# Phytochemical Profiling and Ethnobotanical Study of *Podophyllum hexandrum*

# Royle.: Insights from Langate Forest Division, Jammu and Kashmir

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**ABSTRACT**

# May Apple (*Podophyllum hexandrum* Royle.), a critically endangered Himalayan medicinal herb, possesses enormous medicinal potential. This study was conducted in the Langate Forest Division (LFD) of the Kashmir Valley. Information was gathered about the use of medicinal plants, methods of administration, and the specific plant parts used for treating various ailments by a field survey. Gas Chromatography-Mass Spectrometry (GC-MS) analysis was used to examine the phytochemical profile of the specimens to combine ethnobotanical knowledge with scientific reliability. This study revealed that the herb has a variety of ethno-veterinary and therapeutic applications. Medicinal uses of plants include the treatment of wounds, warts, gastrointestinal issues, and joint discomfort with rhizomes, resin pastes, decoctions, and powders. Its resin contains a significant amount of podophyllotoxin, a potent anticancer drug.  GC-MS analysis of the methanolic rhizome extract identified ten different bioactive compounds with anti-inflammatory, anticancer, and antioxidant properties. These included beta-sitosterol (13.72%) and podophyllotoxin (18.24%). Key threats to (*Podophyllum hexandrum* Royle.) include overharvesting, habitat loss, climate change, and lack of awareness. Therefore, there is a need for sustainable cultivation, habitat protection, and policy enforcement.

**Keywords**: Himalayan medicinal herb, GC-MS analysis, podophyllotoxin, anti-cancer, habitat loss

**1.     INTRODUCTION**

Over time, medicinal plants have been utilized in healthcare as effective treatment options (Ahire *et al.,* 2023; Dar *et al.,* 2023). These plants are used in traditional medicine worldwide owing to their therapeutic value, affordability, and cultural significance. (Nargawe, 2023; Ajewole, 2024). Owing to their economic potential in rural areas, medicinal plants are crucial for biodiversity conservation and sustainable development. (Kingston, 2010). Many modern medications are derived from medicinal plants and plant-based compounds are essential resources for modern medications (Ajani, 2022). Owing to the increasing prevalence of natural remedies and holistic health methods, medicinal plants have become more significant in healthcare investigations and are enhancing global health (Sharma, 2024). Numerous secondary metabolites, such as tannins, terpenoids, alkaloids, flavonoids, phenols, steroids, glycosides, saponins, and anthraquinones, are found in medicinal plants and provide a wide range of health benefits (Cowan, 1999).

The Himalayan May Apple, also known as the Indian May Apple (Podophyllum hexandrum Royle.) is a perennial herb found across the lower Himalayan region, spanning Afghanistan, Pakistan, India, Nepal, Bhutan, and Southwestern China. In India, this species thrives at elevations ranging from 3,000 m to 4,000 m in specific high-altitude areas, including Jammu and Kashmir, Himachal Pradesh, Uttarakhand, Sikkim, and Arunachal Pradesh (Kumar et al. 1997). Primary bioactive compounds in (Podophyllum hexandrum Royle.) include podophyllotoxin, quercetin, lignans, and kaempferol. These compounds possess significant anticancer, antirheumatic, radioprotective, antimicrobial, and antihelminthic properties (Nag *et al.,* 2013; Chaurasia *et al.,* 2011). The people of the ancient Himalayan region used the herbal plant (Podophyllum hexandrum Royle.) in traditional Ayurveda and folk medicine for hundreds of years (Chaudhari, 2014). This herb contains podophyllotoxin and its derivatives, which fight cancer cells while protecting against viral infections and supporting the immune system (Giri and Lakshmi Narasu, 2000).

  Gas chromatography-mass spectrometry (GC-MS) is widely employed in medicinal plant research to analyze and identify bioactive phytochemicals (Kotowska *et al.,* 2011; Brettell & Lum, 2018). Ethnobotanical studies are necessary to acquire the knowledge and practices of local people regarding the use of plants as well as to conserve biodiversity (Chaiyong et al., 2023). These investigations indicate long-standing customs that are significant in places like Asia where the use of medicinal plants has been a part of cultural practice, as well as indigenous knowledge and inventory of beneficial plants (Jatoi *et al.,* 2007). Furthermore, ethnobotanical research provides important insights into pharmaceutical development by overcoming the gap between traditional knowledge and modern scientific confirmation. Multiple issues, such as the excessive harvesting of plants and damaged ecological environments, disrupt the ability to protect these resources for future generations (Sheng, 2001). To ensure that medicinal plants thrive sustainably, efforts must be made to protect intellectual property rights and to limit unregulated plant trade (Yingam, 2024). This study will contribute to the UN's Decade on Ecosystem Restoration (2021–2030) objectives and guide policy frameworks under the CBD's Nagoya Protocol and India's National Biodiversity Action Plan. Therefore, this study bridges critical gaps in ethnobotany, ecology, and pharmacognosy, offering a blueprint for conservation (Podophyllum hexandrum Royle.) in an era of ecological and economic uncertainties.

