RESEARCH PAPER

PUERARIA TUBEROSA: A TRANSLATIONAL JOURNEY FROM TRADITIONAL MEDICINE TO MODERN SCIENTIFIC ADVANCEMENT

Ashish Vishwakarma[1], Vasudev Biswas[1], Md Dilshad[1], Kella Alekhya[2], Mohd Ayub[1], Ajay Sharma[*1], Arya Lakshmi Marisetti[*1],

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[1]Department of Pharmacognosy & Phytochemistry, School of Pharmaceutical Sciences, Delhi Pharmaceutical Sciences and Research University, 110017 New Delhi, India

[2]Assistant Professor, Department of Pharmaceutical Quality Assurance, SRM college of Pharmacy, SRMIST, Kattankulathur 603203, Chengalpattu, Tamilnadu, India.

***Corresponding author:**

Dr. Arya Lakshmi Marisetti

Assistant Professor

School of Pharmaceutical Sciences

Delhi Pharmaceutical Sciences and Research University, New Delhi-110019

Email ID: maryalakshmi@gmail.com

*Corresponding author:

Dr. Ajay Sharma

Professor

School of Pharmaceutical Sciences

Delhi Pharmaceutical Sciences and Research University

New Delhi-110019

Email ID: ajaysharmapharma1979@gmail.com

ABSTRACT

Pueraria tuberosa is medicinal climber belonging to the family Fabaceae and has been used commonly in the practice of Ayurveda as an important medicinal plant for several treatment purposes. This plant contains numerous bioactive compounds such as isoflavones for instance Puerarin, daidzein, genistein and others including flavonoids, glycoside, saponins and terpenoids. This review explores the ethnopharmacology, phytochemistry, pharmacology, toxicology and medicinal uses of *P. tuberosa* based on studies. Research has shown that this plant has important biological effects. These include activity, anti-inflammatory action, antioxidant properties, anticancer effects, hepatoprotective, protection for the kidneys support for immune system regulation, lower levels of fats in the blood brain-enhancing benefits, faster wound healing and prevention of bone loss. Most of these effects come from compounds called isoflavonoids. These compounds work by affecting molecules involved in disease processes such, as DPP-IV, NF-κB and oxidative stress and inflammatory signals. Based on toxicological studies, there is an excellent safety profile when used in therapeutic doses but extended use in higher doses may cause adverse reactions. Even though there is ample evidence from pre-clinical studies demonstrating the therapeutic potential of this plant, there are very few clinical studies and mechanism-based investigations that have been conducted. Thus, more research is needed in this regard to develop therapeutic agents based on *P. tuberosa*. This review highlights the significance of *P. tuberosa* as a promising medicinal plant with significant potential for future pharmaceutical and nutraceutical applications.

KEYWORDS: *Pueraria tuberosa,* Ethnopharmacological, Phytochemistry, Pharmacological activities, Isoflavonoids

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INTRODUCTION

Medicinal plants have been a vital source of medicines since ancient times and still act as one of the key elements in both traditional and contemporary medicine. India has a vast tradition of traditional medicines for instance Ayurveda, Unani, and Siddha along with many other folk medicinal traditions, wherein therapeutic plants are widely used in disease prevention and treatment. There are more than 7,000 herbal medicines listed within the AYUSH system which reflects the country's extensive knowledge of medicinal plants [1]. Amongst the numerous medicinal plants used in Ayurveda, *P. tuberosa* DC., commonly known as Vidarikand or Indian Kudzu belongs to the Fabaceae family is regarded as a significant Rasayana drugs owing to its regenerative, nourishing, cardiotonic, and restorative properties.

crude drug contains sliced and dried tuberous roots, is a perennial climbing shrub with a thick and extensive root system that can grow up to 30 cm in diameter and weighs up to 35 kg with mature tubers weighing usually between 5-10 kg. it is abundantly found in different parts of the Indian sub-continent, including India, Nepal, and Pakistan. *P. tuberosa* tubers have traditionally been utilized for the treatment of fever, respiratory ailments, skin conditions, excessive bleeding during menstrual period, wounds, and debility and as the Ayurvedic pharmacopoeia of India recommends tuber powdered dose in a range of 3-6g for therapeutic purposes [2, 3]. A study of Phytochemical revealed the existence of numerous phytoconstituents in the tubers of *P. tuberosa*, including isoflavones, flavonoids, glycosides, saponins, terpenoids, and steroids. Some of the phytoconstituents which are known for their various biological activities include puerarin, daidzein, genistein, tuberosin, biochanin A, and lupinoside. These compounds were found to possess antioxidant, anti-inflammatory, antidiabetic, immunomodulating, hepatoprotective, nephroprotective, cardioprotective, and anticancer activities, thereby supporting the traditional medicinal claims associated with the plant [4, 5]. Recent pharmacological research has shown that *P. tuberosa* and their important phytochemicals regulate many targets which are responsible for oxidative stress, inflammation, glucose metabolism, lipids, and cellular signal transduction pathways. It has been shown through research that there is great therapeutic efficacy in the management of metabolic diseases, inflammatory conditions, diabetes mellitus, cancer, and toxicity-related disorders to specific organs. Although there is ample scientific data on *P. tuberosa*, yet the ethnopharmacology, phytochemical composition, pharmacological activities, toxicological effects, and therapeutic uses are not well-known [6]. Thus, this current review is meant to systematically collect and scientifically analyze the existing data on the conventional use, chemical composition, biological activities, toxicology, and clinical potential of *P. tuberosa*. This review may help to act as a foundation for upcoming research and the development of new medicinal herbs. The leaves and tuber of *P. tuberosa* is given in (Figure 1).

Figure 1. Leaves and tuber of *P. tuberosa*

MATERIALS AND METHODS

A thorough literature survey was accomplished using numerous electronic records for example Scopus, PubMed, Google Scholar, Web of Science, ScienceDirect, and Springer Link. Relevant scientific articles published until 2026 were searched using the terms "*Pueraria tuberosa*", "Vidarikand", "Indian Kudzu", "Puerarin", "Daidzein", "Genistein", "Phytochemistry", "Ethnopharmacology", "Pharmacological Activities", and "Therapeutic Potential". Original scientific articles, review papers, books, and monographs pertaining to the traditional uses, phytochemistry, pharmacology, toxicity, and medicinal applications of *Pueraria tuberosa* were considered for this study. Duplicate and irrelevant publications were eliminated from this study. This scientific literature was critically evaluated and systematized for summarizing the scientific information on the medicinal properties of *P. tuberosa*.

Vernacular name of *Peuraria. tuberosa* (Roxb. Ex Willd.) DC

There are various name of *P. tuberosa* available in several languages which is depicted in (Table 1) [2].

Table.1 Vernacular name of *Peuraria. tuberosa* (Roxb. Ex Willd.) DC.

Hindi	Vidarikand, Bankumara
English	Indian Kudzu
Sanskrit	Vidari, Vidarika, Bhumikusmanda, Gajavajipriya, Kandapalash, Svadukanda, Iksu-gandha
Assamese	Bhedeleton, Bhuikumra
Bengali	Vidari, Bhumikusmanda, Bhuikumra
Gujrati	Bhoikolu, Bhonykoru, Eagio, Sakharvel, Vidarikanta
Kannada	Gumadi, Belli, Gumadigida, Nelagumbala gudde, Nelagumbula
Malayalam	Mudakku
Marathi	Bhuikohala, Ghodvel

Oriya:	Bhuiankakharu
Punjabi:	Siali, Surala
Tamil:	Nilapoosani
Telugu:	Nelagummuda, Darigummadi

Taxonomy of the *Pueraria tuberosa*

The plant *Pueraria tuberosa* taxonomically classified as Kingdom: Plantae, Subkingdom: Trachebionta. Super division: Spermatophyta, Division: Magnoliphyta, Subclass: Rosidae, Order: Fabales, Family: Fabaceae, Genus: *Pueraria* DC, Species: *tuberosa*[7].

