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Unravelling the Phytochemical and Pharmacognosy Contour of Traditional Medicinal Plant: Pterocarpus Marsupium Roxb

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Abstract

Pterocarpus marsupium Roxb is a traditional medicinal plant commonly acknowledged as “Vengai” and has a long history of usage in tropical and subtropical regions for a variety of purposes in treating several human diseases. Over the years, a lot of commercial and medicinal researchers have focused on resources from various herbs. Extraction and fractionation of this plant have highlighted the presence of alkaloids, proteins, carbohydrates, coumarins, gums, mucilage, fixed oils, anthraquinone glycosides, saponin glycosides, tannins, flavonoids, and phenolic compounds. Several investigational studies have demonstrated that this plant has various pharmacological activities such as analgesic, anti-diabetic, anti-inflammatory, anti-cancer, hepatoprotective, anti-microbial, anti-bacterial, anti-diarrhoeal, memory-enhancing activity, antioxidant, and anti-hyperlipidaemic. It is used alone or with other medicinal plants to provide enhanced therapeutic efficacy for treating various ailments. Our present review is an attempt to unite its phytoconstituents and its pharmacological activities such as antidiabetic, antioxidant, antibacterial, antimicrobial, anticancer, anti-inflammatory, memory-enhancing activity, hepatoprotective, and antihyperlipidaemic activity. In the near future, further investigational studies are needed to isolate and characterize the bioactive compounds present as lead molecules in drug discovery research.

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1. Introduction

Herbal plants are the major resource for traditional medicine as well as for the herbal industry. From ancient times, plants have been used for treating many diseases [1]. Recently, the World Health Organization highlighted that 80% of the worldwide population still depends on herbal medicines for their primary health care needs [2]. India is one of the richest countries in herbal medicine compared to the rest of the world, and it has 15 agro-climatic zones for herbal plants [3]. Ayurveda, Siddha, Unani, and Homoeopathy are the various systems of medicine used in India for several years [4]. The Indian government is promoting the medicinal plants sector through the Ministry of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha & Homoeopathy) [5].

The genus *Pterocarpus* is a large deciduous tree species of the angiosperms group (flower) from the*Leguminosae* family. In this family, about 765 genera and approximately more than 20,000 species are widely distributed throughout the world. The genus *Pterocarpus* includes 227 species, of these, 46 species are accepted, and 30 species are included at the intraspecific rank. *Pterocarpus marsupium* Roxb (*P. marsupium* Roxb) is a popularly well-known species among the *Pterocarpus* genus. Other vernacular names of this plant in India are kino tree or Malabar kino, Vijayasara, Bijasara, Venga, Bibala, Piashala, Chandan Lal, Vengai, and Yegi [6][7]. *P. marsupium* Roxb is native to India, Nepal, and Sri Lanka, and is grown in the deciduous and evergreen forests of central, western, peninsular India, the sub-Himalayan region, and southern regions of India, Bangladesh, Sri Lanka, and Taiwan [8]. In India, *P. marsupium* Roxb is traditionally used in folk medicine, Ayurveda, Siddha, Unani, and Homoeopathy [9].

Earlier phytochemical investigation reports revealed that *P. marsupium* Roxb contains alkaloids, proteins, carbohydrates, coumarins, gums, mucilage, fixed oils, anthraquinone glycosides, saponin glycosides, tannins, flavonoids, and phenolic compounds [10]. It is a rich source of terpenoids, which includes aurone, isoflavonoid glycosides, and associated phenolic compounds such as lupenol, epicatechin, and β-sitosterol [11]. The leaves possess anthelmintic and antioxidant activities. The stem possesses antioxidant, antidiabetic, anti-inflammatory, and antibacterial activities. The bark possesses anti-inflammatory, analgesic, anticancer, antimicrobial, hepatoprotective, and antidiabetic activities. The heartwood possesses antidiarrhoeal and antidiabetic activity.

2. Botanical Description

P. marsupium Roxb is a large deciduous tree that can grow up to 30 m in height. Its bark is scaly, rough, and longitudinally fissured, with a width range of 10-15 mm, and appears grey or greyish-black, while the blaze is pink with whitish markings [4]. The leaves are abundant, alternate without stipules, and unequally pinnate with round petioles[12]. Leaflets are generally 5-7 in number, 8-13 cm long, oblong, elliptic, or rotund, with 15-20 pairs of lateral veins [13].

The heartwood is golden yellowish-brown in colour, with darker streaks, and occurs as uneven pieces of erratic sizes and thickness [14]. On drenching in water, it gives a yellow colour solution with blue fluorescence. It has a strong, hard, and tough fracture with an astringent taste and no odour [13].

Flowers are fragrant, bisexual, and yellow in colour, and possess about 1-5 cm long large panicles[13]. Pods are flat, orbicular, and winged, up to 5 cm in diameter, while seeds are 1-3 in number, bony, and convex in shape. Flowering begins in the month of November, and fruiting continues up to March [15]. Normally, the legumes of the plant contain two seeds [16].

