



***Meconopsis aculeata*: A critically endangered medicinal plant and its multifarious medicinal properties**

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Abstract

Meconopsis aculeata, commonly known as Queen of Himalaya belongs to the family Papaveraceae. It is a crucial herb, used against various diseases and ailments under traditional medicine in Indian, Pakistani, Tibetan and Nepali culture since ancient time. Worldwide, there are approximately 49 species of genus *Meconopsis*, known for its medicinal values till date. As a consequence of specific habitat of Himalaya, environmental conditions and over exploitation, it is under critically an endangered species. The major chemical constituents of the *M. aculeata* are group of naturally occurring compound including Alkaloids, Phenolics, Tannins, Cardiac glycosides, Flavonoids, Saponins, Steroids, Triterpenoids, Carbohydrates, Proteins, Amino acids, Phytosterols, and Phlobatannins. Hardly any scientific literatures are available regarding anti-oxidant, anti-fungal, anti-inflammatory, anti-cancer, and anti-microbial activities of it. Therefore, the present review is designed to delineate only evidence-based depth information regarding ecological, pharmacological, and phytochemical of *M. aculeata*. Some conservation strategies also mentioned for this precious gem of Himalaya. In view of its various therapeutic potentials, this plant species is a subject of considerable modern scientific attention.

Keywords: antimicrobial activities, *Meconopsis aculeata*, papaveraceae, secondary metabolites, conservation strategies

Introduction

In the world, India is the 7th largest country with a total area of 32, 87,263 km² (coordinates: 8.4-37.61N latitude and 68.7-97.251E longitude) and stands in 6th position in regards to mega biodiversity centers. Approximately 6000-7000 flowering plant species out of 17,000-18,000 are evaluated to have medicinal properties usage in traditional knowledge. Literature of traditional medical system advocates that maximum plant species are used in Ayurveda followed by Siddha, Unani, and Tibetan practices. The local tribes of the Himalaya region of India, Pakistan, China, Nepal, and Tibet, are well known for their traditional knowledge concerning the ethnobotanical wealth of various medicinal plant species^[23,10,21].

Himalaya is credited all over the world as a treasure of medicinal, aromatic, and endangered plant species. *Meconopsis aculeata* Royle is the one among them that gained attention because it is an endangered medicinal plant, listed in the Red Data Book of Indian plants^[32]. It is a genus of the flowering, ornamental, decorative plant belonging to the family Papaveraceae, growing at higher altitudes i.e., approximately 4000m above mean sea level. In India, with an estimated 8000 species of medicinal plants, more than 90% of medicinal plants for herbal drug industries are drawn from natural habitats, thereby putting them to severe exploitation^[1]. Out of 49 species of the genus *Meconopsis* growing worldwide, about 38 species are distributed in the west of China including Qinghai, Sichuan, Yunnan provinces, and the Tibet region^[12,47].

It was first described by French botanist Viguier in 1814,^[1] and the species was described by Royle in 1833 from collected specimens. Its natural prominent habitats are Tungnath region of Western Garhwal Himalaya, Uttarakhand (Coordinates: 30°29'23.50"N -79°13'00.64"E), and at Gurez, Harmukh, Thajwas, Nagbaren and Munwarsar in Northwest Himalayan range, of Kashmir valley (330 20 to 340 54 N latitudes and 750 55 to 750 35 longitudes), India.

Literature advocates that *M. aculeata* has been studied in various part of world such as in Pakistan below Makra top, above Nila, above Tambu Naka, Danda Baik, Shingan, Pithoragarh, Bageshwar, Gauri Kund, Suru and Zanskar Valley, Western Himalaya from Kashmir to Kumaon, Ladhak, Sinthan top area of Ananthnag district, Vally of flower, Hemkund, Madhyamhablesheer, Rudra Nath in India, Nepal, China hill area and Tibet etc^[7].

