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Traditional and Contemporary uses, Phytochemistry and Pharmacology of *Psoralea corvlifolia* Linn.

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ABSTRACT

Background: Bakuchi (Psoralea corylifolia Linn.) is an endangered and traditionally important medicinal plant of the family Fabaceae. It is used worldwide for the treatment of several ailments due to the presence of various bioactive constituents that are mainly concentrated in the seeds and fruits of plants. It has been used since time immemorial as a popular drug for shvitra (leukoderma), kustha (skin diseases), osteopathy, rejuvenation, aphrodisiac, etc.

Materials and Methods: Primarily, classical texts of Ayurveda including Brihat trayi (The greater triad), Laghu trayi (The lesser triad), and Nighantu (Lexicons) were reviewed. Establishing an overview, library resources, and online collections of books and other online databases such as Pubmed Central, Scopus, Embase, Web of Science, ERIC, IEEE Xplore, ScienceDirect, DOAJ, JSTOR, Henari, Google Scholar, NepJoL were explored with search words like "Bakuchi", "*Psoralea corylifolia*" for its botanical characteristics, traditional and contemporary uses, pharmacognosy, phytochemical constituents, pharmacology, toxicology, and agricultural and miscellaneous aspects.

Results and Discussion: It was found that Psoralea corylifolia has been used since the Vedic period for the treatment of various skin diseases like psoriasis, and vitiligo in Ayurveda and several metabolic and systemic diseases in Traditional Chinese Medicine, by its various names and formulations. Furthermore, under appropriate dosages no any toxic effect of the plant was reported in an animal experiment conducted by Uthirapathy and Ahamad.

Conclusion: The seed of *P. corilifolia* Linn is commonly used in skin diseases such as Switra (leukoderma), *Vicharchika* (psoriasis) whereas anti-oxidant, anti-diabetic, anti-lipogenic, anti-tuberculous, anti-carcinogenic, memory enhancing, anti-venom and aphrodisiac has also been reported as its major pharmacological activities. Clinical trials can be further conducted to evaluate the pharmacotherapeutics of *P. corylifolia* to develop the well-established evidence-based therapy.

Keywords: Bakuchi, Psoralea corylifolia, Switra, Leukoderma, Psoriasis

INTRODUCTION

Psoralea corylifolia Linn. (PC) belongs to the Fabaceae family which is a versatile herb known for its medicinal and non-medicinal uses. It is abundant in the subtropical plains of Nepal, India, and China.

As an etymology, *Psoralea* comes from the Greek word '*psoraleos*' which means (scabby), and denotes the plants with an uneven surface due to glandular spots or warts¹, it also possesses the meaning of "affected with itch or with leprosy".² Whereas *Corylifolia* is derived from the Greek word 'korus' which means helmet, calcine covering the nut.¹

This plant can be used for various purposes, Traditional Chinese Medicine (TCM) uses its dry fruit and calls it "Buguzhi"3referred to as "Bu-gu-zhi" in Chinese, has great medicinal values since ancient times. PCL is the dried ripe fruit of Psoralea corylifolia L., which has been widely used in traditional Chinese medicine (TCM; homeopathy uses the mother tincture of PC⁴with cosmetic and psychological effects. Studies suggest Psoralea corvlifolia (PC; and Ayurveda describes the use of fruit, seed, and seed pulps, and nut-derived oils for various ailments.5,6 In the vedic period, PC was widely used along with Surya chikitsha (Solar therapy) to treat switra and other venereal diseases. In a brief review of different references in the vedic literature, none of the synonyms of PC were found significantly traceable. Though Somavati had been explained in the Rigveda, its identity with PC can't be established.^{7,8} It seems to be another plant from which sura (drinks of deva) or soma rasa (nectar) were extracted instead.

