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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” have a long history of usage in the tropical and subtropical regions for a variety of purposes in treating several human diseases. The present objective of this study is to provide its phytoconstituents and pharmacological activities of this plant. Extraction and fraction of this plant highlighted the presence of alkaloids, protein, carbohydrates, coumarin, gums, mucilage, fixed oils, anthraquinone glycosides, saponnin glycosides, tannins, flavonoids and phenolic compounds. Several investigational studies demonstrated that this plant has various pharmacological activities such as analgesic, antidiabetic, anti-inflammatory, anticancer, hepatoprotective, antimicrobial, antidiarrhoeal, memory enhancing activity, antioxidant and antihyperlipidemic. It is used alone or with other medicinal plants to provide enhanced therapeutic efficacy for treating various ailments. Our present study is an extensive review relating the plant’s phytoconstituents and pharmacological activities such as antidiabetic, antioxidant, antimicrobial, anticancer, anti-inflammatory, memory enhancing, hepatoprotective and antihyperlipidemics in order to collate the knowledge that already exists about this plant and to emphasize its many uses as a medication.

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1. Introduction

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

The genus, *Pterocarpus* is a large deciduous tree species of angiosperms group (flower) from *Leguminosae* family. In this family, about 765 genera and approximately more than 20000 species are widely distributed throughout the world. The genus *Pterocarpus* includes 227 species, of these, 46 species are accepted and 30 scientific plant names of intraspecific rank. *Pterocarpus marsupium* Roxb (*P. marsupium*) is popularly well-known species among the *Pterocarpus* genus. Other vernacular names of this plant in Indian are kino tree or Malabar kino, Vijayasara, Bijasara, Venga, Bibala, Piashala, Chandan Lal, Vengai and Yegi [6][7]. *P. marsupium* is native to India, Nepal, Sri Lanka and grown in deciduous and evergreen forests of central, western, peninsular India, sub-Himalayan region and southern regions of India, Bangladesh, Sri Lanka and Taiwan [8]. In India, *P. marsupium* is found mostly in the states of Gujarat, Madhya Pradesh, Bihar and Orissa and traditionally used in Ayurveda, Siddha, Unani, and Homoeopathy [9].

Earlier phytochemical investigation reports revealed that *P. marsupium* contains alkaloids, protein, carbohydrates, coumarin, gums, mucilage, fixed oils, anthraquinone glycosides, saponnin glycosides, tannins, flavanoids and phenolic compounds [10]. It has a rich source of terpenoids which includes aurone, isoflavonoids glycosides, associated phenolic compounds includes lupenol, epicatechin and β-sitosterol [11]. The leaf possesses anthelminthic and antioxidant activities. The stem possesses antioxidant, antidiabetic, anti-inflammatory and antimicrobial activities. The bark possesses anti-inflammatory, analgesic, anticancer, antimicrobial, hepatoprotective and antidiabetic activities. The heartwood possesses anti-diarrhoeal and antidiabetic activities.

Although there are several earlier reviews on several phytochemistry, ethnobotany and pharmacological potential of *P. marsupium*, there are very focus on the relevance of its phytoconstitutents and pharmacological activities.

The study was taken up with the objective to provide baseline information on the potential benefits of the plant by investigating the phytoconstitutents role in the depicted pharmacological activities.

2. Botanical Description

P. marsupium is a large deciduous tree which can grow upto 30 m height, barks are scaly, rough and longitudinally

fissured with the width range of 10-15 mm in size which looks like surface grey or greyish-black, blaze pink with whitish marking in colour [4]. Leaves are abundant, alternate without stipules, unequally pinnate with round petioles[12]. Leaflets are generally 5-7 in number, 8-13cm long, oblong or elliptic or rotund, with 15-20 pairs of lateral veins [13].

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

Flowers are fragrant, bisexual and yellow in colour, which possesses about 1-5 cm long large panicles[13]. Pods are flat, orbicular, 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, then fruiting continues up to March [15]. Normally, the legumes of the plant contain two seeds[16].

