Pueraria tuberosa: A Review on Traditional Uses, Pharmacology, and Phytochemistry

Ram Bharti1,2, Bhupinder Singh Chopra1,2, Sachin Raut1,2 and Neeraj Khatri1,2*

1IMTECH Centre for Animal Resources & Experimentation (ICARE), Council of Scientific and Industrial Research-Institute of Microbial Technology (CSIR-IMTECH), Chandigarh, India, 2Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, India

Pueraria tuberosa (Roxb. ex Willd.) DC. (Fabaceae), also known as Indian Kudzu (vidari kand), is a perennial herb distributed throughout India and other Asian countries. Traditionally, tuber and leaves of this plant have extensively been reported for nutritional and medicinal properties in Ayurveda as well as in Chinese traditional practices. The objective of the present review is to compile and update the published data on traditional uses, pharmacological potential, and phytochemistry of compounds isolated from the plant Pueraria tuberosa. P. tuberosa extracts and its purified compounds possess multiple activities such as anticancer, anticonvulsant, antidiabetic, antifertility, anti-inflammatory, antioxidant, anti-stress, antiulcerogenic, cardioprotective, hypolipidemic, hepatoprotective, immunomodulatory, nephroprotective, nootropic, neuroprotective, and wound healing. Tuber and leaf extracts of P. tuberosa contain several bioactive constituents such as puerarin, daidzein, genistein, quercetin, iridoidone, biochanin A, biochanin B, isoorientin, and mangiferin, which possess an extensive range of pharmacological activities. The extensive range of pharmacological properties of P. tuberosa provides opportunities for further investigation and presents a new approach for the treatment of ailments. Many phytochemicals have been identified and characterized from P. tuberosa; however, some of them are still unexplored, and there is no supporting data for their activities and exact mechanisms of action. Therefore, further investigations are warranted to unravel the mechanisms of action of individual constituents of this plant.

Keywords: in vivo studies, pharmacological properties, phytochemical constituents, traditional uses, Pueraria tuberosa

INTRODUCTION

As per the World Health Organization (WHO) estimation, about 65–80% of people all over the world seek herbal therapies to cure primary health conditions (Robinson and Zhang, 2011). Surprisingly, only 15% of the global flora has been assessed for pharmacological potential (De Luca et al., 2012). WHO has published four volumes of the monographs on selected medicinal plants to support the research in the field of herbal medicine (WHO, 2009). In India, Ayurveda, Unani, Siddha, Homeopathy, and Folk medicine are commonly used as traditional alternative medicine practices for treating different ailments. Among the modern civilizations, India has long been known for its rich treasure of medicinal plants, and about more than 7,000 plant remedies have been categorized and documented by the AYUSH system of medicine (National Medicinal Plants Board,
One of the medicinally important plants discussed in this review is *Pueraria tuberosa* (Roxb. ex Willd.) DC. (Fabaceae), also known as Indian Kudzu (vidari kand). It is a rapidly growing large perennial climber with big tuberous roots (Figures 1–4) (Indian Medicinal Plant Database) and is distributed throughout India, Pakistan, and Nepal (Keung, 2002). Liana of *P. tuberosa* has also been found to grow at 4,000 feet in the Himalayan mountain series (Pueraria tuberosa—Vikaspedia, 2020). In Ayurveda, it is known as vidari (vidari kand). The tuber of this plant is sweet (Ayurvedic pharmacopoeia of India, 2001) and is widely used in the treatment of fever, menorrhagia, skin diseases, wounds, bronchial asthma, and jaundice. Apart from the traditional uses of this plant as mentioned in ancient literature like Sushruta Samhita (Sanskrit: सुश्रुत संहिता), several studies have been reported on different pharmacological activities of *P. tuberosa* extracts and its purified compounds, viz., anticancer (Adedapo et al., 2017), anticonvulsant (Basavaraj et al., 2011), antiulcerogenic (Gindi et al., 2010), cardioprotective (Patel, 2005), hepatoprotective (Xia et al., 2013), immunomodulatory (Patel et al., 2016), cardioprotective (Patel et al., 2018), hypolipidemic (Tanwar et al., 2008), hepatoprotective (Xi et al., 2013), antidiabetic (Oza and Kulkarni, 2018a), antifertility (Gupta et al., 2005), anti-inflammatoriy (Tripathi et al., 2013), antioxidant (Shukla et al., 2018a), anti-stress (Verma et al., 2012), antioxidant (Gindi et al., 2010), cardioprotective (Patel et al., 2018), hypolipidemic (Tanwar et al., 2008), hepatoprotective (Xi et al., 2013), immunomodulatory (Patel et al., 2016), and neuroprotective (Shukla et al., 2018b), nootropic (Rao et al., 2008), and wound healing activities (Kambhoja and Murthy, 2007). Previously, Maji et al. (2014) broadly highlighted the phytochemical and therapeutical potential of *P. tuberosa* in various pharmacological activities. However, the information about the doses of plant extracts used and the models implied for the studies (in vitro or in vivo) in different pharmacological activities was missing. In addition, chemical structures of only few phytoconstituents isolated from *P. tuberosa* have been given. Therefore, this review is aimed to provide an up-to-date summary of the literature on traditional uses, doses, and types of studies used to confirm pharmacological activities and phytochemical constituents isolated from *P. tuberosa* plant with their chemical structures and IUPAC names.

**METHODOLOGY**

Relevant literature for this review on *P. tuberosa* has been sourced from PubMed, ScienceDirect, Web of Science, PubChem, Google Scholar, SciFinder, and Scopus database. The articles published in English before September 2020 on traditional uses, pharmacology of extracts, and various phytoconstituents isolated from different parts of *P. tuberosa* were included in this review. The keywords used for retrieving relevant studies were *Pueraria tuberosa* plant, Indian Kudzu, vidari kand, tuber extract, traditional uses, phytochemical constituents, pharmacological activity, and *in silico*, *in vitro*, and *in vivo* studies.

Data inclusion criteria included (a) published/peer-reviewed scientific manuscripts; (b) ethnopharmacological studies; (c) tuber extracts with different solvents; (d) studies on the mechanism of actions of plant extracts and their phytoconstituents; (e) *in silico*, *in vitro*, and *in vivo* studies. Exclusion criteria included (a) repetitive studies and information not meeting the inclusion criteria; (b) studies performed with extracts of other *Pueraria* species; (c) opinion to the editors, case studies, abstracts of the conferences, any unpublished data, and reports.

