Endangered Medicinal Plant *Psoralea corylifolia*: Traditional, Phytochemical, Therapeutic Properties and Micropropagation

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Abstract

*Psoralea corylifolia* is an endangered and medicinally important plant found in tropical and subtropical regions of the world. Its medicinal usage is reported in Indian pharmaceutical codex, the Chinese, British and the American pharmacopoeias and in different traditional system of medicines such as Ayurveda, Unani and Siddha. From its traditional uses in health care and food, extensive phytochemical studies have been reported. The present review reveals that wide ranges of phytochemical constituents have been isolated from the plant and it possesses important activities like antimicrobial, antibacterial, antifungal anti-inflammatory, antitumor, hepatoprotective activit, anti-psoriasis, anthelmintic, antidiabetic, immunomodulatory activities anti AIDS etc. Considering data from the literature, it could be demonstrated that *Psoralea corylifolia* possesses diverse bioactive properties and immense utilization in medicine, health care, cosmetics and as health supplements. As a health food, it is enriched with high therapeutic value with high potential for further development. The present review therefore aims to compile up to date and comprehensive information of *Psoralea corylifolia* with special emphasis on phytochemical and ethno medicinal uses, scientifically documented pharmacological activities and tissue culture methods for conservation.

1 Introduction

Plants are being used as source of medicine since ages. Many medicinal plants are nature’s gift to human beings to make disease free healthy life. India is one of the diverse countries in the world where the medicinal plant sector is a part of time-honored tradition that is respected even today	extsuperscript{1}. India is richly endowed with a wide variety of plants having medicinal value. These plants are widely used by all sections of the society whether directly as folk medicines or indirectly as pharmaceutical preparation of modern medicine	extsuperscript{2}. Over the past five decades focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional system. Medicinal plants are major source and biodynamic compounds of therapeutic value	extsuperscript{3}. More than 80% of the world population in poor and less developed countries depends on traditional plant based medicines for their primary health care needs. Numerous drugs or their precursors used in the current pharmacopoeias originate from plant sources. Natural products or natural product-derived drugs comprise nearly 28% of all the new chemical entities launched into the market in the last 20 years. Medicinal plant-based drugs have added advantage of being simple, effective, and offering a broad spectrum of activity with well-documented prophylactic or curative actions. Medicinal plant products have also proved useful in minimizing the adverse side effects of various chemotherapeutic agents. *Psoralea corylifolia* L. belongs to family Fabaceae (Leguminosae), and is an endangered herbaceous and medicinally important plant. It is found in tropical and subtropical region of the world. It grows in the plains of Central and Eastern India. *Psoralea corylifolia* has multifarious uses as it is an important component of ayurvedic as well as allopathic system of medicines. It is used in the treatment of psoriasis, leucoderma and in many medicinal formulations. It is valued in
Chinese herbal medicine as a tonic remedy and is used to improve general vitality. Interestingly, its medicinal usage is reported in Indian pharmaceutical codex, Chinese, British and the American pharmacopoeias and is found in Ayurvedic systems of medicines such as Ayurveda, Unani and Siddha. In Ayurvedic literature, the properties of Bakuchiol plant is documented as the Sanskrit shiloka states the use of Bakuchiol in various Ayurvedic treatments as in Kushtha (skin disorders); Kesha and Tchyya (skin and hair treatments); Krumi (as a germicidal); Shwasa & Kasa (Bronchial Asthma and Cough); Pandu (Anaemia); and Shotha (Oedema). The Psoralea corylifolia extracts have been reported to possess antibacterial, antifungal, antioxidant, anti-inflammatory, antifilarial, estrogenic, antitumour, and immunomodulatory activity.