During Samhita period, Ayurvedic classics have mentioned the *sodhana* (purification) of PC by immersing in *Bibhitaki kwatha* (decoction of *T.bellerica*) for one night.. This process involving *toya sannikarsha* (contact with water) appears to be similar to the hydrolysis process. On hydrolysis, two benzofuran glycosides, namely isopsoralenoside, and psoralenoside, from the fruits with no trouble get converted into isopsoralen and psoralen.⁹ Thus, hydrolysis makes these alkaloids interconvertible and in simpler form.

The Chikitshasthana, Visha Chikitshitam adhyaya of Charaka Samhita mentions the name Kusthaghna (anti-dermatic disorders) for Khadira (Acacia catechu Linn.) or Prapunnada (Cassia tora Linn.) but not for Bakuchi. In the Brihatrayee, the name of the plant has been coined as Avalguja. Intellectuals like Thakurji have doubted even the name of Somaraji. According to Thakurji, the ethnic name Sevaraja in the forest of Bihar is used for bitter cumin (C. anthelminticum); and that may also be thought for Somaraji. Due to the two significant qualities of Bakuchi such as Visaghna (antidote) and Shawitranasana (eliminate Leucoderma), there is some possibility for an explanation of two varieties of Bakuchi in the classical literature.7 In Bhavaprakash Nighantu with Hindi commentary, KC Chunekar has considered Vernonia anthelmintica Wild. as Somaraji, however, it is the name of Aranyajeeraka.¹⁰ Some of the literature have created a lot of misperceptions by considering Somaraji as Kalajaji (Nigella sativa Linn.); and both as Bakuchi. However, Bakuchi or Somaraji has been recognized as P. corylifolia at present.7 The Charaka Samhita mainly mentions Avalguja as agada. It becomes quite interesting to note that Acharya Charaka hadn't described this plant with the name of bakuchi. Aacharya Susruta used the name Bakuchi for the first time in Kusthachikitshitam adhyaya and Mishrakachikitshitam adhyaya.¹¹ Acharya Vagbhata had used this synonym in the Atishara chikitsha adhyaya and Kustha chikitsha adhyaya in Chikitshasthana and Nasarogavijnaaneevam adhvaya in Uttaratantra of his Astanga Hridayam.12 The Sushruta Samhita mentions it as a treatment for kilas (hypopigmentation disorders of skin) whereas Acharya Vagbhata has mentioned Bakuchi as a rejuvenating drug.

In Bhavaprakash Nighantu, the management of switra with *Bakuchi churna* and *Bakuchi taila* is well explained; and also, as *keshya* (hair growth promoting agent). Bakuchi had rarely been used in the medieval period.¹⁰ In the context of the history in Nepal, the Chandranighantu has mentioned *Bakuchi* as *Vasuchee*.¹³ Ayurvedic Pharmacopoeia of India mentions PC as an official source of a classical drug named *Bakuchi*, has been used in a face serum with Palmitoyl Tripeptide-38, Hydrolyzed Hyaluronic Acid along with Polyherbal and Vitamins have shown positive results in the hydration of the skin.¹⁶

Scientific classification

Kingdom: Plantae SubKingdom: Angiospermae Division: Spermatophyte Class: Dicotyledoneae Natural Order: Fabales Family: Fabaceae Genus: Psoralia Species: *Corylifolia*

Sub Species

Cullen corylifolium Cullen corylifolia Psoralea patersoniar Lotodes corylifolia Trifolium unifolium

Local Names

Bakuchi, bakachi: Nepali13 Bakachi: Newari, Hindi13 Babchi : Unani Bawachi: Urdu Buckidana: Bangladesh Bakuchi: Nepali Babakhi: Persian Ravoli: Sri Lanka Ku Tzu: Chinese Bawchan: German Mahalep: Arabian Boh-Gol-Zhee: Korean and chinese

Rasa Panchak

Rasa: Madhura, Tikta Guna: Guru, Ruksha Veerya: Sheeta Vipaka: Katu Prabhava: Vistambhi, Grahi



Fig 1: Whole plant of *Psoralea corilifolia* Linn. (A), Fruit (B) & Seeds (C)