Botanical description

It has enormous tuberous roots and is a sprawling, deciduous climber or tangled shrub. The three foliolate, pinnately compound leaves have lengthy petioles. Broadly ovate or rhomboid, sub-coriaceous, glabrescent above, and densely covered in silky hairs are the characteristics of leaflets. April is when the flowers bloom. It has a blue or purple color. Racemes 15–27 cm in length were leafless. The calyx was densely silky and 0.4–0.6 cm in length. The corolla was bigger, papilionaceous, and bluish. The fruits were prepared using membranes. Pods are flat, jointed, and 5.0 and 7.5 cm long. It has two to three seeds covered with long, bristly brown hairs [8].

Geographical distribution

The plant *P. tuberosa* found all over the country, ranging from Sikkim to the Western Himalayas, and as high as 4,000 feet in Kumaon. It is distributed over most of Southern India, the hilly regions of Bengal, Mount Abu, and the lower hills of Punjab, excluding extremely humid or arid regions, and can ascend to 1200 m in elevation. Along with India it is also found in Pakistan and Nepal which is shown in (Figure 2) [3, 9].



Figure 2. Geographical Distribution of *P. tuberosa*

Species of *Pueraria* and their distribution

The genus *Pueraria*, including kudzu, is native to China, Japan, south and Southeast Asia, and parts of Oceania. Kudzu has been known and used for centuries as noted in Japanese poems from AD 600. While some Pueraria species have a limited distribution, kudzu is widespread across China and Japan and was introduced to New Guinea and New Caledonia long before yams and sweet potatoes became staple crops. Some other species of Genus *Pueraria* is shown in (Table 2) [3].

Table 2. Some other species of Genus *Pueraria*.

S.no	Species		Distribution
1	*P. pulcherrima*		Eastern Indonesia, Philippines, Papua New Guinea, Kai and Solomon Islands
2	*P. sikkimensis*		India (Sikkim, West Bengal), Bhutan
3	*P. wallichii*		China, Yunnan, Bangladesh, India (E. Himalaya)
4	*P. stricta*		China, Yunnan, Thailand, Myanmar
5	*P. candollei* var. *mirifica* (Synonym: *P. mirifica*)		Bangladesh, India (Assam, Andamans), Thailand, Myanmar
6	*P. tuberosa* (Willd.) DC		India, Nepal, Pakistan
7	*P. lobata* (Willd.) ohwi (Synonyms: *P. thunbergiana Benth*.		Korea, Vietnam, China, and the northeastern provinces of Russia
8	*P. thomsonii*		Korea, Vietnam, China, and the northeastern provinces of Russia
9	*P. bella*		Myanmar, India (Arunachal Pradesh)
10	*P.alopecuroides*		Thailand, Yunnan, China, Myanmar
11	*P. edulis*		India (Manipur, Sikkim), Bhutan, China, Yunnan
12	*P. imbticata*		Thailand, Laos
13	*P. lacet*		Myanmar
14	*P. montana*	var. *lobata*	Australia, South-east, North-east Asia and Oceania introduced to many subtropical region
		var. *chinensis*	China, Bhutan, Hawaii, NE India, Laos, Philippines, Vietnam
		var. *Montana*	East and North-east Asia

15	*P. peduncularis*		India (East Himalaya, Khasi Hills), Myanmar, Bhutan, China, Yunnan, Szechuan, Pakistan
16	*P. phaseoloides*	var. *javanica*	Brunei, Indonesia, Malaysia, Philippines, New Guinea, Solomon Islands, widely introduced in tropical areas
		var. *phaseoloides*	East, South Asia, New Guinea, Africa and South America
		var. *subspicata*	North-east India, Bhutan, Bangladesh, Bangladesh, Thailand.

Traditional uses

Traditionally, Vidarikand has been used to cure various diseases including fever, menorrhagia, skin conditions, injury, respiratory disorders, and hyperbilirubinemia at doses of 3–6 g in powder form [2]. Moreover, it is known to exhibit aphrodisiac, diuretic, galactagogue , energizing [5], and spermatogenic properties [10]. It has been recommended to address the imbalance in all three doses (Vata, Pitta, Kapha), which correspond to various energies within the human body[2]. Powdered tubers are frequently mixed with cow's milk to promote milk production after childbirth and support anabolism. *Piper longum* L. powder is frequently added to treat malnutrition in young people. The powder and honey were combined to relieve heavy menstruation. Further studies suggested that powders of tuber and wheat sautéed in ghee and assorted with milk for treating sexual exhaustion and boosting strength. Furthermore, fresh juice of tuber is combined with sugar and cumin seeds are used therapeutically for spermatorrhea [4].

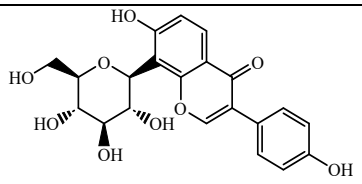
Ethnopharmacology

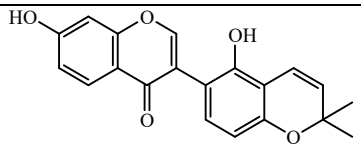
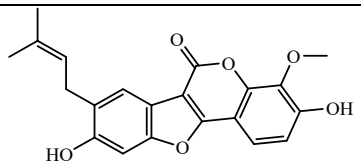
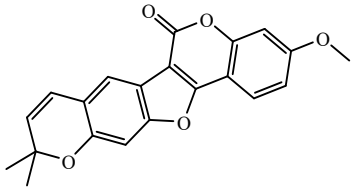
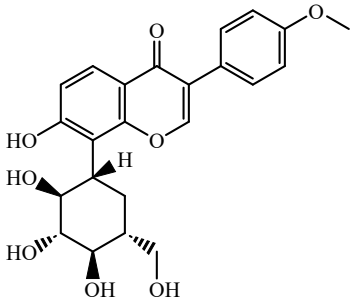
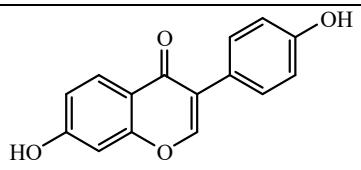
P. tuberosa, also referred to as the popular herb, is considered an important medication in Ayurveda and is classified as a 'Rasayana'. Its tuber is often used therapeutically in traditional and ethno-medical medicine. Aphrodisiac, galactagogue, diuretic, emetic, cardiotonic, rejuvenating agent, expectorant, emollient, laxative, and refrigerant [11]. It is also used as an Ayurvedic medicinal preparation, chyavanprash. The tubers were crushed and used to treat inflamed joints in some parts of India. They were cooked in milk and used as emetics or tonics in Nepal. Santal people have long employed *P. tuberosa* to treat menorrhagia, mild fever, and syphilitic nasal ulcers [3]. People of the eastern ghats of Andhra Pradesh made a paste of *P. tuberosa* tuber and applied it to joints to treat arthritis [12].