**Synonyms (Ayurvedic pharmacopoeia of India, 2001)**

Assamese: Bhedeleton, Bhuiikumra
Bengali: Bhuinkumra, Bhumikusmanda, Vidari
English: Indian kudzu
Gujrati: Bhoikolu, Bhonykoru, Eagio, Sakharvel, Vidarikanta,
Hindi: विदारीकंद (Vidarikanda), बनकुमड़ा (Bankumara)
Kannada: Gumadi belli, Gumadigida, Nelagumbala Gudde,
Nelagumela, Nelagumbula
Malayalam: Mudakku
Marathi: Bhuihkohala, Ghodvel
Oriya: Bhuianakakharu
Punjabi: Siali, Surala
Sanskrit: बनकुमड़ा (Bhumikusmanda), गजवाजपिया (Gajavajipriya), कन्दपलाश (Kandapalash), सुश्रुतसंहिता (Sushruta Samhita), विदारीकंद (Vidarikanda), इंडियन कुड़ु (Indian kudzu)
Telugu: Darigummadi, Nelagummuda

**Scientific Classification (Rawtal et al., 2019)**

Kingdom: Plantae
Subkingdom: Trachebionta
Superdivision: Spermatophyta
Division: Magnoliophyta
Subclass: Rosidae
Order: Fabales
Family: Fabaceae
Genus: *Pueraria* DC.
Species: *Pueraria tuberosa*

**Traditional Uses**

In Ayurveda, vidari kand (*Pueraria tuberosa*) has been described as a plant having good nutritional value. Besides, the plant also possesses aphrodisiac, diuretic, galactagogue (Kirtikar and Basu, 1935), energizing (Maji et al., 2014), and spermatogenic (Chauhan et al., 2013) properties. It has been prescribed for treatment for all three doshas (i.e., for the complications of three different energies, viz., Vata, Kapha, and Pitta) of human body (Ayurvedic pharmacopoeia of India, 1999; Dalal et al., 2013). The powdered form of tuber is primarily used in combination with cow’s milk as a galactagogue agent to abrogate lack of milk production after childbirth and also as an anabolic agent along with *Piper longum* L. (Piperaceae) powder to cure malnutrition in children. For relieving excessive menstruation, the powder is used with honey. A mixture of powdered *P. tuberosa* and wheat or barley fried in ghee (clarified butter) with milk has been advised for sexual enervation and strength. For spermatorrhoea, fresh tuber juice of this plant with cumin seeds and sugar has been used therapeutically (Puri, 2003).
Traditionally, *P. tuberosa* has been used along with other medicinal plants in different combinations to prepare therapeutic Ayurvedic formulation. Some of the important Ayurvedic formulations utilizing *P. tuberosa* are “Ashwagandharishta”, a traditional remedy for epilepsy (Tanna et al., 2012), “Maha visagarbha taila”, a traditional remedy for sciatica and joint disorders (Kumawat et al., 2017), and “Nityananda rasa”, “Sarasvatarista”, “Satavaryadi ghrita” (Ayurvedic pharmacopoeia of India, 2001), “Marma gutika” (Kumar, 2016), and “Vidaryadi ghrita” (Sharma et al., 2018).

Traditional uses of *Pueraria* species, namely, *Pueraria montana* var. *thomsonii* (Benth.) (Fabaceae) and *Pueraria montana* var. *lobata* (Willd.) (Fabaceae), have been reported for their medicinal properties such as antiemetic, antitoxic, cold, countering the effect of alcohol abuse, anti-stress agent, neck stiffness, hypohidrosis, migraines, hypoglycemia, and certain cardiovascular diseases in the Chinese Medicinal Herbs, a book written by Li Shih Chen (Li, 2003; Croom, 2004).

**Pharmacology**

In phytopharmacological/ethnopharmacological research, scientific community should follow best practices in designing and conducting studies and reporting the results of analyzing pharmacological properties of the plant extracts and compounds of natural origin (Heinrich et al., 2020). Therefore, while reporting biological activities of any plant/herbal product, detailed information about the characterization of the plant extracts, their phytoconstituents, doses, duration of treatment, type of models used in the studies, toxicological data, and so forth should be clearly presented for the benefit of research community (Heinrich et al., 2020). Various pharmacological activities of the tuber extracts of *P. tuberosa* have been explored, and a graphical summary of these activities is shown in Figure 5 and Table 1.

**Nephroprotective Activity**

Several studies have shown that *P. tuberosa* plant possesses nephroprotective activities. Oral administration of methanolic tuber extract to cisplatin- (8 mg/kg body weight) induced kidney damaged rats showed a dose-dependent protective effect (Nagwani and Tripathi, 2010). Tuber extract significantly reduced blood urea nitrogen, serum creatinine, glutathione, and superoxide dismutase (SOD) levels. The extract could control deoxyribonucleic acid (DNA) damage and catalase activities, cellular necrosis, and tubular swelling and prevent coagulation of proteins, in contrast to the control group. The nephroprotection of tuber extract of the plant has been attributed to its free radical scavenging activity (Nagwani and Tripathi, 2010). Feeding of biscuits made up of powder of *P. tuberosa* tuber
for 10 days showed significant recovery in cisplatin-induced nephrotoxicity in Swiss mice. However, at higher dose, aspartate aminotransferase and alanine aminotransferase levels were temporarily elevated, so monitoring of liver functions, periodically, is imperative when continuing this regimen for longer periods such as a food supplement for cancer patients undertaking cisplatin chemotherapy (Tripathi et al., 2012). The methanolic extract of *P. tuberosa* ameliorated glycerol-induced acute kidney injury in rats by affecting the lipid peroxidation, SOD, and catalase activity with a lesser accumulation of hyaline casts and a lesser degree of tubular necrosis on histology of the kidney (Yadav et al., 2016a). Water decoction of *P. tuberosa* has also been reported to significantly reverse cisplatin-induced nephrotoxicity in rats (Yadav et al., 2016b). Hydroalcoholic tuber extracts of *P. tuberosa* showed nephroprotective activity in sodium arsenate- (1 mg/kg body weight) induced oxidative kidney tissue damage in rats (Rani et al., 2017). The nephroprotective effect through free radical scavenging activity
was supported in a study, where streptozotocin- (STZ-) induced diabetic nephropathic rats, treated with aqueous tuber extract of *P. tuberosa*, exhibited an upsurge in activity of antioxidant enzymes, lowered oxidative stress, apoptosis, and urinary albumin excretion in a concentration-dependent manner (Shukla et al., 2018a). Methanolic tuber extract of the plant showed substantial protection in diabetic nephropathy induced by the administration of alloxan in rats (120 mg/kg body weight) by decreasing urea and creatinine and improving physiology of the kidney (Yadav et al., 2019). The supplementation of tuber extract of the *P. tuberosa* showed protection of kidney from oxidative stress and cellular injury. It also improved kidney physiology and parameters of kidney function test by reducing cellular apoptosis. These studies indicate that *P. tuberosa* extracts have nephron-protective potential and might lead to promising therapeutic agents for treating kidney diseases.