Botanical description: PC is a large genus of herbs, shrubs, or under shrubs distributed in tropical and sub-tropical regions of the world. It has hairy roots and stems and roots have sharp glands with marks. The leaves are simple, and rounded with mucronated apex. It consists of an axillary, single inflorescence (raceme) with 10 to 30 flowers and a tufted pedicle. The flowers are yellow and bluishpurple colored. The plant bears 5mm long and slightly compressed fruits arranged in 10-30 raceme. Its seeds are campylotropous, bean-shaped oblong, flat, and brownish-black in color with a bitter taste and unpleasant odor.¹⁷ The plant is sown from March and April. Its flowers appear from August to December, and fruit collection is done from October to February, and then after seed collection is done from February to March.¹⁸

Propagation: Propagation of PC is difficult due to low propagation rates and long dormancy¹⁹ and absence of propagules for breeding. The crop is grown directly by sowing seeds that germinate easily. For the whole crop, 8 kg of seeds are needed per hectare. No special pre-treatment is required before germination. Plantation should be done in the field before the onset of monsoon, and the land should be prepared by ploughing 2-3 times with a disc plough. The area is divided into suitable plots. Main and secondary irrigation canals are made ready and the seeds are sown directly in the rows at an optimal distance of 60 x 30 cm for proper crop lift. NPK (nitrogen, phosphorus and potassium) in the ratio of 60:60:30 kg/ha is given as a basal dose and mixed into the soil together with 10 tons/ha of FYM (farm yard manure) as a fertilizer. This crop can be grown as a catch crop in tree plantations in orchards.

Regular weeding (2-3) and hoeing during the early growing season are required to control weeds.¹⁸ The crop is rainfed and can tolerate partial drought conditions. However, after sowing, 2-3 irrigations are required depending on soil conditions and monsoon rain distribution. Manual weeding should be done to keep the plantation free of weeds.²⁰

RESULTS AND DISCUSSION

Phytochemistry: Chemical constituents of fruit are isoflavone, and corylinin, along with six known compounds such as isopsoralen, psoralen, sophoracoumestan A, neobavaisoflavone, daidzin, and uracil.²¹ It also contains corylinal and neobavaisoflavone including the methyl esters of the 2 compounds, psoralenol, 5'-formyl-2',4-dihydroxy-4'-methoxychalcone, and bavachromanol. Chemicals like α -elemene, γ -elemene, β -caryophylenoxide, Limonene, 4-terpineol, linalool, geranylacetate are present in the essential oil of PC.²²

Chemical constituents of seed oil are psoralen, isopsoralen, isobavachalcone, dehydroisopsoralidin, corylin and psoralidin. It becomes quite interesting to know that the most popular constituent of PC i.e. bakuchiol is not present in its seed oil.²³

Newton *et al.* a pigment; probably a hydroxy flavone in the seeds, a monoterpenoid phenol named bakuchiol²⁴ ($C_{18}H_{24}O$, b.p. 145–147°C). It also contains brown fixed oil (10%); raffinose and coumarin compounds, and psoralen and angelicin.²⁵