Moreover, the plant is conventionally used in Ayurvedic system of medicine in some skin diseases and disorders such as psoriasis, vitiligo leucoderma and leprosy in the form of internal as well as external applications. It has been used in the treatment of eczema and hair loss. Roots of the plant are useful in dental caries, fruits are laxative, aphrodisiac, and are used for the treatment of leucoderma, leprosy and in inflammatory diseases of the skin and leaves are good for the treatment of diarrhea. The plant has been used in Ayurvedic medicinal system as a cardiac tonic, vasodilator and pigmentor. The great herb is widely used for the treatment of many kinds of skin diseases like leprosy, leucoderma, psoriasis. Eczema, vitiligo and effective for heart problems, asthma and urinary discharge.

Its natural populations have declined very fast due to indiscriminate and illegal collections, and destruction of its habitats. As a result, it is included in the endangered list of plants. Low germination percentage and viability of the seeds, long gestation periods and delicate field-handling are some of the factors which discourage commercial cultivation of the plant. The germination rate of Psoralea corylifolia seeds are low and span of viability is less which restricts its propagation through conventional method. The development of rapid, large scale propagation protocol for important medicinal plants has become a necessary in order to meet the pharmaceutical needs and also to prevent the plant from becoming endangered. In vitro micropropagation can be an alternative for meeting out the demand within in responsible time and obtain large number of consistently uniform and true to type plant with in short span of time.

2 Active constituents of Psoralea corylifolia

The major active constituents of P. corylifolia are coumifols a-c (prenylflavonoids) that are present in the seeds and other active compound such as psoralen, isopsoralen and neobavaisflavones are found in the dried ripe fruits. Daidzein (4:7 dihydroxizoflavon) and genistein (4:5:7 trihydroxizoflavon) are present in natural plants of P. corylifolia as well as in-vitro cultures. Other active constituents have since been identified, including neoba-vaisflavon, borachin, Bavaistavooz, bavachalcone, bavachromene psoralidin, corylifolin, barachini psoralenoside, isopsoralenoside and coumarin that have been isolated from this plant. A number of chemical constituents, including flavonoids and coumarins, have been isolated from this plant.

3 Traditional Uses

The seed oil is extremely beneficial, externally in numerous skin ailments. In hypopigmented lesions if the skin likes leucoderma and psoriasis respond well, to local application along with oral therapy. In leucoderma, the seed powder of Bakuchi mixed with Haratala Bhasma (Yellow arsenic), in 4:1 proportion and mashed with the cow’s urine. This paste is applied on the lesions of leucoderma. In scabies and ringworm infestations, the bakuchi seed powder mixed with buttermilk is applied externally. In leprosy, the seed oil is recommended orally, with beaten leaf. amalaki and Khadir are valuable adjuvants, with bakuchi, in dermatoses. In chronic skin disease, a mixture of bakuchi and karanja oil is commonly used with Vaseline, Scabies, Psoriasis ringworm and tinea versicular are treated successfully with bakuchi.

4 Pharmacological activities

4.1 Anti-cancer activity

Coumarins are a very common type of secondary plant metabolites with a broad spectrum of biological activities. Psoralidin is naturally occurring furano coumarin isolated from Psoralea corylifolia possessing anticancer and chemo preventive properties. Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) triggers apoptosis in cancer cells with no toxicity toward normal tissues. Endogenous TRAIL plays an important role in immune surveillance and defence against cancer cells. Coumarins can modulate TRAIL-mediated apoptosis in cancer cells, the cytotoxic and apoptotic activities of psoralidin in combination with TRAIL on HeLa cancer cells was determined. The cytotoxicity was measured by MTT and LDH assays. The apoptosis was detected using annexin V-FITC staining and mitochondrial membrane potential was evaluated using DePsipher staining by fluorescence microscopy. Death receptor (TRAIL-R1/DR4 and TRAILR2/ DR5) expression was analyzed using flow cytometry. Psoralidin enhanced TRAIL induced apoptosis in HeLa cells through increased expression of TRAIL-R2 death receptor and depolarization of mitochondrial membrane potential. The study indicates that psoralidin augmented the anticancer effects of TRAIL and confirmed a potential use of coumarins in cancer chemoprevention.