**Antioxidant Activity**

Methanolic and hexane tuber extract of *P. tuberosa* exhibited a strong free radical scavenging activity in a concentration-dependent fashion. These results showed that the methanolic extract of this plant exhibited better activity than the hexane extract in trapping hydroxyl radicals and inhibited lipid peroxidation, which indicated potent antioxidant property (Pandey et al., 2007). Hot water tuber extract of the plant *P. tuberosa*, supplemented with milk in Swiss mice, showed potent antioxidant activities in liver and red blood cells. Besides, a remarkable difference in glutathione levels was also observed in the control (172 µg/ml) and supplemented groups (*P. tuberosa*: 1,212 µg/ml and *P. tuberosa* + milk: 1,308.2 µg/ml). *P. tuberosa* along with milk has antioxidant property as evidenced by higher phagocytic activity, increased immunoglobulin levels, and reduced glutathione and lipid peroxidation (Sawale et al., 2013). *P. tuberosa* extracted with chloroform, acetone, methanol, and hot water was used to determine its antioxidant potential by using ferric reducing antioxidant power (FRAP) assay, metal chelating, phosphomolybdenum, and free radical scavenging using DPPH (2,2'-diphenyl-1-picrylhydrazyl radical) and ABTS (3-ethylbenzothiazoline-6-sulfonic acid) assay. The results showed that acetone extract of *P. tuberosa* has potent antioxidant activity (Viji and Paulsamy, 2015).

**Antidiabetic Activity**

Oral gavage of ethyl acetate tuber extract of *P. tuberosa* (250 mg/kg body weight) to alloxan-induced diabetic rats for seven days showed a pronounced decrease in blood glucose levels (Raghuwanshi and Jain, 2011). Studies suggested that chloroform, petroleum ether, ethanol, and aqueous tuber extracts of *P. tuberosa* confer significant antidiabetic activity in STZ- (50 mg/kg body weight) induced diabetic rats by a single intraperitoneal injection (Tripathi and Kohli, 2013). Water extract of root of *P. tuberosa* showed significant inhibition of dipeptidyl peptidase-4 (DPP-IV) that causes an enhanced half-life of active glucagon-like peptide-1 hormone. This hormone regulates glucose-dependent insulin release from β-cells of the pancreas in rats (Srivastava et al., 2015). In Srivastava et al.’s next study, they found that *P. tuberosa* water extract increased the glucose homeostatic potential through DPP-IV inhibitory pathway.

### Reference

**TABLE 1 | Pharmacological activities of tuber extract of Pueraria tuberosa.**

| Extract                      | Dose tested                        | Pharmacological activity | Model used for study (in vivo or in vitro) | Reference                                                                 |
|------------------------------|------------------------------------|--------------------------|-------------------------------------------|---------------------------------------------------------------------------|
| Aqueous                      | 50 mg/100 g b/w for 35 days        | Antidiabetic             | In vivo                                   | Srivastava et al. (2015); Srivastava et al. (2017); Srivastava et al. (2018); Srivastava et al. (2019) |
| Ethanol                      | 50 mg/100 g b/w for 10 days        | Antioxidant              | In vitro                                  | Patel et al. (2016)                                                       |
| Tuber powder                 | 250 mg/kg b/w                      | Immunomodulatory         | In vivo                                   | Shilpashree et al. (2015)                                                 |
| Aqueous                      | 250 mg/ml given orally to rats for 14 days | Hepatoprotective         | In vivo                                   | Pandey et al. (2019)                                                      |
| Ethanol and methanol         | 125, 250, 500, and 1,000 µg/ml     | Antioxidant              | In vitro                                  | Likhitkar and Pande (2017)                                                |
| Aqueous                      | 200, 400, and 700 µg/ml for 24, 48, and 72 h | Anticancer               | In vitro                                  | Adedapo et al. (2017)                                                     |
| Hydroalcoholic               | 64 and 128 µg/ml for 24 h          | Anticancer               | In vitro                                  | Aruna et al. (2018)                                                       |
| Ethyl acetate                | 31.5–600 µg/ml for 72 h            | Anticancer               | In vitro                                  | Salpathy et al. (2020)                                                    |
| Aqueous                      | 50–100 mg/100 g b/w for 20 days    | Antidiabetic nephropathy | In vivo                                   | Shukla et al. (2017); (2018a); (2018b)                                    |
| Hydroalcoholic               | 20–40 mg/100 g b/w for 14 days     | Antidiabetic nephropathy | In vivo                                   | Tripathi et al. (2017)                                                    |
| Methanolic                   | 20 mg/kg b/w for 14 days           | Antidiabetic nephropathy | In vivo                                   | Yadav et al. (2019)                                                      |
| Methanolic                   | 20 and 40 mg/100 g b/w for 2 days  | Antidiabetic nephropathy | In vivo                                   | Yadav et al. (2016a)                                                     |
| Butanol and ethyl acetate    | 50 mg/100 g b/w for 5 days         | Nephroprotective         | In vivo                                   | Yadav et al. (2016a)                                                     |
| Methanolic                   | 200 mg/ml                          | Antibacterial            | In vitro                                  | Pandya et al. (2019)                                                     |
| Hydroalcoholic               | 50, 100, and 200 mg/kg b/w for 30 days | Neuroprotective         | In vivo                                   | Umarani et al. (2016)                                                    |

*b/w: body weight.*
and the bioactive components robinin and puerarone, and this inhibitory activity was also confirmed by in silico molecular docking (Srivastava et al., 2017). Aqueous extract of tuber of P. tuberosa has further been reported to act as incretin receptor agonist and downregulated β-cells apoptosis and protected STZ-induced diabetes in rats (Srivastava et al., 2018). Aqueous tuber extract of the plant showed an elevated expression of nphrin and SOD and a declined expression of cysteinyl aspartyl specific proteinase 3 (caspase-3), interleukin 6 (IL-6), nuclear factor kappa B (NF-kB), protein kinase C epsilon type (PKCe), tumor necrosis factor alpha (TNF-α), vascular endothelial growth factor (VEGF), matrix metalloproteinase-9 (MMP-9), and hypoxia-inducible factor 1-alpha in STZ-induced diabetic rats (Srivastava et al., 2019). In another experiment, it has been shown that administration of P. tuberosa water extract in alloxan-induced rat diabetic model resulted in decrease in SGOT (serum glutamic oxaloacetic transaminase), SGPT (serum glutamic pyruvic transaminase), and alkaline phosphates level and improved deformed hepatocytes and significant decrease in blood glucose levels as well as apoptosis (Pandey et al., 2019). The tuber extract contains different bioactive compounds that may act as agonists on glucagon-like peptide-1 hormone released from intestine and can also protect β-cells of the pancreas. It also resulted in decreased expression of different inflammatory and apoptotic markers during hypoxic injury to β-cells as evidenced by decreased apoptosis of β-cells. The extract also inhibited DPP-IV enzyme as an incretins receptor agonist, and hence it is emanating from the above studies that P. tuberosa has antidiabetic potential.