M. aculeata is a rich source of primary and secondary metabolites which make it pharmacologically important^[41, 1]. The whole plant body is useful for various disorders, ailments along with antipyretic and analgesic properties^[3, 40, 34, 5]. Out of all genera of *Meconopsis* extensive research has been done worldwide on which *M.*

aculeata is underway and plant extracts of this endangered species may provide a source of new compounds including many drugs that are derived from plant sources for wellbeing. Therefore, the present review is designed to collaborate all information for therapeutic benefits against various diseases to conservation strategies of *M. aculeata*.

Local Names

It is famous as Queen of Himalaya and also known as Achatsarmum, Blue poppy, Kanta, Vanita, Ladak, Gul-e Nilam, AchaK-srmum, Gul-e-Neelam, Landrementok, Ut-Pal sngon-po, Chairingum, etc.

Botany and Ecology

M. aculeata is an endemic, monocarpic, perennial herb that bears a single, unbranched, erect, hard, and prickly stem of about 30–60 cm tall. A single raceme bears many flowers. The flower is showy, actinomorphic, hermaphrodite, complete, and hypogynous. Flowers are shallowly cup-shaped, lateral-facing to semi-nutant has a thin, cylindrical, bristly, and erect pedicel of approximately 2.5 to 13.5 cm in length. Petals are four to six (rarely), obtuse, delicate, thin, soft, obovate, or suborbicular of about 3.7×3.7 cm, blue-purple with wavy margins. Filaments are of filiform, of the same colour as petals but deeper; golden-coloured anthers. Ovary globose to elliptic, densely golden fulvous to bristly, bristles at first appressed, later ascending to sub spreading; styles distinct of about 1.2 cm. Basally thickened in fruiting; stigma lobes free/connate, oblong/spherical. Capsule spheroidal to elliptic-oblong, densely bristly, (3 or) 4-6 (8)-valvate for a short distance from the apex. Seeds reniform, Blooming fond between June - August. Rocky habitats, scree, stream margins; 2400–4200 m. Fruit is many-seeded capsules. Roots are napiform or long and narrow, of approximately 13 cm [6, 33]. Specific habitats are needed for its growth for instance sub-alpine and alpine zones, moist black sandy loam soils, rock crevices, boulders [27], and they bloom between June to August [33].

Molecular Study of *Meconopsis aculeata*

To date, scientists are involved to explore more information of *Meconopsis aculeate* by adopting various molecular approaches. Some researchers have used internal transcribed spacer (ITS) region of nuclear ribosomal DNA and the chloroplast DNA trnL-F region for phylogenetic reconstruction of *Meconopsis* and its close relatives like *Roemeria*, *Papaver*, and *Stylomecon* and identified five clades, which were well supported in the gene trees reconstructed with the nrDNA ITS and cpDNA trnL-F sequences. There are 41 species of Asian *Meconopsis* that did not constitute a monophyletic clade but formed two solid clades (I and V) separated in the phylogenetic tree by three clades (II, III, and IV) of *Papaver* and its allies. Clade V included only four Asian *Meconopsis* species, with the remaining 90 percent of Asian species included in clade I. In this core Asian *Meconopsis* clades, five subclades (Ia-Ie) were recognized in the nrDNA ITS tree. Three species (*Meconopsis discigera*, *M. pinnatifolia*, and *M. torquata*) of subgenus *Discogyne* were embedded in subclade Ia, indicating that the present definition of subgenera in *Meconopsis* should be rejected. These subclades were inconsistent with any series or sections of the present classifications, suggesting that classifications of the genus should be completely revised [17, 28].