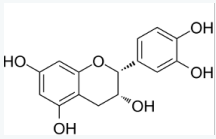
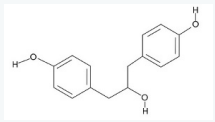
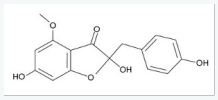
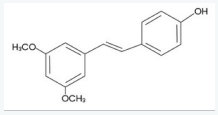
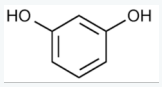
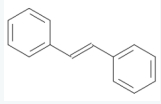
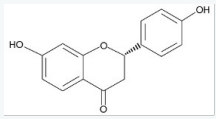
3. Taxonomic classification

Category	Classification
Family	Fabaceae
Domain	Eukaryota
Kingdom	Plantae
Subkingdom	Euphyllophytina
Infraphylum	Radiatopsis
Class	Magnoliopsida
Subclass	Rosidae
Superorder	Fabanae
Order	Fabales
Genus	Pterocarpus
Species	marsupium
Botanical Name	*Pterocarpus marsupium* Roxb [1][4][9][10][14][17].

4. Phytoconstituents

P. marsupium Roxb contains a rich source of flavonoids and polyphenolic compounds. Over years of analysis, researchers have emphasized that the following bioactive phytochemicals, such as about 45% of pterostilbene, 5% of tannins, 0.4% of alkaloids, and proteins, are present [18][19][20][21][22]. Apart from these, there are some primary phytoconstituents such as epicatechin, propterol, marsupin, pterostilbene, resorcinol, trans-stilbene, liquiritigenin, isoliquiritigenin, isoliquiritin, aglycone, pterosupin, catechin, kinotannic acid, kinoin, kino red, β-eudesmol, carsupin, marsupial, marsupinol, pentosan, p-hydroxybenzaldehyde that were obtained from the heartwood and root [22][13]. Some of the phytoconstituents' structures of *P. marsupium* Roxb are given in Table**1**, and phytoconstituents associated with different parts of the plant are depicted in Table **2**.

Table 1. Chemical structure of Phytoconstituents

Name of Phytoconstituents	*Structure of Phytoconstituents*	*Reference*
Epicatechin		[10][12][14][15]
Propterol		[10][12][15]
Marsupin		[1][10][15]
Pterostilbene		[15]
Resorcinol		[10][12]
Trans-stilbene		[10][12]
Liquiritigenin		[12][14][15]

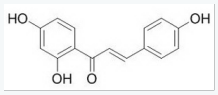
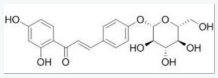
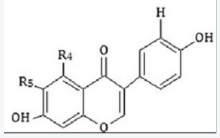
Isoliquiritigrnin		[4][10][12][14][15]
Isoliquiritin		[4][10][14][15]
Aglycone		[19]

Table 2. Phytoconstituents from different parts of P.marsupium Roxb

Parts of plant	***Phytoconstituents***	***Reference***
Flowers	aurone glycosides, 4, 6, 4'-trihydroxyaurone 6-O-rhamnopyranoside and 4,6,4'- trihydroxy-7-methylaurone 4-O-rhamnopyranoside	[10][20]
Roots	flavonoid glycosides 7-Hydroxy-6, 8-dimethyl flavanone-7-O-alpha- L-arabinopyranoside and 7, 8, 4'trihydroxy-3', 5'-dimethoxy flavanone-4'-O-beta-Dglucopyranoside	[10][12]
Heartwood	pterostilbene, isoliquiritigenin, liquiritigenin, carpucin, propterol, propterol-B, oleanolic acid, alkaloid and resin 5, 4'-dimethoxy-8-methylisoflavone, essential oil	[6][21]
Bark	Nonglucosidal tannins, Kinotannic acid, Kinonin, Kinored, Pyrocatechin, Pyrocatechin acid, resin, pectin and gallic acid	[4][10]
Leaves	alkaloids, fixed oils, tannins, proteins, carbohydrates, cardiac glycosides, flavonoids, Isoflavonoids, terpenoids and saponin glycosides.	[10][20]
Stem	alkaloids, glycosides, saponins and tannins, proteins, carbohydrates, cardiac glycosides, flavonoids, and terpenoids	[10][20]

From the heartwood of *P. marsupium* Roxb., three new isoflavone glycosides, viz. retusin 7-glucoside, irisolidone 7-rhamnoside and 5, 7-dihydroxy-6-methoxyisoflavone 7-rhamnoside, were isolated and reported in several studies [16].

5. Pharmacological activities

P. marsupium Roxb. has become an essential source around the world due to its potential therapeutic properties. It is extensively used in various ethnic systems of medicine for the cure of a number of ailments such as leukoderma, elephantiasis, diarrhoea, cough, discoloration of hair, and rectalgia [23]. It is generally non-hazardous and useful in treating jaundice, fever, wounds, diabetes, stomachache, and ulcers [24]. Moreover, *P. marsupium* Roxb. heartwood, leaves, flowers, and gum have been used as one of the major ingredients in various Ayurvedic, homeopathic, and Siddha

formulations due to their ethnic therapeutic activity against diarrhoea, dysentery, fractures, leprosy, leukoderma, skin diseases, sores, boils, constipation, depurative, rectalgia, ophthalmology, haemorrhages, rheumatoid arthritis, lowering the blood glucose levels, as a diuretic, GIT disorders and also aids in the treatment of various neurological problems [16].