3. Taxonomic classification

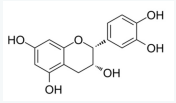
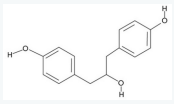
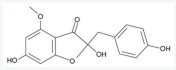
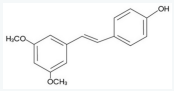
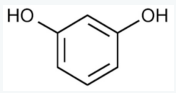
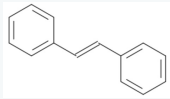
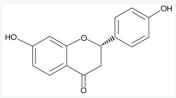
Domain	Eukaryota
Kingdom	Plantae
Subkingdom	Euphyllophytina
Phylum	Tracheophyta
Infraphylum	Radiatopsis
Class	Magnoliopsida
Subclass	Rosidae
Super order	Fabanae
Order	Fabales
Family	*Fabaceae*
Sub-family	Papilionaceae
Genus	Pterocarpus
Species	marsupium
Botanical Name	*Pterocarpus marsupium* Roxb[1][4][9][10][14][17].

4. Phytoconstituents

P. marsupium contains rich source of flavonoids and polyphenolic compounds. Over years of analysis, researchers emphasized that the following bioactive phytochemicals such as 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 and *p*-hydroxybenzaldehyde were obtained from the heartwood and root[22][13]. Some of the phytoconstituents structures

of *P. marsupium* are given in Table 1 and phytoconstituents associated in different parts of plantis 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]

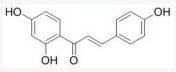
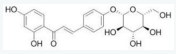
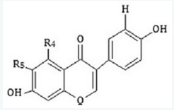
Isoliquiritigrnin		[4][10][12][14][15]
Isoliquiritin		[4][10][14][15]
Aglycone		[19]

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

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,* 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 has become an essential source all 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 ulcer [24]. Moreover, *P. marsupium* heartwood, leaves, flowers and gum have been used one of the major ingredients in various ayurvedic, homeopathic and siddha formulations due to its ethnic therapeutic activity against diarrhoea, dysentery, fractures, leprosy, leukoderma, skin diseases, sores, boils, constipation, depurative, rectalgia, ophthalmology, haemorrhages, rheumatoid arthritis, lowering the blood glucose level, diuretic, gastrointestinal tract disorders also aids in the treatment of various neurological problems [16].

5.1. Antioxidant activity

This plant extract showed not only hypoglycemic activity but exhibited a promising antioxidant effect. The*in vitro* antioxidant activity of ethyl acetate leaf extract of *P. marsupium* was studied by hydroxyl radical scavenging activity, ABTS assay, Ferric reducing ability of plasma (FRAP) assay, Nitrous oxide radical scavenging activity, Total reactive antioxidant potential (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 [25]. Pant *et al.,* investigated the acetone: isopropyl alcohol (1:1) and ethanol extract of stem wood of *P. marsupium* for its antioxidant activity at 5, 20, 40, 60, 80, and 100 µg/mL by 2, 2-diphenyl-1-picrylhydrazyl scavenging method. The study results demonstrated that these extracts showed antioxidant activity in dose dependent manner. Among these two extracts, acetone: isopropyl alcohol (1:1) showed lesser IC_{50} value (36.5 µg/mL), whereas ethanol extract showed IC_{50} 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 [26]. Tippani *et al.,* examined the antioxidant activity methanol extract of *P.marsupium* bark by 2,2-diphenylpicrylhydrazyl (DPPH) method at 0, 10, 20, 40, 80, 100, and 200 µg/mL and compared with ascorbic acid as standard. The result revealed that the extract has dose depend antioxidant activity with IC_{50} value of 53 µg/mL and 34.0 µg/mL for extract and ascorbic acid respectively. They concluded that the extract has closely comparable antioxidant activity with the standard [27]. Bhata and Nayak investigated the various fractions of heart wood of *P. marsupium* on antioxidant enzymes like protein thiols at 75 mg/kg for 30 days. The study results concluded that after the 30 days of treatment the extract significantly reduced the protein thiol level by neutralizing the free radicals by increased utilization [28].

