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COMBATING OF SCORPION BITE WITH PAKISTANI MEDICINAL PLANTS HAVING ETHNO-BOTANICAL EVIDENCES AS ANTIDOTE

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Abstract: Although the majority of serious cases in the world are concerned with snake bite envenomation, but those which are caused by scorpion stings are also famous for causing extreme pain. The present view is an attempt to enlist scientifically ignored medicinal plants of Pakistan exhibiting anti-scorpion venom activity. In this review data of 35 medicinal plants is collected with their families, parts used, distribution in Pakistan, and major constituents present in plant. Amaranthaceae, Astraceae and Euphorbiaceae represent 3 species. Anacardiaceae, Asclepidaceae and Liliaceae represent 2 species. Araceae, Capparidaceae, Ceasalpinaceae, Cyperaceae, Labiatae, Lamiaceae, Meliaceae, Menispermaceae, Oleaceae, Oxalidaceae, Pinaceae, Polygonaceae, Rhamnaceae, Rubiaceae, Solanaceae, Valerianaceae and Zingiberaceae represented single medicinal plant with anti scorpion potential. According to literature, all parts are used in anti scorpion envenomination. Leaves exhibit 30%, whole plant 9%, fruit, bark and seeds 8% anti scorpion activity. Bulb and stems show 5% contribution in this respect and twigs, resins, inflorescence, latex and flowers express 3% potential. This article may assist the researchers to bring innovation in natural product field for scorpion bite envenomation. However, these medicinal plants are still requiring pharmacological and phytochemical investigation in order to be claimed as effective in scorpion bite envenomation.

Keywords: envenomation, antidote, medicinal plants, scorpion bite

History of use of natural products starts from very beginning of the human civilization and the history of plant products brought the most successful remedies because of better compatibility with the human body, and enhanced acceptability in human societies. Another reason for the use the herbal products to treat various ailments is their side effects neutralizing combinations (1). Medicinal plants may be defined as those plants which are a source of some drugs or precursors used to treat, mitigate or to prevent a disease or to bring about a change in physiological and pathological processes.

Medicinal plants exert their effect on society of developing country, both as a source of money and for improving the quality of life and health as 80% of human population prefer herbal remedies (2). Current pharmacopoeia comprises at least 25% drugs of plant origin. Currently, about 121 active compounds are being used or synthetic analogues are obtained from natural resources. So the value of medicinal plants cannot be underestimated (3).

Pakistan occupies an area of about 80,943 km^2 and its dimensions include 60^{o}55' to 75^{o}30'E longitude and 23^{o}45' to 36^{o}50' N latitude. Furthermore, the range of altitude is from 0 to 8611 m. Pakistan is blessed with a mixture of climatic zones and distinctive biodiversity of plants having medicinal importance. There are about 6000 species of higher plants in Pakistan out of which 600 to 700 are used for the sake of medicine. A majority of population of

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Pakistan rely on folk remedies for all sort of diseases whether major or minor. Medicinal plants of Pakistan have the ability to cure and treat any sort of complication from minor headache to severe stomachic to cut and wound (3).

Scorpion bite envenoming in humans is the severe cause of clinical problems and even may lead to death. Scorpion bite is the major cause of mortality and morbidity in humans all over the world. Deaths caused by scorpion bite are 10 times frequent than the deaths caused by poisonous snakes. Scorpion bite envenomation is a major health hazard and its prevalence is the same in magnitude as worldwide (4). About 1000-2000 deaths are caused by scorpion bite each year in Mexico and high mortalities occur in Brazil, Israel, Trinidad, Algeria, India, Pakistan and Jordan (5).

Scorpion venom enhances the excitability of muscle and nerve cells. Some venoms act preferentially on muscle cells, whereas others affect neurons and neurotransmitter release. Scorpion venoms cause the release of serotonin, acetylcholine and noradrenaline (5). The sign and symptoms exhibited by the victim involve both central nervous system and autonomic nervous system. Symptoms include intense local pain followed by dilatation of pupils, diarrhea, hypersalivation and vomiting. After adrenergic activities, cholinergic system results in the release of catecholamine which further causes hypertension, arrhythmias, toxic myocarditis, pulmonary edema, and heart failure (5). Death is caused by respiratory failure and cardiovascular manifestation (6). Antivenom therapy is considered to be the only specific remedy for the treatment of scorpion bite envenoming, however, many others are not convinced because of its questionable usefulness in the treatment of cardiovascular manifestation (7). Because of these drawbacks, medicinal use of plants against scorpion bite is adopted as victims are healed by traditional healers.

