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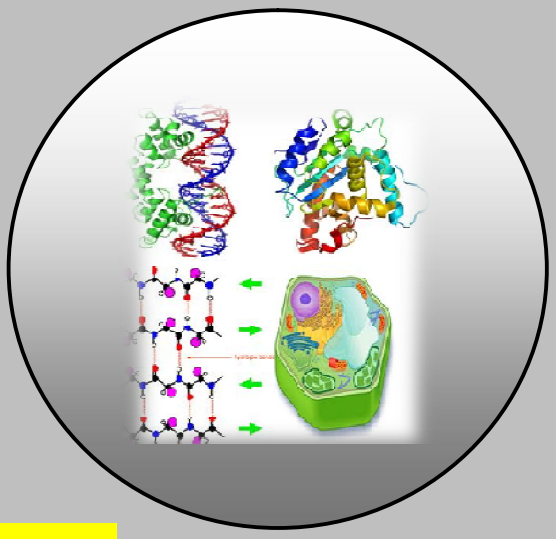

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REVIEW ARTICLE

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An Urgent Need for Conservation of *Podophyllum hexandrum* (Himalyan Mayapple) – An Economically Important and Threatened Plant of Cold Desert of Ladakh, India

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ABSTRACT

Podophyllum hexandrum is enlisted as an endangered plant under IUCN Red list and its high value in medicine needs active participation of scientists, research scholars, NGOS and government to come up with various conservation strategies. Podophyllum rhizomes and fruits are used as an anti-cancerous agents and in treatment of ulcers, hepatic disorders, wounds, cuts, tuberculoses and constipation. It also gives symptomatic relief to certain allergic and inflammatory conditions of skin. Rhizome is called Ol-mo-se in Ladakh which means the remedies for woman problems, and used against various gynaecological disorders in Tibetan system of medicine. Podophyllum is also an effective vermifuge, first stimulating then paralyzing and finally killing Ascaris. Podophyllum resin has a principle compound podophyllotoxin, which has received significant attention for their tumor necrotizing properties. It is currently required for the synthesis of chemotherapeutic drugs like etoposide, teniposide and ethopos etc. Himalayan mayapple is overexploited because the whole plant is uprooted for extraction of podophyllotoxin, which is a serious issue from conservation point of view. Thus, there is an urgent need for conservation and sustainable harvesting of this endangered plant.

Key words: Podophyllum, Podophyllotoxin, Endangered Plant and Conservation.

INTRODUCTION

The genus *Podophyllum* comprises of six species belonging to family Berberidaceae (Hooker, 1897). Out of these six species, *Podophyllum hexandrum* and *Podophllum peltatum* are economically exploited in different parts of world including India, Nepal and U.S.A.

The plant is used as a source of podophyllotoxin required for the synthesis of chemotherapeutic drugs like etoposide, teniposide and ethopos, which are being used for the treatment of several diseases of lung, stomach, pancreatic, testicular, amyeloid leukemia and other cancers (Stathlein and Warburg 1991; Ekston et al. 1998; Holm *et al.* 1989; Leander and Rosen, 1998). It is equally known for its use in the traditional system of medicine as remedy against skin diseases, sunburn and in radioprotection (Goel et al. 1998). On account of its importance and easy identitfication, it has received the attention of many scientists (Jakson and Dewick, 1985; Purohit et al. 1998; Bhadula, 1996; Sultan et al. 2008).