Singh *et al*., examined enzymatic and non-enzymatic antioxidant effect of methanol extracts of*P. marsupium* and *Ocimum sanctum* Linn at as a mixture of both at a dosage of 500 mg/kg body weight to together 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 [29].

5.2. Antidiabetic activity

P. marsupium has been used as a potential antidiabetic agent, ever since prehistoric times. It aids in lowering the 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 hypoglycemic effect and the results have demonstrated that *P. marsupium* repaired the usual insulin secretion by reversing the impairment to the beta cells by

repopulating the islets of Langerhans [21][30][31][32][33]. Mohankumar *et al.,* investigated the aqueous extract of heartwood of *P. marsupium* for its antidiabetic activity using Bio assay method by exposing pancreatic and muscle tissues of mouse. The aqueous extract simultaneously increased the insulin secretion and glucose uptake in concentration dependent manner and concluded that this plant has a potent antidiabetic property in both *in-vitro* as well as *in vivo* [34]. Halagappa *et al*., examined the aqueous extract of *P. marsupium* for antidiabetic activity at 100 and 200 mg/kg. The study result suggested that at 200 mg/kg of dose have effect on postprandial hyperglycemia in type 2 diabetic rats also improved the body weight of the diabetic animals. In addition, it significantly decreases the Tumor necrosis factor (TNF)-α level in type 2 diabetic rats [35]. Jelastin *et al.,* examined the ethanol extract of *P. marsupium* wood and bark for antidiabetic activity in alloxan induced diabetic rats. The study has shown that ethanol extract of *P. marsupium* reduced the blood level and increased plasma insulin level in diabetic rats and highlighted that it can be used for the management of diabetic [36].

Mishra *et al.,* investigated the ethanol extract of heartwood of *P. marsupium* for its antidiabetic activity on streptozotocin induced rats. The crude power, ethanolic extract, hexane and n-butanol fractions showed the improvement on oral glucose tolerance and increase the serum insulin level in a dose dependent manner against its antidiabetic activity [37]. Pant and team performed a comparative antidiabetic activity study on the ethanolic extract of *P. marsupium* stem at 200 and 400mg/kg in mice by oral glucose tolerance test against glimepiride at 0.43 mg/kg. The acute toxicity study results demonstrated that ethanol extract of *P. marsupium* stem is non-toxic in the dose range of 250-1000 mg/kg. The study results demonstrated that blood glucose lowering effect was found to be 57.56%, 51.30% and 55.13% for standard, at 200 mg/kg and 400 mg/kg respectively at 180 min. Also concluded that the antidiabetic activity is time and dose dependent [26]. Gayathri *et al.,* determined the antidiabetic activity of aqueous bark extract of *P. marsupium* at 500 mg/kg in streptozotocin induced diabetic rats and measured the various parameters like plasma insulin, cholesterol, glycosylated haemoglobin, triglycerides, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), a-glutamyl transferase (a- GT) and creatine kinase (CK). The study results demonstrated that the extract normalized the cholesterol, triglycerides, plasma insulin, and glycosylated haemoglobin level also decreased the AST, ALT, ALP, a-GT and CK from its elevated level in the diabetic rats. They concluded that aqueous bark extract of *P. marsupium* showed remarkable antidiabetic effect in metabolic alterations [38]. Mohankumar *et al*., isolated the insulinotrophic activity enriched fraction (AEF) from aqueous extract of *P. marsupium* and investigated for its antidiabetic activity by bioassay method. The study results showed that AEF modulated the biosynthesis of insulin by mimicking sulphonyl urea also prolonged the responsiveness effects on glucose and combat the hyperglycemia adverse effects by increasing and sustaining the glucose-dependent insulin secretion [39]. Singh *et al*., examined antidiabetic effect of methanol extracts of *P. marsupium* and *Ocimum sanctum* Linn at 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 profile were assessed during the study. The study results demonstrated that the extract mixture ameliorated the diabetic associated manifestations by restoring the endogenous antioxidant levels [40]. Radhika *et al*., made a comparative evaluation the methanol extract of *P.marsupium* for its antidiabetic 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 reference standard. Serum biochemical parameters such as triglycerides, Low Density Lipoprotein (LDL), Very Low Density Lipoprotein (VLDL) and High Density