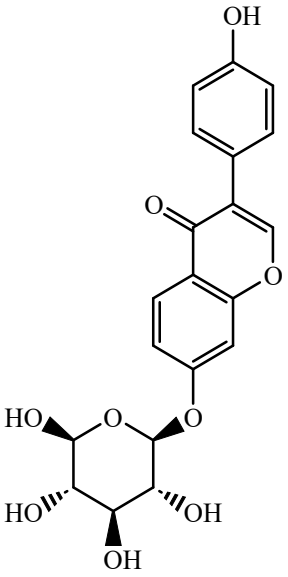
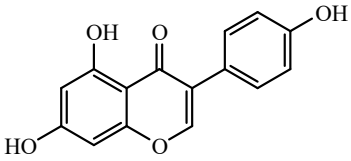
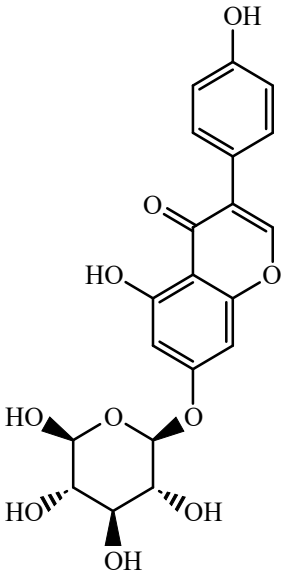
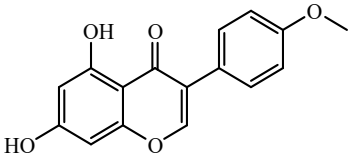
Phytochemistry of *P. tuberosa*

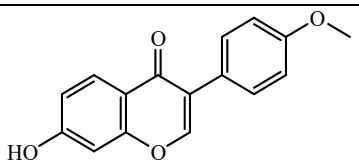
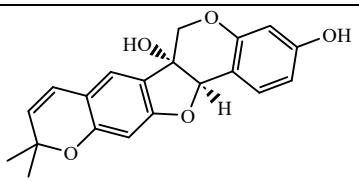
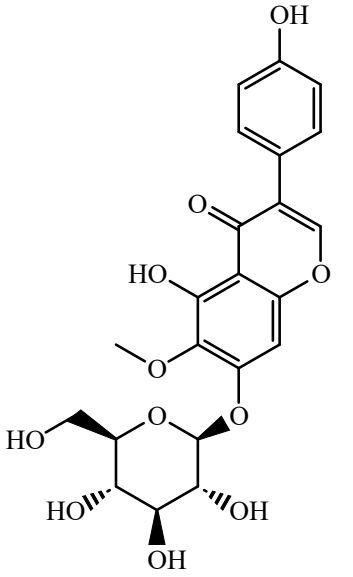
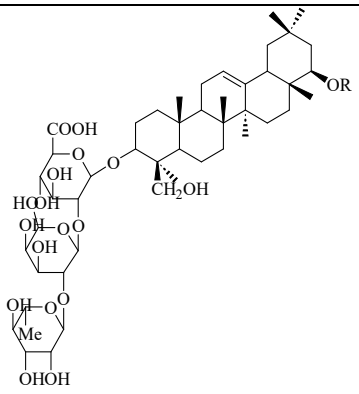
The phytochemical studies of plant *P. tuberosa* tubers have shown that it contains several secondary metabolites including flavonoids, glycoside, anthracene, anthocyanidins, anthaquinone, carbohydrates, catechol compounds, coumarin, hexose sugars, saponins, staroids, terpenoids[5, 13]. Some of the major active compounds given in (Table 3).

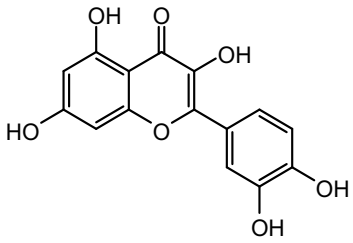
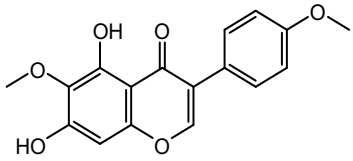
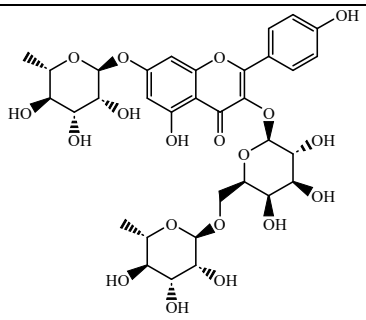
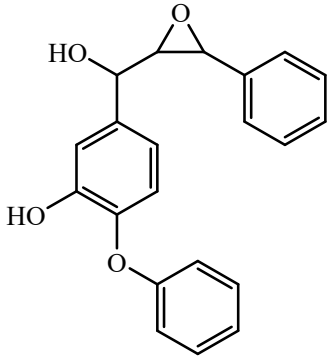
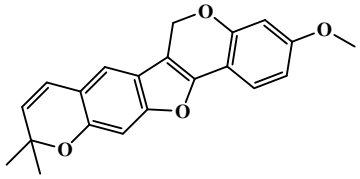
Table 3 Major chemical constituents and their structures

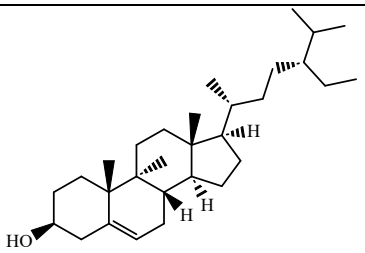
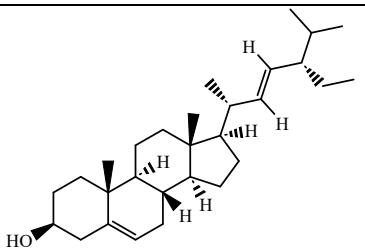
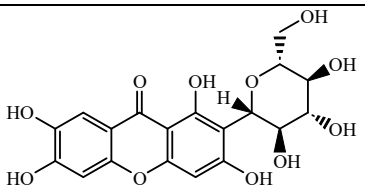
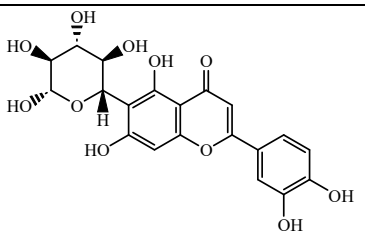
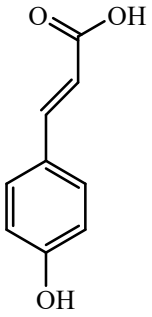
S. no	**Phytochemicals class**	**Major compounds**	**Structure**	**Reference**
1	Isoflavonoids	Puerarin		10

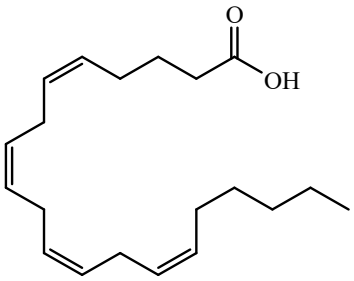
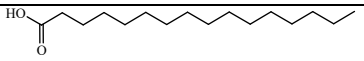
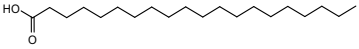
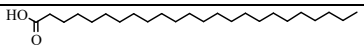
2	Isoflavonoids	Puerarone		[5]
3	Coumstan	Puerarostan		[5]
4	Coumstan	Tuberostan		[5]
5	Isoflavonoids	4-methoxypuerarin		[5]
6	Isoflavonoids	Daidzein		[14]

7	Isoflavonoids	Daidzin		[14]
8	Isoflavonoids	Genistein		[5]
9	Isoflavonoids	Genistin		[5]
10	Isoflavonoids	Biochanin A		[14]

11	Isoflavonoids	Biochanin B		14
12	Pterocarpans	Tuberosin		15
13	Isoflavonoids	Tectoridin		5
14	Steroid	Lupinoside PA4		16

15	Flavonoid	Quercetin		5
16	Isoflavonoids	Irisolidone		5
17	Flavone glycoside	Robinin		5
18	Epoxychalcanol	Puetuberosanol		5
19	Pterocarpanoids	3-o-Methylanhydotuberosin		5

20	Phytosterols	β-sitosterol		[5]
21	Phytosterols	Stigmasterol		[5]
22	Xanthone glycoside	Mangiferin		[17][25]
23	Flavonol	Isoorientin		[10]
24	Organic acids	P-coumaric acid		[5]

25	Organic acids	Arachidonic acid		5
26	Organic acids	Hexadecenoic acid		5
27	Organic acids	Eicosanoic acid		5
28	Organic acids	Tetracosanoic acid		5

PHARMACOLOGICAL ACTIVITY

The plant *P. tuberosa* has been widely investigated for its wide-ranging biological properties, and this is mainly due to the fact that the plant has several phytoconstituents for example isoflavonoids, flavonoids, glycosides, saponins, and others. Several experiments conducted have shown anti-diabetic, anti-inflammatory, antioxidant, anticancer, nephroprotective, hepatoprotective, immunomodulatory, cardioprotective, neuroprotective, anti-osteoporotic, and wound healing effects shown in (Table 4) [5, 6].

