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Review Article

A Review of Two Plants Used Traditionally in Bangladesh for Treatment of Snake Bites

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Abstract

Bangladesh is a developing country with the majority of its population residing in rural areas, which lack modern doctors and hospitals. Poisonous snake bites with resulting fatalities are common in the country, and in absence of modern medical treatment, rural people seek help of traditional medicinal practitioners, who generally use plants for neutralizing snake venom. Abelmoschus moschatus and Achyranthes aspera are two plants used among others to treat snake bites. The present review deals with ethnic uses of these two plants for treatment of snake bites in various areas of the world, reported phytochemical constituents of the two plants, and any reported scientific evidences of any of the phytoconstituent (s) in neutralizing snake venom.

INTRODUCTION

Bangladesh is a developing country with the majority of its population living in rural areas. A typical rural village in Bangladesh does not have readily available modern medical facilities in the form of doctors and hospitals. Moreover, besides human residences comprising of mud houses and adjoining agricultural fields, a rural area may contain groves of trees, shrubs and forests with quite extensive undergrowth, which together with the agricultural fields containing densely cultivated crops form an ideal habitat for both venomous and non-venomous snakes. As such, snake bites are common. A national epidemiological survey found out that there are around 623.4 cases of snake bites per 100,000 person years, and only 3% of the victims visited or could visit a medical doctor or a hospital [1].

Among the most venomous snakes whose bites have been reported from Bangladesh are the monocled cobra or *Naja kaouthia* [2], and the greater black krait (*Bungarus niger*) [3]. Most of the snake bite victims were bitten in their lower extremities [1], possibly because rural people do not wear shoes or any protective gear while working in the fields or walking through dense undergrowth. Treatment expenditure for venomous snake bite, if available, was found to be around US$231 (2012 finding, 1 US$ equaled about 72 Bangladeshi Takas in 2012) [4]. It is to be noted that around a third of the Bangladesh population lives below the poverty level income of US$2 per day. Just alone from this income data, it becomes self-evident that most people bitten by venomous snakes cannot afford modern treatment even if the snake has been identified and there is access to modern treatment centers.

Rural people are dependent on traditional medicinal practitioners (TMPs) for their therapeutic needs unless the disease is complicated, when they may seek out city doctors and hospitals. Most TMP-based medicinal practice is based on phytotherapy where whole plant or plant part is used for treatment in the form of juice, decoction, paste or pills, the administration being either oral or topical depending on the nature of the disease. Venomous snake bites are also treated by TMPs with plants, and TMPs specializing in the treatment of snake bites are commonly known as 'ojhas' [5-8].

While there are a large number of plants used for treatment of snake bites in Bangladesh, this review shall concentrate on just two plants, namely *Abelmoschus moschatus* and *Achyranthes aspera*. Utilizing various databases, the review will focus on similar ethnic uses (treatment of snake bite) of the two plants in other regions of the world, mention the reported phytochemical constituents of the plants, and finally discuss the actual or simulated possibilities of any of the phytoconstituents to neutralize snake venom.

ETHNIC USES OF ABELMOSCHUS MOSCHATUS AND ACHYRANTHES ASPERA FOR TREATMENT OF SNAKE BITES

Abelmoschus moschatus Medik belong to the Malvaceae family and is locally known as kostori; in English it is known as musk-mallow. Leaves and fruits of the plant are used to treat snake bite of any type of venomous snake, although the monocled cobra and the king cobra (*Naja naja*) appear to be the more common venomous snakes behind snake envenomation [9]. Juice obtained by crushing leaves or fruits or both of the plant are administered orally and also applied topically to the bitten area following making a deep incision at the spot and letting blood flow freely. The juice is given orally once, but the topical administration is continued at couple of hour's interval for 24 hours at the least or till the snake-bitten person is considered out of danger.

The Bhil, Meena and Sahariya tribes of Rajasthan, India, take seed paste of *A. moschatus* along with milk orally as an antidote [10]. The plant is also used in Sri Lanka as an antidote to snake bite [11].

Achyranthes aspera L. belongs to the Amaranthaceae family and is locally known as apang; in English it is known as prickly-chaff flower. The Rakhain tribe of Bangladesh (Rakhain name of the plant is chaim-per-on) use leaves, roots and stems of the plant to treat snake bites, while the mainstream TMPs use leaves, seeds and whole plants for the same purpose. As previously mentioned for *Abelmoschus moschatus*, juice from the various parts of the plant are administered both orally and topically.