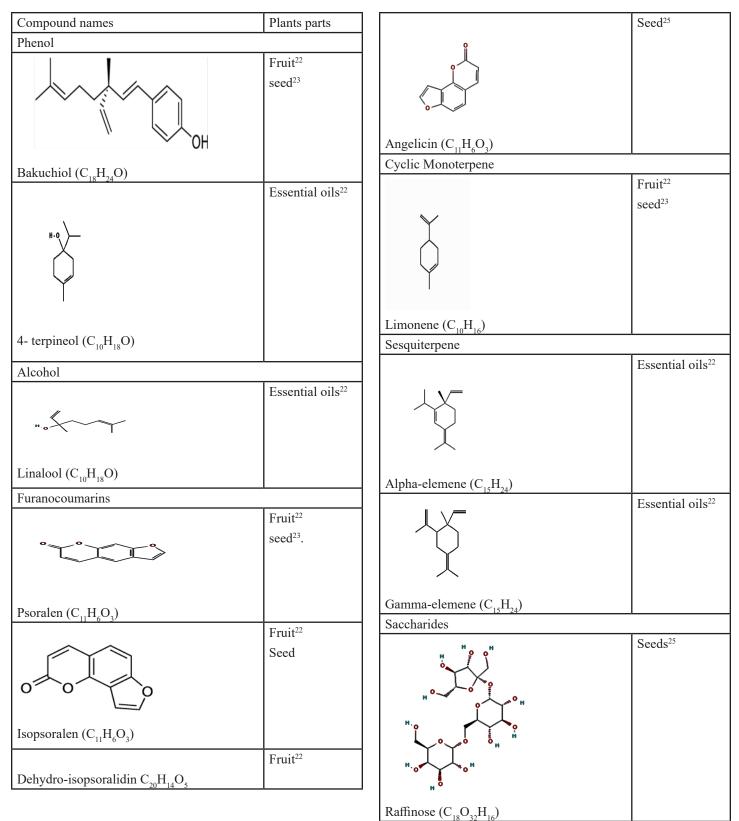
Out of all the above-mentioned chemical constituents, Wang *et al.* investigated a quantitative assay of some important constituents of PC collected from China in three batches with Ultra performance liquid chromatography (UPLC). It was found that the minimum and the maximum value of psoralenoside ranged from 7.42 to 17.04 mg g⁻¹, isopsoralenoside from 6.05 to 14.34 mg g⁻¹, psoralen from 2.37 to 3.90 mg g⁻¹, isopsoralen from 2.53 to 3.65 mg g⁻¹, neobavaisoflavone from 1.59 to 2.96 mg g⁻¹, bavachin from 1.02 to 2.35 mg g⁻¹, psoralidin from 0.45 to 1.91 mg g⁻¹, isobavachalcone from 1.33 to 4.71 mg g⁻¹, corylifol A from 1.02 to 2.40 mg g⁻¹ and bakuchiol from 28.10 to 63.89 mg g^{-1,26}

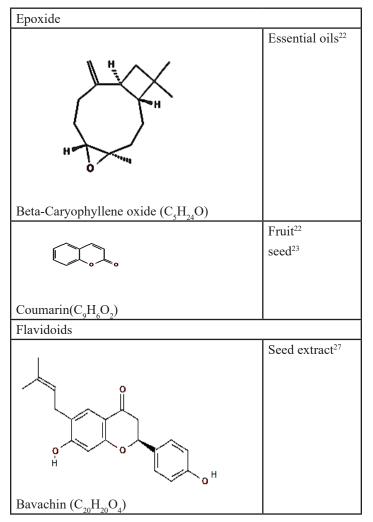
Traditional and contemporary uses: In the *haritkyaadi varga* of *Bhavaprakash Nighantu, Bakuchi* has been described to use as *rasayana* (rejuvenation), and in *Swasa* (asthma), *kasa* (cough), *raktapitta* (excessive bleeding), *pandu* (anemia), *jwar* (fever), *krimi* (helminths) and *prameha* (diabetes).¹⁰ PC is an ingredient of *nila* and *mahanila ghrita* in *Kusthachikitshitam adhyaya*, and in *Unmantha-paali roga* (disease of external ear and auricle) in the *Mishrakchikitshitam adhyaya*.¹¹ it is widely used in traditional medicines, especially for skin diseases. Finally, the Chandranighantu has added its use as *saaraka* (laxative) and

ruchikara (appetiser).13

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Table 2. Phytochemical constituents of P. Corylifolia





In Brihat trayi (Three greater triads) of Ayurveda, Charaka Samhita Sutrasthana mentioned Somaraaji as a Vishaghna (destroys poison), in the Kustha Chikitshaadhyaya where the use of lepa (paste) of bakuchi seed in gomutra (Cow urine) is mentioned in case of leukoderma. In the Arsha Chikitsha adhyaya, the use of bakuchi leaf in Sushka arsha (non-hemorrhoidal piles); and in Palit roga (whitening of hair) and in the Visha Chikitsha adhyaya of Chikitshasthana he had mentioned its uses in sarpa visha (snake poisoning).²⁸