Anti-diabetic

Ethyl acetate extract of *P. tuberosa* tuber administered orally for seven days resulted a notably lowered blood glucose levels in diabetic rats induced by alloxan [18]. Additionally several extracts of *P. tuberosa* including petroleum ether, ethyl alcohol, aqueous and chloroform extracts demonstrated remarkable antidiabetic properties in streptozotocin-induced diabetic rats [19]. The aqueous extract of *P. tuberosa* tubers significantly prohibited DPP-IV, increasing the GLP-1 half-life, which is essential for controlling the glucose-dependent insulin secretion from β-cells in pancreas [20]. In another study, *P. tuberosa* aqueous extract enhanced the glucose homeostatic capacity via the DPP-IV inhibitory route. This inhibitory action was validated through *in silico* molecular modeling of two bioactive compounds, puerarone and robinin [21]. Moreover, aqueous extract from *P. tuberosa* tubers acts as an agonist for incretin receptors, protection against β-cell apoptosis and reduction of streptozotocin induced diabetic complications [22]. The extract also modulated various molecular markers associated with diabetic nephropathy such as nephrin superoxide dismutase, TNF-α, VEGF, MMP-9, HIF-1α, NF-κB, and PKCε, demonstrating its renoprotective and antioxidant potential [23].

Anti-inflammatory

Methanolic tuber extract demonstrated anti-inflammatory activity in contrast to Carrageenan-induced inflammation. The oral administration of extract for nine consecutive days at different doses enhanced antioxidant enzyme levels such as superoxide dismutase, catalase and glutathione while reducing lipid peroxidation and C-reactive protein levels, thereby alleviating oxidative stress and inflammation [24]. Isoorientin present in the tuber had strong anti-inflammatory action in mouse macrophage (RAW 264.7) cell lines treated with lipopolysaccharide, and was useful in reducing inflammation caused by carrageenan in paw oedema and air pouch mouse models. It prevents NF-κB and minimizes the functions of pro-inflammatory genes, such as TNF-α, cyclooxygenase-2, and inducible nitric oxide synthase. Furthermore, the antioxidant enzymes catalase and glutathione S-transferase are activated [25]

Anticancer

In vitro cell viability tests showed that mangiferin exhibited no appreciable toxicity toward normal cell lines, including mouse fibroblast NIH-3T3, RAW 264.7, HEK293, and mouse lymphocytes. In contrast, several cancer cell lines, including K562, MCF7, HEPG2, Jurkart cells, and A549, have demonstrated cytotoxicity [26]. A cell viability experiment was used to examine whether the hydroalcoholic extract of tubers had potential for both apoptosis and anticancer effects. The tuber extract resulted in a 50 percent reduce in viability of human colon cancer cells. The cells also showed increased expression of several pro-apoptotic genes, apoptotic cell death, and DNA fragmentation, which are signs of apoptosis [27]. *P. tubrosa extract-biosynthesized* silver nanoparticles have shown anticancer potential in a

variety of cell lines including breast MCF-7, MDAMB-231, ovarian SKOV-3, and brain U-87 cancer cells. Further investigation of the mechanisms underlying this action is required for therapeutic applications [28].

Anti-stress

The tubers of *P. tuberosa* exhibited substantial anti-stress potential in Wistar rats subjected to stress via cold immobilization. The treatment of animals with a hydro-alcoholic tuber extract (70%) for five days prevented the occurrence of gastric ulceration, decreased serum corticosterone concentrations, and prevented the development of enlarged spleens and adrenal glands. The hydro-alcoholic extract exhibited higher anti-stress properties compared to rhizomes of *Withania somnifera* [29].

Immunomodulatory

Swiss mice were administered a tuber extract with milk as a carrier for 28 days, and the immunomodulatory effects of this mixture were assessed. Compared to the control, The findings revealed a notably elevated level of phagocytic activity and the concentration of immunoglobulin A in the intestine and G in the serum. Additionally, there was a decrease in glutathione content and TBARS levels in the liver and Rbc [30]. This study highlights that both the petroleum ether extract of vidarikand and ashwagandha in Wistar rats of either sex increased the phagocytic action of peritoneal macrophages in clearing carbon particles when evaluating the immunomodulatory activity using a carbon clearance assay [31]. In the mouse model, the phagocytic activity of macrophages was increased and carbon particles in the blood were reduced when the ethanolic extract of tuber was administered at various dosages. Additionally, tuber extract inhibited humoral immunity and cell-mediated immunity, demonstrating the strength of its immunomodulatory action [32].

Nephroprotective

Methanolic extract of *P. tuberosa* demonstrated dose-dependent protection against cisplatin-induced renal toxicity in rats. The tuber extract significantly reduced serum creatinine and blood urea nitrogen levels, enhanced antioxidant status and reduced tubular damage, cellular necrosis, DNA damage and protein coagulation, thereby protecting renal function via its antioxidant and free radical scavenging properties [33]. Moreover, the biscuits fortified with *P. tuberosa* tuber powder given to Swiss mice for 10 days significantly ameliorated cisplatin induced nephrotoxicity, while extended use may require monitoring of liver function due to transient elevations in hepatic enzymes [34]. Additionally, the methanolic extract administered orally for 2 days reduced the acute kidney damage in glycerol induced acute kidney disease by lowering lipid peroxidation, superoxide dismutase, and catalase activity, as well as decreasing hyaline cast deposition and tubular necrosis in the kidney histology [35]. The aqueous tuber extract was administered orally for five days, which strongly reduced cisplatin-induced nephrotoxicity. The nephroprotective efficacy of *P. tuberosa* hydroalcoholic tuber extracts was demonstrated in rats with oxidative kidney tissue damage caused by sodium arsenate [36].

Antioxidant

The extracts of the tubers using hexane and methanol demonstrated strong concentration-dependent activity in scavenging free radicals. According to these findings, the methanolic extract of the plant demonstrated stronger antioxidant properties than the hexane extract by inhibiting lipid peroxidation and capturing hydroxyl radicals [37]. Water decoction of tuber extract mixed with milk and administered to Swiss mice showed strong antioxidant activity in the liver and Rbc. Furthermore, a noteworthy variation in glutathione concentration was noted between the control and augmented groups. *P. tuberosa* and milk both have antioxidant qualities, as shown by decreased glutathione and lipid peroxidation, enhanced immunoglobulin levels, and increased phagocytic activity [36]. Extracts of several solvents, including chloroform, acetone, methanol and decoction, were assessed for antioxidant activity using the FRAP assay, metal chelation, phosphomolybdenum, and free radical scavenging techniques of DPPH and ABTS assays. The findings showed that the acetone extract from the tuber exhibited significant antioxidant properties. [38].

Hypolipidemic

The methanol extract of *P. tuberosa* strongly reduced total serum cholesterol, triglyceride and low-density lipoprotein levels in hypercholesterolemic Wistar rats [39]. It has been suggested that the isoflavones especially puerarin in *P. tuberosa* have been credited for its lipid-lowering effect. In experiments involving rats with hyperlipidemia, puerarin remarkably decreased triglyceride and total cholesterol levels [40]. The hypolipidemic efficacy of aqueous tuber extract in a high-fat diet has been used to develop non-alcoholic fatty liver disease in rats. A high-fat diet along with aqueous tuber extract was administered to the rats, and the finding showed that the extract has a remarkable hypolipidemic effect on lowered triglyceride and cholesterol levels in NAFLD-afflicted rats, manifesting in reduced levels of serum triglycerides and cholesterol [41].

