African Journal of Pharmacy and Pharmacology Vol. 5(20), pp. 2292-2305, 29 November, 2011
Available online at http://www.academicjournals.org/AJPP
DOI: 10.5897/AJPP11.593
ISSN 1996-0816 ©2011 Academic Journals

Full Length Research Paper

Enlisting the scientifically unnoticed medicinal plants of Pakistan as a source of novel therapeutic agents showing anti-venom activity

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Accepted 23 September, 2011

Snake bite envenoming is a global occupational hazard and most of the people of the world trust in traditional medicine for snake poisoning. The present review elaborates scientifically un-investigated/ ignored medicinal plants of Pakistan showing chemical constituents of natural origin with possible mechanisms showing anti-venom activity. This review enlists 35 plants with their families, distribution in Pakistan, parts used traditionally for snake bite treatment and various active principles present in them. Compositae is the most excessive family, with 3 species, followed by Amaranthaceae, Apocynaceae, Asclepiadaceae, Caesalpinaceae, Labiatae, Pinaceae, Polygonaceae and Verbinaceae having 2 species of medicinal plants. While, one plant species belongs to each, Aizoaceae, Araceae, Boraginaceae, Chenopodiaceae, Cucurbitaceae, Euphorbiaceae, Flacourtiaceae, Gentianaceae, Malvaceae, Menispermaceae, Mimosaceae, Oxalidaceae, Papilionaceae, Plantaginaceae, Salvadoraceae and Solanaceae. As an antidote to snake poisoning, the traditional use of leaves (35%) is higher than roots (25%), whole plant (21%), flower (7%), wood (5%), fruit (5%) and milky juice (2%). Among life forms of plants, herbs (55%) are more excessively used as snake bite remedy than shrubs (31%) and trees (14%). This article may help the researchers to bring novelty in the field of natural products for the treatment of snake bite. However, chemical and pharmacological studies are necessary to confirm the anti-venom claims about these medicinal plants of Pakistan.

Key words: Venom, anti-venom, herbal remedy, scientific characterization.

INTRODUCTION

History of natural products is as old as human civilizations. From ancient time, products from plants were the successful remedies due to their enhanced acceptability in human societies, better compatibility with the body and to treat different ailments due to their synergistic and/or side effects neutralizing combinations (Rates, 2001). Plants that are source of some drugs or their precussor in order to prevent, mitigate and cure a disease or to alter physiological and pathological processes are known as medicinal plants. Medicinal plants have an impact in the society of developing countries, not only as a source of income but also for improving health, because 80% of human population rely on herbal remedies (Shah et al., 2009). Modern pharmacopoeia consists of at least 25% of the drugs that come from plant origin, 121 of such active compounds are being in current use or synthetic analogue are obtained from natural precursors. Hence, importance of medicinal plants cannot be under estimated (Shinwari, 2010).

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Figure 1. Map of Pakistan representing distribution of snakes from genus *Naja* (A guide to the Onakoo of Pakistan, 2002).

Pakistan has an area 80,943 km^2 and it lies between 60° 55' to 75° 30' E longitude and 23° 45' to 36° 50' N latitude. Moreover, it has an altitude ranges from 0 to 8611 m, with mixture of climatic zones and distinctive biodiversity of medicinal plants. Pakistan has 6,000 species of higher plants, 600 to 700 of which are used for medicinal purposes. Majority of Pakistan's population depends on folklore remedies for minor and major diseases. Medicinal plants of Pakistan have potentials to treat any sort of disease from headache to stomachic to cut and wound (Shinwari, 2010).

Snake bite envenomation is one of the challenging threats in Pakistan, because 20,000 deaths occur annually due to this reason and numerous cases of chronic physical handicaps are reported (Gutiérrez et al., 2006). Snakes belonging to genus *Naja* are *Naja naja* (●) and *Naja oxiana* (o) are deadly poisonous and are distributed throughout Pakistan (Figure 1). Cytotoxicity, myotoxicity, oedema, pain, necrosis, haemorrhage, fang marks in the skin, diarrhea, burning, convulsions, dizziness, weakness, blurred vision, fever, excessive sweating, tingling and high pulse rate are the major complications of snake bite (Razi et al., 2010; Das, 2009).

Administration of antisera is the most appropriate remedy for snake bite. However, antisera have some side effects, that is, anaphylactic shock, serum sickness, pyrogenic reactions and it is not useful in protecting venom induced nephrotoxicity, haemorrhage, local tissue damage and necrosis. Moreover, antisera development is precious, time consuming, tedious and requires strict storage conditions (Razi et al., 2010). Due to these drawbacks in antiserum therapy, medicinal use of plants against snake bite has long been recognized because traditional healers are first line defense for snake bite victims.