The Bhil, Meena and Sahariya tribes of Rajasthan, India, orally take root extract of *A. aspera* as an antidote to snake bite [10]. Similar to *A. moschatus*, *A. aspera* is also used in Sri Lanka for snake bites [11]. The roots of the plant (*A. aspera*) are grounded and filtrate taken with 2-3 black peppers (fruits of *Piper nigrum* L.) by the tribal communities of Paschim Medinipur district, West Bengal, India, for treatment of snake bite [12]. Root extract is prepared in drinking water and given orally once daily for snake bite by the tribal people of South Surguja, Chhattisgarh, India [13]. The tribals of Kinnerasani region, Andhra Pradesh, India, make a paste of the whole plant. The paste is applied to top of snake bitten area and rubbed down [14].

From the available ethnic reports, it appears that *A. aspera* is used more frequently in the Indian sub-continent countries for treatment of snake bites than *A. moschatus*. It may be mentioned in this context, that throughout the manuscript, snake bites mean bitten by venomous snakes with the poison entering the body (envenomation) and consequential damages, which may even lead to death. Even if death does not occur, such envenomation may lead to tissue damages, pain and inflammation.

PHYTOCHEMICAL CONSTITUENTS OF THE TWO PLANTS

The thus far reported phytochemical constituents of the two plants [15-17] are shown in Tables 1 and 2. Data in Table 1 suggests that the seeds of *A. moschatus* are richer in phytochemicals than other parts from the same plant, and as such should be more pharmacologically active. However, the comparative lack of data on phytoconstituents from other parts of the plant may also simply reflect that they have been under-studied and more research is needed in this area.

More phytochemicals have been identified and reported from *A. aspera* (Table 2) than *A. moschatus*. Since there are more ethnic reports on use of *A. aspera* against snake bites, one or more of these phytochemicals have a greater possibility of neutralizing snake venom and so can serve the purpose of snake venom antidote. Thus the phytochemicals from both plants merit further scientific attention.

DISCUSSION & CONCLUSION

Bites from venomous snakes and consequent envenomation (not all bites can lead to envenomation, which occurs only when venom enters the body) can pose serious problems to people residing in remote areas, or areas where people may lack quick access to hospitals or treatment centers possessing the required anti-venom. This is most often the case in Bangladesh among the rural peoples, where venomous snakes can be found sheltering in houses or in paddy fields, paddy being the foremost crop grown in the country. There are 28 species of venomous snakes in Bangladesh, and a high fatality rate of about 20% from venomous snake bites [18]. However, other countries have similar problem of envenomation from venomous snake bites and lack of timely and appropriate treatment facilities.

In the absence of the requisite anti-venom and modern treatment facilities, most venomous snake-bitten people in rural and smaller urban areas of Bangladesh rely on traditional medicinal practitioners specializing in treatment of venomous snake bites (ojhas). While ojhas can be from the mainstream Bengali-speaking population, a tribal community of people known as the Bedes, specialize more in the treatment of envenomation. The Bedes are a gypsy community in Bangladesh, travelling most of the year by boat from one part of the country to another, selling various items from less precious gem stones to cooking utensils and sundry items, and also treating people suffering from various diseases mainly with medicinal plants. The Bedes have snake charmers and ojhas among them, and both can be performed by the same person. Snake charmers earn their living by showing 'snake dances' in village fairs, where a snake undulate its' body with the sound and movement of the snake charmer's flute. The ojha both catches snakes and treats envenomated persons [19]. Envenomated persons are treated with plants, which are deemed anti-ophidic by the ojha.

Anti-ophidic plants must have the capacity of neutralizing one particular snake's venom or venom of more than one snake. Snake venoms can have quite complex compositions with a mixture of various types of toxins. For instance, *Naja kaouthia* (monocled cobra) venom contains seven different types of cytotoxins, seven phospholipases and eleven different types of neurotoxins [20]. Cumulatively, these toxins can cause a wide range of pathological symptoms including hemorrhage, neurotoxicity, cardiotoxicity, nephrotoxicity, and cytotoxicity [21-23]. However, a given plant also contains hundreds of phytochemicals, which can singly or collectively counteract a snake's venom.

A number of plants are used throughout the world including Bangladesh as anti-ophidic. Common anti-ophidic plants include *Andrographis paniculata*, *Mucuna pruriens*, *Clerodendrum viscosum*, *Abelmoschus moschatus*, *Achyranthes aspera*, *Bixa orellana*, *Hemidesmus indicus*, *Acalypha indica*, *Tamarindus indica*, and *Butea monosperma*, to name only a few. Among these plants, *Andrographis paniculata* has been reported to be useful against venom of *Naja naja*, *Daboia russelii*, and *Echis carinatus* (reviewed in [24]), demonstrating that a single plant extract is capable of acting as an antidote to venoms of different species of snakes.