**2.     Materials and Methods**

**2.1. Study area**

This study was carried out at the Langate Forest Division (LFD), which is located at an elevation of 2000–3500 m above sea level at latitude 34°15'22″ " N and longitude 74°07'52" E (Fig. 1). It covers a total area of 36,061 ha and is situated on the northeastern slopes of the Kazinag and Shamsabari ranges. The Haril in the region mainly has east-facing open slopes, with most of its drainage to the east. The area is mountainous with temperate and sub-alpine climatic conditions and an average annual rainfall of 66-167 mm. The temperature ranges from -10°C to 35°C (Romshoo *et al.,* 2020). The area experiences mild summers and chilly winters, with snowfall occurring from December to February. Broadleaved tree species like *Acer caesium, Prunus cornuta*, and *Robinia pseudoacacia* make up the majority of the forest’s vegetation, while conifer species like *Abies pindrow, Picea simithiana, Cedrus deodara, and Pinus wallichiana,* as well as shrubs like *Rosa webbiana, Berberis lycium*, and *Indigofera heterantha,* are also present (Sajjad *et al.,* 2022).

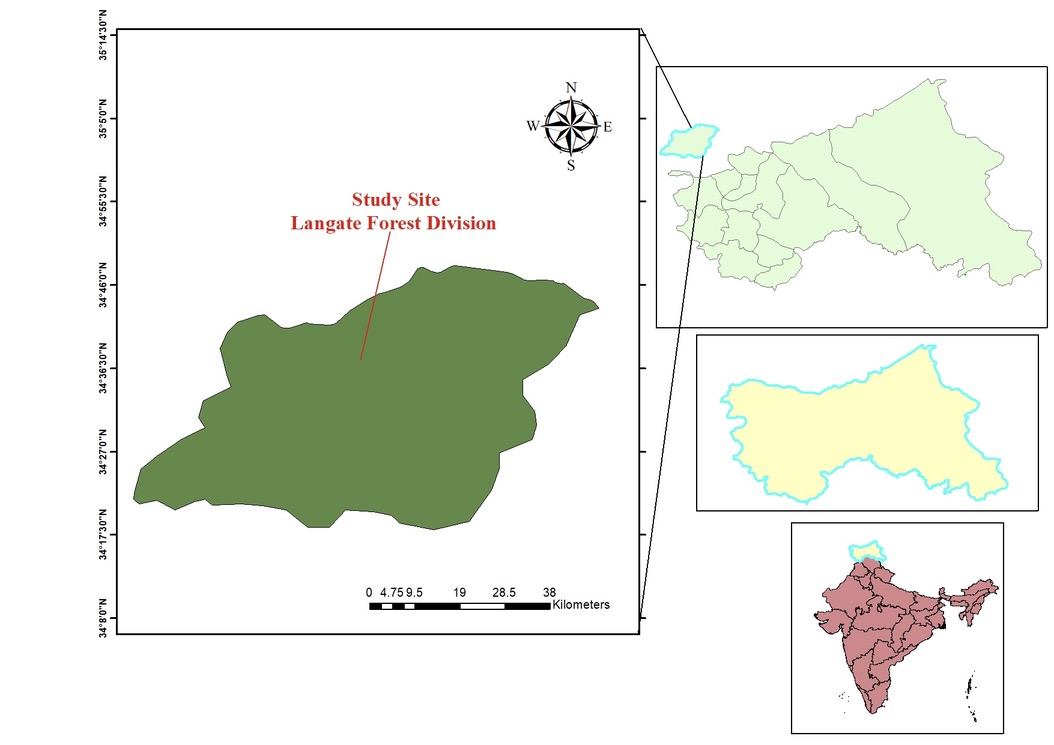


Fig. 1. Study area map of Langate Forest Division

**2.2. Ethnobotanical studies**

To obtain firsthand information about (*Podophyllum hexandrum* Royle.) Field investigations were conducted at the study sites. Ethnobotanical information was provided by gujjars, village heads, and elders. Data regarding the use of medicinal plants, methods of administration, and therapeutic plant parts were gathered through a field survey. The interviewees were selected from various groups based on their proficiency in traditional medicine practices, plant collection activities, and local expertise and experience. This approach ensured that the involvement represented community elders, herbalists, and healers (Focho *et al.* 2009).