According to the literature survey, various plants have been reported previously to be active against snake bite. The following are the few examples: *Acacia catechu* Willd*, Belamcanda chinensis* DC, *Caesalpinia bonduc Roxb, Daphne mezereum* L, *Echinacea angustifolia* DC, *Fagopyrum cymosum* Meissn, *Gentiana lutea* L, *Harpalyce brasiliana Benth, Impatiens balsamina* L, *Liatris squarrosa* Willd*, Macfadyena unguis-cati Gent, Nerium oleander* L*, Ocimum basilicum* L*, Pentaclethra macroloba* (Willd.) Ktze*, Ruta graveolens* L, *Serenoa repens* Small, *Taraxacum officinale* Weber and *Verbascum thapsus* L (Mors et al., 2000). However, to the best of our knowledge and according to the literature search, majority of medicinal plants widespread in Pakistan have not been scientifically evaluated for their anti-venom potentials. Selection of medicinal plants for anti-venom activity is very important and crucial step. Selection can be done by several ways including traditionnal use, chemical content, toxicity, randomized

selection or amalgamation of different criteria (Rates, 2001). In the present article, an effort has been made to enlist scientifically ignored Pakistani medicinal plants having folklore (ethno-botanical) evidences as anti-venoms. It is very essential, primarily because scientific (chemical and biological) studies of such medicinal plants would be helpful for the discovery of novel therapeutic agents, beneficial in snake poisoning in future, and secondly to attract the attention of researchers in order to rationalize their uses as a remedy for snake bite in traditional system of medicine.

DATA COLLECTION

The key words used for the literature search of this article were "Pakistani medicinal plants, anti-venom, ethnobotanical evidences in snake bite and natural products". Data collection was carried out through internet search on Science Direct, Google and PubMed using biological and chemical abstracts. Selection of plants was focused on their potentials as anti-venom in folklore remedies and their references were studied in details. Search was also made to enlist already reported anti-venom constituents with possible mechanism to support the anti-venom characteristics of medicinal plants of Pakistan. The outcome of the results were rechecked and compared with literature.

RESULTS

Humans have been using plants as medicines since the start of civilization. Thus, the plants have important role in human life on this planet. The ascendancy of folklore remedies of medicinal plants as anti-venom has spurred to develop an inventory of such plant species. In this article, 35 medicinal plants occurring in Pakistan and their crucial information have been enumerated in alphabetical order of plant scientific name, family, place (distribution), part used, major constituents and references (Table 1). Those species that are distributed in 25 families of which Compositae stood out with maximum representation with 3 plants species exhibiting anti-snake venom potentials. Amaranthaceae, Apocynaceae, Asclepiadaceae, Caesalpinaceae, Labiatae, Pinaceae, Polygonaceae and Verbinaceae are the families which hold 2 species showing snake envenoming remedy, while, Aizoaceae, Araceae, Boraginaceae, Chenopodiaceae, Cucurbitaceae, Euphorbiaceae, Flacourtiaceae, Gentianaceae, Malvaceae, Menispermaceae, Mimosaceae, Oxalidaceae, Papilionaceae, Plantaginaceae, Salvadoraceae and Solanaceae were found with single medicinal plant of such potential (Figure 2). All species are distributed throughout Pakistan in different places like Cholistan, Ther and Interior Sindh (Table 1). Literature search revealed that each part of the plant has been used in the treatment of snake biting. Leaves represent 35% anti-snake venom features. Among the rest parts of the plant, root form 25%, whole plant 21%, flower 7%, Bark (wood) 5%, fruit 5% and milky juice showed 2% helpfulness in the management of snake poisoning (Figure 3). It was noticed that different medicinal plants were found with different life forms (habits). Among them, herbs (55%), shrubs (31%) and trees (14%) were conspicuous (Figure 4). It seemed that herbs are more effective in snake envenoming than shrubs and trees.