Various phytochemicals have been reported to be active

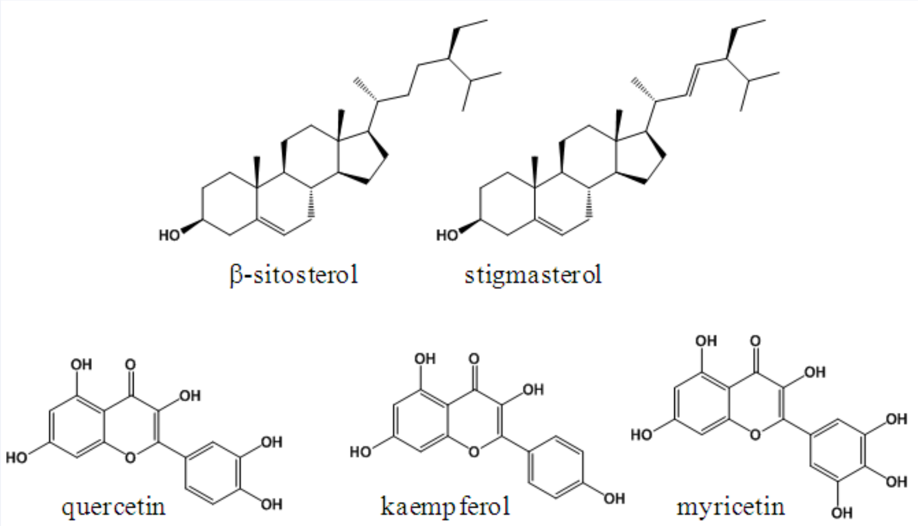

Figure 1 Constituents of *A. moschatus and A.aspera* with known anti-snake venom properties.

Table 1: Reported phytochemical constituents of *Abelmoschus moschatus* [15,16].

Phytochemical constituents of *A. moschatus*
Volatile oil: Myricetin-3-glucoside, cyaniding glycoside, β-sitosterol, farnesyl acetate, 7(Z)-hexadecan-16-olide, 9(Z)-octadecen-18-olide, ambretolide, farnesol, dodecyl acetate, decyl acetate. Seeds: 1-(6-ethyl-3-hydroxypyridin-2-yl) ethanone, 1-(3-hydroxy-5,6-methylpyridin-2-yl) ethanone, 1-(3-hydroxy-6-methylpyridin-2-yl) ethanone, 1-(3-hydroxy-5-methylpyridin-2-yl) ethanone, 2-cephalin, farnesol, ambrettolic acid lactone, furfural, oxacyclonnonadec-10-en-2-one, 5-tetradecenyl acetate, 5-tetradecen-14-olide, (Z)-5-tetradecen-14-olide, malvalic acid, 5-dodecenyl acetate, (Z)-5-tetradecenyl acetate, ergosterol, 2-trans-6-trans-farnesol, decyl alcohol, decyl acetate, trans-trans-farnesyl acetate, campesterol, 12,13-epoxyoleic acid, (Z)-5-dodecenyl acetate, stigmasterol, α-cephalin, sterculic acid, myristic acid. Leaves, petals and flowers: β-sitosterol, myricetin, myricetin-3'-glucoside, quercetin-3'-glucoside, quercetin, kaempferol-3-O-glucoside, kaempferol, cyanidin-3-sambubioside, cyanidin-3-glucoside. Whole plant: Ambrettol, pineol.
α = alpha; β = beta.

Table 2: Reported phytochemical constituents of *Achyranthes aspera* [17].

Phytochemical constituents of *A. aspera*
Leaves, shoots, roots, fruits, seeds, inflorescence: 27-Cyclohexylheptacosan-7-ol, 16-hydroxy-26-methylheptacosan-2-one, 17-pentatriacontanol, ⍰-sitosterol, spinasterol a, 3-acetoxy-6-benzoyloxyapangamide, strigmasta-5,22-dien-3-β-ol, trans-13-docasenoic acid, n-hexacosanyl n-decaniate, n-hexacos-17-enoic acid, n-hexacos-11-enoic acid, n-hexacos-14-enoic acid, 36.47-dihydroxyhenpentacontan-4-one, tritriacontanol, 4-methylheptatriacont-1-en-10-ol, tetracontanol-2, hexatriacontane, 10-octacosanone, 10-triacosanone, 4-triacontanone, betain, betalaine, achyranthine, α-L-rhamnopyranosyl (1→4)-β-D-glucopyranosyl (1→4)-β-D- (1→3)-oleanolic acid, β-D-galactopyranosyl (1→28) ester of saponin A, β-D-glucopyranosyl ester of α-L-rhamnopyranosyl (1→4)-β-D-glucopyranosyl (1→4) β-D-glucuronopyranosyl (1→3)-oleanolic acid, β-d-glucopyranosyl 3β-[O-α-l-rhamnopyranosyl–(1→3)-O-β-d-glucopyranuronosyloxy] machaerinate, β-d-glucopyranosyl 3β-[O-β-d-galactopyranosyl-(1→2)-O-α-d-glucopyranuronosyloxy] machaerinate, ecdysterone. Aerial parts: 20-hydroxyecdysone, quercetin-3-O-β-D-galactoside.
α = alpha; β = beta.