In the Sushrutta Samhita Chikitshasthana, Bakuchi has been mentioned to be used in switra (leucoderma), and in all asadhya kustha (incurable skin diseases), fistula, and worm-infestations Similarly, in the Astanga Hridaya; Bakuchi has been described to use in Amashaya-pakvashayagata visha (poison in stomach and large intestine) in sutrasthana annarakshaadhyaya, pravahika (dysentery) in the atisaarachikitsha-adhyaya and kustha roga (skin diseases) in kusthachikitsha adhyaya of chikitshasthana and in the rasayana-vidhi adhyaya of uttartantra.²⁹ Moreover,

in the *Gunadravyaavali* of the *Dhanwantri Nighantu*, it has been mentioned as *vrishya* (Aphrodisiac), and in *Guduchyaadi varga* as *grahi* (astringent), and *vranapaha* (destroys wounds).³⁰

TCM uses PC and other species by the name *Bol-gol-zhee* or *Bu-gu-zhi* in postmenopausal osteoporosis, vitiligo, and psoriasis³¹; and it is also used for enhancing renal health conditions and spleen meridians.³² Xuenong et al. have added its use in Chinese medicine in formulations for the treatment of diseases like leucoderma and other skin diseases, cardiovascular diseases, nephritis, osteoporosis, and cancer.³³

PC has been successfully used as a remedy for psychroalgia, stomachic, cardiovascular diseases, weak kidneys, and vitiligo in oriental medicine.³⁴ Buguzhi is a Yang tonifying substance in TCM used for curing Yang deficiencies(deficiency of heat, and masculine energy³⁵ which are allied with the sensation of cold, lethargy, and paleness.³⁶

Pharmacological Activities

1. Anti-carcinogenic activity: When the aqueous extract of PC was treated on two proliferating human metastatic cancer cell lines, MDA-MB231 (breast cancer cells) and SKOV-3 (ovarian cancer cells), for 24 hours with various concentrations, it was seen that cell proliferation was inhibited in a dose-dependent manner. The extract concentration of 100 µg/ml had no significant effect on the cells, whereas 1,000 µg/ml of the extract almost completely inhibited colony formation.³⁷ Yang et al. also reported similar effects at similar concentrations on cancerous cells of the lungs.³⁸ Furthermore, Jung et al investigated the expression of epithelial-mesenchymal transition (EMT) related proteins, such as N-cadherin, β -catenin and vimentin, to clarify the effects of the extract on the Lipopolysaccharide-induced EMT. It was found that the aqueous extract successfully repressed the activation of nuclear factor kappa light chain enhancer of activated B cells (NF-KB), which plays a critical role in the epithelial-mesenchymal transition and shows the anti-carcinogenic activity of the plant.37

2. Anti-oxidant activity: Haraguchi *et al.* conducted an experimental study on rats, it was found that bakuchiol prevented lipid peroxidation of mitochondria and protected respiratory enzyme actions in the mitochondrial electron transport system against oxidative trauma.³⁹ Furthermore Seo *et al.* injected its extract in Six-week-old male C57BL/6 mice to examine the free radical scavenging effects of PC seed which Ameliorated Streptozotocin under a 12-hour light and 12-hour dark photoperiod. They calculated the intracellular reactive oxygen species (ROS) level in INS-1 cells (rat insulinoma cells) after treatment with H_2O_2 in the presence or absence of the extract and a significant reduction of the ROS level by 50 µg of the extract was seen. This decrease in the ROS level verifies PC as an anti-oxidant.⁴⁰

3. Anti-inflammatory activity: Lee *et al.* investigated the antiinflammatory properties of isobavachalcone, examining its effects on the endotoxin-induced expression of adhesion molecules in mouse cerebrovascular endothelial cells and leukocyte-endothelial cell adhesion. The expression of ICAM-1 was significantly reduced at both the mRNA and protein levels in brain endothelial cells by Isobavachalcone in a dose-dependent manner.³⁴