Blue poppy is a traditional Tibetan medicinal herb with precious values in which chloroplast genome determined to be 153,761 bp in length with an A+T-biased base composition, and comprised a pair of inverted repeats (IR) regions (26,030 bp), separated by a large single-copy (LSC) region (83,803 bp) and a small single-copy (SSC) region (17,898 bp). A total of 113 gene species were annotated, with 20 of them being completely or partially duplicated and 18 of them harboring one or two introns. Phylogenetic analysis suggests that *M. horridula* is closely related to *Meconopsis racemosa* Maxim [17]. Another molecular investigation done by Xiao and Simpson 2017 showed that molecular phylogeny built by analysing four chloroplast markers are trnL-trnF intergenic spacer, matK, ndhF, and rbcL, and found that the evolutionary relationships revealed by phylogeny disagreed to varying degrees with any infrageneric relationship. This study concludes revised classification based on phylogenetic topology as well as the morphological and cytological patterns reflected by the phylogenetic structure. Finally, results were obtained from the four major clades of *Meconopsis* phylogeny as the bases for infrageneric sections (*Meconopsis* sect. *Meconopsis*, *M.sect. Aculeatae*, *M.sect. Primulinae*, and *M. sect. Grandes*) [45].

Ethnomedicinal Value

The whole plant part of *M. aculeata* is used as medicine. It has strong properties against malarial and bacterial capacity and can be used in drug production [33]. It is used as a Crude drug in the traditional system for curing rheumatic pains, febrifuge, analgesic, and narcotic and to treat the bones especially around the ribs [36, 40, 34, 5]. According to Thakur *et al.*, (2014) [39] Grounded roots of *M. aculeata* along with salt are given for creating resistance to diseases in animals. It removes the colour of veins when turns blue. It can also be given to pregnant women for the substitute of tetanus of their infants or child in any disease [18].

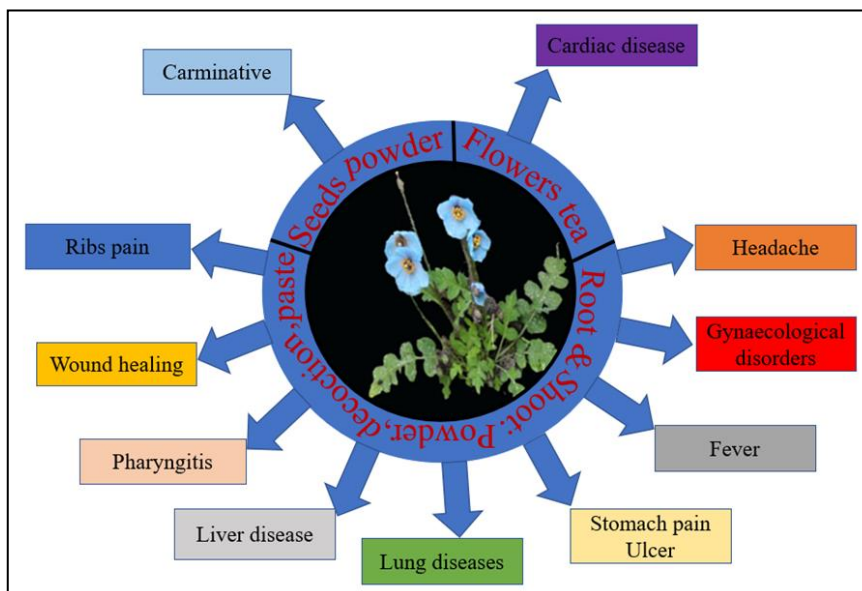


Fig 1: Plant part name and ethnomedicinal /ethnobotanical uses of *Meconopsis aculeata*.

Phytochemical Constituents

Meconopsis aculeata is found the superabundant source of phenols, flavonoids, cardiac glycosides, amino acids, carbohydrates, phytosterols, terpenoids, steroids, etc [8, 1]. The entire plant is used as a tonic and shows cooling potency [11, 40]. It has also been found to possess potent *in vitro* antioxidant effects against various free radicals and can combat oxidative stress disorder [22].