against one or more venom component(s)-induced diverse type of toxicities. Thus ajmaline, reserpine and serpentine from the plant *Rauwolfia serpentina* (Apocynaceae) reportedly inhibited phospholipase A_2 (PLA_2) of *Naja naja* [25, also reviewed in [24]]. Aristolochic acid from *Aristolochia indica* is known to inhibit PLA_2 and edema-inducing activity of *Daboia russelii* [26]; ellagic acid (from *Casearia sylvestris*) to inhibit PLA_2 and PLA_2-induced mycotoxicity and edema of *Bothrops jararacussu* [27]. Anisic acid, gallic acid, glycyrrhizin, myricetin and quercetin reportedly can inhibit snake venom proteases; apigenin, luteolin, β-sitosterol and lupeol acetate can inhibit snake venom hyaluronidases; α-amyrin can inhibit snake venom phosphodiesterases; and anisodamine, resveratrol, and edunol can inhibit the action of whole snake venom [24]. To be noted, this is only a very partial list of phytochemicals active against action of one or other component of snake venoms and not a full list of phytochemicals.

It has been reviewed that about 150 botanical family plants are used in snake bites. The most common families are Fabaceae, Asteraceae, Apocynaceae, Lamiaceae, Rubiaceae, Euphorbiaceae, Araceae, Malvaceae, and Acanthaceae [28]. It is to be noted that *Abelmoschus moschatus* belongs to the Malvaceae family. There are instances of other Malvaceae plants used for neutralizing snake venoms in India. *Abutilon indicum* [29], *Pentace burmanica* [26], and *Sida rhombifolia* [30] are Malvaceae family plants reported to be used against snake bites in India.

Among the reported phytochemicals of *Abelmoschus moschatus* are β-sitosterol, stigmasterol, myricetin, quercetin, and kaempferol (see Table 1, structures shown in Figure 1). Stigmasterol and β-sitosterol can reportedly inhibit myotoxicity of *Crotalus durissus terrificus* [31] and viper venom-induced defibrinogenation, and cobra venom-induced PLA_2 activity [32]. Myricetin and quercetin has been shown to possess anti-hemorrhagic potential against the venomous snake, *Bothrops jararaca* [33]. Kaempferol is known to inhibit hyaluronidase (component in many snake venoms) and delay venom action in mice [34].

Various solvent extracts of the leaves of *Abelmoschus moschatus* have been shown to possess analgesic activity as determined with hot plate and tail flick methods [35]. Amelioration of pain can be an important factor in treatment of snake bites, because snake venoms can cause intense pain [36]. Interestingly, another member of the *Abelmoschus* genus, *Abelmoschus ficulneus* roots have been reported to be used for scorpion bite treatment [37]. Since scorpions can also be venomous [38], it suggests that the *Abelmoschus* genus can prove to be a useful genus for treatment of bites of venomous species.

Leaf extract of *Achyranthes aspera* reportedly neutralized russelii viper's (*Daboia russelii*) venom containing PLA_2 [39]. Among the known phytochemicals of the plant are β-sitosterol and quercetin-3-O-β-D-galactoside (see Table 2, structures given in Figure 1). The anti-venom activities of both β-sitosterol and quercetin have been discussed with reference to *Abelmoschus moschatus*. β-Sitosterol also reportedly possesses analgesic and anti-inflammatory activities [40,41], which would be helpful in easing venom-induced pain and inflammation.

Snake bite, particularly bites of venomous snakes lead to a considerable number of fatalities throughout the world. The major problem in the treatment of snake bites is the lack of easy access to the appropriate anti-venom. From that view point, if venomous snake bites can be treated with readily available, accessible and affordable medicinal plants, it can save the lives of thousands of venomous snake-bitten persons every year. As such, the matter deserves scientific attention and research to validate the ethnic uses of medicinal plants for snake bite treatment, plants like *Abelmoschus moschatus* and *Achyranthes aspera*.

It is not clear or requires studying whether the ubiquitious active anti-venom constituents in these two plants are extraordinarily enriched in these plants and b) whether there are likely to be hitherto uncharacterized small molecule and macromolecules in these plants that may account for, in addition to the cited phytochemicals, the traditional benefit of these plants against venomous snake bite. Also may be it is the combinatorial presence of these phytochemicals within the same plant that makes a difference. Elucidation of the exact mechanism as to how these anti-ophidic plants work needs further scientific investigation

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