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Himalayan Toxic Plants of Defense Importance

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Abstract

In present concept paper, we are introducing the concept of multi-system targeted novel toxic compounds that have been isolated from various poisonous plants of Himalayan region of India for self-defence applications. The selected studied poisonous plants are having dual role as nutraceutical and ethno-pharmacological uses apart from their less explored toxic property. However, future detailed work is required for identification and characterization of the precise toxic chemical components that will be used for the formulation of novel multi-system targeted warfare agents for defensive applications.

Keywords: Poisonous Plants; Multisystem Targeted Toxic Compounds; Defensive Warfare Agents

Abbreviations

IHR: Indian Himalayan Region; m asl: Meter Above Sea Level; RH: Relative Humidity; SGPT: Serum Glutamic-Pyruvic Transaminase; THC: Tetrahydrocannabinol

Introduction

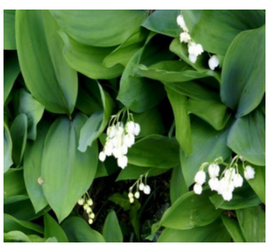
The Himalayan border area are very rich in several plant resources that has yet not been studied in detailed for various defense applications such as emergency food/nutraceutical. Due to the varying altitude, topographic, and climatic conditions, the Himalaya is considered to be a repository of several high value plant resources. Indian Himalayan region (IHR) as a whole supports nearly 50% of the total flowering plants in India. According to an estimate, there are over 816 tree species, 675 edibles and nearly 1743 species of medicinal/toxic value found in the IHR [1]. Such a large diversity of plants may be useful for fulfilling various kinds of needs of our armed forces, particularly for those which, are deployed at extreme environments of high-altitudes. Some of the toxic plants of Himalayan region produce several toxins that have the ability to adversely affect human health in a variety of ways, ranging from relatively mild allergic reactions to serious medical complications, including death [2]. This concept paper proposes the use of many toxic plant resources of Himalayan region that may be exploited for the development of novel multisystem targeted agents for self-defense by using various biotechnological tools.

The use of various poisonous plants for the development of multi-system targeted novel warfare defensive agents has several advantages over other warfare agents like nuclear, microbial and chemical warfare agents. Locally grown poisonous plants are easier and cheaper to multiply and sustain in the natural environment. They are being deadly lethal to animals or livestock including humans and prove to be effective agents for self-defense. They also have nutraceutical and ethno-pharmacological uses and therefore, can be utilized for fulfilling nutritional and medicinal needs during emergency [3]. Figure 1 shows examples of such plants, which have harmful effect on various biological systems like nervous, cardiac, digestive, respiratory, dermal, etc simultaneously for self-defence.

Material and Method

Therefore, in this effort, the Defence Institute of Bio-Energy Research (DIBER) is involved in the identification and characterization of plant resources of Himalayan region, which have poisonous nature and have medicinal and nutraceutical values. Our efforts have led to the identification of several poisonous plants that can be used for the development of novel multi-system targeted warfare agents for defensive applications (Table 1). The seeds or stem/root cuttings of some of these poisonous plants were collected from different cities of India and have been successfully germinated and maintained in culture room under white light (350 mol m^{-2} s^{-1}; 60 ± 2 % RH) at 25°C with 16h light and 8h dark photoperiods. The grown potted plants (~30 cm) were subsequently transferred to glass house for flowering and fruiting at Defence Institute of Bio-Energy Research (DIBER), Haldwani (~424 m asl; 29.22°N, 79.52°E), India.

Figure 1: Concept for development of multi-system targeted agents for defensive applications.

S. No.	Poisonous Plant	Plant photo	Family	Collection site	Propagation mode	Poisonous components	Mode of action
1.	*Heracleum canescens* (Grey-Hairy Hog-weed, Pushki*)*		Apiaceae	Bhowali, Uttarakhand	Seed	Furocumarins	Skin-allergy
2.	*Delphinium brunonianum* (Musk Larkspur, Makhoti)		*Ranunculaceae*	Kashmir valley, Shimla	Seed	Diterpenoid alkaloids, Methyllycaconinite	Cardiotoxic
3.	*Silybum marianum* (Milk Thistle, Dudhpattra)		Asteraceae	NBPGR, Bhowali, Uttarakhand	Seed	Silymarin, KNO_3	Anti-respiratory, Nitrate poisoning
4.	*Aconitum chasmanthum* (Gaping Monkshood, mohri)		Ranunculaceae	Chitral, Kashmir	Seed	Aconitines	Neurotoxin, gastrointestinal
5	*Melia azedarach* (Chinaberry tree, Bakain)		Meliaceae	Chakrata, Haryana	Seed	Terpenoids	Neurotoxic
6	*Convallaria majalis* (European Lily of the Valley)		Asparagaceae	Valley of Flowers, Srinagar	Seed	Cardenolides	Cardiac symptoms
7	*Solanum xanthocarpum* (Thorny Nightshade, Kantakari)		Solanaceae	Bhowali, Uttarakhand	Seed	Solasodine	Anti-spermatogenic, anti-androgenic
8	*Hyoscyamus niger* (Henbane, Khurasani ajwain)		Solanaceae	Village Mana, Vasundhara falls	Seed	Tropane alkaloids	Symptomatic madness