5.1. Antidiabetic activity

P. marsupium Roxb has been used as a potential anti-diabetic agent ever since prehistoric times. It aids in lowering blood glucose levels, protecting the beta cells, and also possesses regenerative properties. Various investigational studies have been performed on numerous animal classes (rats, dogs, and rabbits) to study the hypoglycaemic effect, and the results have demonstrated that *P. marsupium* Roxb repaired the usual insulin secretion by reversing the impairment to the beta cells by repopulating the islets of Langerhans [21][25][26][27][28][29]. Mohankumar *et al.* investigated the aqueous extract of the heartwood of *P. marsupium* Roxb for its anti-diabetic activity by the bioassay method by exposing pancreatic and muscle tissues of mice. The aqueous extract simultaneously increased the insulin secretion and glucose uptake in a concentration-dependent manner and concluded that this plant has potent antidiabetic properties both *in vitro* as well as *in vivo* [30]. Halagappa *et al.* examined the aqueous extract of *P. marsupium* Roxb for anti-diabetic activity at 100 and 200 mg/kg. The study results suggested that at a 200 mg/kg dose, it has an effect on postprandial hyperglycaemia in type 2 diabetic rats and also improved the body weight of the diabetic animals. In addition, it significantly decreased the TNF-α level in type 2 diabetic rats [31]. Jelastin *et al.* examined the ethanolic extract of *P. marsupium* Roxb wood and bark for antidiabetic activity in alloxan-induced diabetic rats. The study has shown that the ethanol extract of *P. marsupium* Roxb reduced the blood glucose level and increased plasma insulin level in diabetic rats, highlighting that it can be used for the management of diabetes [32].

Mishra *et al.* investigated the ethanolic extract of the heartwood of *P. marsupium* Roxb for its anti-diabetic activity on streptozotocin-induced rats. The crude powder, ethanolic extract, hexane, and n-butanol fractions showed improvement in oral glucose tolerance and increased the serum insulin level in a dose-dependent manner against its anti-diabetic activity [33]. Pant and his team performed a comparative anti-diabetic activity study on the ethanolic extract of *P. marsupium* Roxb stem at 200 and 400 mg/kg in mice by oral glucose tolerance test against glimepiride at 0.43 mg/kg. The acute toxicity study results demonstrated that the ethanolic extract of *P. marsupium* Roxb stem is non-toxic in the dose range of 250-1000 mg/kg. The study results demonstrated that the blood glucose-lowering effect was found to be 57.56%, 51.30%, and 55.13% for the standard, at 200 mg/kg, and 400 mg/kg respectively at 180 min. It was also concluded that the anti-diabetic activity is time and dose-dependent [34]. Gayathri *et al.* determined the anti-diabetic activity of the aqueous bark extract of *P. marsupium Roxb* at 500 mg/kg in streptozotocin-induced diabetic rats and measured various parameters like plasma insulin, cholesterol, glycosylated haemoglobin, triglycerides, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), α-glutamyl transferase (α-GT), and creatine kinase (CK). The study results demonstrated that the extract normalized cholesterol, triglycerides, plasma insulin, and glycosylated haemoglobin levels and also decreased the AST, ALT, ALP, α-GT, and CK from their elevated levels in the diabetic rats. They concluded that the aqueous bark extract of *P. marsupium Roxb* showed a remarkable anti-diabetic effect on metabolic alterations [35]. Mohankumar *et al.* isolated the insulinotropic activity-enriched fraction (AEF) from the aqueous

extract of *P. marsupium* Roxb and investigated its anti-diabetic activity by the bioassay method. The study results showed that AEF modulated the biosynthesis of insulin by mimicking sulphonylurea and also prolonged the responsiveness effects on glucose and combated the hyperglycaemia adverse effects by increasing and sustaining glucose-dependent insulin secretion [36]. Singh *et al.* examined the anti-diabetic effect of methanol extracts of*P. marsupium Roxb* and *Ocimum sanctum* Linn as a mixture of both at a dosage of 500 mg/kg body weight to both non-diabetic and alloxan-induced diabetic adult female Wistar rats. Parameters such as tissue lipids along with corticosterone, oestrogen, and progesterone profiles were assessed during the study. The study results demonstrated that the extract mixture ameliorated the diabetic-associated manifestations by restoring the endogenous antioxidant levels [37]. Radhika *et al.* made a comparative evaluation of the methanol extract of *P. marsupium* Roxb for its anti-diabetic activity at the dose of 200 mg/kg and 400 mg/kg in streptozotocin-induced diabetic rats with glibenclamide at 2.5 mg/kg as a reference standard. Serum biochemical parameters such as triglycerides, LDL, VLDL, and HDL were also assessed. The extract showed significant diabetic activity by improving the peripheral utilization of glucose and exerting an extra-pancreatic effect. In addition, the extract significantly decreased triglycerides ($p<0.01$), LDL ($p<0.01$), VLDL ($p<0.001$), and increased HDL ($p<0.05$) and concluded that the extract has potent anti-diabetic activity [38]. Dhanabal *et al.* prepared an alcohol extract from the bark of *P. marsupium* Roxb, subsequently fractionated with different solvents like chloroform, butanol, toluene, and ethyl acetate, and investigated its anti-diabetic activity along with its related metabolic alterations in alloxan-induced diabetic rats. The study results demonstrated that among the different fractions, the butanol fraction showed more activity than the other fractions and also controlled the diabetic metabolic parameters such as total protein, triglyceride, cholesterol, SGOT, SGPT, and alkaline phosphatase [39].

