BIOACTIVE CHEMICALS AND PHARMACOLOGICAL SIGNIFICANCE OF IMPORTANT MEDICINAL PLANTS OF NORTH WESTERN HIMALAYA

Abstract

The Indian Himalayan region (IHR) stands as a colossal storehouse of medicinal plants, boasting unparalleled biodiversity. Over countless generations, these plants have been harnessed for their curative properties, becoming an integral part of traditional healing practices. This abundance of botanical treasures holds the promise of therapeutic solutions for a multitude of ailments, with many species teetering on the brink of endangerment. These plants derive their therapeutic potency from a complex interplay of chemical compounds within their various parts. In recent years, their appeal has surged owing to their perceived advantages, notably their limited adverse side effects when compared to conventional allopathic medications. However. this newfound popularity has birthed an alarming over-exploitation. The relentless demand for medicinal plants has initiated a precarious decline in their populations. Of particular the Himalayan concern are Western medicinal species, such as Aconitum heterophyllum, Podophyllum hexandrum, Picrorrhiza kurroa, Swertia chiravita, and Valeriana jatamansi, which have permeated both national and international trade. Roots of Aconitum heterophyllum, renowned for their antipyretic, astringent, stomachic, and properties. aphrodisiac have garnered substantial attention. P. hexandrum stands out for its well-documented anti-cancerous attribute. Meanwhile, the bitter-tasting P. kurroa and S. chirayita hold immense potential as anti-diabetic agents. Given these pressing concerns and the immense therapeutic potential these plants harbor, this chapter endeavors to shed light on the

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looming threats confronting Western Himalayan medicinal plants. It also delves into the imperative matter of conservation, unraveling the chemistry underpinning their medicinal efficacy and exploring their vast pharmacological promise. In doing so, we strive to underscore the critical importance of preserving these invaluable botanical resources for the betterment of human health and the protection of our natural heritage.

Keywords: Medicinal plants, Threats, Conservation, Chemistry, Therapeutic properties

I. INTRODUCTION

The Himalayan Region is a treasure trove of traditional medicinal knowledge and a rich repository of biodiversity, housing approximately 18,000 plant species, including a substantial collection of Medicinal and Aromatic Plant species (MAPs). Within this botanical wealth, the Indian Himalayas are home to a remarkable 1,748 plants renowned for their therapeutic benefits, as highlighted by Joshi et al. (2016). This indigenous knowledge of medicinal plants is deeply woven into the tapestry of Himalayan culture, permeating every facet of daily life. It stands as a lifeline for the healthcare of rural communities, particularly the economically disadvantaged. Astonishingly, between 65% and 80% of people in impoverished nations already rely on medicinal plants for their healthcare needs, a fact underscored by the World Health Organization (WHO) in 2011. What sets these MAPs apart is their potential to supplant allopathic medications. Their allure lies in the presence of unique chemical compounds, affordability, and a lower incidence of adverse side effects. Recent times have witnessed an exponential surge in the market for herbal products, with many Himalayan MAPs in high demand as essential inputs for these products. Remarkably, amidst the world's estimated 300,000 plant species, only 15% have been subjected to evaluation for their pharmacological potential, as noted by De Luca et al. (2012). This underlines the vast untapped potential within natural sources.

The herbal product market is now a burgeoning industry, contributing around USD 62 billion to international markets. It is noteworthy that India's current contribution is a mere 2.5%, a fraction of its potential. Projections indicate that this sector's value could escalate to USD 5 trillion by 2050, signaling an unprecedented growth trajectory. To meet this surging demand for medicinal and aromatic plants (MAPs) sustainably and equitably, it is imperative to engage all stakeholders. This holistic and inclusive approach should encompass farmers, collectors and traders. Their active involvement is vital for the expansion of India's herbal sector, ensuring that it thrives as a beacon of both natural health and economic prosperity.