Hepatoprotective

Oral Administration of butanolic tuber extract was effectual in decreasing the hepatotoxic effects of carbon tetrachloride in rats. Exposure to carbon tetrachloride and tert-butyl hydroperoxide, D-galactosamine, resulted in

hepatocyte damage. CCl4 significantly increased lactate dehydrogenase (LDH), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels [42].

Wound healing

In the wound healing activity, to assess the capacity of *P. tuberosa*, excision and incision wound models were used. The outcomes exhibited a marked wound healing effect, especially with extracts containing methanol and ethyl acetate [43].

Antifertility

The anti-fertility activity of *P. tuberosa* was most prominently elicited by its ethanolic and butanolic extracts. Several other solvents including hexane, chloroform, methanol, petroleum ether, and benzene showed notable effectiveness in inhibiting implantation, specifically in rats and mice. Notably, the water extract showed no discernible antifertility effects in any of the three animal species examined. Analysis of the biological characteristics of *P. tuberosa* showed that significant estrogenic and progestational activity was present in all its fractions [44]. The lengthening of the oestrous cycle was observed in the ethanolic tuber extract of rats [45]. Male rat fertility was found to decrease when tuber extract was administered orally. This reduction was attributed to a decrease in the generation of spermatids and the concentration of sperm in the testes and cauda epididymides [46]. The reproductive structures of female albino rats exhibited dose- and duration-dependent effects when *P. tuberosa* tuber crude powder and extracts (alcoholic and hot water) were administered orally. Treatment causes uterine glands to atrophy without compromising the lumen, which decreases the size, height, and quantity of uterine glands in the endometrium [47].

Nootropic activity

The nootropic action of *P. tuberosa* tuber extracts was assessed via amnesia caused by scopolamine and diazepam in mice and rats. The inflection ratio observed in the enhanced plus-maze trial was quite high and similar to that of the standard medication piracetam. The aqueous and alcoholic extracts administered orally corrected the learning and memory impairment caused by scopolamine, hypothermia caused by clonidine, and head twitches caused by lithium in experimental rats. The extract exhibits a nootropic effect due to its flavonoids interaction through the cholinergic, GABAergic, adrenergic, and serotonergic systems. [48].

Antiostioporotic activity

Effectiveness of an ethyl acetate fraction rich in antioxidants (FRAC) derived from a *P. tuberosa* tubers extract in combating menopausal osteoporosis in rats. Femur weight, length, and thickness were markedly increased by FRAC treatment. Urine hydroxyproline, calcium, and phosphorus levels improved dose dependently, reflecting a beneficial effect on biochemical markers and bone volume. Moreover, FRAC reduced uterine weight following ovariectomy, resulting in an increase in body weight. According to histopathological research, FRAC therapy restores normal bone structure. According to docking studies, the anti-osteoporotic mechanism may involve genistein and daidzein. Taken together, menopausal osteoporosis may be treated with FRAC derived from *P. tuberosa* [49].

Cardioprotective

The tuber powder of *P. tuberosa* weighing about 3gm/day was given to patient with ischemic heart disease for 1 year. The case study confirmed an inclusive substantial cardioprotective consequence; resting mean blood pressure was decreased from 96.66 to 90.00 mm Hg without disturbing the resting heart rate, and the heart rate at peak exercise was correspondingly decreased suggesting improved workout acceptance [50].

Table 4. Reported pharmacological activities of *Pueraria tuberosa* tuber's extract

S.no	Extract	Doses	Duration	Activity	Model used	Ref.
1	Aqueous	50 mg/100gram b/w	-	Anti-diabetic	*In vivo*	[20] [21] [22] [23]
		50 mg/100 g b/w	35 days			
		50 mg/100 g b/w	10 days			
2	Ethanol	100-400 mg/kg b/w	5 days	Immunomodulatory	*In vivo*	[32]

3	Methanol and water	250 mg/kg b/w	5 days	Immunomodulatory	*In vivo*	[31]
4	Aqueous	250 mg/ml	14 days	Hepatoprotective	*In vivo*	[51]
5	Ethanol and methanol	1000 µg/ml	-	Antioxidant	*In vitro*	[52]
6	Aqueous	200 µg/ml	1 day	Anticancer	*In vitro*	[53]
		400 µg/ml	2 days			
		700 µg/ml	72 hr			
7	Ethyl acetate	31.5- 500 µg/ml	72 hr	Anticancer	*In vitro*	[54]
8	Aqueous	50-100 mg/100 g b/w	20 days	Anti-diabetic nephropathy	*In vivo*	[55] [56] [57]
10	Hydroalcoholic	20 mg/100g, 40 mg/100g b/w	14 days	Anti-diabetic nephropathy	*In vivo*	[58]
11	Methanol	20 mg/kg b/w	14 days	Anti-diabetic nephropathy	*In vivo*	[59]
		40 mg/kg bw	7 days			
12	Methanol	20 and 40 mg/100 g b/w	48 hr	Nephroprotective	*In vivo*	[35]
13	Butanol and ethyl acetate	50 mg/100 g b/w	5 days	Nephroprotective	*In vivo*	[60]
14	Methanol	200 mg/ml	--	Antibacterial	*In vitro*	[61, 62]
15	Hydroalcoholic	50, 100, 200 mg/kg b/w	30 days	Neuroprotective	*In vivo*	[61]

Pharmacological activity of phytoconstituents of *P. tuberosa*

The extract of *P. tuberosa* tubers is acknowledged for its constituents, including, anthracene, anthocyanidins, anthraquinone, glycosides, carbohydrates, catecholic compounds, coumarins, flavonoids, glycosides, hexose sugars, saponins, steroids, terpenoids, and volatile oils, which possess various pharmacological activities detailed given in (Table 5).

Table 8 Pharmacological activity and Mechanism of actions of phytoconstituents of *Pueraria tuberosa*

S.no	Active compound	Dose	Model	Pharmacological activity	Mechanism of action	Ref.
1	**Puerarin**	10 and 100 µM,	*In vivo*	Anti-diabetic	Enhancing the activity of PPARγ leads to increased expression of its downstream targets including GLUT4 and adiponectin	[63] [64, 65]
		20, 40, 80 mg/kg b/w for 56 days			By inhibiting the SIRT1/FOXO1 (Sirtuin signaling pathway/Forkhead box protein O1) pathway.	
		100 µm for 24 h	*In vivo*	Antioxidant	Via the Gβ1/P13K/AKT-Nrf2 signaling pathway, estrogen receptor-dependent induction of HO-1 enhances antioxidant defense capacity.	[66] [67]
		2.5 mg/kg b/w per day for 2 weeks			Restricting the activity of p38, ERK, and IκB along with lowering production of reactive oxygen species suppresses macrophage activation.	

		300 mg/kg/day for 4 weeks	*In vivo*	Hypolipidemic	Encouragement of liver excretion of bile acids and cholesterol	[40]
		50, 100, and 200 mg/kg b.w	*In vivo*	Hepatoprotective	Due to a combination of inhibiting lipid peroxidation and enhancing the antioxidant enzyme activity.	[68]
		600 mg, once daily for 1 week,	*In vivo*	Fibrinolytic	Enhance superoxide dismutase, reduce lipid peroxidation and promote fibrinolysis activity	[69]
		10–40 μM,	*In vitro*	Anti-inflammatory	The suppression of INOS, COX-2, and CRP expression is facilitated by the inhibition of NF-κB activation at transcription level.	[70] [71]
		50 mg/kg b/w/day for 14 weeks	*In vivo*		Decreased levels of inflammatory mediators (TNF-α, IL-1β, COX2 and MMP-14) are accompanied by inhibition of HDAC1/HDAC3 signaling.	
		50 or 100m mg/kg for 28 days	*In vivo*	Nootropic	Activity through modulating the glutamatergic and GABAergic system	[72]
		50 and 100 mg/kg	*In vitro*	Anxiolytic	Activities linked to the HPA axis's adjusted stress hormone levels and neurosteroids production.	[73]

		40- 80 mg/ kg¯1/day *i.p*	*In Vivo*	Antihypertensive	Elevated the phosphorylated eNOS protein level while concurrently reducing the expression levels of angiotensin-2 type 1 receptor and caveolin-1.	[74]
		≥300 mg/kg per day orally	*In vivo*	Anti-fertility	Uterine expression of estrogen receptors and progesterone disrupts the conducive uterine milieu necessary for implantation, thereby preventing implantation.	[75]
		10mg/kg, 30mg/kg and 50mg/kg	*In vivo*	Nephroprotective	Suppressing the signaling pathway of TLR4/NF-κB	[76]
		10 µM and 50 µM	*In vivo*	Anticancer	NF-κB induction in breast cancer cells through P65 and IkBa phosphorylation inhibition	[77]
2	**Genistein**	10 nmol/L to 5 µmol/L	*In vitro*	Antidiabetic	Works on the pancreatic beta cells, promoting the cAMP/PKA signaling cascade and producing an insulinotropic effect.	[78, 79]
		0.2 g/kg	*In vivo*		Improve the absorption and utilization of lipids and carbohydrates.	