5.2. Antioxidant activity

This plant extract showed not only hypoglycaemic activity but also exhibited a promising antioxidant effect. The in vitro antioxidant activity of the ethyl acetate leaf extract of *P. marsupium* was studied by hydroxyl radical scavenging activity, ABTS assay, FRAP assay, NO radical scavenging activity, TRAP assay, reducing power assay, and hydrogen peroxide (H_2O_2) radical scavenging activity. The study results demonstrated that the leaf extract has very good antioxidant activity [40]. Pant *et al.* investigated the acetone: isopropyl alcohol (1:1) and ethanol extract of stem wood of*P. marsupium* Roxb for its antioxidant activity at 5, 20, 40, 60, 80, and 100 µg/ml by the 2,2-diphenyl-1-picrylhydrazyl scavenging method. The study results demonstrated that these extracts showed antioxidant activity in a dose-dependent manner. Among these two extracts, acetone: isopropyl alcohol (1:1) showed a lesser IC50 value (36.5 µg/mL), whereas the ethanol extract showed an IC50 value of 61.94 µg/mL. In addition, they highlighted that phytoconstituents such as flavonoids, alkaloids, glycosides, phenols, steroids, coumarins, tannins, and terpenoids are responsible for its antioxidant activity [34]. Tippani *et al.* examined the antioxidant activity of the methanolic extract of*P. marsupium* Roxb bark by the DPPH method at 0, 10, 20, 40, 80, 100, and 200 µg/mL and compared it with ascorbic acid as a standard. The result revealed that the extract has dose-dependent antioxidant activity with IC50 values of 53 µg/mL and 34.0 µg/mL for the extract and ascorbic acid, respectively. They concluded that the extract has closely comparable antioxidant activity [41]. Bhatta and Nayak investigated the various fractions of the heartwood of *P. marsupium* on antioxidant enzymes like protein

thiols at 75 mg/kg for 30 days. The study results concluded that after 30 days of treatment, the extract significantly reduced the protein thiol level by neutralising the free radicals through increased utilisation [42].

Singh *et al.* examined the enzymatic and non-enzymatic antioxidant effects of methanol extracts of*P. marsupium Roxb* and *Ocimum sanctum* Linn as a mixture of both at a dosage of 500 mg/kg body weight to both non-diabetic and alloxan-induced diabetic adult female Wistar rats through its lipid peroxidation level. The study results demonstrated that the extracts showed antioxidant activity by re-establishing the endogenous antioxidant levels to the pre-diabetic conditions [37].

5.3. Antibacterial and Antimicrobial activity

Kachhawa and coworkers investigated the antibacterial activity of*P. marsupium* (stem) methanolic extract at the concentrations of 200, 100, 50, and 25 mg/mL against Gram-positive (*Bacillus coagulans*) and Gram-negative (*E. coli*) bacteria and compared it with ciprofloxacin as a standard (0.001 mg/mL) by the disc diffusion method. The study results demonstrated that the extract showed antibacterial activity against both types of bacteria, and the results were comparable with the standard [43]. Singh *et al.* investigated the acetone: isopropyl alcohol (1:1) and ethanol extracts of*P. marsupium* Roxb stem (50 mg/mL) for their antibacterial activity against Gram-positive (*Staphylococcus aureus, Bacillus cereus*) and Gram-negative bacteria (*Escherichia coli, Salmonella typhi*) and compared them against ofloxacin 50 µg/mL. Their study results demonstrated that the acetone: isopropyl alcohol (1:1) extract showed a zone of inhibition (8 mm) against Gram-positive bacteria, but no activity was observed against Gram-negative bacteria. In addition, the ethanol extract did not show any antibacterial activity against both Gram-positive and Gram-negative bacteria [37].

A comparative antimicrobial activity study between ethanol and aqueous extracts of fresh barks of*P. marsupium* Roxb by the cup plate agar diffusion method against Gram-positive (Staphylococcus aureus, Bacillus sterothermophilus) and Gram-negative (Escherichia coli, Klebsiella pneumoniae) bacteria at 400 and 800 µg/mL of extract was compared with ciprofloxacin at 20 µg/mL as a standard. The study results concluded that both extracts showed concentration-dependent antibacterial activity, whereas the alcohol extract was more potent than the water extract. In addition, they highlighted that the presence of tannins and flavonoids may contribute to its antimicrobial activity [44].

