

International Journal of Biomolecules and Biomedicine (IJBB)

ISSN: 2221-1063 (Print), 2222-503X (Online) http://www.innspub.net Vol. 18, No. 2, p. 11-18, 2024

REVIEW PAPER

OPEN ACCESS

Exploring pharmacologically significant bioactive compounds of *Psoralea corylifolia* L.- A review

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Key words: Bioactive compounds, Pharmacological activities, Novel drugs, Psoralea corylifolia

Abstract

Article Published: 12 April 2024

Psoralea corylifolia, a Chinese medicinal plant belonging to the Fabaceae family, has long been esteemed in various traditional medicine systems. Recent scrutiny into its phytochemistry and pharmacology unveils a treasure trove of secondary metabolites, totaling 63, delineated into six structural categories: flavonoids, meroterpenes, furanocoumarins, coumestans, steroids, and phenolic compounds. Foremost among these compounds is bakuchiol, a meroterpene gaining traction in the cosmetic industry for its noted anti-aging and anti-acne properties. Furanocoumarins like psoralen and isopsoralen exhibit efficacy in treating psoriasis and vitiligo by inducing skin pigmentation. Moreover, the spectrum of bioactivities demonstrated by other secondary metabolites from *P. corylifolia* is vast, encompassing antibacterial, anti-inflammatory, antioxidant, antidiabetic, anti-obesity, hepatoprotective, estrogenic, osteogenic, and anticancer effects. Looking ahead, the study underscores both challenges and opportunities for advancing research and development in this domain. Key focal points include optimizing extraction and isolation techniques, standardizing and controlling the quality of plant materials and extracts, elucidating mechanisms of action and molecular targets, and assessing the safety and toxicity profiles of secondary metabolites. In conclusion, P. corylifolia emerges as a botanical gem, poised to unlock novel pharmaceutical and cosmetic avenues. Its multifaceted pharmacological potential underscores its significance in contemporary medicine and warrants further exploration and harnessing of its bioactive constituents.

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Introduction

Psoralea corylifolia, often known as "Babchi" or "Bu gu zhi" in traditional Chinese medicine, is a perennial herbaceous plant from the Fabaceae family. *P. corylifolia* is indigenous to Asia, particularly China and India, and has a centuries-long history of use in traditional medical systems (Pandey *et al.*, 2016).

P. corylifolia is regarded in traditional Chinese medicine (TCM) for its diverse medicinal characteristics, and it has been used to cure a wide range of diseases, from skin problems to reproductive health difficulties. The seeds, fruits, and roots of P. corylifolia are highly valued for their therapeutic properties and have been used in a variety of herbal compositions and cures. P. corylifolia has long been valued for its dermatological properties, particularly in the treatment of skin disorders including psoriasis, eczema, and vitiligo. Its seeds contain bioactive substances, including furanocoumarins like psoralen and psoralen, which have long been used to enhance and relieve symptoms of skin pigmentation dermatological conditions.

Pharmacological research on P. corylifolia, extends far beyond its dermatological applications. This botanical marvel boasts a wide array of medicinal properties, including anti-inflammatory, antioxidant, antidiabetic, and hepatoprotective qualities. These diverse pharmacological effects underscore the plant's significance in traditional medicinal practices and its potential as a valuable therapeutic agent in modern pharmacology.As the demand for natural remedies and traditional medicines continues to rise, there is a parallel increase in interest regarding the pharmacological potential of botanicals like P. corylifolia. This plant's chemical diversity and bioactive components present promising opportunities for drug discovery and development. Considering the escalating incidence of chronic illnesses and the emergence of antibiotic resistance, there's an urgent need to identify innovative therapeutic agents with various modes of action. P. corylifolia emerges as a compelling plant due to its multifaceted pharmacological activity and historical utilization in traditional medicine. The forthcoming study on P. corylifolia will delve into its phytochemistry and pharmacology, providing a comprehensive examination of its bioactive ingredients and therapeutic potential. By synthesizing previous advancements in the field, the study aims to illuminate P. corylifolia's promise for drug discovery and development. Through meticulous exploration, researchers endeavour to unlock the full spectrum of benefits offered by this botanical treasure, paving the way for novel pharmaceutical interventions, and contributing to the advancement of medical science.

