxic (Dey and De, 2012d), antioxidative (Dey and De, 2012e), antihistidin (Dey and De, 2012f) properties.

Plants are used against scorpion sting in the traditional medicinal systems throughout the world (Hutt and Houghton, 1998). Reports on traditional phytotherapy against scorpion envenomation are available from the countries like India, Mexico, Trinidad, Thailand (Brahmane et al., 2011; Izquierdo et al., 2010; Uwonggul et al., 2005; Lans et al., 2001) and many others. Earlier, Hutt and Houghton (1998) have provided a list of ethnobotanicals used against scorpion bite. In the present review, the authors present a pioneer effort to document the pharmacological investigations of medicinal plants used for the purpose.

Scorpion sting is known to cause a number of physiological disturbances and clinical manifestations such as pulmonary edema (Goncalves et al., 2012), myocardial damage (Maheshwari and Tanwar, 2012), intracerebral haemorrhage (Dube et al., 2011), brachial plexopathy (Rubin and Vavra, 2011), renal failure (Malhotra et al., 1978; Naqvi et al., 1998) etc. Prolific release of neurotransmitters especially acetylcholine and catecholamines is associated with scorpion envenomation (Ismail, 1995; Natu et al., 2010). Children are also severely affected by scorpion venom (Bahloul et al., 2010).

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Acidosis, tachypnea and myocarditis are the symptoms associated with children affected by scorpion bite (Prasad et al., 2011). Experimental envenomation in dogs and rabbits was also found to induce acute myocarditis in the animals (Murthy and Zare, 1998). Although, it was found that the certain scorpion venom toxicity depends on the age and mammalian species (Tiwari and Deshpande, 1993), acute myocarditis, caused by scorpion can be fatal in children as well as in adults (Kari and Zolfaghrian, 1986). Srinivasan et al. (2002) have prepared a molecular database named “SCORPION” involving scorpion toxins.

Scorpion envenomation is a common global phenomenon and regarding the effectiveness, the use of antivenin is some sort of controversial (Tuuri and Reynolds, 2011) requiring a protocol for standard antivenin treatment (Karnad, 2009). Anti-Scorpion Venom Serum (ASvS) or prazosin is commonly used in the treatment of scorpion venom toxicity associated clinical symptoms (Natu et al., 2010) and some have noted the efficacy of ASvS over other treatments (Deshpande, 2010). Several researches have been performed regarding the use, safety, utility and efficacy of ASvS or prazosin (Bawaskar and Bawaskar, 2007, 2011; Thirunavukkarasu and Chandrasekaran, 2011; Mills and Ford, 2011). Dobutamine has also been experimented as a possible antidote to scorpion sting (Gupta et al., 2010). Cost effectiveness of such anti venin therapy (Brown and Landon, 2010) has to be another primary concern especially for the developing and under developed countries. The venom protein was found to be neutralized in vitro by heat and chemical treatments such as hydrochloric acid and acetic acid which were also effective in vivo. The chemicals were found to decrease the total protein, free amino acids and protease activity of the venom and also reduced the mortality in experimental animals (Venkateswarlu et al., 1988). A sodium channel blocker was successfully used to neutralize the Leiurus quinquestriatus venom induced effects in vitro and in vivo (Fatani et al., 2000).

Keeping aside the dangerous and fatal aspects of the venom, it is found to be effective against cancer (Zhang et al., 2009) and HIV (Chen et al., 2012) and has shown antibacterial (Peramal Samy et al., 2007; Diaz et al., 2009), virucidal (Li et al., 2011), antistegocariosis (Haldar et al., 2010), antiproliferative and apoptogenic (Gupta et al., 2007) properties. Therapeutic ability of animal venoms is considered as one of the prime aspects of research and scorpion venom along with snake, bee and other insects may serve as potential candidates against different human ailments. The objective of the study is to document the pharmacologically active botanicals against scorpion venom in vitro and/or in vivo.

**Enumeration:** The present review compiles a total number of nine medicinal plants tested for scorpion antivenin ability. Most of the reports come from Mexico followed by Egypt, Thailand, Jordon, India, Saudi Arabia and USA. Considering the traditional aspects of such therapy, most of the investigated plants were actually reported from the ethnic use as antivenin. Various scorpions have been used as source of the venom such as Mesobuthus tamulus, Heterometrus laoticus, Centruroides impidus impidus and Leiurus quinquestriatus. The plant names are mentioned along with the plant part(s), solvent system(s) used for extraction and isolated active principle(s) (if any). Studies were performed either in vitro or in vivo or both. For in vitro investigations isolated guinea-pig ileum, rabbit and guinea-pig jejunum and trachea or chick embryonic fibroblast cell have been used for the assay of antitoxin and anti fibroblast cell lytic activity of the venom respectively. For in vivo experimentation mice/rat model has been used. The following table (Table 1) alphabetically lists the botanicals pharmacologically tested for scorpion anti venin properties.