Kalaivani *et al.* examined the antimicrobial activity of the ethanol leaf extract of*P. marsupium* Roxb against *E. coli, S. aureus, A. niger*, and *C. albicans* and compared it with ciprofloxacin at 5 µg/disc for bacteria and fluconazole at 100 units/disc for fungi by the disc diffusion method. The study results outlined that the extract has both antibacterial and antifungal activity and highlighted that *E. coli* had the highest [22 mm] and *C. albicans* had the lowest [12 mm] zones of inhibition [45].

Londonkar and Hugar conducted the extraction from *P. marsupium* Roxb bark with different solvents such as distilled water, methanol, chloroform, and petroleum ether. The extracts were investigated for their antimicrobial activity against gram-positive (*S. aureus* and *E. faecalis*), gram-negative (*S. typhimurium*, *E. coli*, *E. aerogenes*, and *S. dysenteriae*) and a fungus (*A. niger*) at the concentration of 100 mg/mL and compared with standard Cefixime (30µg) for positive and Piperacillin (30µg) for negative bacteria, and Amphotericin B (20mcg) for fungi, respectively. The study results

demonstrated that the order of antimicrobial activity was found to be methanol > aqueous > petroleum ether > chloroform respectively [46]. Deepa *et al.* investigated the ethanol extract of *Pterocarpus marsupium* Roxb stem bark for its antimicrobial activity at 0.1, 0.3, 0.6, 1.25, 2.5, 5 mg per ml by agar well diffusion method against *Bacillus polymyxa*, *Vibrio cholerae*, and *Candida albicans* using Gentamycin and Amphotericin as controls. The ethanol extract of *P. marsupium* Roxb stem bark showed significant antimicrobial activity at 1.25 mg/ml against *Bacillus polymyxa*, *Vibrio cholerae*, and microbial activity at 25 mg/ml against *Candida albicans*. They also concluded that the antimicrobial activity might be due to its phytoconstituents such as alkaloids, tannins, glycosides, steroids, and flavonoids of the extract [47]. Gayathri and Kannabiran examined the antimicrobial activity of the aqueous extract of *Hemidesmus indicus* root, *Ficus bengalensis* bark, and *P. marsupium* Roxb bark. The study emphasized that aqueous extracts of *P. marsupium* Roxb had the minimum inhibitory concentration range between 0.04 and 0.08 mg and concluded that the extract showed significant antimicrobial activity against all the microorganisms. They also suggested that secondary metabolites such as saponins and tannins could be responsible for its antibacterial activity [48]. Another research analysis revealed the antimicrobial activity against gram-positive (*Enterococci* and *Staphylococcus aureus*) and gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) microbes and also inhibits *Candida albicans*, a fungal strain [49].

Rajgovind and his team photosynthesized copper nanoparticles from *P. marsupium* and evaluated their antimicrobial activity against gram-positive (*S. aureus*, *S. epidermidis*, *B. cereus*) and gram-negative (*E. coli*, *P. vulgaris*, *K. pneumoniae*) bacteria by the agar diffusion method and compared them with gentamycin as the standard. The synthesized nanoparticles showed antimicrobial activity against all the microbes, with the maximum zone of inhibition for *K. pneumoniae* [50].

Shrestha *et al.* extracted *P. marsupium* Roxb bark with methanol and investigated its antimicrobial activity against four American Type Culture Collection strains (*E. coli, K. pneumoniae, S. Typhimurium*, and *S. aureus*) and eight multidrug-resistant strains (*E. coli, methicillin-resistant S. aureus, K. pneumoniae, A. baumannii, C. freundii, Xanthomonas* species, *M. morganii, P. aeruginosa*) by agar well diffusion technique. The study results revealed that *P. marsupium* exhibited potent antibacterial activity against the clinical isolates of MDR bacteria [51]. Bhat and his team evaluated the antimicrobial activity of the alcohol extract of the heartwood of *P. marsupium* against Gram-positive (*Enterococci* and *S. aureus*) and Gram-negative (*E. coli* and *P. aeruginosa*) bacteria and a fungal strain *C. albicans* at 25, 50, and 100 µg/ml. The study results revealed that the extract has dose-dependent antibacterial activity and didn't show any antifungal activity. Also, they highlighted that secondary metabolites such as triterpenes, tannins, saponins, and flavonoids could be responsible for its antimicrobial activity [52]. The antibacterial effect of the methanol extract of *P. marsupium* Roxb bark was investigated against *B. cereus, E. coli, K. pneumoniae*, and *V. cholerae* and compared with streptomycin sulphate as a standard. It was concluded that the extract showed higher antibacterial activity against *K. pneumoniae* [53].

5.4. Anti-cancer activity

Vijayarekha *et al.* performed the extraction of *P. marsupium* Roxb bark with three different solvents such as ethanol, chloroform, and aqueous and evaluated its anticancer activity against the human prostate cancer cell line (PC-3) and the

human cervical cancer cell line (HeLa) by DNA fragmentation assay method. The study results demonstrated that the ethanol and chloroform extracts showed an apoptosis effect by lysis of cells bound with apoptotic bodies [54].