II. THREATS TO MEDICINAL AND AROMATIC PLANTS

The relentless over-exploitation of medicinal and aromatic plants (MAPs) in the Himalayan region stands as the primary driver behind their depletion and increasing scarcity. According to Goraya and Ved's findings in 2017, a staggering 95% of the MAPs used by local Indian communities are sourced from the wild. Furthermore, this study unveiled a concerning statistic - approximately 72% of medicinal plant species and 50% of the annual quantities used by the domestic herbal industry are also harvested from the wild. This insatiable demand for herbal remedies has led to unchecked collection, resulting in a significant loss of biodiversity and the ruthless depletion of numerous MAPs, as noted by Nishteswar in 2014. Adding to the challenge is the looming specter of climate change. The Himalayan ecosystems, highly sensitive to environmental shifts, are facing the brunt of these changes. However, limited research has been devoted to assessing the precise impacts of climate change on medicinal herbs in this region. Recent studies, such as the one conducted by Das et al. in 2016, have started to shed light on this issue. They reveal how climate change is altering the distribution and diversity of Himalayan medicinal plants, affecting their flowering patterns and vegetative growth periods, ultimately diminishing their productivity. As a direct consequence of these compounding factors, approximately 120 medicinal plant species in the Indian Himalayan Region have been classified as endangered, critically endangered, near threatened, or data deficient, as documented by Samant et al. in 1998 and Ved *et al.* in 2003. Urgent and comprehensive efforts are imperative to conserve and sustainably manage these invaluable resources to ensure their survival for future generations.

III. CONSERVATION OF MEDICINAL PLANTS

Himalayan Medicinal plants face significant threats due to extensive harvesting from wild populations, a practice that can lead to a point where a species reproductive capacity is irreversibly diminished. To counter this, various conservation strategies are imperative. Among these, ex situ conservation stands out as a valuable complement to in situ methods, particularly for slow-growing and sparsely distributed endangered medicinal plants. Ex situ conservation involves cultivating and acclimatizing threatened species outside their natural habitats. This approach serves a dual purpose: it ensures the survival of these valuable plants and can generate substantial quantities of plant material for drug production. This is especially critical given the escalating demand for medicinal plants. Herbal industries have increasingly embraced ex situ conservation as it guarantees a sustained supply of plant resources. However, a challenge lies in the scattered and often limited information regarding the cultivation techniques of certain medicinal plants. Streamlining and enhancing this knowledge base is essential for the effective implementation of ex situ conservation efforts, ensuring the continued availability of these vital medicinal resources.

IV. NEED FOR UNDERSTANDING THE CHEMISTRY OF PLANTS?

Plants, as part of their evolutionary strategy, produce an array of chemical compounds that confer advantages. The chemical profile of medicinal plants plays a pivotal role in defining their species-specific traits and pharmacological properties, making them invaluable in medical applications. The intricate relationship between the synthesis of bioactive substances and the accumulation of elements is governed by various levels of molecular regulation, as elucidated by Lovkova *et al.* in 2001. These plant-derived compounds, often referred to as secondary metabolites, hold tremendous potential as pharmaceutical agents. Their known pharmacological activities form the scientific foundation for their utilization in modern medicine. Understanding the chemistry of these compounds is of paramount importance for the development of novel drugs and for enhancing the processes of isolation, purification, and analysis, thus driving advancements in pharmaceutical research and applications.

V. CHEMICAL CONSTITUENTS AND THERAPEUTIC POTENTIAL OF IMPORTANT MEDICINAL PLANTS

- 1. Aconitum heterophyllum Wall. ex Royle Common Name: Patrees and Atees Family: Ranunculaceae IUCN Status: Endangered
 - **Description:** It is an erect biennial herb, 30-100 cm long. The leaves are alternate, shortly stalked or sessile, glabrous and dark green in color. The cauline leaves are amplexicaul, and the lowest parts leaves are petiolated. Flowers are complete bluish

purple coloured, 2-3 cm long, Fruit is a capsule having many dark brown coloured seeds.