4. Neuroprotective activity: Lee *et al.* found that isobavachalcone inhibited LPS-induced ICAM-1 expression and adhesion of leukocytes to the endothelial cell of the brain by blocking TLR4 signaling and thus, it can potentially reduce the inflammation-related neuronal injury in the brain diseases. Hence it can be used as a neuroprotective due to its anti-inflammatory activity.³⁴

5. Anti-viral activity: In a study by Cho *et al.* found that isopsoralen (IC50=28.95 μ m) effectively inhibited the lytic replication of murine gamma herpesvirus 68 (MHV-68) in a dose-dependent manner.⁴¹ Sundaram *et al.* conducted a study on mice and nonhuman primates and found that the psoralen-inactivated dengue virus vaccine was seen to be immunogenic.⁴² In a study by Darnell *et al.*, it was reported that the presence of psoralen boosted the inactivation of severe acute respiratory syndrome coronavirus (SARS- CoV).⁴³ The above examples showing the anti-viral properties of the plant encourage further research to establish its effect and clinical application in other viral diseases like HIV/AIDS, hepatitis, etc.

6. Antibacterial activity: He *et al.* studied on determination of minimum inhibitory concentration (MIC) and minimum bactericide concentration (MBC) of corylifolinin. It was found that *corylifolinin* exhibited relatively strong antibacterial activity against *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* with the zone of inhibition of 15.1 and 13.1 mm at the concentration of 2.5 mg/mL respectively.⁴⁴

7. Anti-diabetic activity: Lee *et al.* investigated targeting 3T3-L1 pre-adipocytes of mice with type 2 Diabetes Mellitus (DM), it was found that bavachin a phytoconstituent isolated from PC facilitates glucose uptake by differentiated adipocytes and myoblasts via glucose transporter 4 (GLUT4) translocation by activating the Akt (a protein kinase B) and 51 AMP-activated protein kinase (AMPK) pathway in the presence or absence of insulin and augments insulin sensitivity. Hence it may help manage type-2 DM.²⁷

8. Memory Enhancing Effect/ Neurine tonic: Ning *et al.* studied psoralen with different concentrations of 10, 50 and 100 nm, and it was found that psoralen had good potential therapeutic effects on neurodegenerative diseases and central nervous system injury as it could successfully control the particular gene expression profile of neural stem cells, prevent their proliferation, and help their differentiation into astrocytes.⁴⁵ Furthermore, it also showed an effect on Alzheimer's disease in an experiment conducted by Chen et al.³referred to as "Bu-gu-zhi" in Chinese, has great medicinal values since ancient times. PCL is the dried ripe fruit of Psoralea corylifolia L., which has been widely used in traditional Chinese medicine (TCM Luang et al. after a study found the significant improvement on the learning and memory ability of APP/PS1

mice. Regarding their mechanism they found the expression of PC on estrogen receptor α and β , follicle stimulating hormone receptor and luteinizing hormone receptor in the hypothalamus of the mice and based on which they concluded PC as neurine. Hence, it could act as a memory enhancing drug.⁴⁶

9. Derma care: Gidwan *et al.* conducted a clinical trial on 30 patients suffering from eczema in which all the checklists and signs of the disease were cured in a duration of two fortnight using an ointment containing extract of PC as a main ingredient. To rule out the effect of PC, they also used a placebo in another group of patients who did not get cured. This clinical trial is the best proof of the effectiveness of the plant.⁴⁷

10. Osteogenic effects: Ge *et al.* used an osteoblast cell namely MC3T3-E1 as a cellular model for a series of experiments and established the osteogenic effect of PC on MC3T3-E1 cells. They by the literature review found 23 important compounds in PC which had a total of 71 osteogenic differentiation related targets. Finally, their results of alizarin red stain verified that PC might pointedly promote the formation of mineralized nodules as well as osteogenic gene expression compared to that in the control.⁴⁸