DISCUSSION

Plants efficacy to neutralize snake venom may be due to certain chemical compounds possessing anti-lethal effects (Mors et al., 2000). Among them steroids, triterpenes, acids (benzoic acid, cinnamic acid, chlorogenic acid and aristolochic acid derivatives), phenylpropanoid derivatives, curcuminoids, coumarins, flavonoids, polyphenols and polysaccharides have been isolated and tested as anti-venom previously (Table 2). In this article, authors found that folklore reported medicinal plants have potentials of anti-venom due to the presence of copious forms of flavonoids, steroids, tannins, triterpenoides and coumarins, while a single substance does not reproduce the full activity of an extract rather more than one active constituent present in the plants acting synergistically on various target structures (receptors and enzymes). Commonly, these chemical constituents are considered 'multifunctional', in the sense that they exhibit more than one pharmacological or biochemical property (Table 2). Therefore, multi-func-tionality has built an illustration in the capacity of such chemical substances to stick to proteins, hence obstruct the functions of many macromolecules. We suggest that these substances are responsible for observed protection but the time has come to validate pharmacologically traditional evidences of Pakistani medicinal plants as antidote for snake victims.

Search was also made to enlist already reported anti-venom constituents with possible mechanism to support the anti-venom characteristics of medicinal plants of Pakistan (Afzal et al., 2009).

Conclusion

In the present article, folklore use of enlisted 35 medicinal plants as anti-snake venom spread in Pakistan are recorded and documented. Nowadays, importance of such medicinal plants has been realized because many of them proved to be effective as antidote for snake poisoning. However, there is a need for detailed scientific verification especially chemical investigations. Furthermore, studies with new active constituents are essential for the understanding of physiology, pathology and pharmacology of snake bite as well as other related disorders.

Table 1. Scientifically ignored medicinal plants of Pakistan possessing ethno-botanical evidences as antidote in snake poisoning.

S/N	Botanical names of plant	Family	Occurrence in Pakistan	Part used in snake bite	Chemical constituents (if any)	References
1	*Ageratum houstonianum* Mill	Compositae	District Attock	Leaves and inflorescence juice is used as antidote to snakebite.	Precocene-II, precocene-I and β-caryophyllene.	(Ahmad et al., 2006; Kurade et al., 2010)
2	*Albizia lebbeck* (L.) Benth	Mimosaceae	Karachi, Sind, Punjab, Kutch, Indus dalta	All parts are recommended in snakebite.	Alkaloid, tannins, carbohydrate, flavanoids, proteins, echinocystic acid and amino acids.	(Baquar, 1989; Chulet et al., 2010; Ahmad, 2007)
3	*Althaea officinalis* Linn	Malvaceae	Morgah biodiversity park, Rawalpindi	Leaves and roots are used for snake bite.	Fatty oil, butyric acid, phytosterin, mucilage and starch.	(Husain et al., 2008; Chopra et al., 1956)
4	*Amaranthus viridus*	Amaranthaceae	Common throughout Pakistan	Leaves are effective in snake bite.	Rutin, 5, 7, 3', 4', tetrahydroxy flavonol -3-rhamnoglucoside and quercetin 5, 7, 3', 4', - tetrahydroxy flavonol. Proteins, fat and carbohydrates	(Baquar, 1989; Ashok et al., 2009; Ahmad and Javed, 2007)
5	*Amaranthus hybridus* L.	Amaranthaceae	Peshawar	Leaves are used as an antidote to snake bite	Alkaloid, flavonoid, saponin, tannins, phenols, hydrocyanic acid, phytic acid, vitamin A, vitamin B_1, vitamin B_2, vitamin B_3, vitamin B_6, vitamin C, vitamin E, minerals (Na, K, Ca, Mg, Fe, Zn, P) and amino acids	(Shah et al., 2006; Akubugwo et al., 2007)
6	*Artemisia scoparia* Walds and Kit	Compositae	Punjab plains to 2000 m and Baluchistan	Whole plant is used as antidote to snakebite	Essential oil, crystalline lactone scoparin, 01-phenyl-penta-2,4-diyne, beta-pinene, limonene and (*E*)-beta-osimene	(Baquar, 1989; Jhomi et al., 2005; Chopra, 1956; Ahmad et al., 2006)
7	*Bauhinia variegate* L.	Caesalpinaceae	Margala hills National Park Islamabad, sub Himalayan tracts from Indus eastward	Root is used as an antidote to snake poison	Gum, tannins and fatty oil	(Baquar, 1989; Ahmad, 2009)

Table 1. Contd.