- **Distribution:** The plant is usually found in sub-alpine and alpine zones of the Himalayas, at 2000-5000 m above mean sea level. In India, *A. heterophyllum* is distributed in Jammu and Kashmir, Himachal Pradesh and Uttarakhand states. In Himachal Pradesh, it has been reported from Chamba, Kangra, Kinnaur, Kullu and Lahaul and Spiti districts.
- Climate and Soil: Atees grows well in sub-alpine and alpine climate. Sandy loam and slightly acidic soil, and favours pH around 6, is best for seed germination, survival and good rhizome yield.
- **Propagation:** It's propagation can be done through seeds and rhizome.
- Chemical Constituents: The plant possesses many chemical constituents, of which alkaloids and flavanoids are the important one having broad spectrum of activity. In addition, polysaccharides and other fatty acids have been extracted from the plant. The plant contains alkaloids viz. benzoylmesaconine, mesaconitine, aconitine, hypaconitine, heteratisine, heterophyllisine, heterophyllisine, heterophyllisine, heterophyllisine, heterophyllisine, heterophyllidine, atidine, isotisine, hetidine, hetisinone and benzolylheteratisine (Punia *et al.*, 2022). Tubers of *A. heterophyllum* contain a noncrystalline, non-toxic alkaloid atisine (0.4%). Nearly 0.79% of total alkaloids in the plants are in the root. Aconite acid, tannic acid, a mixture of oleic, palmitic, stearic glycerides and vegetable mucilage are also present in the species.

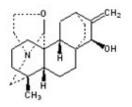


Figure 1: Chemical Structure of Atisine

- **Therapeutic Potential:** Evaluation of *A. heterophyllum* for its therapeutic potential by scientific studies has proved that it possesses anti-diarrhoeal, anti-inflammatory, anti-hypertensive, anti-bacterial, anti-obesity, hypolipidemic, anticholinergic properties. Besides, it also exhibits antioxidant activity and immunomodulatory effects.
- 2. Podophyllum hexandrum Royle Common Name: Bankakri Family: Berberidaceae IUCN Status: Endangered

- **Description:** It is a perennial herb up to 30-50 cm tall. Stem is simple, leafy without top. Leaves are alternate, long stalked, often having purple spots, round, 6-10 inch in width, deeply divided from the middle or base into 3-5 lobes, sharply toothed and with deep incision. Fruit is 1-2.5 inch long, berry, scarlet colored when ripened and ovoid shaped with abundant seeds. Roots are perennial and bears 1 aerial reproductive shoot and 4-5 vegetative shoots. Reproductive shoots generally have 2 or extremely 3 leaves, however vegetative shoot bear a single leaf (Airi *et al.*, 1997).
- **Distribution:** The plant is native to the lower elevations of Himalayas like Afghanistan, Bhutan, India, Nepal, Pakistan and China. In India, *P. hexandrum* is mostly found in alpine Himalayas (3000-4000 msl) of J & K, Himachal Pradesh, Uttarankhand, Sikkim and Arunachal Pradesh.
- Climate and Soil: The species thrives best as undergrowth as well as in forests in well drained humus rich soil in temperate and subalpine zones.
- **Propagation:** The crop is propagated through seed as well as rhizome cutting.
- Chemical Constituents: *Podophyllum hexandrum* is reported to contain a number of compounds e.g. epipodophyllotoxin, podophyllotoxone, aryltetrahydronaphthalene lignans, flavonoids such as quercetin, quercetin-3-glycoside, podophyllotoxin glycoside, kaempferol and kaempferol-3-glucoside. The rhizomes and roots of the plant contain anti-tumor lignans such as podophyllotoxin, 4'-demethyl podophyllotoxin and podophyllotoxin 4-O-glucoside. Among these lignans, podophyllotoxin (Fig. 1.) is most important for its use in the synthesis of anti-cancer drugs etoposide, teniposide and etophos. *P. hexandrum* contains 7–16 % podophyllin resin, which is higher than that found in *P. peltatum* (3-4%) (Rather and Amin, 2016).