**2.3. Collection of plant specimens**

### Rhizomes of this species were collected from the wild ( mawar and rafiabad ranges of Langate Forest Division) for extraction and chemical characterization experiments. The plant specimens were accurately identified through comparison with authenticated herbarium vouchers.

**2.4. Phytochemical Screening**

The rhizomes were first dried before being ground into a fine powder, and the extract was then filtered and condensed. GC-MS was used to identify the chemicals present in the samples (Parveen *et al.,* 2016). The methanolic extract was analyzed using a gas chromatography-mass spectrometer at a predetermined temperature. Retention time and area percentage values were used to identify chemicals in the chromatograms generated by the GC-MS analysis (Biswal & Kumar Panda, 2023; Sebastian *et al.,* 2020). The biological activities of the identified compounds were reviewed to relate them to the traditional uses reported by local communities.

**3.     Results:**

**3.1. Ethno-botanical Uses**

The Langate area in the District Kupwara Kashmir utilises (*Podophyllum hexandrum* Royle.) as a multipurpose herb for veterinary and medicinal applications. Rhizome paste with resin helps to treat warts, skin infections, and wounds and shows anti-cancer properties (Table 1).

**3.2. Phytochemical Screening**

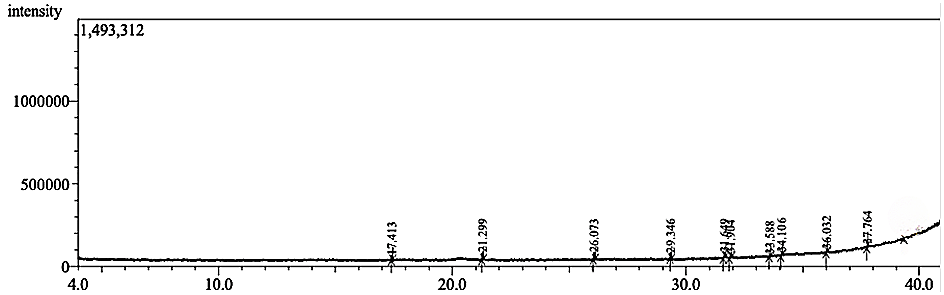
GC-MS analysis of a methanolic extract of the rhizomes of (*Podophyllum hexandrum* Royle.) revealed ten phytochemicals.  These ten chemicals are primarily composed of beta-sitosterol (13.72%) and podophyllotoxin (18.24%) (Fig. 2) (Table 2). These chemicals exhibit anti-cancer effects and function as antioxidants and anti-inflammatory agents, suggesting their potential applications in medicine (Table 3).

**Table 1. Ethnobotanical uses of *(Podophyllum hexandrum* Royle.)in Langate forest division**

|  |  |  |  |
| --- | --- | --- | --- |
| **Use Category** | **Specific Use** | **Part of Plant Used** | **Preparation**  **Method** |
| **Medicinal** | Treatment of warts, skin infections, and  Wounds | Rhizome, Resin | Paste or poultice applied topically |
| Anti-cancer  properties (source of podophyllotoxin) | Rhizome | Extracted resin used in modern medicine |
| Treatment of gastrointestinal disorders (e.g., diarrhea,  constipation) | Rhizome | Decoction or powder consumed orally |
| Anti-inflammatory and analgesic(joint  pain,arthritis) | Rhizome, Leaves | Paste applied to affected areas |
| **Ethnoveterinary** | Treatment of parasitic infections/antiseptic  in livestock | Rhizome | Mixed with fodder or applied topically |