9	*Arisaema triphyllum* (Saapbhutta)		Araceae	Dogaon, Uttarakhand	Seed	Calcium oxalate	Skin allergy
10	*Cannabis sativa* (Marijuana, Hemp, bhang)		Cannabaceae	Haldwani	Seed	Cannabinoids	Psycho-tropic

Table 1: List of the poisonous plants of the Himalayan region that may be used for the development of novel multi-system targeted agents for defense applications.

Himalayan Toxic Bio-Resource

Heracleum canescens (also called as Grey-Hairy Hogweed, Pushki) is found in the central western Himalayas at altitudes of 2300m asl. The sap of *Heracleum* species contains photosensitizers that cause contact phototoxic dermatitis: a family of photocytotoxic compounds called furanocoumarins. The highest levels of furanocoumarins, including angelicin, are found in hogweed leaves but are also present in its stems and inflorescences. Furanocoumarins confer an ecological advantage to the plant, as they possess both insecticidal and antimicrobial properties, thus protecting the plant from pathogen and insect attack. In mammalian cells, exposure to furanocoumarins causes both carcinogenic and mutagenic changes by virtue of their unusual ability to intercalate directly into host DNA. After integration into the host DNA, exposure to light energy can result in further collation of these bioactive tricyclic molecules which then undergo additional reactions with pyrimidine bases on the complementary DNA strand, giving rise to inter-strand cross-linking. Cross-linking within the DNA strands induces apoptosis and inhibits further cell proliferation [4]. Besides these, it is also traditionally used as food additives, spices and flavoring agents. Moreover, these plants are widely used in folklore medicine for the treatment of many disorders such as inflammation, flatulence, stomachache, epilepsy, psoriasis, and as carminative, wound healing, antiseptic, anti-diarrheal, tonic, digestive, pain killer, analgesic, and anticonvulsant agents [5].

Delphinium brunonianum (Musk Larkspur, Makhoti) is a high-altitude plant, found at 4300 - 5500m asl. It contains diterpene alkaloids viz. aconitum and delphinium that have been used mainly for preparation of a wide spectrum of poisons as well as medicines for many centuries. Extensive biological and pharmacological studies performed have shown that delphinium alkaloids affect substantially the cardiac and central nervous systems. Thus, at present, a number of diterpene alkaloids have been identified that exert analgesic, anti-inflammatory, anti-epileptiform and cardiovascular effects. The high toxicity of various species of Delphinium plants is attributed to the norditerpenoid alkaloids present. These plants still continue to be the main cause of extensive cattle poisoning resulting in substantial losses for the cattle-breeding industry.

Silybum marianum (Milk thistle, dudhpattra) is found at high altitudes regions of Himalayan states. Its leaf sap contains silymarin toxins that may cause allergic skin reactions, bloating, blood clots, impotence, itching, nausea, non-specific muscle and joint effects, sexual dysfunction and vomiting. Reported cases observed with cattle and sheep poisoning with ingested plant material, which contains potassium nitrate that combines with haemoglobin to form methaeglobin that lead to incapable of to combine with oxygen and ultimately may cause respiratory distress. Its milk thistle extracts also have been used as traditional herbal remedies for almost 2000 years. The extracts are still widely used to protect the liver against toxins and to control chronic liver diseases. Recent experimental and clinical studies suggest that milk thistle extracts also have anticancer, antidiabetic, and cardioprotective effects [6]. Silymarin and its active constituent, silybin, have been reported to work as antioxidants scavenging free radicals and inhibiting lipid peroxidation [7].

Aconitum chasmanthum (Gaping Monkshood, mohri) is found in the meadows of the Himalayas, from Pakistan to Nepal, at altitudes of 2300 - 4300 m asl. The whole plant is highly toxic and even skin contact causes numbness in people. The main alkaloid of these plants is aconitine, a highly toxic diterpenoid alkaloid, which is known to suppress the inactivation of voltage-dependent Na^+ channels by binding to neurotoxin binding site 2 of the α-subunit of the channel protein [8]. These alkaloids are highly cardiotoxins and neurotoxins. Severe aconite poisoning can occur after accidental ingestion of the wild plant or consumption of an herbal decoction made from aconite roots. In traditional Chinese medicine, aconite roots are used only after processing to reduce the toxic alkaloid content. The dried pulverized roots are mixed with butter and given as ointment on abscess and boils also mixed with tobacco and uses as "Naswar". Soaking and boiling during processing or decoction preparation will hydrolyze aconite alkaloids into less toxic and non-toxic derivatives. However, the use of a larger than recommended dose and inadequate processing increases the risk of poisoning [9].