8	*Calotropis procera* (Wild.) R.Br	Asclepiadaceae	Greater Cholistan desert, Karak district	Milky latex of plant is applied on snakebite area to neutralize poison.	Calotropin, calotropagenin, uscharine, calotoxin, calactin and voruscharine	(Khan, 2002; Schmid and Bencze, 1953; Mahran et al., 1973; Chopra, 1956)
9	*Cassia occidentalis* Linn	Caesalpinaceae	Mostly found in Lahore-Islamabad Motorway (M-2), waste places in rawalpindi district and Baluchistan	Roots are used for snakebite.	Emodine, oxymethyl-anthraquinones, toxalbumin, tannic acid, mucilage and fatty oil.	(Ahmad, 2007; Baquar, 1989)
10	*Cedrus deodara* G. Don	Pinaceae	Chitral, Swat, Astor, Hazara division, Murree hills and in Kashmir.	Wood (bark) is used for snakebite.	Gum, essential oil, cholesterin and ascorbic acid in needle.	(Hussain et al., 2006, Baquar, 1989)
11	*Chenopodium album* Linn	Chenopodiaceae	Margala hills National Park, Islamabad.	Fruit and roots are used as antidote to snake bite.	Essential oil, carotene and vitamin C.	(Shinwari, 2000; Baquar, 1989)
12	*Cissampelos paperia* Linn	Menispermaceae	Sind, Punjab plains up to 2000 m.	Leaves are used for snake bite.	Sepeerine, bebeerine, cissampelline, hyatin and hyatinin.	(Shinwari, 2000; Baquar, 1989)
13	*Coccinia grandis* Linn	Cucurbitaceae	Lasbela, Karachi and Indus delta.	Plant is effective against snake biting.	Triterpenoides, carotenoides, flavonoids, alkaloids and fatty acids.	(Farrukh et al., 2008; Baquar, 1989; Singh et al., 2007)
14	*Enicostemma hyssopifolium* (Willd.) Verdoorn	Gentianaceae	Karachi, Sind, Indus delta, Kutch and Jhellum district.	Fresh plant is grinded and applied on area of snakebite.	Flavonoids with glycosides (apigenin, genkwanin, isovitexin, swertisin, saponarin, 5-*O*-glucosylswertisin, 5-*O*-glucosylisoswertisin), alkaloid (erythrocentaurin) and ophelic acid.	(Baquar, 1989; Ghosal and Jaiswal, 2006; Chopra, 1956; Khan, 2009)
15	*Euphorbia caducifolia* Haines	Euphorbiaceae	Karachi, Sind, Baluchistan and Indus delta.	Milky juice of leaves is effective in snakebite.	Triterpenes are found in latex (euphol, tirucallol, cycloartenol and cyclocaducinol).	(Baquar, 1989; Afza et al., 1989; Khan, 2009)

Table 1. Contd.

16	*Flacourtia indica* (Burm.) Merr.	Flacourtiaceae	Sub-Himalayan zone 600 - 1000 m, Rawalpindi district, Poonch, Punjab and Swat	Leaves are crushed and applied topically on the point of snakebite	Phytosterol, β-sitosterol-β-D-glucopyranoside, ramontoside, butyrolactone, lignan disaccharide, flacourtin and coumarins (scoparone and aesculetin)	(Baquar, 1989; Gnanaprakash et al., 2010; Khan, 2002)
17	*Leucas capitata* Desf.	Labiatae	Margala hills National Park Islamabad, Trans-Indus, Swat, Rawalpindi, Poonch, Dir, Chitral and Lower Hazara	Whole plant is used for snake bite	Essential oil and alkaloids	(Shinwari, 2000; Baquar, 1989)
18	*Marrubium vulgare* Linn	Labiatae	Ziarat juniper forest Baluchistan, Khuram, Swat, Thal, Chitral, Fort Sandeman	Roots are remedy for the bite of rattlesnakes	Bitter substances, essential oil and marrubin	(Flora of Zairat, 2008; Baquar, 1989)
19	*Nerium indicum* Mill	Apocynaceae	Throughout Pakistan	Leaves, roots and flowers are used against snake bite	Cardiotoxins, neriodorin, nerioderin, odorin and karabin	(Naqvi et al., 1994; Baquar, 1989)
20	*Oxalis corniculata* Linn	Oxalidaceae	In shady places in Sind, NWFP, Chitral, Hunza and Hazara	Leaves are used in snakebite	Acid potassium oxalate, isoorientin, isovitexin and swertisin	(Mizokami et al., 2008; Chopra, 1956; Baquar, 1989; Qureshi et al., 2009)
21	*Pinus roxburghii* Sargent	Pinaceae	Murree hills, Swat, Dir, Hazara (600 - 1500 m)	Wood and oleoresin is used in snakebite	A-carene, B-carene, A-pinene and B-pinene	(Baquar, 1989)
22	*Plantago lanceolata* Linn	Plantaginaceae	Throughout Pakistan, except Sind, Western Himalaya, Salt Range, Waziristan	Roots are remedy for the bite of rattlesnakes	Plant contains glucoside aucubin	(Baquar, 1989; Flora of Zairat., 2008)

Table 1. Contd.