		2 g/kg	*In vivo*	Hypolipidemic	Mediates the mRNA expression of several genes connected to the liver's digestion of fatty acids, cholesterol, and steroids.	[80]
		5, 10, 25 µM for 24 hours	*In vitro*	Antioxidant	Stimulate Phosphatase and tensin homolog lost on chromosome 10 expression and activates AMPK (AMP-activate protein kinase) to enhance the production of antioxidant enzymes.	[81, 82]
		0.5, 1 and 2 mg/kg/day, (15 days)	*In vivo*	Hepatoprotective	Reduced hepatic microsomal enzyme levels, reduced oxidative stress markers- malondialdehyde and nitric oxide, boosted anti-oxidation by increasing GSH, & decreased inflammatory markers such as MPO, IL-1β, and COX-2 expression.	[83]
		6-60 mg/kg/day/b.w for 3 months	*In vivo*	Fibrinolytic	Expression levels of tissue plasminogen inhibitor, plasminogen activator inhibitor-1 and C-reactive protein were elevated.	[84][68]
		2.0 or 20 mg/kg daily, or 3.2 or 32 mg/kg for 72 hr	*In vivo*	Anti-inflammatory	Inhibited synthesis of IL-1β, IL-6, and tumor necrosis factor- alpha in blood and liver when exposed to lipopolysaccharide (LPS).	[85 86]

		50 µM			Reduced NF-κB p65 translocation induced by hemolysate and also reduced TNF-α, MCP-1, and ICAM- expression.	
		10 mg/kg b/w	*In vivo*	Nootropic	Enhances short-term spatial memory deficit due to Aβ (β-amyloid) by lowering oxidative stress and activating an estrogenic pathway.	[87]
		1.0 mg/kg, for 96 hr	*In vivo*	Anxiolytic	Agonistic impact on estrogen receptor-β, which produces effects that are identical to anxiolytic effects from other +Ve modulators of estrogen receptor-β	[88]
		1 mg/kg b/w between days 16-60	*In vivo*	Antihypertensive	Reduced blood pressure, maintained renal ultra-structural authenticity, and revived ACE, PKC-βII, eNOS expression	[89]
		2.5–10 mg/kg orally once daily (2 weeks)	*In vivo*	Neuroprotective	Control of Mitochondria-mediated apoptosis channels and ROS inhibition triggered NF-κB activation.	[90]
		10^{-5}-10^{-10} μmol,	*In vitro*	Cardioprotective	Antagonizes the apoptosis by suppressing caspase-expression and enhancing the ratio of Bcl-2/Bax.	[91]

		5 mg/kg, *I.p*	*In vivo*		Decreased post-ischemic contractile recovery and pressure in low flow ischemia, enhanced heart function by inhibiting $Na+/Ca^{2}+$ exchanger and facilitating mitochondrial permeability transition pore opening.	
		2 mg $ml^{-}1$	*In vitro*	Antifertility	Prevent spermatozoa from adhering to the zona pellucida and prevent sperm cells from undergoing the acrosomal process by inhibiting protein tyrosine kinase receptors.	[92]
		50 mg/kg/day	*In vivo*	Wound healing	Action is mediated via traditional estrogen receptor-dependent pathways.	[93, 94]
		0.2,1,and 5mg/kg b/w/day			Delayed wound healing was alleviated, and wound angiogenesis was enhanced through the inhibition of Foxo1, iNOS activity and oxidative stress.	
		10mg/kg/week 3 times for 10 weeks	*In vivo*	Nephroprotective	Decrease in oxidative stress, apoptosis 2/and kidney inflammation observed in diabetic mice.	[95]

3	**Daidzein**	0.2 g/kg,	*In vivo*	Antidiabetic	Increased glucokinase activation along with inhibition od fatty acid synthase, phosphoenolpyruvate carboxykinase, G6phosphatase, β-oxidation and CPT.	[78, 79, 96]
		10µmol/L-20µmol/L			Increased the glucose absorption by adipocytes in response to insulin by up regulating the GLUT4 and IRS-1 expression through PPARγ stimulation.	
		5-200 µM for 24, 48, or 72 h	*In vitro*	Antioxidant	Increased mRNA and protein expression along with increased activity of catalase and total superoxide dismutase, including CuZn-SOD and Mn-SOD.	[97]
		5, 25mg/kg bw for 5 weeks orally	*In vivo*	Hepatoprotective	Inhibit apoptosis via acting as an antioxidant, which in turn lowers caspase-3 over expression	[98]
		12.50–50 µM,	*In Vitro*	Anti-inflammatory	Enhancing PPARγ expression lowers inflammation in the adipose tissues, that may help to alleviate insulin resistance in obese individuals.	[99]
		1 g/kg b/w for (12 weeks	*In vivo*			
		12.5-100mg/kg	*In vivo*	Immunomodulatory	Stimulated the IgM and IgG titer manifested as the HA titer. And increase in the delayed-type hypersensitivity reaction (DTH)	[100]

		5 mg/kg	*In vivo*	Nootropic	Improve cognitive dysfunction and learning memory through p-CREB/BDNF signaling channel and cholinergic system activation.	[101]
		20 mg /kg	*In-vitro*	Antidepressant	Via fatty acid amide hydrolase suppression and regulation of corticosterone levels.	[102]
		10 mg/kg	*In vivo*	Neuroprotective	Through decreasing the generation of oxygen free radicals.	[103]
4	**Daidzin**	Oral 400mg/kg (14 days)	*In vivo*	Antidiabetic	The inhibitory effect on blood glucose is achieved via accelerating intake of muscle glucose and inhibiting alpha glucosidase.	[104]
		5 to 100 µM	*In vitro*	Antioxidant	Increased mRNA and protein expression, along with increased activity of catalase and total superoxide dismutase, including CuZn-SOD and Mn-SOD.	[97]
		25, 50, 100 and 200 mg/kg. *I.p*	*In vivo*	Hepatoprotective	Due to a reduction in oxidative stress and its anti-apoptotic properties.	[105]
5	**Genistin**	20, 40, 60mg/kg b/w	*In vivo*	Cardioprotective	Via blocking the NF-κB and P2X7	[106]

		50, 100 µM (48 h)	*In vitro*	Anti-adipogenic, Anti-lipogenic	Initiate AMP-activated protein kinase-α, and suppress transcription factor 1c that binds to sterol regulatory elements binding (SREBP-1c)	[107]
6	**Tuberosin**	50, 100, 300, and 600 mg/ml	*In vitro*	Antioxidant	Due to its capacity to repress the development of iNOS proteins, decrease LPS induced NO generation in a dependent on concentration way.	[108]
7	**Lupinoside PA4**	20 µg/ml,	*In vitro*	Anti-diabetic	IR-b and Akt phosphorylation can be stimulated by increasing insulin signaling.	[17]
		1.5mg/200g b.w (12 days)	*In vivo*			
8	**β-sitosterol**	20mg/kg orally for 8 weeks	*In vivo*	Anti-colitis	Preventing lipopolysaccharide from attachment to toll like receptor 4 within the NF-κB pathways	[109]
		0.25µg/ml and 2.5µg/ml	*In vitro*	Anti-proliferative	MDM2 expression and STAT6 phosphorylation were suppressed while the p53 expression was enhanced, leading to poly ADP-ribose polymerase cleavage and caspase-3 initiation.	[110]