**DISCUSSION**

*Andrographis paniculata* has also been reported for snake venom neutralization capacity (Nazimuddin et al., 1978). Species of *Aristolochia* and *Viter* are also reported for the same (Alam and Gomes, 2003; Dey and De, 2012g). Pharmacologically active cyclic hexapeptides bouvardin and deoxybouvardin were isolated from *Bouvardia ternifolia* (Jolad et al., 1977). *Aristolochia elegans*, on the other hand, is reported for antiprotozoal and anti mycobacterial activities due to the compounds fargesin and cubebin (Jimenez-Arellanes et al., 2012). A. elegans has been investigated extensively for phyto-constituents (Hussein and El-Sebakhy, 1974; Wu et al., 2000, 2002; Shi et al., 2004) many of which may contribute to its antivenin ability. Monodesmosidic saponins actantulosides A-F and other related compounds were isolated from *Barringtonia acutangula* (Barua et al., 1961; Pal et al., 1994; Mills et al., 2005). Akbar (2011) has reviewed *Andrographis paniculata* for an array of biomolecules present in the plant with diverse pharmacological efficacy. Aristolochic acid (8-methoxy-6-nitrophenanthro [3,4-d] [1,3] dioxe-5-carboxylic acid)
<table>
<thead>
<tr>
<th>Species name</th>
<th>Plant parts used/solvent/compound</th>
<th>Scorpion used</th>
<th>Proposed mechanism of action/comment</th>
<th>In vitro studies</th>
<th>In vivo studies</th>
<th>Traditional relevance/country of research</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ambrosia maritima</em></td>
<td>Plant/methanol</td>
<td>Leiusurus quinquestriatus</td>
<td>Hepatoprotective</td>
<td>No</td>
<td>Male albino rats</td>
<td>Egypt</td>
<td>Mansour et al. (2007a)</td>
</tr>
<tr>
<td><em>Ambrosia maritima</em></td>
<td>Plant/methanol</td>
<td>Leiusurus quinquestriatus</td>
<td>Renal tissue protective</td>
<td>No</td>
<td>Rats</td>
<td>Egypt</td>
<td>Mansour et al. (2007b)</td>
</tr>
<tr>
<td><em>Ambrosia maritima</em></td>
<td>Plant/methanol</td>
<td>Leiusurus quinquestriatus</td>
<td>Skeletal muscles and intestinal tissue protective</td>
<td>No</td>
<td>Rats</td>
<td>Egypt</td>
<td>Mansour et al. (2011)</td>
</tr>
<tr>
<td><em>Andrographis paniculata</em></td>
<td>Plant/ethanol</td>
<td>Melesobrachus tamulus</td>
<td>Partial venom neutralization activity/no survival benefit</td>
<td>Yes</td>
<td>Mice</td>
<td>India</td>
<td>Brahmane et al. (2011)</td>
</tr>
<tr>
<td><em>Andrographis paniculata</em></td>
<td>Plant/water</td>
<td>Heterometrus laoticus</td>
<td>Anti fibroblast cell lytic activity/anti venom activity with low cytotoxicity</td>
<td>Chick embryonic fibroblast cell</td>
<td>No</td>
<td>Thailand</td>
<td>Uawonggool et al. (2005)</td>
</tr>
<tr>
<td><em>Aristolochia elegans</em></td>
<td>Roots and aerial parts/hexane and methanol</td>
<td>Centruroides limbicus</td>
<td>Antitoxin activity</td>
<td>Isolated guinea-pig ileum</td>
<td>No</td>
<td>Mexico</td>
<td>Izquierdo et al. (2010)</td>
</tr>
<tr>
<td><em>Aristolochia elegans</em></td>
<td>Roots/hexane and methanol</td>
<td>Centruroides limbicus</td>
<td>Significant in vitro antitoxin activity, lower in vivo protection</td>
<td>Guinea pig ileum</td>
<td>Mice</td>
<td>Mexico</td>
<td>Jimenez-Ferrer et al. (2005b)</td>
</tr>
<tr>
<td><em>Barringtonia acanthocalyx</em></td>
<td>Plant/water</td>
<td>Heterometrus laoticus</td>
<td>Anti fibroblast cell lytic activity/anti venom activity with low cytotoxicity</td>
<td>Chick embryonic fibroblast cell</td>
<td>No</td>
<td>Thailand</td>
<td>Uawonggool et al. (2005)</td>
</tr>
<tr>
<td><em>Booivardia ternifolia</em></td>
<td>Roots/hexane and methanol</td>
<td>Centruroides limbicus</td>