Diabetes mellitus can lead to cell damage and apoptosis through oxidative stress. Dar and his team investigated glucose uptake and apoptosis in HepG2 cells under oxidative stress conditions. The apoptosis effect of the methanol extract of *P. marsupium* Roxb heartwood was assessed through a fluorescence microscope. The study results revealed that the extract reduced cell damage and apoptosis in HepG2 cells at the concentration of 93.75 µg/mL [55].

Pterostilbene, a *stilbenoid (polyphenolic compound)*, was isolated from the heartwood of*P. marsupium* Roxb by Chakraborty *et al.* and investigated for its anticancer activity against breast (MCF-7) and prostate (PC3) cancer cell lines. Isolated pterostilbene showed anticancer activity by fragmenting DNA, forming apoptotic bodies, and distorting the cell membrane. They highlighted the mechanism behind its apoptotic effect by inhibiting cell proliferating factors such as Akt, Bcl-2, and enhancing apoptotic signals like Bax and caspases in mitochondria. In addition, it prevents two metastasis inducers, Matrix metalloproteinase 9 (MMP9) and α-methyl acyl-CoA racemase (AMACR) [56].

Gosetti *et al.* identified volatile, non-volatile, and metal in the aqueous extract of*P. marsupium* heartwood and examined its anticancer potential in A431, HeLa, REN, and PC-3 cell lines, comparing it with Imatinib mesylate as a positive control. The observed results concluded that the aqueous extract of *P. marsupium* heartwood has anticancer activity against all the cell lines with the IC50 values of 8.7, 9.8, 12.5, and 13.4 µg/mL for A431, HeLa, REN, and PC-3 cell lines, respectively [57].

5.5. Anti-inflammatory activity

Londonkar *et al.* performed a comparative anti-inflammatory activity study by the protein denaturation method between aqueous and methanol extracts of *P. marsupium* bark and diclofenac sodium as a standard. The study results revealed that both extracts have distinct anti-inflammatory activity, which was comparable with the standard with the IC50 values of 45±1.6 µg/mL, 45±0.94 µg/mL, and 55±0.24 µg/mL for the methanol extract, aqueous extract, and diclofenac sodium, respectively [58].

Pant *et al.* investigated the acetone: isopropyl alcohol (1:1) extract of*P. marsupium* Roxb stem wood for its anti-inflammatory activity in Swiss albino mice at 200 mg/kg/oral and 400 mg/kg/oral and compared it with indomethacin as a standard at 5 mg/kg/oral for 6 h. The paw edema was induced by administering 0.05 mL of undiluted fresh egg white in the sub-plantar region. The study results revealed that the extract has anti-inflammatory activity by decreasing the elevated TNF-α in serum in a time- and dose-dependent manner, with the inhibition activity at 5 h being 52.96%, 45.18%, and 47.03% for the standard, 200 mg/kg, and 400 mg/kg, respectively [37].

Patil and his team developed a hydrogel from the hydroalcoholic extract of*P. marsupium* Roxb heartwood and evaluated its anti-inflammatory activity in carrageenan-induced rat hind paw edema for 8 h, comparing it with a marketed formulation (Enacgel). The investigational results revealed that the formulated hydrogel showed more significant anti-inflammatory activity (43.70%) than the marketed formulation (17.03%) [59].

Yadav performed an anti-inflammatory activity assessment based on the individual and combined bark extracts of *P. marsupium* and *C. nurvala* at 250 µg/mL each and compared them with diclofenac sodium at 100 µg/mL as a standard. Anti-inflammatory activity was assessed based on hypotonicity-induced membrane lysis of human red blood cells. The study results revealed that anti-inflammatory activity was found to be 74.49%, 42.88%, 38.26%, and 59.52% for the standard, *P. marsupium*, *C. nurvala*, and combined extract, respectively. The study results suggested that the combination of these extracts produced a synergistic effect and that phytoconstituents such as phenols, flavonoids, and alkaloids are mediating the anti-inflammatory activity by preventing numerous inflammatory enzymes [60].

Elevated inflammatory cytokines were observed during hyperglycaemic conditions. A study performed by Halagappa and team examined the anti-inflammatory effect of the aqueous extract of the heartwood of *P. marsupium* Roxb at doses of 100 and 200 mg/kg in Type 2 diabetic rats for 4 weeks. Diabetes was induced in neonatal rats by administering streptozotocin (90 mg/kg, i.p.). The results revealed that the extract significantly decreased the elevated TNF-α in serum ($P<0.001$). They also highlighted that the presence of flavonoids in the extract might be responsible for its anti-inflammatory activity. Furthermore, they evaluated the bioactive fraction (2.5% and 5%) of *P. marsupium* extract for its anti-inflammatory activity by measuring tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) in diabetic rats for 45 days at 50, 100, and 200 mg/kg body weight. The study results demonstrated that the bioactive fraction at 5% in the dose of 200 mg/kg body weight showed significant anti-inflammatory activity by reducing oxidative stress, tumour necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) as inflammatory cytokines [31].