4.2 Antimicrobial activity

Psoralea corylifolia reported the presence of fourteen compounds which include aromatic, sesquiterpenes,
furocoumarins, sterols, fatty acid and their methyl esters. P. corylifolia seeds represented a unique chemical composition with considerable antimicrobial activity which not only validates their traditional medicinal uses but also indicates their potential as a source of natural antimicrobial compound.

Rao GV et al. 2010 isolated g-cadinene, bakuchio, psoralen, isopsoralen and psoraldin from the seeds of acetone extract of Psoralea corylifolia. The compound bakuchiol showed an excellent antibacterial activity than its crude extract35.

4.3 Antibacterial

Three new prenylfлавonoids, namely corylifols A-C (1-3), were isolated from the seed of P. corylifolia showed antibacterial activity against Staphylococcus aureus and S.epidermidis.

4.4 Antitumour activity

The plant possess potent inhibitory activity against 4 species of fungi viz. Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum and Microsporum gypseum36.

4.5 Anti-tumour activity

The volatile fraction (fraction I) and three other fractions (fraction II, III, IV) from methanol extract of P. corylifolia L. were isolated. The Fraction IV significantly inhibits the growth of cancer cells (KB, KBv200, K562 and K562/ADM) in a dose-dependent manner37.

4.6 Antidiabetic activity

Jitpal k et al. 2011 investigated the anti-diabetic and anti-oxidant potential of ethanolic extract of seeds of Psoralea corylifolia in streptozotocin( STZ) nicotineamide induced type 2 – diabetic rats. The findings indicates that Psoralea corylifolia has significant anti-hyperglycemic and antioxidant activity38.

4.7 Anti-AIDS activity

Psoralea corylifolia is also used against treatment of AIDS. Psoralen and Isopsoralen, the main active compounds isolated from Psoralea corylifolia are being investigated against AIDS39.

4.8 Anti-inflammatory activity

Neobavaisoflavone is one of the flavonoids found in Psoralea corylifolia. Neobavaisoflavone significantly inhibited the production of reactive oxygen species (ROS), reactive nitrogen species (RNS) and cytokines: IL-1β, IL-6, IL-12p40, IL-12p70, TNF-α in LPS+IFN-γ – or PMA– stimulated RAW264.7 macrophages40.

4.9 Larvicidal bioassay

The essential oil of Psoralea corylifolia produced significant larvicidal activities in terms of LC50 and LC90.

4.10 Pesticidal activity

The pure compound 6-(3-methyl but -2-enyl) 6-7 dihydroxycoumestan 1 isolated from chloroform extract of the seed of P. corylifolia and exhibited pesticidal activity against both adults and different instars of Tribolium castaneum Hebrst41.

4.11 Genotoxicity testing

Genotoxicity testing by comet assay The DNA damage studies were carried out using Single Cell Gel Electrophoresis (SCGE), commonly known as comet assay.

4.12 Anthelmintic effect

The alcoholic extracts of seeds of Psoralea corylifolia demonstrated anthelmintic activity on two-enzyme system taking rat brain as a model for Ascaridia galli42.

4.13 Hepatoprotective activity

The aqueous extract of seed furnished one hepatoprotective compound, bakuchiol 1, together with two moderately active compounds, bakuchicin 2 and psoralen 3, on tacrine-induced cytotoxicity in human liver- derived Hep G-2 cells43.

4.14 DNA Damage protection activity

Bhawya D et al. 2011 reported that ethanol, methanol and water extracts of Psoralea corylifolia showed significant antioxidant potency compared to other solvent extracts and also possess metal chelation and reducing power activity, protection against DNA damage and possess antibacterial activity. Hence it suggested that seeds of Psoralea corylifolia have potential application in food systems as an antioxidant and probably in biological systems as a nutraceutica44.

4.15 DNA polymerase and topoisomerase II inhibitors

An ethanol extract of seed caused strong DNA polymerase inhibition in a whole cell bioassay specific for inhibitors of DNA replication enzymes. Bioassay directed purification of the active compounds led to the isolation of the new compound corylifolin 1 and the known compounds led to the isolation of the new compound bakuchiol 2 as DNA polymerase inhibitors45.