		20 mg/kg b/w (32 days)	*In vivo*	Nephroprotective	Notable enhancement observed in biochemical, histological parameters and immuno-histochemical assessments accompanied by increase in expression of Nrf2 gene.	[111]
9	**Biochanin A**	10, 20, 40 mg/kg (4 weeks)	*In vivo*	Anti-diabetic	Due to elevated level of SIRT1 expression observed in pancreatic tissue.	[112]
		5-20μM for 1 hr.	*In vitro*	Antitoxic against 2,3,7,8-tetrachlorodibenzo-p-dioxin	Suppression of TCDD-triggered triglycerine depletion in 3T3-L1 adipocytes indicated improved differentiation of 3T3-L1 preadipocytes to adipocytes contrasted to cells solely subjected to TCDD.	[113]
		2-4 μM	*In vitro*	Vasodilatory	Suppression of L-type calcium channels.	[114]
		2.5–100 μM	*In vitro*	Anti-inflammatory	Via decreasing the proteins expressions iNOS, COX-2, MyD88, and TLR-4 along with initiation of Akt and ERK1/2 pathways.	[115]
10	**Biochanin B**	3.45 μmol/L in Vero cells, 3.98	*In vitro*	Anti-enterovirus 71	Suppress expression of COX-2 and PGE2 generation caused by EV71 through the MAPKs pathway involving ERK, p38 and JNK.	[116, 117]

		µmol/L in SK-N-SH cells.				
		1 and 100 µM for 2 weeks	*In vivo*	Hypertrichosis	Suppressing activation of caspase caused by Fas/Fas ligand, therefore preventing apoptosis.	[118]
		5,10,20mg/kg bw.	*In vivo*	Anti-diabetic	Suppressing apoptosis of islet β cells and encouraging their renewal as well as enhancing insulin secretion, hepatic glycogen production and glycolysis.	[119]
		15,50,75mg/kg bw for 5 days.	*In vivo*	Nephroprotective	Reduced expression of p53 by enhancing the over expression of murine doubleminute 2 and MDMX.	[120]
		0-280 µM (24-48 hrs)	*In vitro*	Anticancer	Reducing the ERK phosphorylation level to prevent ovarien cancer cells from proliferating, migrating, and invading.	[121]
		2.5, 5, and 10 µM for 1 day	*In vitro*	Neuroprotective	Focusing the NF-κB signaling pathway in BV2 microglia cells, potentially mediated by ERβ related process.	[122]

		30 µM for 1 day	*In vitro*	Anti-inflammatory	Suppresses HMGB1 via increasing SIRT1 transcription, leading to HMGB1 deacetylation in RAW267.7 cells treated with LPS.	[116]
		5 mM	*In vitro*	Cardioprotective	Enhancing autophagy to reduce ischemia/reperfusion-induced cellular death in aging cells.	[123]
		25,50,100mg/kg bw for 8 days	*In vivo*	Anticolitis	Through Suppressing the stimulation of NLRP3 Inflammasome channels.	[124]
		150 µmol/L for 12, 24, and 48 h	*In vitro*	Anticancer	Enhancing the tumor inhibiting potential of everolimus via blocking Akt activation. Further enhanced the PTEN and p-4EBP-1 while suppressing the p-mTOR and p-p70S6K expression	[125]
		50mg/kg bw for 28 days	*In vivo*			
		100mg/kg bw for 14 weeks	*In vivo*	Hepatoprotective	Enhanced fatty liver by promoting lysosome biogenesis through TFEB activation.	[126]
		31.25µg/ml	*In vivo*	Anti-inflammatory	Via blocking the MAPK/JNK and TRIF MAPK/ERK or MyD88 pathways	[127]

		25mg/kg bw for 10 days	*In vivo*	Anxiolytic	Reduction of inflammation and hyperexcitabilty via suppression of NMDA receptor and CBP in basolateral amygdala.	[128]
11	**Irisolidone**	1, 5, and 10 μM for 12 h	*In vitro*	Anti-ischemia	Enhanced cell survival and reduce apoptosis	[129]
		50,100,200mg/kg bw for 30 days	*In vivo*		Suppressed mitochondrial membrane potential and enhanced overall ATPase activity.	
		5 or 10 μM for 90 min	*In vitro*	Anti-gastritic	By suppressing the ingress of immune cells notably neutrophils through the CXCL-4 or IL-8 release regulation.	[130]
		20-50mg/kg for 4 days	*In vivo*			
		20 mg/kg b/w	*In vivo*	Anti-colitis	Via preventing toll like receptor4 and the total number of gut proteobacteria from binding to lipopolysaccharides	[131]
13	**Puerarone**	-	*In silico*	Antidiabetic	Via DPP-4 inhibition	[21]

14	**Quercetin**	15mg/kg bw for 7 days	*In vivo*	Hepatoprotective	Reduced the rise in MDA, improved GSH level and action of SOD along with reduced the sinusoidal congestion and liver vacuolar degradation	[132]
		100mg/kg bw for 30 days	*In vivo*	Neuroprotective	Suppress oxidative stress via reducing reactive oxygen species.	[133]
		5-100µM	*In vitro*			
		100 mg/kg b/w (6 days)	*In vivo*	Intestinal damage repair	Stimulation of cell expansion within the crypt instead of apoptosis suppression	[134]
15	**Tectoridin**	75mg·kg^{-1}·b/w	*In vivo*	Anti-alcoholism	Act by reducing the alcohol content	[135]
16	**p-coumaric acid**	100mg/kg b/w (7 days)	*In vivo*	Immunomodulatory	Likely Due to suppression of NF-κB gene activity, possibly resulting in decrease in TNF-α expression.	[136]
		8 mg/kg b/w (7days)	*In vivo*	Cardio-protective	Due to its antihypertrophic, antilipidemic, and ability to scavenge free radicals, suppressed heart hypertrophy as well as alterations in lipids, lipoproteins and ECG.	[137]

		100mg/kg b/w for 21 days orally	*In vivo*	Nephroprotective	Because of its metal chelating action and elevation of metallothionein content.	[138]
		100 mg/kg bw orally	*In vivo*	Antidiabetic	by the pancreatic stimulation of GLUT 2	[139]
		30 mg/kg b/w	*In vivo*	Neuroprotective	Minimize cognitive impairments caused by muscarinic cholinergic inhibitors	[140]
		100mg/kg bw for 26 days	*In vivo*	Anti-arthritic	via suppression of NFjB and kinase pathway (ERK, JNK, p-JNK)	[141]
		50 and 100 µmol/L	*In vivo*	Anti-oxidant	Via decrease the reactive oxygen species	[142]
		10–100 µM	*In vitro*	Hepatoprotective	Preventing nuclear breakdown, cytotoxicity, ROS generation, and mitochondrial depolarization	[143]
		50, 100, and 200 mg/kg b/w	*In vivo*		Via preventing the Bax, caspases expression such as AST, ALT, ALS, LDH	
		0–4,000 µmol/L for 24 and 72 h	*In vitro*	Anticancer		[144]