It contains phytoconstituents for instance alkaloids, phenolics, tannins, cardiac glycosides, flavonoids, saponins, steroids, triterpenoids, carbohydrates, proteins, amino acids, phytosterols, phlorotannins in its various extracts such as hexane solvent, ethyl acetate, methanolic and aqueous solvent. Terpenoids are a very important constituent found in *M. aculeata* making them pharmacologically crucial because it provides anti-inflammatory, anticancer, anti-malarial, anti-viral, and anti-bacterial properties [29, 31, 5] and helps in the inhibition of cholesterol synthesis. The presence of terpenoids produces it attracting to mites and consume the herbivorous insects [24] have been identified in the plant.

Methanolic extract of plant areal part showed isolate phenols (10.2%) > tannins (0.40%) > alkaloids (0.28%) in overall, whereas rhizome showed overall extract percentage of alkaloids, (4.30%) phenols (0.46%) and tannins (0.15%) along with the presence of tannins, cardiac glycosides, flavonoids, saponins, steroids, proteins, phlobatannins in less amount *i.e.* aerial part of *M. aculeata* contains the highest percentage of phenols, while as the highest percentage of alkaloids were recorded in rhizome part [22]. *M. aculeata* showed the highest total flavonoid content (TFC) in the ethyl acetate extracts with 15.637 ± 0.085 mg QE g^{-1} [41]. Yoshida *et al.*, 2006 [46] demonstrate that ferric ions and a supramolecular pigment such as commelinin or protocyanin are involved in the flower color development of the Himalayan blue poppy, *Meconopsis grandis*.

M. aculeata has potential for defense against many diseases since ancient times in Tibetan and Indian culture but lack of knowledge regarding phytochemical constituent and biological activities of it making this species inferior against other well-defined species such as *M. horridula* showed the highest level of tumor inhibition activities [38, 15, 20, 33].