According to the survey of literature, activity of many plants against scorpion bite has been reported previously. Few examples include: *Arisaema intermedium* Bl, *Asparagus adsendens* Roxb, *Pinus roxburghii* Sargent, *Allium cepa* L., *Amaranthus virdis* L, *Adiantum venustum* D. Don, *Alnus nitida* (Spach.) Endl, *Artemisia biennis* Willd, *Valeriana jatamansi* Jones, *Artemesia maritime* L., *Rumex hastatus* D. Don, *Oxalis corniculata* L., *Achyrathus aspera* L., *Calotropis gigantea* R. Br, *Prosopis cineraria* L. Druce, *Ricinus communis* L., *Pisticia integrimma*, *Adiantum capillus-veneris* L., *Euphorbia caducifolia* Haines (E. neriifolia Auctt.), *Sarcostemma viminale* L., *Rubia manjith*, *Curcuma longa* L., *Cleome gynandra*, *Colocasia esculanta*, *Euphorbia thymifolia* L. However, according to the literature review and to the best of our knowledge, a majority of medicinal plants present abundantly in Pakistan have not been scientifically examined for their anti scorpion activity. A critical and crucial step in antivenom activity is the selection of medicinal plant. There are several ways on the basis of which selection can be done. It includes: traditional use, toxicity, chemical constituents, amalgamation of different criteria or randomized selection (8).

Present article is an endeavor to enlist medicinally important and scientifically ignored plants of Pakistan having ethno-botanical evidences as anti venoms. Its significance can be estimated from the fact that scientific studies of such plants would open a new era in the discovery of novel therapeutic agents, beneficial in scorpion bite, and secondly it would attract the attention of researchers to rationalize the use of these plants as a treatment for scorpion bite in traditional system of medicine.

DATA COLLECTION

Data were collected by literature search. The key words used for collection of data for this article were “anti scorpion, medicinal plants of Pakistan, ethno botanical evidences in scorpion bite and natural products”. Data were collected through internet search on Pub Med, Google and Science Direct using chemical and biological abstracts, plants were selected on the basis of their anti scorpion venom potential in folklore remedies and studied their reference in detail. Previously reported anti scorpion venom constituents are also enlisted with possible mode of action to support anti scorpion venom properties of medicinal plants of Pakistan. The outcome was again checked and compared with the literature.

RESULTS AND DISCUSSION

History of use of natural products starts from very beginning of the human civilization. From very beginning of the history plant products were the most successful remedies because of better compatibility with the human body, enhanced acceptability in human societies. In this article, 35 medicinal plants distributed at various places in Pakistan have been enlisted in alphabetical order of scientific name, place of distribution, family, part used, major constituents and references (Table 1). These species are distributed in 24 families among which Euphorbiaceae and Umbelliferae have maximum representation with 3 plants. Adiantaceae,

Table 1. Medicinal plants of Pakistan used in scorpion bite envenomation.