**Anti-Stress Activity**

Adult male Wistar rats subjected to cold immobilization stress, pretreated with 70% hydroethanolic tuber extract of P. tuberosa (200 and 400 mg/kg body weight) for 5 days, showed significant protection from gastric mucosal damage, reduced corticosterone level in the blood, and no enlargement of spleen and adrenals as compared to Withania somnifera (L.) Dunal (Solanaceae) rhizome extract (100 mg/kg body weight). These studies established the anti-stress effect of P. tuberosa (Pramanik et al., 2011). In a human trial, hypertensive patients were divided into two groups: group 1 was given capsules with 0.75 g tuber powder, whereas group 2 was given placebo capsules with lactose powder administered for 12 weeks. Group 1, treated with 1.5 g (twice a day) tuber powder of P. tuberosa for 12 weeks, showed a gradual decrease in systolic, diastolic, and mean blood pressure as well as a tolerant decrease in fibrinogen and increased plasma fibrinolytic activity (Verma et al., 2012). In stress-mediated disorders, the hypothalamic-pituitary-adrenal (HPA) axis is dysregulated which changes the levels of corticosteroids in plasma and monoamine in the brain. The extract of this plant might act on mucosal layer of the gastrointestinal, cardiovascular, and nervous (HPA) system, suggestive of anti-stress activity by a reduction in stress hormones.

**Antidiabetic Nephropathic Activity**

STZ-induced diabetic rats with nephropathy were given tuber extract of P. tuberosa (30 mg/100 g, body weight) for 20 days and exhibited a significant reduced severity of diabetic nephropathy by enhanced expression and activity of MMP-9 and degrading the accumulation of extracellular matrix in kidney tissue (Tripathi et al., 2017). Levels of nphrin, a biomarker of early glomerular injury, in the kidney of diabetic nephropathic rats were restored after treatment with tuber extract of P. tuberosa (Shukla et al., 2017). The diabetic nephropathic inflammatory response is mediated by NF-κB and its activated phosphorylated derivative (pNF-κB). Improved levels of these transcription factors and inflammatory cytokines (IL-6 and TNF-α) in the kidney of STZ-induced (55 mg/kg body weight) diabetic nephropathic rats were observed, and treatment with extracts from the tuber of P. tuberosa significantly negated these changes in a dose-dependent manner (Shukla et al., 2018b). Amelioration of renal damage was evaluated by renal functional tests, histopathology, and oxidative stress in alloxan-induced diabetic nephropathy. P. tuberosa methanolic extract showed renal protection by decreasing urea and creatinine and improved kidney physiology and histopathology changes through antioxidant mechanisms (Yadav et al., 2019). These studies are indicative of nephro-protection offered by P. tuberosa in diabetic nephropathy; however, this protective effect needs to be further explored, including studies on the protection of renal and glomerular cells mediated by different signaling pathway in the antidiabetic nephropathy.

**Anti-Inflammatory Activity**

The ethyl acetate and methanolic tuber extracts of P. tuberosa showed considerable anti-inflammatory potential compared to the control and standard drugs, ibuprofen, and nitrofurazone ointment in the rat paw edema method (Kambhoja and Murthy, 2007). The methanolic tuber extract of the plant significantly prevented the carrageenan-induced inflammation by lowering the glutathione content, catalase, SOD activity, and enhancing lipid peroxidation and C-reactive proteins in rats in a sequential manner (Tripathi et al., 2013). Isoorientin, isolated from the tuber of P. tuberosa plant, showed significant anti-inflammatory activity in LPS-treated mouse macrophage (RAW 264.7) cell line. It was also effective against carrageenan-induced inflammation on paw edema and air pouch mouse models. These studies revealed the downregulation in the expression of proinflammatory genes such as inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), TNF-α, and inactivation of NF-κB. Moreover, there was activation of antioxidant enzymes, catalase and glutathione-S-transferase (Anilkumar et al., 2017). The anti-inflammatory property of extracts of P. tuberosa in these studies appears to be mediated by lipid peroxidation, inactivation of the NF-κB pathway, and downregulation of proinflammatory cytokines.

**Immunomodulatory Activity**

Immunomodulatory activities of plant extract (0.4%) with milk as a carrier given to Swiss mice for 28 days were evaluated. The result showed a significantly higher phagocytic activity and immunoglobulin concentration, reduced glutathione content, and thiobarbituric acid reactive substances level compared to the control (Sawale et al., 2013). Reversed phase high-performance
liquid chromatography (RP-HPLC) analysis of ethanolic tuber extract of the plant revealed that bioactive compounds involved in the immunomodulatory activities are genistein (1.37%), daidzein (1.70%), and puerarin (8.31%). Oral administration of these extracts builds up innate and humoral immune responses against sheep red blood cells challenged rats (Maji et al., 2014). The immunomodulatory activity of petroleum ether extract of P. tuberosa was evaluated by carbon clearance assay (Granulopectic index). The extract and Withania somnifera (L.) Dunal (Solanaceae) at 250 mg/kg body weight (Medicinal Plant Names Services, e) exhibited enhanced phagocytic activity of peritoneal macrophages to clear the carbon particles (Shilpashree et al., 2015). The ethanolic extract of tuber increased the phagocytic activity of macrophages in the mice model. The extract also inhibited both the cell mediated and humoral immunity, which supports its potent immunomodulatory activity (Patel et al., 2016).

Anticancer Activity
There is no significant toxicity of mangiferin isolated from tuber of P. tuberosa on normal cell lines (mouse fibroblast NIH-3T3, RAW 264.7, HEK293, and mouse lymphocytes) in cell viability assay in vitro; however, it is cytotoxic to various cancer cell lines like K562, MCF7, HEPG2, Jurkat cells, and A549 (Bulugonda et al., 2017). Furthermore, the anticancer and apoptotic potential of the hydroalcoholic tuber extract of P. tuberosa was investigated by cell viability assay. The extract showed a 50% inhibition of cell viability against human colon carcinoma (HT-29) cells at a concentration of 63.91 µg/ml. Cells also exhibited DNA fragmentation that is the hallmark of apoptosis, apoptotic cell death, and increased expression of certain proapoptotic genes (Aruna et al., 2018). The silver nanoparticles biosynthesized with aqueous extract of the P. tuberosa showed in vitro anticancer potential on different cancer cell lines (breast MCF-7 and MDA-MB-231; ovarian SKOV-3; brain U-87 cancer). However, the mechanism behind this activity needs exploration for therapeutic use (Satpathy et al., 2018). Antioxidant-enriched fraction also exhibited in vitro cytotoxicity in the breast (MCF-7 and MDA-MB-231) and ovarian (SKOV-3) cancer cells (Satpathy et al., 2020).