Lipoprotein (HDL) were also assessed. The extract showed significant diabetic activity by improving the peripheral utilization of glucose and extra pancreatic effect. In addition, the extract showed 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 a potent antidiabetic activity [41]. Dhanabal *et al.*, prepared alcohol extract from the bark of *P. marsupium*, subsequently fractioned with different solvents like chloroform, butanol, toluene and ethyl acetate. These fractions were investigated for its antidiabetic activity along with its related metabolic alterations in alloxan-induced diabetic rats. The study results demonstrated that among the different fractions, butanol fraction showed more activity than other fraction; in addition it controlled the diabetic metabolic parameters such as total protein, triglyceride, cholesterol, Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT) and alkaline phosphatase [42].

5.3. Antimicrobial activity

Kachhawa and coworkers investigated the antibacterial activity of *P. marsupium* (Stem) methanol extract at the concentration of (200, 100, 50 and 25 mg/mL) against gram positive *Bacillus coagulans* and gram negative *Escherichia coli* (*E. coli*) and compared with ciprofloxacin as standard (0.001 mg/mL) by disc diffusion method. The study results demonstrated that extract showed antibacterial activity against both bacterial and the results were comparable with the standard [43]. Singh *et al.,* investigated the acetone: isopropyl alcohol (1:1) and ethanol extract of *P. marsupium* stem (50 mg/mL) for its antibacterial activity against Gram-positive bacteria such as *Staphylococcus aureus (S. aureus), Bacillus cereus* (*B. cereus*) and Gram-negative such as *E. coli, Salmonella typhi* and compared against ofloxacin 50 µg/mL. They study results demonstrated that the acetone: isopropyl alcohol (1:1) showed zone of inhibition (8 mm) against gram positive bacteria, no activity was observed against gram negative bacteria. In addition, ethanol extract didn't show any anti-bacterial activity against both gram positive and gram-negative bacteria [40].

A comparative antimicrobial activity study between ethanol and aqueous extract of fresh barks of *P. marsupium* by cup plate agar diffusion method against gram + ve bacteria like *S. aureus, Bacillus sterothermophilus* and gram – ve bacteria like *E. coli*, *Klebsiella pneumoniae* at 400 and 800 µg/mL of extract and compared with ciprofloxacin at 20 µg/mL as standard. The study results concluded that both extract showed concentration dependent antibacterial activity whereas alcohol extract was more potent antibacterial activity than water. In addition, they highlighted that presence of tannin and flavonoids may contribute to its antimicrobial activity [44].

Kalaivani *et al*, examined the antimicrobial activity of ethanol leaf extract of *P. marsupium* by against *E. Coli, S. aureus, Aspergillus niger* (*A. niger*) and *Candida albicans* (*C. albicnas*) and compared with Ciprofloxacin 5µg/disc for bacicria Fluconazole 100 units/disc for fungi by disc diffusion method. The study results outlined that the extract has both antibacterial and antifungal activity also highlighted that *E. coli* had highest (22 mm) and *C. albicans* had lowest (12 mm) zone of inhibition [45].