No.	Botanical name	Family	Occurrence in Pakistan	Part used	Chemical constituents	Ref.
1	*Achyranthes aspera* L.	Amaranthaceae	Pind Dadan Khan	The paste of leaves is applied on scorpion bite	Saponins, oleonolic acid, dihydroxy ketones, alkaloids, long chain compounds	(11, 12)
2	*Adiantum capillus-veneris*. L.	Adiantaceae	Morgah biodiversity park Rawalpindi	Leaves	Triterpenoids, adiantulupanone, phenyl propanoids, flavonoids, β-sitosterol, shikimic acid and quinic acid, saponin glycoside	(9, 13)
3	*Adiantum venustum* D. Don	Adiantaceae	District Buner, NWFP	Fronds	Flavanoids, alkaloids, saponins and carbohydrates	(14)
4	*Allium sepa* L.	Liliaceae	Nara Desert, Sindh	Bulb and leaves	Tannins, flavonoids, volatile oils	(15, 16)
5	*Amaranthus virdis* L.	Amaranthaceae	Balakot, Kawai, Jared, Mahandri and Kaghan Upper Siran	The paste of the root is applied on scorpion sting	Rutin, 5,7,3”,4”, tetrahydroxy flavonol-3-rhamnoglucoside and quercetin 5,7,3”,4”,-tetrahydroxyflavonol, proteins, fat and carbohydrates	(4, 6, 17)
6	*Artemisia maritime* L.	Asteraceae	Paras, Chanul; Kawai; Manur; Kaghan, Naran	The poultice of the flowering tops is given to relieve pain, bite of snake and sting of scorpion	Santonin, flavanoids, polar terpenic constituents	(17, 18)
7	*Arisaema flavum*	Araceae	Sub-alpine regions/ Kaghan valley	Rhizome		(19)
8	*Asphodelus tenuifolius* Cav.	Liliaceae	Kadhi areas of Khushab	The paste of leaves	Alkaloids	(20, 21)
9	*Azadirachata indica* A. Juss	Meliaceae	Godi khel & its outskirts hilly areas, District Karak	Bark, leaves, twigs and seeds	Alkaloids, Aiplai	(1, 22)
10	*Calotropis gigantean* R. Br.	Asclepiadaceae	Pind Dadan Khan	Latex is externally applied on scorpion bites.	Calotropin, calotropagenin, uscharine, calotoxin, calactin and voruscharine	(11, 23-26)
11	*Cassia occidentalis* L.	Caesalpinaceae	Lahore-Islamabad Motor way (M-2)	Roots	Emodine, oxymethyl-anthraquinones, toxalbumin, tannic acid, mucilage and fatty oil.	(27)
12	*Cleome gynandra*	Capperdiceae	Common weed in Karachi, Sind, Punjab during monsoon	Leaves, seed, root, juice	Alkaloids, flavonoids, steroids, saponins, carbohydrates, proteins, phenols, and glycosides	(4, 28)
13	*Colocasia esculenta*	Araceae	Corm juice is used in scorpion bite	Leaf juicej	Anthocyanins, cyanidin 3-glucoside, pelargonidin 3-glucoside and cyanidin 3-rhamnoside	(4, 29, 30)
14	*Cyperus niveus* Retz	Cyperaceae	Lahore -Islamabad Motor way (M-2)	Root	Flavonoles, phenolic acids, aurone	(27, 31)

Table 1. cont.

No.	Botanical name	Family	Occurrence in Pakistan	Part used	Chemical constituents	Ref.
15	*Eclipta alba* (L.) *Hassk.*	Asteraceae	Peshawar Khyber Pakhtun Khwa (KPK)	Leaves	Wedelolactone, demethylwedelolacton, stigmasterol, α-terthienymethanol, desmethyl-wedelolactone-7-glucoside, alkaloid, apigenin, luteolin, weldic acid, 25-β-hydroxyverazine, ecliptine, nicotine	(32, 33)
16	*Euphorbia caducifolia* Haines = *E. neriifolia* Auctt.	Euphorbiaceae	Greater Cholistan desert of Pakistan	Milky juice of leaves	Triterpenes are found in latex (euphol, tirucallol, Cycloartenol and cyclocaducinol.	(4, 34, 35)
17	*Euphorbia thymifolia* L.	Euphorbiacea	Karachi, Sind, Lasbella, Indus delta, Turbat	Whole plant juice is recommended in scorpion bite.	Steroids, tannins, flavonoids, sugars	(4, 36)
18	*Lagenaria siceraria*	Cucurbitacae	Sahiwal district of Punjab, Pakistan	Pulp of fruit	Alkaloids sterols, saponins, and carbohydrates	(37-39)
19	*Mangifera indica* L.	Anacardaceae	District Dera Ismail Khan KPK	Inflorescence of mango	Phenols, pentagalloyl glucopyranose	(39, 40)
20	*Ocimum basilicum* L.	Lamiaceae	Mahal Kohistan (Khirthar National Park)	Leaves	Caffeic acid, rosmarinic acid, apigenin	(41)
21	*Olea ferruginea* Royle	Oleaceae	Lahore-Islamabad Motorway (M-2)	Root	Alkaloids, terpenoids, saponins, tannins, sugars, phenolics, flavanoids, cardiac glycosides	(5, 27)
22	*Oxalis corniculata* L.	Oxalidaceae	In shady places in Sind, NWFP, Chitral, Hunza and Hazara	Leaves	Acid potassium oxalate, isoorientin, isovitexin and swertisin	(4, 6, 10, 43, 44)
23	*Pinus roxburghii* Sargent	Pinaceae	District Buner, NWFP, Murree hills, Swat, Dir, Hazara (600-1500 m)	Resin	α-Carene, β-carene, α-pinene and β-pinene	(6, 44)
24	*Pisticia integrimma*	Anacardiaceae	Upper Siran	Galls, bark	Tannins, essential oil, resin, triterpenic acid, pistacienoic acid, triterpene alcohol and triterpenoic acid	(10, 34, 45)
25	*Prangos pabularia* Lindle.	Umbelliferae	Chitral Gol National Park (CGNP) Pakistan	Leaves	Coumarins, furocoumarins, alkaloids, phenolic acids and lactonic constituents	(23, 46)
26	*Prosopis cineraria* (L.) Druce	Mimosaceae	Pind Dadan Khan	Bark is used in scorpion sting	Flavanoids, tannins, phytosterols, carbohydrates, alkaloids, proteins and aminoacids.	(11, 47)
27	*Ricinus communis* L.	Euphorbiaceae	Pind Dadan Khan	Seeds	Flavanoids and tannins	(11, 48)
28	*Rubia manjith*	Rubiaceae	Swat	Stems	Rubiadin	(49)
29	*Rumex hastatus* D. Don	Polygonaceae	Common throughout Hazara.	Leaves, juice, seeds	Hastatusides A and B, resveratrol, rumexoside, torachrysone-8-yl β-D-glucopyranoside, rutin, nepodin, and orientaloside, flavonoid	(17, 39)