**Table 2. Phytochemicals Identified by GC-MS Analysis of Methanolic Extract of *(Podophyllum hexandrum* Royle*.)* Rhizomes**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Peak Name** | **Retention time** | **Area %** | **Name of compound** | **Molecular Formula** | **Molecular Weight** |
| 1 | 17.413 | 10.97 | Campesterol | C₂₈H₄₈O | 400.69 g/mol |
| 2 | 21.299 | 18.24 | Podophyllotoxin | C₂₂H₂₂O₈ | 414.41 g/mol |
| 3 | 26.073 | 13.72 | Beta-sitosterol | C₂₉H₅₀O | 414.71 g/mol |
| 4 | 29.346 | 4.16 | Octadecanoic acid | C₁₈H₃₆O₂ | 284.48 g/mol |
| 5 | 31.649 | 8.01 | D-allose | C₆H₁₂O₆ | 180.16 g/mol |
| 6 | 31.904 | 7.51 | (9Z)-octadec-9-enoicacid | C₁₈H₃₄O₂ | 282.47 g/mol |
| 7 | 33.588 | 3.81 | Retinol | C₂₀H₃₀O | 286.45 g/mol |
| 8 | 34.106 | 12.38 | 2,2'-Benzylidenebis(3-methylbenzofuran) | C₂₆H₂₂O₂ | 382.46 g/mol |
| 9 | 36.032 | 7.88 | Sucrose | C₁₂H₂₂O₁₁ | 342.30 g/mol |
| 10 | 37.764 | 10.32 | Ethyl iso-allocholate | C₂₆H₄₄O₅ | 436.63 g/mol |

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**Fig. 2.** GC-MS Chromatogram of methanolic extract of(*Podophyllum hexandrum* Royle.)

**Table 3. Bioactive Compounds Identified by GC-MS in *(Podophyllum hexandrum* Royle*.)* Rhizomes: Structures and Therapeutic Uses**

|  |  |  |  |
| --- | --- | --- | --- |
| **Compound Name** | **Therapeutic Uses** | **References** | **Structure** |
| **Campesterol** | Cholesterol-lowering effects, Anti-cancer properties, Antiangiogenic | (Choi *et al* 2007;Vanmierlo *et al.,* 2012; Bae *et al.,* 2021), |  |
| **Podophyllotoxin** | Used to treat genital warts, Anticancer, Antiviral | (Giri and Narasu, 2000; Edwards *et al.,* 1988) |  |
|  |  |  |  |
| **Beta-sitosterol** | Antioxidant, Cholesterol-lowering agent, Food fortification | (Patch *et al.,* 2006; Arivarasu, 2023; Abumweis & Jones, 2008). |  |
| **Octadecanoic acid** | Antimicrobial, Anti-inflammatory and Anticancer | (Yonezawa et al., 2008; Desbois and Smith; Harvey et al., 2010) |  |
| **D-allose** | Anti-cancer, Anti-tumor, Anti-inflammatory, Anti-oxidative, Anti-hypertensive | (Zare *et al.,* 2023; Lim & Oh, 2011). |  |
| **(9Z)-octadec-9-enoicacid** | Cardiovascular benefits and Skin-conditioning properties | (Harvey *et al.,* 2010; Subramanian *et al.,* 2019). |  |
| **Retinol** | Essential for vision, Immune function, and Skin health | (Jun *et al.,* 2021; Sorg *et al.,* 2006; Hammerling, 2016). |  |
| **2,2'-Benzylidenebis(3-methylbenzofuran)** | Antidiabetic, Antioxidant | (Li *et al.,* 2013; Akinmoladun *et al.,* 2021) |  |
| **Sucrose** | Immunomodulatory, Hypertonic, Stabilizer and Cryoprotectant | (Struck *et al.,* 2014; Tomaszewska *et al.,* 2018) |  |
| **Ethyl iso-allocholate** | Antimicrobial, Antioxidant, Anti-inflammatory, Anticancer, Antitumor, Antiarthritic, and Antibacterial | (Tyagi & Agarwal, 2017) |  |

**4. Discussion**

In this study, we investigated the traditional applications and phytochemical composition of (Podophyllum hexandrum Royle.) within the Langate Forest Division of Kupwara District in Kashmir. This study highlights the significance of this endangered species in terms of its ecological role, therapeutic value, and cultural history.

4.1 **Traditional Uses**

In the Langate area of Kashmir, locals depend on the Himalayan May apple (Podophyllum hexandrum Royle.) for medicinal purposes. Podophyllotoxin has antiviral and anticancer properties; people use the rhizome and resin of the plant to treat wounds and skin-related diseases. It is used to produce etoposide and teniposide, two cancer medications. (Giri & Narasu, 2000; Kumar et al., 2015). In addition to its established veterinary uses, Podophyllum hexandrum Royle.) has traditionally been used to heal wounds and parasites in cattle because of its inherent antifungal properties (Kumar et al., 2015). The increasing demand for podophyllotoxin and the endangered status of the plant highlights the need for sustainable production methods, such as cell cultures or biotransformation, to protect this valuable resource (Farkya et al., 2004; Giri and Narasu, 2000).