		100 mg/kg b/w for 30 weeks	*In vivo*		Suppresses Grp78 activation in cancer cells via stimulating the pathway of PERKeIF2α-ATF-4-CHOP	
18	**Robinin**	50mg/kg bw for 10 days	*In vivo*	Cardioprotective	Via modifying the TGF-b1 signaling pathway	[145]
		6 µg/ml	*In vitro*	Immunomodulatory	Through blocking the signaling pathway of TLR4-NF-κB	[146]
		0.125–0.50 mg/ml	*In vitro*	Antioxidant	Capable of preserving the stroma cells, PF, lowering ROS levels and keeping mitochondrial function constant	[147]
19	**Tuberostan**	-	*In silico*	Anti-diabetic	Demonstrated the strongest interactions with GLP-1R, GIP-R active site amino acid residues.	[22]
20	**Isoorientin**	25 nM and 100 µM (16 hrs.)	*In vitro*	Anti-inflammatory	Suppressed the COX-2 expression	[25]
		10,20mg/kg, b/w for 1 day	*In vivo*		Reduced the COX-2, TNF-α, IL-1β, iNOS, and 5-LOX expression	

21	**Mangiferin**	20 and 40 μM for 16 h	*In vitro*	Anti-inflammatory	Decreased expression of TNF-α, iNOS, and COX-2 and elevated concentrations of anti-inflammatory cytokine IL-10	[26]
		10 mg/kg, 20 mg/kg b/w for 24 h	*In vivo*			
22	**Stigmasterol**	200 mg/kg and 400 mg/kg b/w (orally 16 weeks)	*In vivo*	Chemo-preventive	Enhanced the lipid peroxide concentration and DNA damage Due to oxidative stress.	[148]

TOXICOLOGY

The safety profile of *P. tuberosa* has been assessed via acute and repeated-dose toxicity studies showed in accordance with OECD guidelines. Acute toxicity study showed that oral administration of the aqueous tuber extract in doses of 2,000 and 5,000 mg/kg body weight did not cause any deaths or behavioral changes, suggesting a high safety margin and LD_{50} more than 5,000 mg/kg body weight. In the same way there were no notable changes in body weight, hematology, renal markers, and pathologic examinations after a single-dose study. Repeated-dose studies have however shown dose-dependent toxic effects at higher doses. Aqueous tuber extract administered at doses of 250-2,000 mg/kg body weight for 28 days led to 100% mortality at 2,000 mg/kg by 21st day [149]. The cause of death in histopathology is due to toxicity to the liver, as the result is necrosis of hepatocytes and inflammation with degeneration of the hepatic tissue. However, there were no apparent changes in the structures of the spleen, adrenals, heart, intestine, and reproductive organs, with normal sperm counts maintained. Further studies on the toxicity aspect revealed that the continuous use of the methanolic extract from the tubers may lead to dose-dependent hepatic injury. High levels of serum hepatic enzymes, congestion of the sinusoids, infiltration of inflammatory cells, and necrosis of the hepatocytes were observed in animal experiments exposed to higher doses. Nonetheless, there was no nephrotoxicity and hematological toxicity seen at doses that were therapeutically significant. This makes the use of the herb relatively safe at therapeutic levels. All things considered, it is evident from the data presented here that the P. tuberosa herb has a relatively safe safety profile at therapeutic doses; nonetheless, long-term use at high doses would be associated with hepatotoxicity. Thus, additional chronic, reproductive, genotoxicity, and clinical safety studies are needed [150].

FORMULATIONS

P. tuberosa has traditionally been used to make curative Ayurvedic formulations in conjunction with other medicinal herbs. Significant Ayurvedic preparations that include *P. tuberosa* are 'Ashwagandharishta', a conventional treatment for epilepsy [151], and 'Maha vishagarbha taila', a traditional solution for sciatica and joint issues [152], and “Nityananda rasa”, “Sarasvatarista”, “Satavaryadi ghrita”, Manmathabhra Rasa, Pugakhanda (Aparah), “Marma gutika” [153], and “Vidaryadi ghrita” Chawanprash, Indrokta rasayan, Brimhani gutika, Sukumar tail [154].

FUTURE PERSPECTIVE

The phytochemical and biological activities of *P. tuberosa* have been widely studied, majority of the available evidence is based on *in vitro* and preclinical studies. As a result, there is an absolute necessity to conduct clinical trials in order to govern its efficacy, safety and therapeutic application in the management of various diseases. The standardization of the extracts along with the determination of markers such as puerarin, daidzein, genistein, and robinin is recommended for further research [5, 6]. Complete pharmacokinetic, bioavailability and metabolic studies are also essential to better recognize the ADME of its bioactive compounds. Additionally advanced approaches including network pharmacology, molecular docking and omics-based technologies may provide deeper insights into the molecular mechanism underlying the therapeutic applications of *P tuberosa*. Further advances in delivery techniques such as phytosome formulation, nanoparticle formulations, and other nano-formulations can increase its bioavailability and enhance the pharmacological properties of its active components. Long-term toxicological studies, reproductive toxicological tests, and clinical safety trials are required to ensure the safety of this herb for long-term use [149, 150]. All these studies will support in the conversion of this traditional medicinal plant into a scientifically validated phytopharmaceutical and nutraceutical agent.

CONCLUSION

Pueraria tuberosa is a useful medicinal plant with a history of use in traditional system of medicine and increasing scientific evidence supporting its therapeutic efficacy. Phytochemical studies have suggested the presence of numerous bioactive components in *P. tuberosa* in which most of the phytochemicals are isoflavonoids including puerarin, genistein, daidzein and robinin. Many experimental studies have shown that P. tuberosa possess several medicinal properties for instance antidiabetic, antioxidant, anti-inflammatory, nephroprotective, hepatoprotective, cardioprotective, neuroprotective, anti-stress, immunomodulatory, wound healing, and anti-osteoporotic, thereby validating many of its traditional medicinal properties. The toxicological studies suggest a favorable safety profile at therapeutic doses, though extended use at higher doses may cause adverse effects, emphasizing the need for comprehensive long term safety evaluation. In spite of encouraging preclinical findings, clinical evidence leftovers limited and additional studies are vital to establish safety, efficacy, pharmacokinetic and optimal dosage regimens in humans. Further research related to the standardization of extracts, pharmacological mechanisms, biomarkers, and delivery systems will probably promote the development of phytopharmaceutical and nutraceutical products based on *P. tuberosa*. Overall, *P. tuberosa* seems to be a auspicious source of medicinal compounds with potential medical application in the future.

CONFLICT OF INTEREST

NA

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NA

ABBREVIATIONS

P (Pueraria), NF-κB (Nuclear factor-kappa B), PPARγ (Peroxisome Proliferator Activated Receptor Gamma), GLUT (Glucose Transporter), SIRT1 (Silent information regyulator sirtuin 1), ERK (Extracellular signal-regulated kinase), INOS (Inducible nitric oxide synthase, COX-2 (Cylcooxiginase-2), CRP (C-reactive protein), IL-1β (Interleukin-1 beta), MMP-14 (Matrix metalloproteinase-14), HDAC1 (Histone deacetylase 1), GABA (Gamma-aminobutyric acid), HPA (Hypothalamic-pituitary adrenal), TLR4 (Toll-like receptor 4), mRNA (Messenger ribonucleic acid), MPO (Myeloperoxidase), GSH (Glutathione), TNF-α (Tumor necrosis factor alpha), MCP-1 (Monocyte chemoattractant Protein-1), ICAM (Intercellular adhesion molecule), ACE (Angiotensin converting enzyme), PKC (Protein kinase C), CPT (carnitine palmitoyltransferase), IRS-1 (Insulin receptor substrate 1), CuZnSOD (Copper-zinc superoxide dismutase), MnSOD (manganese superoxide dismutase), HA (Hemagglutination assay), MDM2 (Mouse double minute 2), STAT 6 (Signal transducer and activator of transcription 6), NRF2 (Nulcear factor erythoid 2- related factor 2), TCDD (Tetrachlorodibenzo para dixon), JNKs (Jun N-terminal kinase), HMGB 1 (High mobility group box 1), NLRP3 (Nucelotide-binding oligomerization domain), PTEN (Phosphatase and tensin homolog), p-mTOR (phosphorylated Mammalian Target of Rapamycin), TEFB (Transcription factor EB), MDA (Malondialdehyde)

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