23	*Rhazya stricta* Dcne.	Apocynaceae	Plains between Indus and Jhellum, Karachi, Sind, Lasbella,Khyber, Malakand, Dargai, Salt Range and Attock.	Fruit and leaves are antidote to snakebite	Flavonoids (rhazianosides A and rhazianosides B), glycosides (isorhamnetin-3-7-rhamnoside, 3-7-rhamnoside and roblnin), triterpenes (Beto-sitosterol, Mg quinate and urosoic acid), enzymes (strictosidine synthase and NADPH dependent tetrahydroaistonine) and alkaloids	(Baquar, 1989, Treimer and Zenk, 1979; Kaneko and Namba, 1967; Andersen et al., 1987; Kaneko and Namba, 1967; Panhwar and Abro, 2007)
24	*Rumex hastatus* D.Don	Polygonaceae	Hazara division.	Juice of leaves is used for snakebite	-	(Jan et al., 2008)
25	*Rumex vesicarius* Linn	Polygonaceae	Sind, Baluchistan Coasts, South Waziristan, Peshawar, Salt Range, Abbottabad, Hazara, Hasan Abdal, Margalla, up to 1200 m	Leaves are used for snakebite	Minerals (Ca, Cu, Fe, Mg, K, Na, Zn), proteins, lipids, ascorbic acid, tocopherol, citric acid, malic acid and oxalic acid	(Baquar, 1989; Chopra et al., 1956; Alfawaz, 2006)
26	*Salvadora persica*	Salvadoraceae	It is found abundantly all over the Pakistan	Leaves and flowers are used for snake biting	Carbohydrates, alkaloid (salvadorine), steroids, terpenoids, saponins, flavonoids (quercetin and kaempferol)	(Almas, 2001; Kamil et.al., 1999, a, b, c; et al., 2000a, b)
27	*Sarcostemma viminale* Linn.	Asclepiadaceae	Greater Cholistan desert	Roots are powdered and poultice is applied on the area of snakebite	Beta-amyrin, friedelin and viminalol	(Khan, 2002; Torrance and Marais, 2006)
28	*Sauromatum guttatum* Schott.	Araceae	Swat, Hazara, Chikar, Rawalpindi, Murree and Kashmir	Stimulating poultice in snake bite	Lectins, Dimethyl sulphides, p-caryophyiiene, indole, skatole, ammonia, trimethylamine and primary amines	(Nasir , 1978; Baquar, 1989; Smith and Meeuse, 1966; Borg- Karlson et al., 1994; Chen and Meeuse, 1971; Shinwari and Khan, 2000)

Table 1. Contd.

29	*Solanum xanthocarpum* Schard & Wendl	Solanaceae	Common in waste places from plains to 1500 m; throughout Pakistan	Root is used for snakebite	Solanocarpine, solanocarpidine, solanines and carpesteral.	(Baquar, 1989; Shah et al., 2006)
30	*Taraxacum officinale* Weber	Compositae	Common throughout Punjab and Baluchistan from 350 - 6000 m	Leaves and roots are antidote to snakebite	Taraxacin, taraxacerin, tataxerine, taraxerol, taraxasterol, homotaraxasterol, 3,4 dioxycinnamic acid, flavoxanthin, inulin, citric acid, pheyloxyacetic acid, riboflavin, sitosterol, sitosterin, stigmasterol and coumestro.	(Baquar, 1989; Stuart, 1979; Chopra, 1956; Ahmad et al., 2006)
31	*Trichodesma indicum* (Linn) R.Br	Boraginaceae	Plains to 1400 m throughout Pakistan	Leaves are antidote to snakebite	Fatty acids and non-steroidal compounds.	(Baquar, 1989; Panhwar and Abro, 2007; Hassan et al., 1982)
32	*Verbena officinalis* Linn	Verbinaceae	Mostly distributed in Potwar Plateau, moist mountains and arid/semi-arid mountains including Northern Balochistan, Sulemania range, Waziristan, Kurram agency, Gilgit and Chitral	It is recommended for snake bite	Glucoside, verbenalin and verbenin.	(Khan et al., 2006; Baquar, 1989)
33	*Vicia sativa L.*	Papilionaceae	Kallar Kahar, Rawalpindi, Hasan Abdal, Abbottabad	Whole plant is used for snake poison	Hydrocynic acid, vicianine and glucosides	(Ahmad, 2008; Baquar, 1989)
34	*Vitex negundo* Linn	Verbenaceae	Charkotli hills, Batkhela district, Malakand	Leaves are used for snake bite	Alkaloid, essential oil and nishindine.	(Baquar, 1989; Barkatullah and Hussain, 2009)
35	*Zaleya pentandara* (L.) Jeffery	Aizoaceae	Mostly in the coastal areas of Pakistan	It is recommended for snake bite	-	(Khan et al., 2006)