The Plant

The term *Podophyllum* is derived from an ancient Greek word means "foot leaf" and commonly known as mayapple because its fruits ripen in springs. (Chaurasia et al. 2012). *Podophyllum* is a herbaceous perennial plant, the stem grow 30 - 40cm tall, with palmately lobed umbrella like leaves up to 20-40 cm in diameter and 3-9 shallowly to deep incised lobes. The plant produces several stems from a creeping underground rhizome; some stems bear a single leaf and do not produce any flower or fruit, while flowering stems produce a pair or more leaves with 1-8 flowers in the axil between the apical leaves (Hooker, 1897). The flowers are white, yellow or red, 2-6 cm diameter with 6-9 petals, and mature into 2-5cm long green, yellow or red fleshy fruit (Dahiwal and Sharma 1999; Khakrawal et al. 2008) results in dormancy, poor seed germination and poor seedling germination. The flower of the taxon is solitary, erect, cup-shaped, bisexual actinomorphic and gamosepalous bearing deciduous petaloid sepals and six obovate/ oblong polypetalous petals. Stamens are 6 with anthers dehiscing along lateral slits. Ovary is superior, multilocular bearing ovules on marginal placenta (Dahiwal and Sharma 1999; Singh and Rawat, 2000; Khakrawal et al. 2000). In *Podophyllum* mature ovule is anatropous, bitegmic and pseudocrassinucellate. Ontogenetically, ovule arises as a mass of homogenous tissue on the central placenta. *Podophyllum* is evolutionarily advanced among other members of Berberidaceae in having pseudocrassinucellate bistomic ovule (Sreeniva et al. 2010).

Podophyllum propagates vegetatively by rhizome formation and sexually by seeds. The plant raised from rhizome cutting takes 12 years to produces far-sized marketable rhizome, whereas the plants raised from seedling takes even longer time (Bhadwar and Sharma 1963). Laverty and Plowright (1998) observed a significant increase in *Podophyllum hexandrum* fruit and seed production when population of *P. hexandrum* and *Pedicularis canadensis* are grown together and when insect pollinators regularly visited populations of both the taxa. This increase in seed production cross pollination was also observed with Bombus sp. (Swanson and Sohmer 1976). Successful propagation of *P. peltatum* using invitro technique has been reported by Moraes Cerdeira et al. 1998. This plant shows a higher survival rate in medium containing non- sterile (NS) sand (Moraes et al. 2004). Krochmal *et al.* (1974) were unable to germinate its seeds even after finding 88% of viable seeds with tetrazolium test. Bhadrwar and Sharma (1963) tried variety of treatment on seeds of *P. hexandrum*, but were unsuccessful. Success was achieved only after seeds were sown with fruit pulp. Such seeds germinated in 9-10 months.

Similar results were found in *P. peltatum* (Meijer 1974). According to Rust and Roth (1981), turtle ingested seeds germinated faster and had higher probability of survival than non-ingested seeds. Seed dormancy in *Podophyllum* has been considered to be a major constraint in seeds and most of the earlier reports recommended dormancy breaking pretreatments such as chilling, gibberellic acid (GA_3) etc. Several workers have reported the use of different treatment for blocking endosperm and/or mechanical or coat imposed dormancy in *P. hexandrum.* Khakrawal et al. (2008) were successful in overcoming the endosperm dormancy through excised embryo culture. During the development of *Podophyllum,* Watson and Lu (1999) observed that several factors like the current or future reproductive status, the genotype and the environment to which the plant was exposed might influence the timing of shoot senescence's.

The widely distributed *Podophyllum* grows over diverse habitats, from the extreme below zero winter temperature of north climates to high summer temperature of southern climates (Krochmal et al. 1974). Amercian mayapple grows in typical southern Appalachain cave soil with alluvial and coalluvial material at pH varying between 4.5 - 7.6 (Zhelijakov et al. 2009).

Medicinal uses

Podophyllum rhizomes and fruits are used as anti-cancerous agents and in treatment of ulcers, hepatic disorders, wounds, cuts, tuberculoses and constipation (Sharma *et al.* 2006). In past few years *Podophyllum* resin and its active principle podophyllotoxin have received significant attention for their tumor necrotizing properties. *Podophyllum* has been used in treatment of warty lesions on the skin and neoplasm occurring in the regions of body accessible to tropical therapy. It is also used in dermatological infections (Allevi et al. 1993).

Podophyllum is an effective vermifuge, first stimulating, then paralyzing and finally killing *Ascaris*. It also gives symptomatic relief to certain allergic and inflammatory conditions of skin. *Podophyllum* is also being used for controlling some form of cancer; the limiting factor is the severe gastro- intestinal discomfort while used in high doses. The drug podophyllotoxin has certain cytotoxic effects similar to that of colchicines (mitotic arrest, nuclear fragmentation, other evidence of cellular damage) as mitosis inhibitors. It is also used as anti-malarial and antifungal agents with immune modulator activities (Leander K & Rosen B, medicinal uses of podophyllotoxin, US Patent, 1988). It has been reported that after the major discovery of the anticancerous properties of podophyllotoxin derivatives, the US annual demand for *P. peltatum* rhizome was more than 130 tonnes in 1970 (Mejir, 1974).