Other Pharmacological Properties
P. tuberosa has been attributed as one of the most sought plants that proved to be effective against multiple diseases and ailments. Alcoholic and aqueous extracts of P. tuberosa tuber were studied for nootropic effect in mice and rat models of amnesia induced by scopolamine and diazepam. The inflexion ratio observed was considerably high and comparable with piracetam, the standard drug in an elevated plus-maze experiment. Flavonoids present in the P. tuberosa tuber extracts have been reported for nootropic effect by interacting with cholinergic, adrenergic, serotonergic, and GABAergic system (Rao et al., 2008). The neuroprotective properties of this plant were also studied in chronic foot-shock stressed rat model showing unpredictable and inescapable nature of physiological malfunctions, increase in anxiety level, decrease in male sexual indices, and behavioral changes. All these symptoms were abolished by this plant's tuber extract (Pramanik et al., 2010). Neurotoxicity induced by sodium arsenate was ameliorated by hydroalcoholic extract which strengthens its memory and restores muscle strength and locomotor activity. Biochemical and histopathological changes are suggestive of the protective property of the extract in maintaining normal functional status of the brain in arsenate neurotoxicity (Umarni et al., 2016).

Alcoholic tuber extract of P. tuberosa was studied for anticonvulsant activity in pentalene tetrazole, strychnine, and maximal electroshock-induced convulsions in animals. Different doses of the extract (50, 100, and 200 mg/kg body weight) were compared with the standard drug, diazepam (5 mg/kg body weight). The medium and high doses exhibited potent anticonvulsant activity as compared to the control group (Basavaraj et al., 2011). The ethanolic and methanolic extract of leaf, stem, and tuber of P. tuberosa showed a wide range of antimicrobial activity against bacteria, Escherichia coli, Bacillus cereus, Salmonella paratyphi, and Staphylococcus aureus, as well as fungi, Candida albicans, Aspergillus fumigates, and Alternaria solani, on agar diffusion assay (Sadguna et al., 2015). The tuber extracts of P. tuberosa with different solvents exhibited a wide range of antimicrobial activity on selected bacterial and fungal pathogens (Aruna et al., 2016). The chloroform and water extracts of tuber of P. tuberosa showed significant antibacterial activity against Klebsiella pneumoniae and Staphylococcus aureus and methanol extract on Staphylococcus aureus and Streptococcus agalactiae (Pandya et al., 2019). The metabolites in P. tuberosa extracts may be behind the mechanism involved in the antimicrobial action, which may interact with the microbial cell membrane resulting in microbial cell death. The antiulcerogenic activity of aqueous leaf extract of P. tuberosa on cold restraint stress, pyloric ligation, and ethanol-induced gastric ulcer rat models was observed. There was significant inhibition in gastric lesions by 76.6% in cold restraint stress, 80.1% in pyloric ligation, and 70.6% in ethanol-induced rat models (Gindi et al., 2010).

In metabolic disorders also, P. tuberosa extracts exhibited a hypolipidemic effect. Oral administration of butanol tuber extract of P. tuberosa at a dose of 150 mg/kg body weight showed a pronounced protective effect against CCl4-induced hepatotoxicity in adult male rats (Shukla et al., 1996). Rats maintained on high cholesterol diet upon the treatment demonstrated a substantial reduction in serum cholesterol, triglycerides (TG), low-density lipoproteins (LDL), and very-low-density lipoproteins (VLDL) levels (Tanwar et al., 2008). These results were corroborated in another study where nonalcoholic fatty liver disease (NAFLD), induced in rats by feeding a high fat diet, was treated with water extract of this plant. Antioxidant activity with reduced lipid peroxidation and enhanced activities of SOD and catalase enzymes were observed. A similar finding was observed by Tripathi et al. in the NAFLD rats model which also showed a reduction in serum TG and cholesterol values (Tripathi and Aditi, 2020). The ethanolic extract of P. tuberosa showed a dose-dependent immunosuppressant activity as evident by a decrease in antibody titer and also a reduction in hematological
| Purified compound studied | Model used for study | Dose tested | Pharmacological activity | Conclusion | References |
|---------------------------|---------------------|-------------|--------------------------|------------|------------|
| **Puerarin** (C_{21}H_{20}O_{9}) | In vivo | 10 mg/kg b/w for 7 days | Nephroprotective | Suppression of oxidative stress production and 5-nitroxylation of proteins in the diabetic kidneys and MMP-9 | Zheng et al. (2014) |
| | In vivo | 20, 40, and 80 mg/kg b/w/day for 8 weeks | Antidiabetic | Hypoglycemic effect which supports its antidiabetic property and renal protective effects via the mechanism of attenuating SIRT1/FOXO1 pathway | Xu et al. (2016) |
| | In vivo | 2.5 mg/kg b/w/day for 2 weeks | Antioxidant | Suppressed mRNA expression and activity of Bcl-2, Bcl-xL, and p38 activity and active caspase-3 production | Tanaka et al. (2016) |
| | In vivo | 10 and 50 μM | Anticancer | Suppressed NO and MMP-9 | Liu et al. (2017) |
| **Daidzein** (C_{15}H_{10}O_{4}) | In vivo | 0.01, 0.1, 1, 10, and 100 μmol/L | Antidiabetic | Improved insulin sensitivity and reduced diabetic foot ulcers | Yu et al. (2017) |
| | In vitro | 0.78–200 μM; in vivo: 0.5–50 μM | Antioxidant | Suppressed macrophage activation by inhibiting IκB, ERK, and p38 activity and reactive oxygen species production | Liu et al. (2017) |
| | In vitro | 12.50–50 μM | Anticancer | Reduced the cell viability and colony formation in a concentration-dependent manner and inhibited tumor growth | Zheng et al. (2017) |
| | In vitro | 2.5–20 mg/kg b/w for 27 days | Anticancer | Induced G2/M cell cycle arrest and suppressed the ovarian tumor growth | Hua et al. (2018) |
| **Genistin** (C_{21}H_{20}O_{10}) | In vivo | 10 and 20 mg/kg b/w 3 times a week for 30 weeks | Anti-stress | Reduced hippocampal LTP and reduced oxidative stress through an estrogenic pathway and reduced oxidative stress | Palanisamy and Venkataraman (2013) |

(Continued on following page)
| Purified compound studied | Model used for study (in silico/in vitro/in vivo) | Dose tested | Pharmacological activity | Conclusion | References |
|---------------------------|--------------------------------------------------|-------------|-------------------------|------------|------------|
| Lupinoside PA4 [5]        | In vitro/in vivo                                  | 20 ng/ml; in vivo: 1.5 mg/200 g b.w. for 12 days | Antidiabetic | Stimulated IR-β and akt phosphorylation | Dey et al. (2007) |
| Tuberosin [6] (C20H18O5)  | In vitro                                         | 50, 100, 300, and 600 ng/ml | Antioxidant | Inhibited LPS-induced NO production in a concentration-dependent manner, expression of iNOS proteins | Pandey and Tripathi (2010) |
| 3-O-methylanhydrotuberosin [7] (C21H18O4) | In vitro                                         |                     | Pharmacological activity not reported |            |            |
| Puerarostan [8] (C21H18O6) | In vitro                                         |                     | Pharmacological activity not reported |            |            |