**1.1.      Phytochemical Profiling (GC-MS Analysis)**

GC-MS analysis revealed that the rhizomes of (Podophyllum hexandrum Royle.) contain various bioactive compounds. The most common compound identified, accounting for 18.24% of the sample, was the cancer-preventive compound podophyllotoxin (Jiang et al., 2007; Qadir et al., 2020). The presence of significant levels of other secondary metabolites such as campesterol, beta-sitosterol, and D-allose in (Podophyllum hexandrum Royle.) Therefore, rhizomes may have medicinal potential. Research supports the anti-aging properties of d-allose (Eun et al., 2020).    Although the amount generated depends on the culture and extraction techniques, it might yield a range of beneficial chemical compounds (Bhattacharyya et al., 2013; Qadir et al., 2020). Further research is needed to optimize the extraction process for industrial use in cancer drug production.

1. **Threats, Conservation Challenges and Recommendations**

Threats to medicinal plants and their conservation illustrate how humans impact the environment and climate. Overharvesting of medicinal plants, particularly those with limited distribution and high economic value like (*Podophyllum hexandrum* Royle), poses a significant threat to their population and long-term survival (Kakkar *et al.,* 2023; Mathela *et al.,* 2021). Increasing market demand often leads to unsustainable collection practices, causing a rapid decline in wild populations (Mathela *et al.,* 2021). This is especially concerning for species such as (*Podophyllum hexandrum* Royle), which contains higher amounts of the valuable compound podophyllotoxin than other plants, making it a prime target for exploitation (Kumar *et al.,* 2015). Climate change significantly affects the Himalayan region, with predicted temperature increases of 5-6°C and rainfall increases of 20-30% (Salick *et al.,* 2014). These changes are likely to affect various plant species in the region, including those with specific habitat requirements such as (*Podophyllum hexandrum* Royle). The vulnerability of such species is often linked to their sensitivity to environmental changes and their limited adaptive capacity (Jamwal *et al.,* 2021). To address this, it is essential to do a study to track the effects of climate change adaptive management (Ebeling & Yasué, 2008; Kingsford, 2011; Shafi *et al.,* 2021) and encourage climate-resilient behaviours (Li *et al.,* 2022).   Cultivation strategies and strengthened harvesting regulations are crucial to safeguard endangered medicinal plant species. This approach has been supported by various studies. For instance, (Kougioumoutzis *et al.,* 2024) emphasize the importance of proactive measures, such as awareness raising, establishing plant micro-reserves, assisted translocation, and promoting sustainable harvesting to protect medicinal plants in the face of climate and land-use changes. Similarly, Shafi *et al.*, (2021) highlighted the need for multiplication and cultivation strategies and resource management for medicinal plant conservation. The findings of Ebeling and Yasué (2008) regarding the effectiveness of protected areas in reducing deforestation and protecting medicinal plants are consistent with our study.   Furthermore, Pilatti *et al.*, (2010) emphasised the importance of ex-situ conservation methods, such as seed banks and cryobanks, which permit the long-term conservation of a wider genetic base and provide additional safeguards against risks to field conservation. Tackling these interrelated challenges would require enhancing governance and imposing strict restrictions on the overharvesting of medicinal plants (Kingsford, 2011). These approaches, combined with protected areas and ex situ conservation methods, form a comprehensive strategy for safeguarding endangered medicinal plants and their habitats (Kougioumoutzis *et al.,* 2024).

1. **Conclusion**

In Kashmir's Langate Forest Division, a study shows the ethnobotanical usage of *Podophyllum hexandrum* Royle.) in addition to its vital ecological relevance and therapeutic benefits. The plant's therapeutic characteristics, particularly in the treatment of cancer, are supported by podophyllotoxin and other bioactive components. Ethnobotanical research indicates that traditional consumers of this herb have been using it for hundreds of years, but overharvesting and habitat damage pose a serious threat to its sustainability. Appropriate preventive measures must be put in place right away to preserve this vital species. The study shows that combining ancient knowledge with contemporary scientific methods is necessary to address future sustainable depletion. Fostering cultivation and enacting stringent laws for collecting in the wild are essential to the protected conservation of (*Podophyllum hexandrum* Royle.). Future Research should focus on three primary areas: (1) new cultivation techniques that reduce the requirement for wild collection; (2) documented cultural practices to inform conservation plans; and (3) alternative biotechnological techniques such as tissue culture for the manufacture of podophyllotoxin. Tests of community-based conservation models must be conducted alongside the evaluation of how climate change affects habitat suitability. Both the promotion of agricultural activities and strategies to safeguard protected wild populations should be established by the evaluation of policy research.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

Author(s) hereby declare that NO generative AI technologies have been used during the writing or editing of this Manuscript.

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