4.16 Antipsoriasis

Arusha S et al. 2013 documented that ethanol seed extracts exhibited significant effect of anti-psoriatic and anti-bacterial activity. The seed extracts showed significant effect on psoriasis which was concluded by measuring mean thickness of epidermis and histopathological reports and anti-bacterial studies by zones of inhibition and MIC46.

5 Micropropagation

In vitro techniques have been increasingly applied for mass propagation and conservation of germplasm as it has superiority over conventional method of propagation and offer some distinct advantage over alternative strategies. The development

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of rapid, large scale propagation protocol for important medicinal plants has become a necessity in order to meet the pharmaceutical needs and also to prevent the plant from becoming endangered. The germination rate of *Psoralea corylifolia* seeds are low and span of viability is less which restricts its propagation through conventional method. Low germination percentage and viability of the seeds, long gestation periods and delicate field-handling are some of the factors which discourage commercial cultivation of the plant *in vitro* micropropagation can be an alternative for meeting out the demand within in responsible time and obtain large number of consistently uniform and true to type plant with in short span of time.

Consumer demand for high quality medicinal herbs is increasing at a slow, but steady, rate. Many of these herbs are harvested exclusively from stagnant to declining wild populations. One of the possible methods of protection of endangered taxon is multiplying and conservation of plants by *in vitro* cultures. Biotechnological approaches, specifically plant tissue culture plays a vital role in search for alternatives to production of desirable medicinal compounds from plants. The gradual decline in the population of *Psoralea corylifolia* demand launching of conservation effort so as to ensure continuous and ample supply by establishing a balanced cycle of harvest and renewal. Such conservation efforts would ensure continuous and ample supply of this valuable material which is in great demand by the pharmaceutical industry. Due to micropropagation it reduces cost and completion of life cycle can be attained within reasonable time, reducing risk of extinction to the wild population. An observation at the post-germination growth stage revealed that *Psoralea corylifolia* is a slow-growing species[46].

5.1 Micropropagation through apical meristem

The Apical meristems was used as the explants cultured on Murashige and Skoog (1962) medium (MS) supplemented different concentrations and combinations of plant growth regulators, 6-Benzylaminopurine (BAP), Kinetin (Kn), 1-Naphthaleneacetic acid (NAA) and B5 vitamins + 2 ml/ltr. Glycine (MBC). Results: Highest Shoot regeneration (95%) results were obtained on MS medium containing BAP (12 μM) with NAA (10.0 μM) and Kn (15.0 μM) generating shoots (6.12 shoots). BAP 12 μM found to be best for shoot multiplication.

5.2 Micropropagation through cotyledonary node

Cotyledonary node of *Psoralea corylifolia* gave rise to multiple shoots when cultured on MS medium supplemented with different concentrations of BAP and Kn. The highest rate of shoot multiplication was obtained in MS containing 2.22 μM BAP. The regenerated shootlets were rooted on MS basal medium with different concentrations of IBA. The maximum number of roots was produced on the medium containing 4.92 μM of IBA. The plantlets, thus developed were hardened and successfully established in soil. Tissue culture raised plants exhibited normal growth, flowering and pod setting[46].

5.3 Micropropagation through axillary meristem

Shoot induction on Murashige and Skoog medium supplemented with various auxins and cytokinins individually and in various combinations has been achieved by using axillary and apical meristems. MS medium fortified with 0.5- 2.0 mg/l BAP and 0.2mg/l NAA was found to be effective individually. The medium with 0.5mg/l BAP + 0.2 mg/l NAA responded better as compared to other combinations. 3-6 shoots having 2-3cm length has been initiated from axillary meristem were excised and further used for shoot multiplication on MS fortified with high concentration of growth hormones to produce shoots[47].