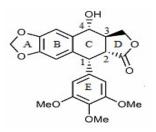


Figure 2: Chemical structure of Podophyllotoxin

- **Therapeutic Potential:** Podophyllotoxin possess anti-cancerous property (Motyka *et al.*, 2023), besides, plant is also known for having anti-fungal, anti-microbial, anti-inflammatory, anti-spasmogenic, hypolipidemic, immunosuppressive, antioxidative, analgesic and cathartic activities.
- 3. *Picrorrhiza kurroa* Royle ex Benth Common Name: Kutki Family: Scrophulariaceae IUCN Status: Endangered

- **Description:** The species is a 20-30 cm tall perennial herb. Leaves are 5-10cm in length, mostly radical however, cauline are absent or only showing up as bracts during the fruiting stage. Flowers are very small, in dense spicate racemes and white or pale blue-purple coloured. A two-celled spherical capsule is a fruit. Rhizomes are irregularly curved, cylindrical and 15-25 cm long. They are greyish-brown in color and have jointed nodes where they branch and root.
- **Distribution:** It is found in the Himalayan region, between 3000 and 5000 msl, in Pakistan, India, Nepal, Bhutan, and southern China. It is only found in the Western Himalayas, which reach as far as the highlands in Yunnan, China. It can be found in the upper altitudes of the Himachal Pradesh districts of Chamba, Kangra, Mandi, Shimla, Kinnaur, Lahaul and Spiti.
- Climate and Soil: *Picrorrhiza kurroa* thrives well in cool and moist localities. It grows best in soil with a sandy clay texture. It requires porous soil layers that enable the rhizomes beneath to extend horizontally so that they can develop aerial sprouts from the nodes.
- **Propagation:** Plant is propagated through seeds and stolon cuttings. However, planting through stolon cutting is best suited for achieving higher productivity in short time.
- Chemical Constituents: Iridoids, alkaloids, terpenes, phenolics, acetophenones, and cucurbitacins are only a few of the chemical substances found in the plant. The main chemical compound of the species is kutkin, which includes picrosides I, II, III (Fig. 2) and kutkoside. Additionally, *P. kurrooa* contains 4-hydroxyl-3-methoxyacetophenone, veronicoside, phenol glycosides, various cucurbitacin glycosides and pikuroside.
- **Therapeutic Potential:** Kutki has hepatoprotective, antioxidant, immunemodulatory, anticancerous, anti-inflammatory, anti-microbial, anti-diabetic, antiasthmatic, nephro-protective, analgesic, cardio-protective properties (Salma *et al.*, 2017).

- 4. Valeriana jatamansi Jones ex Roxb Common Name: Tagar, Mushkbala Family: Valerianaceae IUCN Status: Endangered
 - **Description:** *Valeriana jatamansi* grows upto 50 cm tall. The thick rootstock has long, fibrous roots (6-10 cm thick) and knotted by unequal circular ridges. There are two sorts of leaves: radical and cauline. The cauline leaves are few, tiny, entire or lobulate, radical leaves are cordate-ovate (2.5-8 cm), toothed or sinuate and have long stalk. White or pink-tinged flowers grow in flat-topped corymbose clusters on upright, almost leafless peduncles.
 - **Distribution:** *Valeriana jatamansi* is common in IHR, from Kashmir to Bhutan and Khasi Hills. It is found naturally at an altitude ranging from 1800 to 3000 m in NW Himalayas and between 1200 m and 1800 m in Assam and NE India.
 - Climate and Soil: The plant favors a temperate climate and typically grows in steep slopes, damp, rocky, disturbed grassy slopes and on stones with coarse sandy loam soil.
 - **Propagation:** It is propagated through seed and rootstock cutting.
 - Chemical Constituents: The major chemical constituents from roots and rhizomes of *V. jatamansi* are valepotriates (Fig. 3), flavonoids, flavone glycosides, terpenoids, and phenolics. Valepotriates (upto 3.82%) are among the main compounds of this herb and include valtrate, acevaltrate and didrovaltrate.