(Continued on following page)
TABLE 2 | (Continued) Pharmacological activities of phytoconstituents of Pueraria tuberosa.

| Purified compound studied | Model used for study | Dose tested | Pharmacological activity | Conclusion | References |
|--------------------------|----------------------|-------------|--------------------------|------------|------------|
| | | | | | |
| 25, 50, and 100 mg/kg b/w for 8 days | Anti-diabetic | Reduced insulin resistance and attenuated hyperglycemia in type II diabetes, which could be due to increased expression of SIRT1 in pancreatic tissues | Wang et al. (2015) |
| 30 µM for 24 h | Anti-inflammatory | Inhibited βT3-induced CCK-2 expression and PGS2 production via MAPKs pathway including ERK, p38, and JNK | Kim et al. (2016) |
| 150 and 300 µM | Cardioprotective | Pretreatment with formononetin reduced myocardial tissue injury, improved cardiac function, and decreased apoptosis in heart tissue | Huang et al. (2018) |
| 5 mM | Cardioprotective | Formononetin-treated cells were morphologically normal compared to the cells undergoing childhood induced death (cd) and were protected against apoptosis induced by formononetin treatment | Huang et al. (2018) |
| 20–100 µM for 24 h | Nephroprotective | Formonoetin-treated cells were morphologically normal compared to the cells undergoing childhood induced death (cd) and were protected against apoptosis induced by formononetin treatment | Lee et al. (2018) |
| 25, 50, and 100 mg/kg b/w for 8 days | Antibacterial | Inhibited HMGB1 release by increased HMGB1 acetylation via upregulating SIRT1 in a PARP-dependent manner | Wang et al. (2018) |
| 150 µM for 12, 24, and 48 h; in vivo 50 mg/kg b/w for 4 weeks | Anthocyanin | Inhibited MUP/MB489 cell survival in a dose- and time-dependent manner, and tumor volume shrinkage from 472.7 to 253.6 mm³ on day 30 in xenograft model | Zhou et al. (2019) |
| 15 mg/kg b/w | Anticancer | The tumor inhibition rate was 50.17% in the mice treated with formononetin by oral gavage. | Zhang et al. (2019) |
| 100 mg/kg b/w for 14 weeks | Hepatoprotective | Promoted the lysis of some bioluminescent and autophagy hypersensitive fusion, relieving the kidney damage in autophagic flux and further inducible autophagy | Wang et al. (2019) |
| 40–60 mg/kg b/w for 10 days | Hepatoprotective | Ameliorated hepatic cholestasis by upregulating expression of SIRT1 and activating PPARs | Yang et al. (2019) |
| 20 and 40 mg/kg b/w for 10 weeks | Neuroprotective | Reduced the levels of inflammatory cytokines IL-1β and TNF-α and tau hyperphosphorylation in mice hippocampus | Fu et al. (2019) |

(Continued on following page)
| Purified compound studied | Model used for study (in silico/in vitro/in vivo) | Dose tested | Pharmacological activity | Conclusion | References |
|---------------------------|-----------------------------------------------|-------------|-------------------------|------------|------------|
| In vitro | 31.25 μg/ml | Anti-inflammatory | LPS-induced inflammation in zebrafish was attenuated by formononetin mainly by restraining the MyD88 or TRIF MAPK/ERK and MAPK/JNK pathways | Luo et al. (2019) |
| In vivo | 25 mg/kg b/w for 10 days | Anti-stress | Reduced the neural excitability and the protective upregulation of GABA receptors | Wang et al. (2019) |
| In vivo | 10, 20, and 40 mg/kg b/w for 16 weeks | Nephroprotective | Enhanced creatinine clearance and reduced oxidative stress burden along with increased SIRT1 expression in kidney tissues | Oza and Kulkarni (2019) |
| In vivo | 10 mg/kg b/w | Anticancer | Inhibited EGFR-Akt axis and promoted FBW7-mediated Mcl-1 ubiquitination | Yu et al. (2020) |
| In vitro | 5–100 μM | Antioxidant | Stimulated catalase and total superoxide dismutase (CuZn- and Mn-SOD) activity, and mRNA and protein expression | Choi and Kim (2014) |
| In vitro/in vivo | 1, 5, and 10 μM for 12 h; in vivo: 50, 100, and 200 mg/kg b/w for 30 days | Anti-ischemia | In vitro, increased cell viability and attenuated apoptosis; in vivo, inhibited mitochondrial membrane potential (MMP) and increased total ATPase activity | Yin et al. (2016) |
| In vitro/in vivo | 5 or 10 μM for 90 min; in vivo: 20–50 mg/kg for 4 days | Anti-gastric | Pretreatment with irisolidone increased the area of hemorrhagic ulcerative lesions caused by ethanol and suppressed stomach myeloperoxidase activity, CXCL4 secretion, and NF-κB activation | Kang et al. (2017) |
| In vivo | 20 mg/kg b/w | Anticolitic | Alleviated colon shortening and myeloperoxidase activity in mice with TNBS-induced colitis | Jang et al. (2019) |
| In vivo | 20 μg/kg b/w | Anticoagulant | Glycosylation of 4′-methoxypuerarin, caused steric hindrance to weaken the DNA binding affinity and had no significant inhibition on DNA amplification | Chen et al. (2020) |
| Puerarone | In silico | Antidiabetic | Strong affinity to VEGFR-1 and VEGFR-2 along with 93.881% human intestinal absorption | Srivastava et al. (2017) |
| Purified compound studied | Model used for study | Dose tested | Pharmacological activity | Conclusion | References |
|---------------------------|----------------------|-------------|--------------------------|------------|-------------|
| Quercetin (C15H10O7)      | In vivo              | 15 mg/kg b/w for 7 days | Hepatoprotective | Accelerated the regeneration after partial hepatectomy | Kantor et al. (2016) |
|                           | In vitro/in vivo     | 5–100 µM intraperitoneal for 30 days | Neuroprotective | Protected neuronal cells from amyloid beta induced oxidative stress | Li et al. (2017) |
|                           | In vivo              | 100 mg/kg b/w for 6 days | Intestinal damage repair | Increased intestinal and mucosal weight and prevented methotrexate-induced intestinal damage | Sukhotnik et al. (2018) |
| Tectoridin (C22H22O11)    | In vivo              | 25–400 mg/kg b/w | Anti-alcoholism | Strongest clearance rate of ethanol | Zhang et al. (2019) |
|                           | In vivo              | 100 mg/kg b/w for 7 days | Immunomodulatory | Decreased the expression of inflammatory mediator TNF-α and circulating immune complexes | Phagawat et al. (2013) |
|                           | In vivo              | 8 mg/kg b/w for 7 days | Cardioprotective | Prevented cardiac hypertrophy by virtue of its antihypertrophic, antilipidemic, and anti-radical scavenging | Roy and Prince (2013) |
|                           | In vivo              | 100 mg/kg b/w for 3 weeks | Neuroprotective | Cardiac mitochondrial chelating activity | Narasaiah and Rassol (2014) |
|                           | In vivo              | 100 mg/kg b/w | Anti-diabetic | Modulated glucose and lipid metabolism via GLUT2 activation in the pancreas | Amalan et al. (2016) |
|                           | In vivo              | 30 mg/kg b/w | Neuroprotective | Increased the total activity of fEPSP dose-dependently after high frequency stimulation and attenuated scopolamine-induced block of fEPSP in the hippocampal CA1 long-term potentiation area | Kim et al. (2017) |
|                           | In vivo              | 100 mg/kg b/w for 26 days | Anti-arthritic | Suppressed the paw edema, body weight loss and inflammatory cytokines and chemokines levels (TNF-α, IL-6, IL-1β and MCP-1) in serum and ankle joint of arthritic rats | Nego et al. (2017) |
|                           | In vivo              | 50 mg/kg b/w | Hepatoprotective | Suppressed hepatic apoptosis via ROS-mediated DNA damage and inflammation by modulating the mitogen-activated protein kinase (MAPK) signaling axis in an ROS-dependent manner | Ghant et al. (2018) |
|                           | In vivo              | 100 mg/kg b/w for 2 weeks | Neuroprotective | Protected with p-coumaric acid significantly reduced malondialdehyde (MDA) levels, whole-brain infarct volume and hippocampal neuronal death together and increased vascularity and supersede dilatation activities | Sakamura and Thong-asa (2019) |
|                           | In vitro/in vivo     | 2–4,000 µM, for 24 and 72 hr | Antioxidant | Downregulated Gpr78 and activated UPR mediated apoptosis both in vitro and in vivo models of colon cancer | Sharma et al. (2019) |
|                           | In vivo              | 60 and 100 µg/mL | Antioxidant | Significantly increased the survival rate of Caenorhabditis elegans under the oxidative stress condition and increased lifespan by 20% for both 60 and 100 µg/mL, compared to the control | Yui et al. (2019) |
|                           | In vivo              | 50 mg/kg b/w for 6 weeks | Anti-diabetic | Enhanced anti-inflammatory, anti-extremophagic, and antioxidant defense systems in streptozotocin-treated mice | Shabani et al. (2019) |
|                           | In vivo              | 10–100 µM, for 90, 100, and 200 mg/kg b/w | Hepatoprotective | No effect on cell viability up to 60–80 µM concentrations on HepG2 cells in vitro, p-coumaric acid at 200 mg/kg exhibited higher protection on ethanol-induced hepatic injury in rats | Sabitha et al. (2020) |