Traditional uses exploration

P. corylifolia has a long history of traditional use across different cultural systems, dating back centuries. In traditional Chinese medicine (TCM), it is revered for its versatile therapeutic properties and is used to treat various ailments. Traditional uses include the management of skin disorders such as psoriasis, eczema, and vitiligo, attributed to its ability stimulate skin pigmentation and alleviate to symptoms. Additionally, it is employed for its antiinflammatory, antimicrobial, and analgesic properties, making it a popular choice for treating inflammatory conditions and infections (Zhou et al., 2020). Furthermore, P. corylifolia is utilized to improve reproductive health, enhance libido, and address menstrual irregularities. Scientific evidence supporting these traditional uses continues to accumulate, validating the efficacy of P. corylifolia in traditional medicine systems.

Pharmacological activities review

Bioactive compounds derived from Psoralea corylifolia exhibit а broad spectrum of pharmacological activities, making it a valuable candidate for therapeutic interventions. Studies have demonstrated its anti-inflammatory properties, attributed to compounds like bakuchiol and flavonoids, which inhibit pro-inflammatory mediators. Additionally, P. corylifolia extracts possess potent antioxidant activity, scavenging free radicals and protecting cells from oxidative damage. Furthermore, its antimicrobial properties have been

investigated, showing efficacy against various bacterial and fungal pathogens. Moreover, *P. corylifolia* compounds display antidiabetic effects by regulating glucose metabolism and insulin sensitivity. Hepatoprotective properties have also been reported, with compounds like bakuchiol exhibiting liver-protective effects against toxins and oxidative stress. Furthermore, research suggests anticancer potential, with *P. corylifolia* compounds demonstrating cytotoxic effects on cancer cells and inhibiting tumor growth through various mechanisms.

Pharmacological activities of P. corylifolia compounds

Pharmacological properties and anti-inflammatory activity: Numerous studies have demonstrated the anti-inflammatory properties of *P. corylifolia* extracts and isolated compounds. Psoralen and bakuchiol, two major bioactive constituents of *P. corylifolia*, have been shown to inhibit inflammatory mediators such as tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and cyclooxygenase-2 (COX-2). These compounds exert their anti-inflammatory effects by suppressing the nuclear factor-kappa B (NF-κB) signaling pathway and reducing the production of pro-inflammatory cytokines (Wang *et al.*, 2020, Khushboo *et al.*, 2019)

Immunomodulatory activity: Ρ. corylifolia compounds exhibit immunomodulatory effects by regulating the activity of immune cells and modulating cytokine production. Isopsoralen, a bioactive furanocoumarin, has been reported to enhance the proliferation and function of T while inhibiting the activity of lymphocytes inflammatory cytokines. Additionally, flavonoids present Ρ. corylifolia extracts in exert immunomodulatory effects bv modulating macrophage activation and dendritic cell function (Ali et al., 2018; Dong et al., 2020).

Anti-cancer activity: The anti-cancer potential of *P*. *corylifolia* has garnered significant attention in recent years. Psoralen and isopsoralen have shown promising anticancer effects against various cancer

cell lines, including breast, lung, prostate, and skin cancer. These compounds exert their anti-cancer activity by inducing apoptosis, inhibiting cell proliferation, and suppressing angiogenesis. Moreover, bakuchiol, a phytoestrogen present in *P. corylifolia*, exhibits anti-cancer properties by targeting estrogen receptor signaling pathways in hormone-sensitive cancers.

Anti-diabetic activity: *P. corylifolia* extracts and bioactive compounds have been investigated for their potential anti-diabetic effects. Bakuchiol and flavonoids from *P. corylifolia* have demonstrated hypoglycemic activity by enhancing insulin sensitivity, promoting glucose uptake, and inhibiting gluconeogenesis. These compounds also exert protective effects against diabetic complications such as nephropathy and retinopathy.

Anti-microbial activity: The antimicrobial properties of *P. corylifolia* have been attributed to its bioactive constituents, including psoralen and flavonoids. These compounds exhibit broad-spectrum antimicrobial activity against bacteria, fungi, and viruses. Psoralen has been particularly effective against methicillin-resistant Staphylococcus aureus (MRSA) and Candida albicans, while flavonoids demonstrate inhibitory effects against various pathogenic microorganisms.