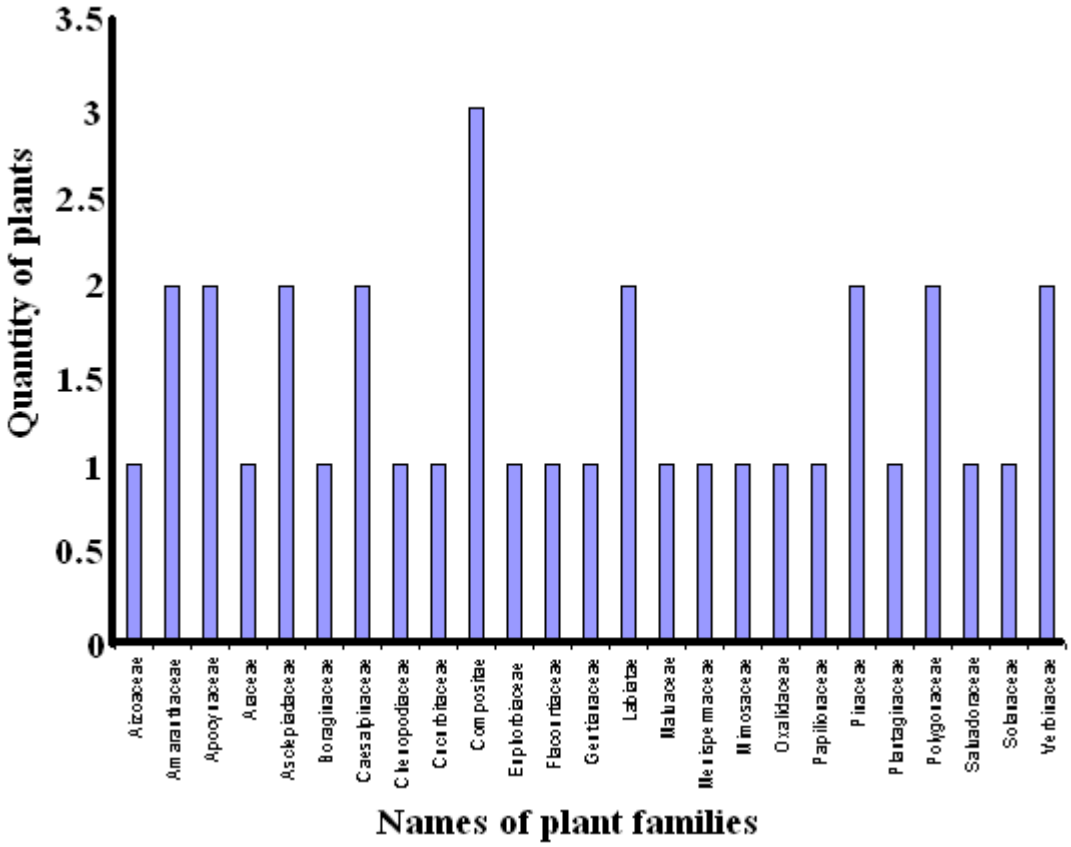

Figure 2. Various families with their number of plants having anti-venom potentials.