11. Aphrodisiac Activity: Tayade *et al.* conducted a study on the effect of methanolic extract of PC whole plant on streptozotocin (STZ) induced diabetic Wistar rats weighing 150–180 g. Diabetes mellitus was induced with a single 65 mg/kg intravenous injection of STZ (a toxin specific for insulin-producing cells) in saline-sodium citrate buffer. The diabetic Wistar rats were treated with methanolic extract of PC for fourteen days; and compared with the diabetic control and normal control group. It was found that the animals treated with all tested compounds at tested dose levels showed a significant increase in the sexual attraction of the male like the number of licking, number of anogenital sniffing towards females, and number of genital grooming towards self; which was not seen in the diabetic rats with the problem of erectile dysfunction.⁴⁹

12. Antimycobacterial activity: Newton *et al.* studied fortythree plant species for *in vitro* antimycobacterial activities. It was found that 24.36% of methanol soluble seed extract of PC showed Minimum Inhibitory Concentration (MIC) for *Mycobacterium aurum* at 62.5 µg/ml and *M. bovis* at 83.6 µg/ml whereas negligible for *M. smegmatis*²⁴ whereas effects for *M. Tuberculosis* was not stated. This shows the anti-mycobacterial effect of the plant.

13. Toxicology: Chen *et al.* mentioned PC as a poisonous plant in their book entitled "Lei's Treatise on Preparing Drugs". With the thorough study of fresh PC, increasing amounts of evidence have established that the chronic or excessive administration of PC and its active ingredients can cause hepatotoxicity, nephrotoxicity, phototoxicity, developmental toxicity, and reproductive toxicity.³³

Some of the previous studies on seeds of PC reported that acute toxicity produced acute dermatitis followed by blistering and edema, whereas sub-acute toxicity resulted in hepatotoxicity associated with nausea and vomiting, sleeplessness, malaise, diarrhea, headache, and mental misery.⁵⁰ Chronic toxicity affects the eyes, liver, kidneys, and immune system.²⁵ Khushboo *et al.* investigated a mixture of psoralen, isopsoralen, and imperatorin; and resulted in hypertrophy of the kidney, liver, and spleen in rats at a daily dosage of 2.5 mg/75 g for 60 days.²⁵

In the animal experimental study conducted by Uthirapathy and Ahamad with 500 mg/kg of alcoholic extract of PC administered for 90 days, histology of the liver and the kidneys showed very minor inactive inflammatory changes; whereas no toxicity symptoms were seen till the dose of 2000 mg/kg when orally fed in a single dose toxicity test, also no such changes to heart, GIT, lungs, and brain was observed. It was finally concluded that the higher (>1000mg/kg) and long-term usage of PC may be harmful to the liver and kidneys.⁵¹

To rule out dosing in humans, it can be calculated as;

Human Equivalent Doses (mg/kg) =

The correction factor (Km) = Body weight (kg)/ Body surface area (m²) where the Km ratio for rat to human =0.162.⁵²

Therefore, Human Equivalent Dose (HED) = 500 x 0.162= 80mg/ kg

Hence, a dosage of 3.2 - 6.4 gm extract seems to be appropriate for a 60 kg human where dosages greater than 6.4 gm can cause hepatotoxicity.⁵¹ Comparing these with the dosage of *bakuchi* given in Bhavaprakash Nighantu which is 1-3 gm of churna¹⁰ and equivalently less than the alcoholic extract, suggests that the dose mentioned in Ayurveda exhibits no toxicity at all.