Rageeb *et al.* examined the methanol and aqueous extracts of *P. marsupium* Roxb stem bark for their anti-inflammatory activity at 100 mg/kg and compared them with ibuprofen at 60 mg/kg as a standard. Paw oedema was induced in albino rats by carrageenan. The result revealed that both extracts showed significant anti-inflammatory activity and outlined that the presence of flavonoids in the extract could be responsible for its anti-inflammatory activity [61].

5.6. Memory-enhancing activity

Dementia is a syndrome – usually characterized as a mental disorder – which leads to deterioration in intellectual ability and involves the impairment of memory. It is considered a major influencing factor in causing the specific brain disease known as Alzheimer's disease. Chauhan *et al.* investigated the methanol extract of *P. marsupium* Roxb for its memory-enhancing activity in albino mice at 25 and 50 mg/kg p.o by elevated plus-maze and Morris's water maze test. In the elevated plus-maze model, administration of the extract significantly increased the inflexion ratio and reduction in transfer latency, whereas in Morris's water maze models, it enhanced the impairment in learning and memory. The study outlined that the extract showed the memory-enhancing effect by facilitating cholinergic transmission [62].

Vangalapati *et al.* assessed the memory-enhancing activity of the aqueous extract of *P. marsupium* heartwood on diabetic rats at 250 mg/kg and 500 mg/kg b.w. based on Morris's water maze. Diabetes was induced by the intraperitoneal route injection of Streptozotocin (STZ) & Nicotinamide (NA). The investigational results revealed that the extract showed a beneficial learning and memory effect in diabetic rats [63].

5.7. Hepatoprotective activity

Mankani and his team investigated CCl4-induced hepatotoxicity in rats with methanol and aqueous extracts of *P. marsupium* stem bark as hepatoprotective agents at 25 mg/kg/day based on liver function biochemical parameters such as total bilirubin, serum protein, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase activities, and histopathological studies of the liver, and compared with standard silymarin at 100 mg/kg/day for 14 days. The study results revealed that both extracts restored the liver functional biochemical parameters and showed normal hepatic cords, absence of necrosis, and lesser fatty infiltration. However, among these two extracts, the methanol extract showed more potent activity than the aqueous extract. In addition, they concluded that the presence of a higher content of flavonoids could be responsible for its hepatoprotective activity [23].

Saidurrahman and his team evaluated the hepatoprotective effect of the ethanol leaf extract of *P. marsupium* Roxb against paracetamol-induced liver damage in rats at 200 mg/kg/day and 400 mg/kg/day by measuring various biochemical markers such as AST, ALT, ALP, total cholesterol, bilirubin, and liver weight. The study results were compared with 100 mg silymarin/kg/day as standard. The study results demonstrated that the extract showed potent hepatoprotective activity by inhibiting oxidative stress and altering the biochemical markers [64].

Devipriya *et al.* conducted a study on the hepatoprotective activity of *P.marsupium* extracts at 100 mg/kg orally against the CCl4-induced hepatotoxicity model and measured various marker enzymes like ALT, AST, ALP, LDH, and bilirubin. The study results revealed that the extract significantly increased the marker enzyme levels in the CCl4-induced hepatotoxicity model [65].

Gupta and his team examined the hepatoprotective activity in streptozotocin-induced diabetic rats at 100 and 300 mg/kg b.wt for 21 days and assessed the hepatic LPO, GSH, SOD, serum AST, ALT, and creatinine as hepatoprotective parameters. The study determined that the plant extract reduced the hepatic LPO, increased GSH, SOD, AST, ALT, and creatinine content, and concluded that the extract showed a hepatoprotective effect in diabetic rats [66].

Jadhav and Dhikale developed a polyherbal formulation comprising the extracts of *Bauhinia variegata*, *Pterocarpus marsupium*, and *Oxalis corniculata* and investigated its hepatoprotective activity in carbon tetrachloride-induced hepatotoxic female Albino Wistar strain rats for 4 days. Changes in histopathology of the liver and quantification of SGOT, SGPT, ALP, and serum bilirubin were considered as hepatoprotective assessment parameters and compared with the marketed tablets Liv-52 as a standard. The study determined that the polyherbal formulation to be a hepatoprotective agent by increasing the SGOT, SGPT, ALP, and serum bilirubin also showed less hepatocyte cell damage [67].

5.8. Anthelmintic activity

Helminthic diseases are worm infections caused by parasitic worms. Panda *et al.* performed an investigation of various extracts such as ethanol, ethyl acetate, n-butanol, and petroleum ether extract of leaves of *Pterocarpus marsupium* at 20, 40, and 60 mg/mL and determined the paralysis and death time in Indian earthworms *Pheretima posthuma* as the test worm and compared with albendazole 10 mg/mL as a standard. The study determined that petroleum ether, ethanol, and

the standard showed paralysis in 7.14, 8.41, and 6.33 min respectively; death in 15.33, 16.17, and 14.27 min respectively. The strategic and hypothesized study concluded that the extracts of petroleum ether and ethanol showed substantial dose-dependent and significant anthelmintic activity which was comparable with the standard [68].