All parts of *Melia azedarach* (Chinaberry tree, Bakain) tree are poisonous. Even eating as few as 6 berries can result in death of humans. Birds that eat too many seeds have been known to become paralyzed. Also, its bark and fruit extract is used to kill parasitic roundworms. In Manipur, its leaves and flowers are used as poultice in nervous headache. Its leaves bark and fruit are also used as insect repellant. Its seed-oil and wood-extract is used in rheumatism and asthma, respectively. Toxicity and pathological studies showed that the meliatoxins from *M. azedarach* are responsible for most but not all of the symptoms resulting from the ingestion of whole fruit [10]. In addition, limonoids from M. azedarach showed various biological activities like insecticidal, insect antifeedant and growth regulating activity on insects as well as antibacterial, antifungal, antimalarial, anticancer, antiviral and a number of other pharmacological activities on humans [11].

Convallaria majalis (European Lily of the Valley) it's all parts are poisonous due to Cardenolides and saponins toxins. Cardenolides have a digitalis like activity and causing cardiac conduction disturbances [12]. Few cases of animal poisoning reported in *C. majalis,* which contains cardiac glycosides (digoxin) due to immunologically cross-reactive compounds [13].

Solanum xanthocarpum (Thorny Nightshade, Kantakari) contains toxic compound called as solasodine. Its chronic administration in mammals causes testicular lesions resulting in a severe impairment of spermatogenic elements, reduction in acid phosphatase enzyme activity, decrease in serum enzymes (Serum Glutamic-Pyruvic Transaminase (SGPT), alkaline phosphatase), triglycerides, non-esterified fatty acid levels etc. Solasodine administration in dogs definitely rendered the male infertile as evidenced by the absence of sperms [14]. Apart from these it is an important medicinal herb in Ayurvedic medicine. Various studies indicated that *S. xanthocarpum* possesses antiasthmatic, hypoglycemic, hepatoprotective, antibacterial and insect repellent properties [15].

Hyoscyamus niger (Henbane, Khurasani ajwain) is found in the Himalayas at altitudes of 2100 - 3300 m asl. All part of this plant contains toxic alkaloids such as hyoscyamine, atropine, tropane and scopolamine that causes various harmful effects like bronchodilating, antisecretory, urinary bladder relaxant, spasmolytic, hypnotic, hallucinogenic, pupil dilating, sedative etc. Clinical studies showed that its acute poisoning may lead to mydriasis, tachycardia, blurred vision and photophobia, arrhythmia, hyper reflexia, auditory, visual or tactile hallucinations, confusion, disorientation, delirium, aggressiveness, and combative behavior changes [16]. Apart of these, it is also used in homoeopathic and traditional medicines.

Arisaema triphyllum (Jack-in-the pulpit, Saapbhutta) is a poisonous plant. The toxicity of Arisaema species is due to its content of calcium oxalate, a compound derived from oxalic acid, as well as enzymes that trigger the release of histamine in the blood stream of persons who ingest the leaves. Needle like calcium oxalate crystals causes painful oropharyngeal edema, hypersalivation, aphonia, oral ulceration, esophageal erosion, and hypocalcemia upon contact with lips, tongue, oral mucosa, conjunctiva, or skin [17].

Cannabis sativa (Marijuana, Hemp, bhang) has been used for centuries for the effects of its psychoactive resins. The term "marijuana" typically refers to tobacco like preparations of the leaves and flowers. The plant contains more than ~400 toxic chemicals. The cannabinoid, 9-tetrahydrocannabinol (THC) is the major psychoactive toxic constituent. "Hashish" is the resin extracted from the tops of flowering plants and generally has a much higher THC concentration that has been widely used as psychoactive effects [18].

Conclusion

The studied poisonous plants are having dual role as nutraceutical and ethno-pharmacological uses apart from their less explored toxic property. Therefore, they may be used for the formulation of future novel multi-system targeted defensive warfare agents. However, future detailed work is required for identification and characterization of the precise poisonous chemical components by using various biotechnological tools.

Author Contribution Statement

SMG conceived the idea, helped in execution of lab study and wrote this concept paper. KM contributed in the execution of the laboratory work and collection of toxic Himalayan bio-resources. SKD and MB contributed in critically revising the draft and updating the manuscript for publication. All authors read and approved the manuscript and declared that no competing interests exist.

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