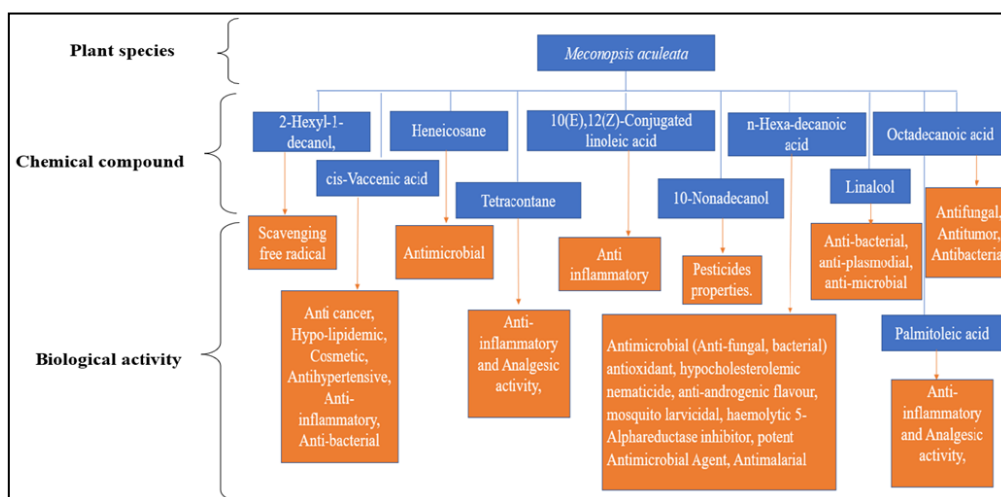


Fig 2: Bioactive compound and chemical constituents of *Meconopsis aculeata*

Biological Activities

Anti-oxidant and anti-inflammatory activities

Natural antioxidant bioactive compounds in diets reduced the risk of degenerative diseases such as cancer, diabetes, cardiovascular and neurodegenerative disease. In addition, natural bioactive antioxidant compounds have been widely used in the food industry to prolong shelf-life, because synthetic antioxidants such as butyl hydroxyanisole and butylhydroxytoluene (BHA and BHT, respectively) reported toxicity [37, 5]. Total phenolics (1.68-3.76 mg GAEg⁻¹), flavonoids (1.02-2.3 mg QEG⁻¹), flavonols (0.69-1.46 mg QEG⁻¹), tannins (1.25-3.83 mg TAEg⁻¹/g), and proanthocyanidin (0.34-0.81 mg CEG⁻¹) were reported that can prevent DNA damage, lipid peroxidation and protein oxidation in living cells. Antioxidant activity such as ABTS 2.33–2.67, DPPH 1.03–2.35, acetone (80%) was shown best for harnessing reducing antioxidant FRAP activity (1.76 mM AAE 100 g⁻¹ dw) and nitric oxide scavenging NO antioxidant activity (0.92 mM AAE 100 g⁻¹ DW) as compared to other solvents whereas ethanolic (60%) DPPH observed in *M. aculeata* [5, 41]. It possesses free radical scavenging activity and can act as a potent source of antioxidants against oxidative stress-related diseases [22; 44], phenolics and flavonoids are recognized for their multiple biological effects including anti-oxidants, anti-inflammatory, anti-microbial, anti-carcinogenic properties, etc [35], It is effective against the disorder of lungs, liver, and inflammation [38]. Hassan *et al.*, (2020) [22], conducted an experiment on methanol extract of *M. aculeata* and their results revealed that administration of CCl₄ caused a significant increase in serum AST, ALT, and LDH levels whereas consumption of *M. aculeata* extract prevents neutrophil infiltration and tissue necrosis in the liver samples of treated animals so can be used as hepatoprotective due to its antioxidant property.