5.9. Antihyperlipidemic activity

Many natural herbs and shrubs, including *P. marsupium* extracts, are continuously screened for their potential hypolipidemic effect or antihyperlipidemic activity. Singh *et al.* carried out an extensive study by combining therapy with the methanol extract of *O. sanctum* leaves and *P. marsupium* heartwood against non-diabetic and oxidative stressed alloxan-induced diabetic rats for 15 days and measured serum triglycerides, VLDL, HDL, and hepatic cholesterol as parameters for lipidemic activity. Wistar female rats with a dosage of 500 mg/kg (combination therapy) revealed that *P. marsupium* heartwood exhibited a potential anti-lipidemic effect by maintaining the serum triglycerides, VLDL, HDL, and hepatic cholesterol. The study results concluded that the combination of these two extracts showed the greatest lipid-lowering potential, which can be used as corrective measures on the metabolic machinery responsible for diabetic dyslipidemia [37].

Jahromi and Ray investigated the antilipidemic effect of ethyl acetate from the heartwood of*P. marsupium* in diet-induced and Triton-induced hyperlipidemic model rats for 14 days at 75 mg/kg/b.w. and measured lipidemic parameters such as serum triglyceride, total cholesterol, and LDL- and VLDL-cholesterol levels. The study results revealed that the extract significantly reduced all lipidemic parameters in both animal models [69].

Mohire performed a comparative study between the aqueous extract of the heartwood of*P. marsupium* at 0.25, 0.5, 1, 2, and 4 mg/mL and digitoxin at 0.25, 0.5, and 1.0 mg/mL for its cardiotonic effect in isolated frog heart perfusion technique. The study results showed that at a low concentration (0.25 mg/mL), there was an increase in the height of the force of contraction and a decrease in heart rate, whereas at higher concentrations, a significant increase in the height of the force of contraction and a decrease in heart rate were observed. Also, they concluded that the extract showed a narrow therapeutic window, very good cardiotonic activity, and a wide margin of safety [70].

A study performed by Gunasekaran *et al.* {m/100/} observed the neuroprotective effect of the aqueous extract of*P. marsupium* Roxb at 100 mg and 200 mg/day on the pain threshold response in streptozotocin-induced diabetic neuropathic pain for 8 weeks. At the end of 8 weeks, a formalin-evoked pain model was followed, and parameters such as TNF-α, IL-1β, IL-6, and pain threshold response were measured. The study results demonstrated that the extract significantly prevented the TNF-α, IL-1β, and IL-6 levels and significantly increased the pain threshold response. Further, they highlighted that the extract showed a neuroprotective effect due to its anti-inflammatory and neuroregeneration mechanisms in STZ-induced neuropathic pain [71].

Gupta *et al.* examined the alcoholic extract of*P. marsupium* heartwood at doses of 100, 200, and 400 mg/kg for its nephroprotective effect in diabetic nephropathy rats. Various parameters such as kidney weight, serum creatinine, blood urea nitrogen, serum uric acid, urea, urine volume, urine albumin, oxidative stress markers such as lipid peroxidation,

catalase, superoxide dismutase, and creatinine clearance were estimated during the study. The study results concluded that at higher doses, the extract showed a significant reduction of kidney weight, serum creatinine, blood urea nitrogen, uric acid, total protein, and remarkably decreased the urine volume and urine protein, while increasing the urine creatinine and creatinine clearance; it also significantly increased SOD, GSH, and catalase. The histopathological results confirmed that the extract prevented kidney damage. Finally, they concluded that the extract showed a dose-dependent nephroprotective effect [72].

6. Conclusion

In recent years, ethnomedicinal studies have received much attention as they shed light on the numerous little-known and unknown medicinal virtues, especially of plant origin. *P. marsupium* Roxb can serve as an effective remedy for the detrimental effects posed by synthetic derivatives and drugs prevalent in this modern age. Due to the high availability and use of *P. marsupium* Roxb in the formulation of diabetic medications, India is notoriously known to be the Diabetic capital of the world. Various investigational studies have been carried out to shed light on the recent progress of the plant's bioactive phytochemicals and diverse pharmacological effects. The presence of bioactive phytoconstituents in the extracts of *P. marsupium* Roxb is very well scrutinized and documented by various researchers; however, there is no clear information about which kind of phytoconstituents possess what kind of pharmacological activity. Our present review summarized the high biomedical activities of *P. marsupium* Roxb such as antidiabetic, antioxidant, antibacterial, antimicrobial, anticancer, and anti-inflammatory activity. Therefore, various pharmacological screenings of *P. marsupium* Roxb have revealed its therapeutic potential and represent it as a valuable pharmaceutical plant with several medicinal properties. As pharmacologists are looking forward to developing new drugs from natural sources, the development of modern drugs from *P. marsupium* Roxb can be emphasized for the control of various diseases. Systematic research and development work should be undertaken for the conservation of *P. marsupium* Roxb and the development of products for their better economic and therapeutic utilization.

Statements and Declarations

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