(Continued on following page)
| Purified compound studied | Model used for study | Dose tested | Pharmacological activity | Conclusion | References |
|---------------------------|---------------------|-------------|--------------------------|------------|------------|
| Hydrotuberosone [19] (C20H18O6) | In vivo | Topical application | Wound healing | Excision and incision wound model | Kambhoja and Murthy (2007) |
| Puetuberosanol [20] (C21H18O4) | In vivo | 50 mg/kg b/w for 10 days | Cardioprotective | Modulation of TGF-β1 signaling pathway in doxorubicin-induced cardiac toxicity in Sprague Dawley rats | Janeesh and Abraham (2014) |
| | In vitro | 6 μg/ml | Immunomodulatory | Inhibited TLR4-NF-κB signaling pathway | Janeesh et al. (2014) |
| | In vitro | 0.125–0.50 mg/ml | Antioxidant | The total antioxidant capacity (TAC) in robinin was significantly higher and best maintained the follicular morphology | Dos Santos Morais et al. (2019) |
| Tuberostan [22] (C21H16O5) | In silico | — | Anti-diabetic | In molecular docking study, tuberostan showed best interaction for GLP-1R with binding energy at 8.15 kcal/mol and dissociation constant at 1061624.125 pM | Srivastava et al. (2018) |

Pharmacological activity not reported.
TABLE 2 | (Continued) Pharmacological activities of phytoconstituents of Pueraria tuberosa.

| Purified compound studied | Model used for study (in silico/in vitro/in vivo) | Dose tested | Pharmacological activity | Conclusion | References |
|---------------------------|-----------------------------------------------|-------------|------------------------|------------|-----------|
| Isoorientin (C_{21}H_{20}O_{11}) | In vitro | 0.1–100 µM | Anti-inflammatory | Inhibited COX-2 activity by 64% | Sumalatha et al. (2015) |
| IUPAC name: 2-(2,3-dihydroxyphenyl)-5,7-dihydroxy-6-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]chromen-4-one | | | | | |
| | In vitro/in vivo | 10 μM | Anti-inflammatory | Inhibited the expression of COX-2 in vitro and decreased the expression of COX-2, TNF-α, iNOS, and 5-LOX in dose-dependent manner in carrageenan-induced inflammation in mice | Anilkumar et al. (2017) |
| Mangiferin (C_{19}H_{18}O_{11}) | In vitro | 100 µM | Anti-inflammatory | Inhibited COX-1 and COX-2 activity by 79.4% and 45.9%, respectively | Sumalatha et al. (2015) |
| IUPAC name: 1,3,6,7-tetrahydroxy-2-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]xanthen-9-one | | | | | Bulugonda et al. (2017) |
| Stigmasterol (C_{29}H_{48}O) | In vivo | 200 mg/kg and 400 mg/kg b/w | Chemo-preventive | Induced a significant decrease in 7,12-dimethylbenz(a)anthracene (DMBA)-induced skin tumor | Ali et al. (2015) |
| IUPAC name: [(3S,8S,9S,10R,13R,14S,17R)-17-[(E,2R,5S)-5-ethyl-6-methylhept-3-en-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol] | | | | | |

In vivo: body weight.
parameters in the drug-induced myelosuppression model (Babu et al., 2016). Crude powder (3 g daily) of *P. tuberosa* tuber was given to a human patient with ischemic heart disease for twelve months. The case study demonstrated an overall significant cardioprotective effect; resting mean blood pressure was reduced from 96.66 to 90.00 mm Hg without affecting the resting heart rate, and the heart rate at peak exercise was also reduced, indicating better exercise tolerance (Verma et al., 2009).