Podophyllum hexandrum provides a reproductive effect in in-vitro and invivo models. The ripen fruits of *Podophyllum* species are said to be edible and also used against fever in traditional system of medicine in India. Rhizome are called Ol-mo-se in Ladakh which means the remedies for woman problems, these are used against various forms of gynaecological disorders in Tibetan system of medicine and in Ladakh (Ballabh and Chaurasia, 2007). The whole plant but especially the root is cholagogue, cytostatic and purgative.

The plant contains podophyllin which has an anti-mitotic effect. It is therefore, specially used in the treatment of ovarian cancer (Pugh et al. 2001). The roots are also antirheumatic (Duke et al. 1985). The plant is highly poisonous and should only be used under the supervision of a qualified practitioner and it should not be prescribed for pregnant woman (Bown, 1995).

It is currently being used as a lead compound for a semi–synthesis of anticancerous drugs etoposide, teniposide, etophos etc. which are used for the treatment of lung, testicular cancers and certain leukemia (Imbert, 1998). The aqueous-ethanoic (AEE) extract of high altitude *Podophyllum hexandrum* has earlier been reported to render a radioprotective effect against lethal gamma radiation in-vitro model. AEE has also been reported to posses metal chelating and DNA protecting properties. Podophyllin, a resin used as catharic, an anthelmentic and misuse as a lethal poison in 1974. Podophyllin reported as cancer growth inhibitor agent in animals (Jackson and Dewick, 1984). *Podophyllum peltatum* rhizomes have a long medicinal history among native of North American tribes who used rhizome powder as a laxative or an agent that expel worm (anthelmintic). Its powder was also used to treat warts and tumerous growth on skin.

Threat to *Podophyllum* and its conservation

Podophyllum is a hardy plant which thrive upto about - 20^{o}C (Knight, 1990). It takes years to become established but is very long lived in a suitable habitat (Facciola, 1990). According to reports, about 37.3 tonnes of rhizomes of *P. hexandrum* were uprooted during 1995-2000 in H.P. *P. hexandrum* has been overharvested to meet the demands of pharmaceutical industries. The entire plant is harvested due to presence of podophyllotoxin in its rhizome. That is why the species has acquired the endangered status (Gupta and Sethi, 1983; Foster 1993; Bhadula et al. 1996; Airi *et al.* 1997). Leaves of *P hexandrum* contain higher amounts of podophyllotoxin in comparison to *P. peltatum.* Himalayan mayapple is overexploited because the whole plant is uprooted for extraction of podophyllotoxin which is a serious issue from conservation point of view (Canel *et al.* 2001; Moores et al. 2001). In view of overexploitation due to its medicinal importance, a conservation strategy should be devised to increase its population number by propagating the plant through seed in a short period thereby compensating or reducing the harvesting pressure on rhizome.

Exploitation of *Podophyllum* from the wild is prohibited for export from India under CITES (Convention on International Trade In Endangered Species of wild flora and fauna). Only cultivated/ artificially propagated plant species is allowed for export under cover of CITES export permit and Legal Procurement Certificates (LPC) or certificate of cultivation from the designed authorities. *Podophyllum hexandrum* needs study of its variability and population under different locations with scientific basis and its ex-situ and in-situ conservation. National Medicinal Plant Broad, India has initated efforts towards conservation of rare, endangered and threatened medicinal plants throughout the country (Kaul et al. 1998).

CONCLUSION

Podophyllum is enlisted as an endangered plant under IUCN Red list and its high value in medicine needs active participation of scientists, research scholars, NGOS and government to come up with various conservation strategies. *Podophyllum* has wide scope of organized scientific study on its different aspects. Though the cultivation practices were standardized at several location but still quality and quantity of its bioactive compounds under different zones from wild and cultivable land is not systematically reported. Standardization of quality podophyllotoxin contents from cultured plantlets is another area of organized study due to its endangered status. Similarly, sustainable harvesting methods are urgently required.

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