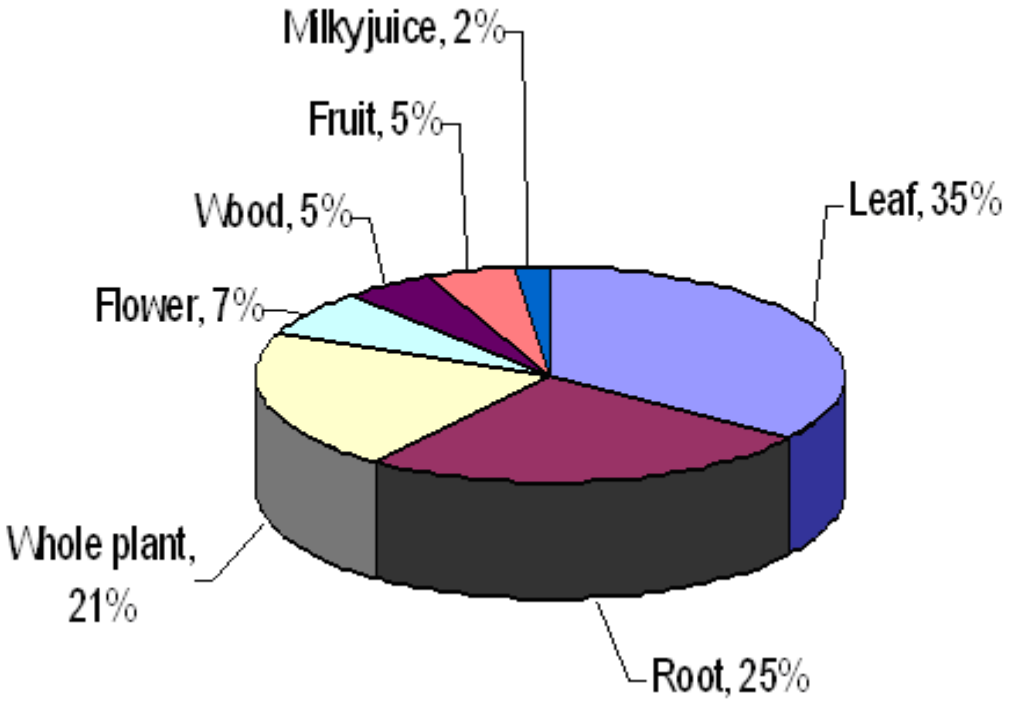

Figure 3. Percentage of different parts of plants used in the treatment of snake poisoning.

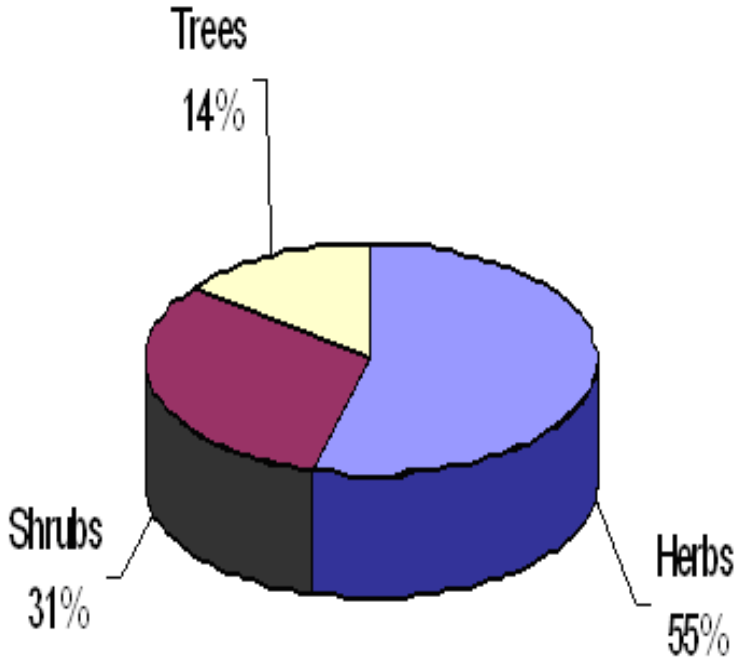

Figure 4. Different life forms of medicinal plants effective in snake bite.

Table 2. Reported chemical substances possessing anti-venom activity found in various plants.

S/N	Class	Chemical constituent	Possible mechanism / anti lethal effect	References
1	Steroids	Sitosterol (70% protection)	Anti-inflammatory	(Mors et al., 2000)
		Sitosterolin	Anti-inflammatory	
		Stigmasterol (analogue of sitosterol)	Anti-inflammatory	
		Dehydrocholic acid (80% protection)	By complex formation	
		Cholesterol (60% protection)	Cholesterol combines with lysolecithin thus produces antihemolytic effect.	
		Corticosteroids	Protective mechanism comparable to antivenom steroids due to chemical analogy.	
		Tigogenin (40% protection)	Anti-inflammatory	
		Hecogenin (20% protection)	Anti-inflammatory	
		α-spinasterol	Anti-inflammatory	

Table 2. Contd.