Neuroprotective activity: *P. corylifolia* compounds possess neuroprotective properties that may have implications for the treatment of neurodegenerative diseases. Bakuchiol, in particular, has been shown to exert neuroprotective effects by reducing oxidative stress, inhibiting neuroinflammation, and promoting neuronal survival. These mechanisms contribute to the potential therapeutic utility of *P. corylifolia* in conditions such as Alzheimer's disease and Parkinson's disease.

Mechanisms of action

The pharmacological effects of *P. corylifolia* compounds are mediated by their interactions with

key molecular targets involved in various cellular pathways. These include modulation of transcription factors (e.g., NF- κ B), cytokine signaling pathways (e.g., TNF- α , IL-6), apoptotic regulators (e.g., Bcl-2, caspases), and hormone receptors (e.g., estrogen receptor). The multifaceted nature of *P. corylifolia* bioactive compounds allows for their pleiotropic effects on diverse physiological processes.

Phytochemistry of Psoralea corylifolia

P. corylifolia, a member of the Fabaceae family, boasts a rich phytochemical profile across its various plant parts. The seeds, fruits, roots, and aerial parts of P. corylifolia harbor a diverse array of chemical constituents. Notably, the seeds are particularly rich in bioactive compounds, including furanocoumarins such as psoralen and psoralen, flavonoids, meroterpenes, coumestans, steroids, and phenolic compounds. These compounds contribute to the plant's pharmacological activities and therapeutic potential. Furthermore, different extraction methods have been employed to isolate and characterize these constituents, shedding light on their structural diversity and potential applications in medicine (Patel and Sharma, 2021).

Flavonoids

Flavonoids are a class of polyphenolic compounds found abundantly in plants. In *P corylifolia,* flavonoids such as flavones, flavonols, and flavanones have been identified. These compounds contribute to the plant's antioxidant properties and may also exhibit anti-inflammatory and anticancer activities.

Flavonoids are a diverse group of plant secondary metabolites that are characterized by their chemical structure containing 15 carbon atoms, arranged into two aromatic rings (A and B) connected by a threecarbon bridge (C). Flavonoids are often represented by various symbols to denote their chemical structure. Here are some commonly used symbols for flavonoids:

General flavonoid structure

The basic structure of a flavonoid is often represented the arrangement of the three rings (A, B, and C) and their connections. Rings A and B:

Sometimes, rings A and B are represented using letters:

Ring A: Denoted as C6-C3, Ring B: Denoted as C6-C3 Hydroxyl Groups (OH): Hydroxyl groups attached to the rings are typically represented by 'OH' (Fig. 1).

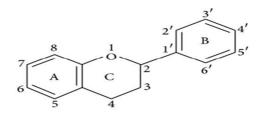


Fig. 1. Rings A and B are represented using letters

Flavonoid Subclasses: Different subclasses of flavonoids have additional features in their structure, and their symbols may vary accordingly (Fig. 2.). For example:

Flavones: Presence of a carbonyl group at C4 position. Flavonols: Presence of hydroxyl groups at C3 position.

Flavanones: Absence of double bond at C2-C3 position.

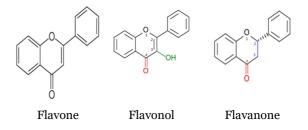


Fig. 2. Flavonoid subclasses

Specific flavonoids: Symbols for specific flavonoids are often represented using chemical notations or simplified structures based on the general structure.

It is important to note that while these symbols provide a simplified representation of flavonoid structures, actual flavonoids can vary greatly in their chemical composition and properties.

Meroterpenes

Meroterpenes are hybrid compounds containing both terpenoid and polyketide moieties. *P. corylifolia* is

known to contain meroterpenes such as bakuchiol, which has gained attention for its anti-aging and antiacne effects in the cosmetic industry.

Meroterpenes are a class of natural products that contain both terpenoid (derived from isoprene units) and non-terpenoid moieties. Their chemical structures can vary widely, incorporating different combinations of terpenoid and non-terpenoid components. As such, there isn't a standard set of symbols specifically for meroterpenes as there might be for simpler chemical structures like flavonoids.

However, meroterpenes can be represented using general chemical notation conventions, highlighting their terpenoid and non-terpenoid components. Here are some common symbols and conventions used in representing meroterpenes.