Ayurveda mentions Milk, ghee, and butter As an antidote for PC.25

14. Adverse reactions: Jadav et al. reported that Furanocoumarins like psoralen present in *Bakuchi* were found to make skin hypersensitive and caused phyto-photodermatitis in a few cases.³⁸

Excessive doses of *Bakuchi* can hamper the health of the kidney and liver as well as change the color of the urine and stool into orange or brown.⁵⁴ It also may cause hyperacidity and gastritis.²⁵ Moreover, Khushboo *et al.* mentioned the adverse effects like nausea, vomiting, and significant irritations in her toxicity study on PC seeds.²⁵

15. Contraindications: PC was not peculiarly seen as contraindicated. However, Asad *et al.* found inhibiting of the anticoagulating activity of *Naja naja karachiensis* toxin.^{55,56} Rubia cordifolia and Stenolobium stans (11% extracts This shows that the plant extract may be contraindicated with anti-coagulant application; and also supports the anti-venom property of the plant.

16. Warnings: According to the adverse effect evaluation criteria taken into consideration in the study by Patil et al. in the use of a *lepa* named *dhyas* powder, PC being whose main constituent, application of the medication shall be stopped when any severe

adverse effects are seen like severe burning, highly swelling, inflammation, watery discharge, fever, etc. or no any changes seen in the lesion after application of medication for 1 month.⁵⁷

16. Precautions: *Bakuchi* should be taken in the recommended dose and duration, as high doses and long-term use may cause hyperacidity and gastritis.²⁵ Some products like curd, pickles, fish, etc. should be avoided in case of vitiligo treatment with *Bakuchi* churna as they are considered *apathya* (don't do) with treatment.²⁵ PC Should be used only under medical supervision in case of pregnancy, nursing mother, and pediatric.^{25,54}

The scientific community asks questions about its mechanism of action. PC is considered toxic based on merely available evidences on liver, kidneys, and other organs. Thus, any occurrence of such a patient may be due to improper use of the drug beyond the toxicity level. The ayurvedic reference "rogah sarvepi jaayante mandaagni" (all types of diseases evolve because of diminished digestive power) suggests that the patient may further have been ineligible due to his/her weak digestive fire instead. Asodhita (impure) PC without proper ayurvedic anupana, may also be the cause for such incidents as reported by Nam et al.⁵⁰ The toxicity conducted by Uthirapathy and Ahamad found no side effects or toxicity under the therapeutic dose.⁵¹ The upper limit of dose of PC is 6.4 gm. Bhavaprakash Nighantu, an Ayurvedic authoritative classical literature recommends dosages of 1-3 gm that are safe and are within the limit of experimental calculation dose of the same plant.

In his study, Richard *et al.* found that combination of Psoralen and ultraviolet A (PUVA) was significantly effective as compared to Psoralen alone. However, PUVA showed enough evidences of having carcinogenic potency.⁵⁸ Contradictory to the result of Richard *et al.*, Yang *et al.* have reported the anticarcinogenic properties of PC extract.³⁸ Ayurveda prescribes the crude form of a single herb or polyherbal formulation which has merely been reported side effects, adverse reactions, or toxic effects. Long-term use of a single molecule can show adverse reactions or unwanted effects as reported by Richard. Hence, robust research works are needed to establish the safety measures and efficacy of the medicinal herb.

Based on the above study, clinical trials can be conducted to establish the various aspects of uses of PC in evidence-based practices. As per ayurvedic principles of medicinal uses of plants, it recommends purification of raw materials, detoxification in the formulation and use of *anupana (vehicle)* in correct duration of time. In the era of side effects and drug resistance in modern medicine, herbs can play a significant role and hold a good position in treatment.

CONCLUSION

The seed of *P. corilifolia* Linn is commonly used in skin diseases such as *Switra* (leukoderma), *Vicharchika* (psoriasis). The plant contains benzofuran glycosides, coumarins, flavonoids, meroterpene, saccharides, and sesquiterpenes like other groups of compounds that collectively show anti-oxidant, anti-diabetic, antilipogenic, anti-tuberculous, anti-carcinogenic, memory enhancing, anti-venom and aphrodisiac as the major pharmacological activities. *Churna* and *taila* are the used dosages form according to Sri Bhava Mishra. Based on the toxicology report it can be concluded that it has almost no toxicity nor any significant adverse effect when used under proper dosages and time.

CONFLICT OF INTEREST: None

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