5.4 Micropropagation through leaves

Leaves segments, shoot segments and root segments excised from *in vitro* raised seedlings were used as explants. Among three explants used, leaves segments were best for callus induction as compared to shoot and root segments. The concentration of 2, 4-D (18 μM) + kinetin (2.0 μM) was sufficient to induce callus in 95% of cultures from leaf segments. Leaf segment derived calli were greenish yellow and friable. Higher number of shoots (6.15 shoots) was obtained BAP (14 μM) with NAA (10.0 μM) and Kn (10.0 μM) from leaf derived callus. The %age of shoot generates from shoot derived callus (70.5%) is higher than shoot generates from root derived callus (40.3%). Regenerated shoots were rooted on MS medium supplemented with different plant growth regulators and best response (92%) was observed with IBA (0.5μM).

5.5 Micropropagation through hypocotyle

Hypocotyl explants was used as the explants cultured on Murashige and Skoog (1962) medium (MS) supplemented with different concentrations and combinations of plant growth regulators. The highest response was observed in ms medium containing 3mg/l of BA benzyladenine and 1 NAA and 5AA(ascorbic acid) and 5mg/l of (CH) casein hydrolysate. the regenerated shoots were rooted on half strength ms basal medium supplemented 3 mg/l IBA. Rooted shoots were effectively transfered to garden soil farmedy soil, and sand 2:1:1 mixture subsequently plants were successfully aclimatised,.During acclimatisation plants were irrigated with 50 ml one-eight strength MS basal salt solution devoid of sucrose and inositol But supplemented with 3 mg/l of IBA and Bavistin (BV).The plants were subsequently established in the field[46].

5.6 Micropropagation through nodal segments

Nodal explants was used as the explants cultured on Murashige and Skoog (1962) medium (MS) supplemented with different concentrations and combinations of plant growth regulators, The highest response was observed in MS medium
containing 5mg/l of BA benzyladenine and addition of 100mg/l of (CH) casein hydrolysate in medium enhanced the growth of regenerants. The regenerated shoots were rooted best in half MS basal medium supplemented with0.5mg/l IBA. Rooted shoots were hardened successfully and maintained in nursery90.

5.7 Callus induction

Callus induction depended on the different concentration of plant growth regulators as well as type of explants in the callus-inducing medium. Leaf segments, shoot segments and root segments excised from in vitro raised seedlings were used as explants. Among three explants used, leaf segments were best for callus induction as compared to shoot and root segments. The concentration of 2, 4-D (18 μM) + kinetin (2.0 μM) was sufficient to induce callus in 95% of cultures from leaf segments. Leaf segment derived calli were greenish yellow and friable. Higher number of shoots (6.15 shoots) was obtained BAP (14 μM) with NAA (10.0 μM) and Kn (10.0 μM) from leaf derived callus. The %age of shoot generates from shoot derived callus (70.5%) is higher than shoot generates from root derived callus (40.3%). Regenerated shoots were rooted on MS medium supplemented with different plant growth regulators and best response (92%) was observed with IBA (0.5μM)90.

6 Conclusions

Plants are the main repository of all kind of biochemical’s which are produced as primary and secondary metabolites. These metabolites are industrially important as they constitute the major chunk of pharmaceutically important drugs. As a result of their huge demand in modern market they are overexploited from their natural habitat, resulting in disappearance of many plant species. Widespread harvesting of medicinal plants will lead to loss of genetic diversity and income to poor people who benefit greatly from the collection and trade in plants. From the review of the literature, we conclude that development of appropriate can ensure availability of uniform and disease-free propagules for cultivation and management of threatened plants on farmland. Conventional breeding is slow and horticultural tools may not be sufficient to meet the future demand for these plants. Therefore, plant tissue cultures are being potentially used as an alternative new strategy for conservation of this important plant species.

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8 Conflict of interests

No conflict of interest among all authors of this work

9 Author’s contribution

NGN and MK carried out literature review and draft the manuscript. RS participated in collection of data. All authors read and approved the final manuscript.

10 References


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