2	Triterpenes	Oleanolic acid, Lupeol (20% protection) Ursolic acid, Taraxerol, Taraxasterol, α-Amyrin, β-Amyrin, Friedelin (40% protection), Epifriedelinol, Alnusenone, Betulinic acid (40% protection) Betulinol (40% protection), Bredemeyeroside (80% protection), Echinocystic acid, Cycloartenol, Quinovic acid, Presenegenin, Alnusenone, Gymnemagenin Gypsogenin,	All possess anti-snake venom and anti-inflammatory properties due to five-ring structure of a triterpenes and related conformation are important for achievement of liable pharmacophore.	(Mors et al., 2000)
3	Hydroxy benzoic acid derivatives	Primveroside 2-hydroxy-4-methoxybenzaldehyde 2,4-dihydroxybenzoic acid (83% protection) Protocatechuic acid (80% protection) 4-O-methyl ether of 2,4-dihydroxybenzoic acid 4-O-methyl ester of 2,4-dihydroxybenzoic acid 4-hydroxy-3-methoxy-benzaldehyde Veratrum aldehyde Gentisic acid (2,5-dihydroxy- benzoic acid) 3,4-dihydroxybenzaldehyde Monomethyl ether of 2,6-dihydroxybenzoic acid (40% protection)	Anti-inflammatory activity Tyrosinase inhibitor Rest all of all produces effects (1) By attaching proteins, occupying critical binding sites. (2) By conjugation with compounds of primary metabolites. (3) By chelation (seizing of metal atoms). (4) By phenolases oxidation of phenols to quinones, which ultimately condense with proteins resulting in copolymerization.	(Mors et al., 2000; Mason, 1955)
4	Cinnamic acid derivatives	Caffeic acid and caffeic acid derivatives (verbascosides, rosmarinic acid, Myricerone caffeate and oligomers of caffeic acid). Ferulic and isoferulic acid	Caffeic acid is a strong lipoxygenase inhibitor and antihepatoxic activity. Myricerone caffeate is selective endothelin receptors antagonist.	(Mors et al., 2000)
5	Chlorogenic acid	3-0-caffeyl-D-quinic acid (caffeic acid esterified with quinic acid) 60% protection.	Lipoxygenase inhibitor and anti-hepatoxic activity.	(Mors et al., 2000)
6	Phenylpropanoid derivatives	Cynarin (1,5-dicaffeoylquinic acid) 20% protection	Choleretic and anti-hepatoxic activity.	(Mors et al., 2000)

Table 2. Contd.

7	Curcuminoids	Curcumin Demethoxycurcumin Bis demethoxycurcumin Ar-turmerone	Anti-inflammatory, anti-hepatoxin, anti-mutagenic, anti-carcinogenic, lipoxygenase and prostaglandin-endoperoxide synthase inhibition.	(Kiso et al., 1983; Amman and Wahl, 1990; Ferreira et al.,1992; Mors et al., 2000)
8	Coumarins	Coumarin, Herniarin (7-methoxy-coumarin), Ayapin (6,7- methylenedioxy-coumarin), 7,8-dihydroxycoumarin (7-O-gluco-side of daphnetin), Suberenone, Marmin, Bergapten (20% protection) Monoterpenoid dorstenin Fernolin	Not clearly known however, inhibitions of various enzymes are reported.	(Brown, 1977; Mors et al., 2000)
9	Flavonoids	Primetin (5,8-dihydoxyflavone), Free quercetin (40 - 80% protection), Rutin (quercetin 3-0-rutoside, 20 - 80% protection), Hesperetin, Pinostrobin, Naringenin, Apigenin (40% protection), Kaempferol, luteolin, diosmetin, isorhamnetin, morin, myricetin, quercitrin and isoquercitrin, isoflavonoids (Tectoridin, 7-O-glucoside of tectorigenin, iridin, 7-O-glucoside of irigenin, derricidin produces 70% protection) Pterocarpans (cabenegrins A-I 22, A-II and edunol), Coumestans (wedelolactone, produces 40% protection, demethylwedelolactone).	Anti-venom activity is due to inhibition of phospholipases A_2 and some flavonoids by lipoxygenase inhibition. Other reported activities are anti-inflammatory, anti-hepatoxin, anti-hypertensive, anti-arrhytmic, hypocholesterolemic and anti-allergic in general.	(Lindahl and Tagesson, 1997; Mors et al., 2000)
10	Aristolochic acids	Aristolochic acid	It forms a 1:1 complex with phospholipase A_2 and causes a change in the secondary structures of the proteins.	(Vishwanath et al., 1987)
11	Vegetable tannins (poly phenols)	Persimmon tannin, Ellagitannins, Eufhorbins A and B	It is due to protein-tannin interaction (enzyme inhibiting activity of tannins)	(Haslam, 1989; Mors et al., 2000)
12	Polysaccharides	Mixture of polysaccharides, especially heteroglycan and others produce more than 30% protection.	Antiinflammatory and immunomodulating property can be extended to anti-venom activity.	(Barbi, 1992; Varlen et al., 1989; Mors et al., 2000)

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