Terpenoid moiety: Isoprene units: Represented by the isoprene structure, often abbreviated as $'CH_2=C(CH_3)-CH=CH_2'$.

Monoterpenes: Represented by two isoprene units joined together (C10H16).

Sesquiterpenes: Represented by three isoprene units joined together (C15H24).

Diterpenes: Represented by four isoprene units joined together (C20H32).

Triterpenes: Represented by six isoprene units joined together (C30H48).

Tetraterpenes: Represented by eight isoprene units joined together (C40H64).

Non-terpenoid moiety: Non-terpenoid components can vary widely and may include aromatic rings, aliphatic chains, or other functional groups. They are typically represented using standard chemical notation.

Bridging groups: Bridging groups connecting the terpenoid and non-terpenoid moieties are represented using chemical bonds or structural diagrams.

Specific meroterpenes: Specific meroterpenes may have their unique structural features or substituents, which are represented using chemical notation or simplified structural diagrams. It is important to note that meroterpenes encompass a diverse group of compounds with varied structures, so their representation can be complex and specific to individual molecules. Detailed structural diagrams or chemical formulae are often used to accurately represent their structures (Kumar and Singh, 2020).

Platensimycin: Platensimycin is a meroterpene antibiotic produced by certain strains of bacteria. It contains a tricyclic sesquiterpene moiety fused to a polyketide-derived portion. Its structure can be represented as (Fig. 3):

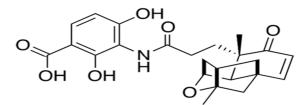


Fig. 3. Platensimycin

Furanocoumarins

Furanocoumarins are a class of compounds characterized by a furan ring fused to a coumarin moiety. *P. corylifolia* is rich in furanocoumarins, including psoralen and isopsoralen, which have been traditionally used for the treatment of skin disorders such as psoriasis and vitiligo due to their ability to induce skin pigmentation.

Furanocoumarins are a class of organic compounds that belong to the larger group of coumarins. They are characterized by the presence of a furan ring fused to a coumarin nucleus. Furanocoumarins are found in various plant species and are known for their biological activities, including their role in plant defense mechanisms and their phototoxic effects on human skin. Here are two isomers of Furanocoumarins (Fig. 4):

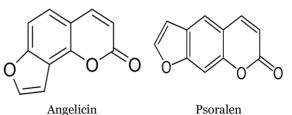


Fig. 4. Two isomers of Furanocoumarins *Coumestans*

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Coumestans are a group of phenolic compounds with a coumarin structure. *P. corylifolia* contains coumestans with diverse biological activities, including estrogenic effects and potential anticancer properties.

Coumestans are a class of natural compounds belonging to the group of phytoestrogens, which are plant-derived substances that can exert estrogenic effects. They are structurally like coumarins but contain a benzofuran moiety fused to a benzopyran ring system. Coumestans are found in various plants, particularly in legumes such as clover and alfalfa. Here's a structure of a coumestan (Fig. 5).

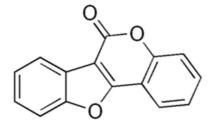


Fig. 5. Structure of a coumestan

In this structure, the benzopyran ring system is represented by the central ring, which consists of a benzene ring fused to a pyran ring. The benzofuran moiety is attached to the benzopyran ring system, typically at the C-3 position.

R1 and R2 represent various substituents that may be present on the benzopyran or benzofuran ring, which can vary depending on the specific coumestan compound.

Like furanocoumarins, coumestans can have different substitution patterns and functional groups, leading to a diverse array of compounds within this class. More complex coumestan structures may include additional rings or substituents, which would be represented in more detailed structural diagrams.

Steroids

Steroids are a class of lipids characterized by a fourring structure. While less common in *P. corylifolia* compared to other plant families, steroids such as β sitosterol and stigmasterol have been identified in the plant and may contribute to its pharmacological activities.

Steroids are a class of organic compounds with a characteristic molecular structure composed of four fused rings: three cyclohexane rings (designated as rings A, B, and C) and one cyclopentane ring (designated as ring D). These rings are labeled from A to D, and they are numbered starting from the one carbon atom that participates in the fusion. The basic structure of a steroid is often represented as follows (Fig. 6).