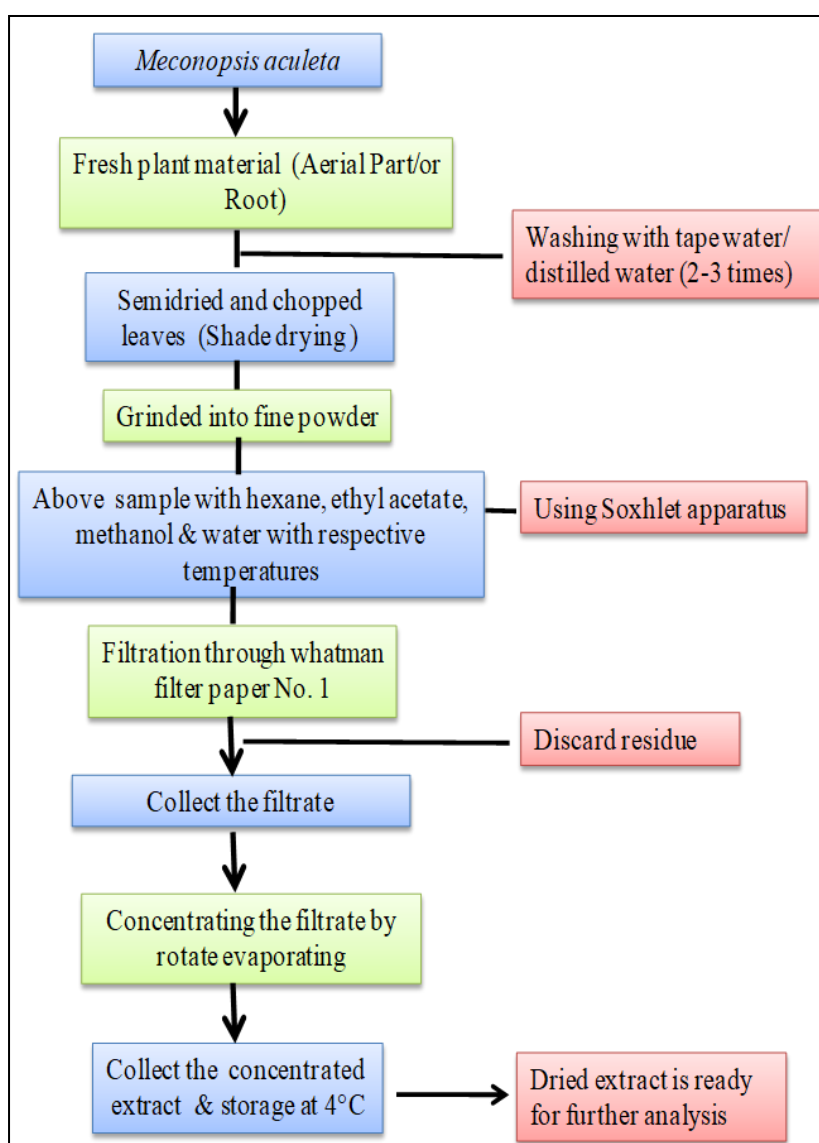


Fig 3: Procedure used in the extraction of *Meconopsis aculeata*

Anticancer activities

M. aculeata is a good source of flavonoids and alkaloids show anti-cancerous properties [28]. Besides these, due to the abundant presence of secondary metabolites including alkaloids, flavonoids, and phenylpropanoids, the plant showed strong anti-cancerous functions. Alkaloids are the main bioactive compounds of this plant.

Antimicrobial (bacterial and fungal) activities

Medicinal plants also possess various types of Antifungal properties [31, 19]. An experiment conducted by Tsering & Praveen, (2021) [41] on antimicrobial properties of *M. aculeata* revealed that plant samples were effective against the bacteria and the fungus cultures and the minimum inhibitory concentration (MIC) against the bacteria and fungi was 2.50 µg ml⁻¹. Antibacterial and fungal activities of *M. aculeata* showed that the MIC was variable in various extracts such as in petroleum ether extracts MIC was 2.50 µg ml⁻¹, 5.00 µg ml⁻¹, and 10.00 µg ml⁻¹ against *A. niger*, *E. coli* and *S. mutans* respectively whereas in chloroform and ethanol extracts MIC was 10.00 µg ml⁻¹ against *V. vulnificus*, and in methanol and water extracts it was 20.00 µg ml⁻¹ against *S. aureus*. In chloroform extracts MIC against *T. islandicus* was 20.00 µg ml⁻¹.

According to Tsering and Praveen, (2021) [41] presence of n-hexadecanoic acids, squalene, dibutyl phthalate, beta-amyrin, alpha-amyrin, and cis-vaccenic acid, eugenol, Lup-20(29)-en-3-ol, acetate, (3. beta.-), hentriacontanone, eicosyl, dotriacontinal, palmitoleic, 2-propenoic acid, A'-Neogammacer 22(29)-en-3-ol acetate, linalool, etc in the extract of *Meconopsis aculeata* are superintending for antimicrobial properties in species. This information will be helpful for the scientific community in exploring more antimicrobial activity in *M. aculeata*.

Threats to *Meconopsis aculeata*

Himalaya is privileged with considerable diversity of endemic plant species but undergoing unreasonable extraction of wild medicinal plants, endangering many of its high-value gene stocks. *M. aculeata* is one of the rarely found medicinal plant species, confined to the Himalayan range only, grow during May to October where flowering is observed from mid-July to August and fruiting from mid-August to September. From November to April, due to environmental conditions, seeds become dormant and germination percentage, growth, and development of plants get suppressed which play a role against conservation [30].

The cytological basis for the low viability of seed germination is the stickiness of chromosomes and irregular spindle activities are under the control of genetic factors caused by low-temperature stress conditions that prevail in the area when the plants enter the flowering stage. This phenomenon is known as cytomixis affect the meiotic course in the microsporocytes, resulting in reduced pollen fertility and pollen grains of variable sizes [27].