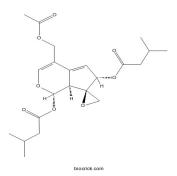


Figure 4: Chemical Structure of Valepotriate

- **Therapeutic Potential:** Rhizomes and roots of *V. jatamansi* have antipyretic, cooling, diuretic, hypotensive, stimulant and sedative properties. They are useful in epilepsy, nervous unrest, hypochondriasis, hysteria and skin diseases.
- Angelica glauca Edgew. Common Name: Chora or Gandrayan Family: Apiaceae IUCN Status: Endangered

- **Description:** It is a 1-2 meter tall upright perennial herb. Large, petiolated, tripinnate, alternating leaves with very long rachises are typical. A compound umbel with umbels of many orders is an inflorescence. Fruit is mericarp, oblong, smooth, flat and pale white to brown, on maturity. Seeds are flat, pale whitish to brown, with five ridges and winged.
- **Distribution:** *A. glauca* is only found in sub-alpine and alpine parts of the Himalayas, where it is endemic. Its distribution area covers the Himalayan mountain ranges in Afghanistan, Pakistan and parts of India, with elevations ranging from 2000 to 4000 m. The plant is found in the Western Himalaya between 2700 and 3700 meters, in alpine scrub and forest shadows, from Kashmir to Uttarakhand.
- Climate and Soil: It requires cool and temperate climate for optimum growth. Well drained, loamy soil rich in organic matter and without water stagnation is ideal for the plant growth.
- **Propagation:** The plant propagates through seed and rootstock splits. The collection of seeds from primary and first lateral umbel is advantageous, as seed set is higher (Gautam and Raina, 2019).
- Chemical Constituents: The plant harbors several phthalides, *i.e.* (Z)-ligustilide, (Z)-butylidene phthalide and (E)-butylidene phthalide. The main compounds found in the plant root oil are transligustilide (72%) followed by Z-3-butylidenephthalide (6%), α-phellandrene (3-4%), β-phellandrene (3%), p-cymene (1-2%) and spathulenol (1-2%). Some other components also found are α-pinene, β-trans-ocimene, γ-terpinene, sabinol, α-santalene, β-eudesmol etc.
- **Therapeutic Potential:** Root oil is having anti-inflammatory, anti-oxidant, anti-fungal, anti-bacterial, anti-cancerous and analgesic properties.
- Swertia chirayita Karst.
 Common Name: Chirayita, Chirata, Bhunimba Family: Gentianaceae IUCN Status: Endangered
 - **Description:** The plant is an erect pluri-annual herb of 70 to 120 cm height. Tap root of 5-10 cm long, light yellow in colour. Radical leaves (lanceolate shaped, 5-7 nerved) in dense rosettes that are noticeable up until the emergence of the main branch and have a purple underside are present. Flowers present in large panicles are greenish yellow coloured. Fruit is an oval capsule containing 20 to 45 seeds. During the first year of growth, it remains as low stature plant without any visible shoot, but with abundant radicle leaves. During the second year, shoot development commences attaining a height of 60 to 150 cm, which bears cauline leaves, flowers and fruits.
 - **Distribution:** It is a naturally found in the temperate IHR and grows at an altitude of 1200-3000 m from Kashmir to Bhutan and in the Khasi hills at 1200-1500m.

- Climate and Soil: The plant inhabits temperate regions in the Himalayas. Loamy to sandy loam, friable, and well-drained soils are suitable for its cultivation. The crop can be grown in areas having mild rainfall (100 cm) in rainy season and in areas with long cold winter, receiving snowfall frequently.
- **Propagation:** *Swertia chirayita* is usually propagated through seeds after collecting the mature seeds in autumn.
- Chemical Constituents: The wide-range biological activities of *S. chirayita* are attributed to the presence of a diverse group of pharmacologically bioactive compounds belonging to different classes such as xanthones and their derivatives, lignans, alkaloids, flavonoids, terpenoids, iridoids, secoiridoids and other compounds such as chiratin, ophelic acid, palmitic acid, oleic acid, and stearic acid (Patil *et al.*, 2013). Amarogentin and amaroswerin (Fig. 4.) are the two major chemical constituents found in the plant and belonging to secoiridoid glycoside group of compounds.



Figure 5: Chemical structure of Amarogentin

• **Therapeutic Potential:** Species is used as anthelmintic, hepatoprotective, hypoglycemic, antimalarial, antifungal, antibacterial, cardiostimulant, antifatigue, anti-inflammatory, antiaging, antidiarrheal, as protectant of the heart and also help in lowering blood pressure and blood sugar (Schimmer and Mauthner, 1996).

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