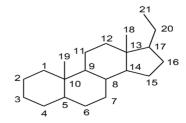


Fig. 6. The basic structure of a steroid

In this representation, the four rings are depicted, with the cyclopentane ring (ring D) being the smallest and the three cyclohexane rings (rings A, B, and C) being larger.

Carbon atoms within each ring are numbered: The side chains and functional groups attached to the rings are not shown in this simplified representation. Steroids exhibit a wide range of biological activities and are important in various physiological processes. They can be further classified into subclasses based on their functional groups and structural modifications, such as:

Sex steroids (e.g., testosterone, estrogen, progesterone) involved in sexual development and reproduction. Corticosteroids (e.g., cortisol, aldosterone) involved in regulating metabolism and immune response.

Anabolic steroids, which are synthetic derivatives of testosterone used to promote muscle growth and enhance athletic performance.

Actual steroid molecules can have diverse substituents and functional groups attached to the

rings, leading to a wide variety of compounds within this class. More complex steroid structures may include additional rings or complex substituents, which would be represented in more detailed structural diagrams (Wang *et al.*, 2021).

Phenolic compounds

Phenolic compounds are characterized by the presence of one or more phenol groups. *Psoralea corylifolia* contains various phenolic compounds with antioxidant, anti-inflammatory, and antimicrobial properties, contributing to its traditional medicinal uses.

Phenolic compounds are a diverse group of organic compounds characterized by the presence of one or more hydroxyl groups attached to an aromatic benzene ring. They are widely distributed in nature and play important roles in various biological processes, including plant defence mechanisms, antioxidant activity, and pigmentation. Here's a simplified representation of the basic structure of a phenolic compound (Phenol) (Fig. 7).

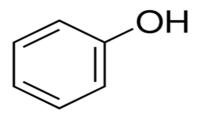


Fig. 7. The basic structure of phenolic compound (Phenol)

In this representation, the benzene ring is depicted, which consists of six carbon atoms arranged in a hexagonal ring with alternating single and double bonds. The hydroxyl group (-OH) is attached to one of the carbon atoms of the benzene ring.

Phenolic compounds can vary widely in their structure, and they may contain additional substituents or functional groups attached to the benzene ring. Some common variations include:

Multiple hydroxyl groups attached to different positions on the benzene ring. Methoxy (-OCH3) or

other alkyl groups attached to the benzene ring. Additional aromatic rings attached to the phenolic ring, forming complex structures like flavonoids or lignans (Fig. 8).

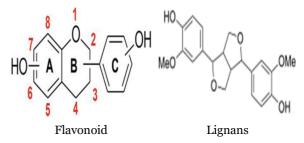
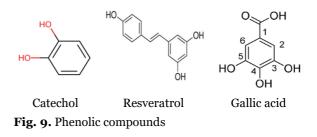


Fig. 8. Two isomers of Furanocoumarins

Phenol (hydroxybenzene), the simplest phenolic compound. Here are a few examples of phenolic compounds-Catechol, which contains two hydroxyl groups attached to adjacent carbon atoms on the benzene ring. Resveratrol, a polyphenolic compound found in grapes and red wine, known for its antioxidant properties. Gallic acid, a phenolic acid found in various fruits and plants, often as a component of tannins (Fig. 9).



These examples illustrate the diversity of phenolic compounds and their importance in biological systems. Detailed structural diagrams or chemical formulas would be used to represent more complex phenolic structures with additional substituents or functional groups.

Overall, the diverse array of secondary metabolites present in *P. corylifolia* contributes to its pharmacological activities and traditional therapeutic uses. Understanding the chemical diversity of these compounds is essential for elucidating their biological activities and exploring their potential applications in medicine and other fields (Zhao and Jiang, 2018) and (Gupta and Mahajan, 2020).

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Conclusion

P. corylifolia- derived bioactive compounds exhibit a wide range of pharmacological properties, including anti-inflammatory, immunomodulatory, anti-cancer, anti-diabetic, anti-microbial, and neuroprotective activities. These effects are attributed to the interactions of *P. corylifolia* compounds with molecular targets involved in key cellular pathways. However, further research is warranted to elucidate the underlying mechanisms of action and optimize the therapeutic potential of *P. corylifolia*-derived compounds. *P. corylifolia* represents a promising source of novel therapeutic agents with potential applications in various disease conditions.

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