*P. tuberosa* root extract, given to male Wistar rats (100 mg/rat per day) for 60 days, affected the fertility of rats as shown by a reduction in weight of testes, epididymis, prostate, and the seminal vesicle. Studies also showed a considerable decrease in the quantity of mature Leydig cells, cauda epididymis, and sperm motility (Gupta et al., 2005). The antioxidant-enriched fraction from the tuber extract of *P. tuberosa* against menopausal osteoporosis in ovariectomy-induced osteoporosis in rats was studied and found that it improved biochemical parameters, controlled the increased body weight, and decreased uterus weight following ovariectomy as well as restoration of typical bone structure and trabecular width of the femur (Satpathy et al., 2020). Incision and excision wounds were treated with methanolic and ethyl acetate tuber extract of *P. tuberosa*. The extracts showed potent wound healing property in comparison to ibuprofen, and nitrofurazone ointment (Kambhoja and Murthy, 2007).

### Phytocchemistry

The crude tuber extracts of *P. tuberosa* are known to contain alkaloids, anthracene, anthocyanidins, anthraquinone, glycosides, carbohydrates, catecholic compounds, coumarins, flavonoids, glycosides, hexose sugars, saponins, steroids, terpenoids, and volatile oils (Ratnam and Venkata Raju, 2009; Rawtal et al., 2019). Therefore, many studies have been undertaken to individually analyze and characterize the activities of different phytoconstituents of the plant. Vaishnav et al. could grow a callus culture of *P. tuberosa* and identified four isoflavonoids, viz., puerarin [1], daidzein [2], genistin [3], and genistein[4] (Vaishnav et al., 2006; Satpathy et al., 2017). Lupinopside PA4 [5] was isolated from methanolic extract of *P. tuberosa* using HPLC, and its structure was determined by 1D, 2D NMR, and Q-TOF-MS (Dey et al., 2007). Pandey and Tripathi extracted tuberosin [6], 3-O-methylhydrotuberosin [7], and puerarostan [8] from ethanolic tuber extract; the same was confirmed by UV, IR, and NMR spectral data (Pandey and Tripathi, 2010). β-Sitosterol [9] was quantified in the methanolic root extract of *P. tuberosa* by high-performance thin layer chromatography (HPTLC) method (Mhaske et al., 2009). Liquid chromatography–mass spectrometry (LC–MS) analysis of ethanolic extract was found to contain puerarin, daidzein, biochanin A [10], and biochanin B [11] (formononetin) (Chauhan et al., 2013). Daidzin [12], irisinolide [13], 4-methoxypuerarin [14], puerarone [15], quercetin [16], and tectoridin [17] are the flavonoid compounds and p-coumaric acid [18], which have been reported to be isolated from tuber of *P. tuberosa* (Majju et al., 2014) and aqueous tuber decoction shown to contain daidzein, genistin, hydroxytuberosone [19], puerarin, puertuberosanol [20], robinin [21], tuberosin, and tuberostan [22] (Shukla et al., 2017). Mass spectrometry and 2D-NMR techniques were used to isolate isoorientin [23] and mangiferin [24] from methanolic extract from *P. tuberosa* (Sumalatha et al., 2015). Phytochemical analysis of *P. tuberosa* extract using HPTLC revealed the presence of carbohydrates, proteins, alkaloids, flavonoids, saponins, phenols, and tannins (Viji and Paulsamy, 2018). Satpathy et al. showed the presence of 23 bioactive molecules including stigmasterol [25], β-sitosterol, and stigmasta-3,5-dien-7-one by gas chromatography–mass spectrometry analysis of antioxidant-enriched fraction prepared from *P. tuberosa* (Satpathy et al., 2020). We have listed various phytoconstituents isolated from *P. tuberosa* and provided detailed information about their chemical structures, IUPAC names, and pharmacological activities, as well as associated references, in Table 2. The chemical structures of phytochemical compounds from *P. tuberosa* were drawn using “ChemDraw JS 19.0”; https://chemdrawdirect.perkinelmer. cloud/js. IUPAC (International Union of Pure and Applied Chemistry) names have been taken from PubChem database.

### Toxicology of Pueraria tuberosa

The acute (single dose of 2,000 and 5,000 mg/kg body weight) and repeated dose (250, 500, 1,000, and 2,000 mg/kg body weight for 28 days) toxicity studies with water extract of the tuber of *P. tuberosa* were conducted in rats as per OECD (Organization for Economic Co-Operation and Development) guidelines. The survival rate and biochemical and histological changes were studied. No adverse effect was reported in single-dose acute toxicity, but in repeated dose toxicity studies, 100% mortality was observed on day 21 at 2,000 mg/kg body weight, and histological examination of the visceral organs showed that this mortality could be due to hepatotoxicity (Pandey et al., 2018). However, histological evaluation of different organs using hematoxylin and eosin staining did not observe any morphological alterations in the spleen, adrenal glands, and heart. The size and shapes in crypts and villi of the intestine and seminiferous tubules were intact with normal spermatozoa count in testis (Pandey et al., 2019). In another experiment on acute toxicity study of poly-herbal formulation (containing *P. tubrosa*), “Dhatryadi Ghrita” methanolic extract did not show any untoward effects in mice (Pal and Mishra, 2019).

### CONCLUSION AND FUTURE DIRECTIONS

The scientific community worldwide has shown an interest in discovering the disease combating potential of natural flora and bioactive compounds therein. A wide pool of literature suggests that these phytochemicals hold the immense potential of eliminating diseases, and many such plant-based drugs have long been used in many parts of the world. Markedly, the tuber and leaf of *P. tuberosa* plant have been used from ancient times in the traditional practices. Previous literature has shown that leaf and tuber extracts of the plant contain several bioactive
constituents that possess an extensive range of pharmacological activities. Some of the isolated compounds, namely, puerarin, irsosidione, genistein, daidzein, biochanin A, biochanin B, isoerocitrin, and mangiferin, have been studied for various medicinal purposes and demonstrated several pharmacological activities like anticancerous, antidiabetic, anti-inflammatory, antioxidant, antiviral, cardioprotective, fibrinolytic, hepatoprotective, hypolipidemic, immunomodulatory, neuroprotective, nephroprotective, nootropic, vasodilatory, and wound healing. The bioactive constituents of *P. tuberosa* can individually or synergistically exert their therapeutic effects. Apart from puerarin, daidzein, genistein, irsosidione, and biochanin, many more compounds have been identified from *P. tuberosa*; however, underlying mechanisms of action of compounds isolated from this plant are not completely known. Thus, exploration of pharmacological mechanisms of individual bioactive constituents and their toxicity/clinical studies shall be the focus of future investigations. The extensive range of pharmacological properties of *P. tuberosa* could provide us a new interesting path for future research and may present new perspectives for the disease management.

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**AUTHOR CONTRIBUTIONS**

RB was responsible for the methodology, writing the original draft, and data curation. BC and SR were responsible for data curation and reviewing and editing the manuscript. NK was responsible for conceptualization, data curation, writing, reviewing, and editing the manuscript.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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