Table 1. cont.

No.	Botanical name	Family	Occurrence in Pakistan	Part used	Chemical constituents	Ref.
30	*Sarcostemma viminale* L.	Asclepiadaceae	Greater Cholistan desert of Pakistan	Roots	β-Amyrin, friedelin and viminalol	(50, 51)
31	*Trachydium roylei* Lindl.	Umbelliferae	Droneel Sosoom Lutkhoo, 2476 m Chirtal Valley, Pakistan		Leaves	(52)
32	*Valeriana jatamansi* Jones	Valerianaceae	Swat Kohistan, Pakistan	Rhizome	Phenols, flavonoids, tannins	(14, 40)
33	*Ferula narthex* Boiss.	Umbelliferae	Harcho nullah near the atwashi village, Kamari, Damusar, Zail, Kluma, Bubin, Chillim, Rattu, Astore, Boosthon, Doian, Gudai and at the hill of Majini Harai Bulashbar nullah in a scarcity.	Gum resin is used in scorpion sting	Luteolin and pinene	(3)
34	*Skimmia laureola* M. Roem	Rutaceae	Hilly areas of NWFP	Whole plant		(53)
35	*Phyla odiflora* L.	Verbenaceae	Sindh	Leaves		(54)

Amaranthaceae, Anacardiaceae, Araceae, Asclepidaceae, Astraceae and Liliaceae are the famililies which have 2 species exhibiting anti scorpion activity. Caesalpinaceae, Capparidaceae, Cucurbitaceae, Cyperaceae, Lamiaceae, Meliaceae, Mimosaceae, Oleaceae, Oxalidaceae, Pinaceae, Polygonaceae, Rubiaceae, Rutaceae, Valerianaceae and Verbenaceae represented single medicinal plant with anti scorpion potential (Fig. 1). The literature reveals that all the plants are distributed at various places throughout Pakistan. According to literature, all parts are used in anti scorpion envenomination. Leaves exhibit 39%, roots 15%, stems and seeds 10% bark 8%, and whole plant 5% anti scorpion activity. Whole plant, resin, and flowers have 5% contribution in this respect and latex express 3% potential (Fig. 2).

Unlike the extensive studies on plants used against snake bite, no specific reports on pharmacological or clinical studies are found about the efficacy of plants against scorpion bite. The efficacy of plants against scorpion sting may be associated with the presence of various phytochemicals, while symptomatic relief may be due to anti-inflammatory, anti-pruritic and analgesic effects.