Because of the ethnobotanical importance of *M. aculeata*, owing to increasing market demand, the local indigenous population and pharma companies utilize it for commercial purposes especially when uprooting the whole plant causing the loss of herbal gems. Himalaya has been Cattles such as goat and sheep are the main dairy animals in hilly areas when these animals graze in sensitive areas due to improper graze management made these plants graze in early-stage. Climate change, avalanches are other factors responsible for the decline population of species as it significantly disturbs the plant population and habitat. Such overexploitation made it enlisted in the IUCN red list of 1997 in the endangered category [42, 43]. Majid *et al.*, (2015) surveyed for 3 years and found that only 39 mature plant species are available and categorized under critically endangered as per IUCN alphanumeric classification CR B1(i), (ii), (iii), (iv), and CR D.

Conservation Strategies of *Meconopsis aculeata*

The uprooting of plants made areas susceptible to plant growth as the soil becomes barren can cause landslide and deforestation as well [30]. For protection and management of such medicinal plants, confined only to some high-altitude areas, medicinal plant conservation societies (MPCS) should be established for the conservation of medicinal plants including threatened species from the local population under the observation of specialists of the field.

For rehabilitation and reintroduction of threatened species, ecological niche modelling could be of great help in predicting the potential habitats of threatened species. These implements will help in socio-economic conditions for the benefit of local, indigenous populations [15]. Sustainable land use may also be helpful in conservation.

In conservation strategies, seed germination studies are prime vital tools for reintroduction and management programs because it's a critical stage in the life history of plants. Under favorable conditions, seeds get to germinate. However, due to climate change, favorable conditions for seed germination may not persist for long enough and disturb the establishment of seed. Thus, increasing the chances of seedling mortality and thereby contributing to the decrease of population regeneration. Therefore, under control conditions *in vitro* seed germination of *M. aculeata* demonstrate under different media and supplements such as MS medium supplemented with Zeatin (4 mg l⁻¹) + NAA (0.5 mg l⁻¹) for pure germination, while for shoot germination seedlings on MS medium supplemented with Zeatin (2 mg/l) + IAA (0.1 mg l⁻¹) performed whereas MS medium supplemented with Zeatin (2 mg/l) + IAA (0.1 mg l⁻¹) recorded *in vitro* root regeneration. This protocol can be followed for *in-vitro* seed germination percentage of *M. aculeata* for the production of quality seedlings in large quantities to conserve species from the natural collection. In the same experiment hardening of sapling was achieved in 15 days with a survival rate of 60% is also a good sign towards conservation of plant [2].

A reliable *in-vitro* propagation method for *M. aculeata* and other Himalayan medicinal herbs can be produced for conservation purposes for the benefit of all. Danthonia grassy slope and mixed herbaceous is the most preferred habitat for medicinal plant species. Therefore, could be marked as control sites for future monitoring and assessment of population status for foreseeable future. Intensive habitat-based survey and phenological studies would be required for conservation, development, and sustainable harvesting plan of medicinal plants [15].

Toxicity

The root of *M. aculeata* is considered toxic due to the presence of narcotic alkaloids which may cause lethality. Therefore, it is suggested to take in prescribed amount for a limited duration to avoid its consequences. Sometimes its excessive use may cause harm to consumers^[33].

Conclusion

Meconopsis aculeata is cramped to the Himalayan range as it gets feasible environmental conditions to grow in the area. Due to seasonal dependence, climate change, cytological deformities, overexploitation, and unexploited knowledge about phenological parameters dwindle density of *M. aculeata* is impoverishing day by day. Therefore, it becomes critically endangered. Because of its ethnomedicinal properties plant should be commenced and promoted for further phenological, phytochemical, and antimicrobial studies so that this Himalayan gem can be conserved for human welfare and socioeconomic benefits. The available scientific research on *M. aculeata* has shown that it is an important broad-spectrum medicinal plant species. The detailed information presented in this review provides evidence for its ethnobotanical, molecular, phytochemical, pharmacological & traditional uses. This review article is based on the studies related to *M. aculeata* to date that will improve our future research view.

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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