<td>Antagonistic to secretagogue effect of poison on pancreas</td>
<td>No</td>
<td>Mice</td>
<td>Mexico</td>
<td>Jimenez-Ferrer et al. (2005a)</td>
</tr>
<tr>
<td><em>Booivardia ternifolia</em></td>
<td>Roots/hexane and methanol</td>
<td>Centruroides limbicus</td>
<td>Significant in vitro and in vivo</td>
<td>Guinea pig ileum</td>
<td>Mice</td>
<td>Mexico</td>
<td>Jimenez-Ferrer et al. (2005b)</td>
</tr>
<tr>
<td><em>Eryngium creticum</em></td>
<td>Leaves and roots/water and ethanol</td>
<td>Leiusurus quinquestriatus</td>
<td>Inhibitory effect to haemolytic activity of the venom/ethanol extract enhanced haemolytic</td>
<td>No</td>
<td>Jordan</td>
<td>Jordan</td>
<td>Alkofahi et al. (1997)</td>
</tr>
<tr>
<td><em>Eryngium creticum</em></td>
<td>Roots/water</td>
<td>Leiusurus quinquestriatus</td>
<td>Inhibitory effect on tracheal and jejunal contractions caused by the venom</td>
<td>Isolated rabbit and Guinea-pig jejunum and trachea</td>
<td>No</td>
<td>Jordan</td>
<td>Affif et al. (1990)</td>
</tr>
<tr>
<td><em>Ginkgo biloba</em></td>
<td>Leaves</td>
<td>Leiusurus quinquestriatus</td>
<td>Protease inhibitory and anti oxidase effective/plant extract in combination with aprotinin</td>
<td>No</td>
<td>Male wistar rats</td>
<td>Saudi Arabia</td>
<td>Fatani et al. (2006)</td>
</tr>
<tr>
<td><em>Vitis vinifera</em></td>
<td>Leaves/hexane and methanol</td>
<td>Centruroides limbicus</td>
<td>Lower in vitro antitoxin activity no in vivo protection</td>
<td>Guinea pig ileum</td>
<td>Mice</td>
<td>Mexico</td>
<td>Jimenez-Ferrer et al. (2005b)</td>
</tr>
<tr>
<td><em>Red grape</em></td>
<td>Seeds/proanthocyanidins</td>
<td>Leiusurus quinquestriatus</td>
<td>Possibly by enhancing antioxidative system and cardioprotective effect by isolated proanthocyanidins</td>
<td>No</td>
<td>Mice</td>
<td>USA</td>
<td>El-Alfy et al. (2008)</td>
</tr>
</tbody>
</table>
isolated from species of Aristolochia, has also been reported for antiophidian properties (Girish and Kemparaaju, 2005).

**CONCLUSION**

Several compounds present in the reported plants are known to possess protein binding and enzyme inhibitory principles which may be directly or indirectly related to the pharmacological activity of the crude extracts of the plants against scorpion venom. However, further research is needed to potentiate this speculation. Antiophidian claims of certain botanicals is encouraging since snake venom neutralizing ability of some plant extracts and isolated compounds can be correlated with their scorpion antivenin ability. Further investigation in this regard may lead to the discovery of certain common antidote which can be applied against snake, scorpion and other insect venoms effectively. Most of the experiments conducted in this area primarily concentrate on in vitro and in vivo assays. To elevate the potential of herbal remedy to the next level of drug discovery programs, extensive clinical trials are required considering the toxicological considerations of certain herbal preparations. Thus, the ethnic claims of anti venin therapy can be considered as the starting point of any potential drug discovery venture. In the present scenario of poverty and remoteness of medicine centers especially in the third world countries the safety, efficacy and cost effectiveness of the antivenins are of prime importance. Less development of side effects and occurrence of drug resistance are the other two aspects of phyotherapy, which are to be considered while developing plant based antivenin as an alternative and complementary therapy to the conventional antivenin treatment.

**REFERENCES**


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