The phytochemicals concerned with such an effect are expected to be unusual but another study (9) reveals that for snake bite, common constituents of certain plants used for this activity in Brazil, such as β-sitosterol and some flavonoids like quercitin, exhibit anti-inflammatory action. These compounds may be present in adequate quantity in various species enlisted in the table that would result in a remarkable effect in scorpion sting as well. Another possible mechanism may involve complexation of constituents with venom and subsequent prohibition to act on receptors.

Another mechanism may involve quick antagonism or metabolism of catecholamines released as a result of interaction of venom with receptors. The intensity of envenomation effect can also be reduced by non-specific stimulation of the immune system that would result in neutralization or phagocytosis of the pep-

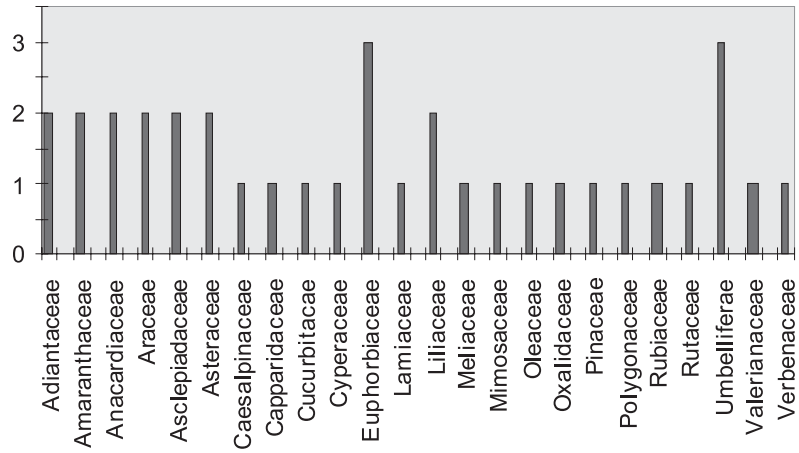

Figure 1. Various families with their number of plants having anti-scorpion venom potentials

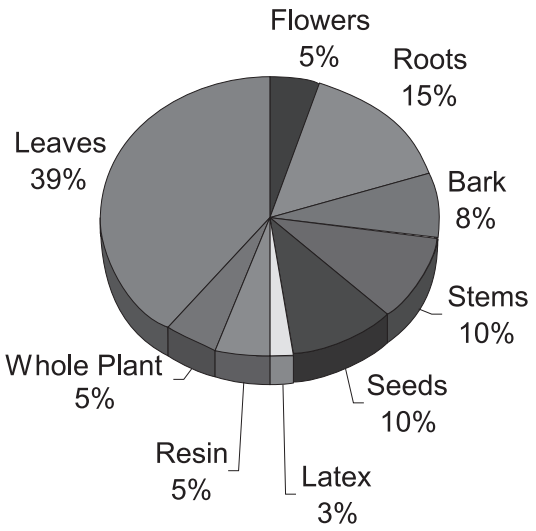

Figure 2. Percentage of different plant parts used in scorpion bite envenomation

tides of venom. Phospholipase enzymes play significant role in the cascade which leads to pain and inflammatory responses. The inhibition of these enzymes may relieve scorpion envenomation (10). In this article, authors have gathered the data about folklore reported medicinal plants of Pakistan having potentials of anti-scorpion venom. These plants contain various types of flavonoids, steroids, triterpenoids, alkaloids, tannins and coumarins. Full activity of a plant cannot be attributed to a single constituent; instead, full activity of a plant extract is due to the synergistic effect of various constituents on various target structures (enzymes and receptors). Usually chemical constituents are multifunctional as they perform more than one biochemical or pharmacological functions simultaneously.

CONCLUSION

In this article, data of 35 medicinal plants is collected which are used in the folklore treatment of scorpion sting in various parts of Pakistan. It is quite evident that till now there are many unexplored plants that can be used to treat scorpion bite. These plants can be used as alternative remedy for the treatment of scorpion sting if they are validated scientifically. Though scorpion bite envenomation is not a big problem yet it is unlikely that some clinically and medicinally important compounds can be isolated and used as important tools in pharmacological investigations. Therefore, there is a great need for phytochemical investigation of these plants as it may assist understanding the pharmacology, physiology and pathology of scorpion bite and other related complications.

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