Londonkar and Hugar have done the extraction from *P. marsupium* bark with different solvents such as distilled water, methanol, chloroform and petroleum ether. The extracts were investigated for its antimicrobial activity against gram + ve bacteria such as *S. aureus* and *Enterococcus faecalis (E. faecalis*), gram – ve bacteria such as *Salmonella typhimurium*,

E. coli, *Enterobacter aerogenes* and *Shigella dysenteriae* and a fungus *A. niger* at the concentration of 100 mg/mL and compared with standard Cefixime (30µg) for +ve and piperacillin (30µg) for -ve bacteria's 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 *P. marsupium* 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 (B. plymyxa), Vibrio cholera* (*V. cholera*) and *C. albicans* using Gentamycin and Amphotericin as controls. The ethanol extract showed significant antimicrobial activity at 1.25 mg/mL for *B. plymyxa, V. cholera* and at 25 mg/mL against *C. albicans*. From the study, they concluded that the antimicrobial activity might be due to its phytoconstituents such as alkaloids, tannin, glycosides, steroids and flavanoids 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* bark. The study emphasized aqueous extracts of *P. marsupium* 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. Also, suggested that secondary metabolites such as saponins and tannins could be responsible for its antibacterial activity [48]. Another research analysis revealed the anti-microbial activity against the gram positive bacteria such as *Enterococci* and *S. aureus* and negative bacteria such as *E. coli* and *Pseudomonas aeruginosa* (*P. aeruginosa*) and a fungal strain *C. albicans* [49].

Rajgovind and team photo synthesized copper nanoparticle from *P. marsupium* and evaluated for its anti-microbial activity against gram + ve (*S. aureus, Staphylococcus epidermidis, B. cereus*) and gram – ve (*E. coli, Proteus vulgaris, K. pneumoniae*) bacteria by agar diffusion method and compared with gentamycin as standard. The synthesized nanoparticles showed antimicrobial activity against all the microbes, whereas it had maximum zone of inhibition for *K. pneumonia* [50].

Shrestha *et al*., extracted *P. marsupium* bark with methanol and performed antimicrobial activity against four American type culture collection (*E. coli, K. pneumonia, S.Typhimurium and S. aureus*) and eight Multidrug resistant strains (*E. coli, methicillin-resistant S. aureus, K. pnemoniae, Acinetobacter baumannii, Citrobacter freundii, Xanthomonas species, Morganella morganii, P. aeruginosa)* by agar well diffusion technique. The study results revealed that *P. marsupium* exhibited good antibacterial activity against the clinical isolates of MDR bacteria [51]. Bhat and team evaluated the antimicrobial activity of alcohol extract of heart wood of *P. marsupium* against gram + ve (*Enterococci and S. aureus*) and negative (*E. coli and P. aeruginosa*) bacteria's and a fungal strain *C. albicans* at 25, 50 and 100 µg/mL. The study results revealed that the extract showed dose dependent anti-bacterial activity against the examined bacteria's and didn't show any antifungal activity against *C. albicans*. Also, they highlighted that secondary metabolites such as triterpenes, tannins, saponins and flavonoids could be responsible for its antimicrobial activity [52]. Antibacterial effect of methanol extract of *P. marsupium* bark was investigated against *B. cereus, E. coli, K. pneumoniae* and *V. cholera* and compared with Streptomycin sulphate as standard and concluded that the extract showed higher antibacterial activity against *K. pneumonia* [53].

5.4. Anticancer activity

Vijayarekha *et al*., performed the extraction of *P. marsupium* bark with three different solvents such as ethanol, chloroform and aqueous and evaluated for its anticancer activity against Human prostate cancer cell line (PC-3) and Human cervical cancer cell line (HeLa) by DNA fragmentation assay method. The study results demonstrated that ethanol and chloroform extract showed apoptosis effect by lysis of cells bound with the apoptotic bodies [54]. Diabetes mellitus can lead to produce cell damage and apoptosis through oxidative stress. Dar and team investigated the glucose uptake and apoptosis in HepG2 cells against oxidative stress condition. Apoptosis effect of the methanol extract of *P. marsupium* heartwood was assessed through fluorescence microscope. The study results revealed that the extract reduced cell damage and apoptosis effect in HepG2 cells at 93.75 µg/mL [55].

Pterostilbene, is a stilbenoid (Polyphenolic compound) was isolated from heart wood of*P. marsupium* 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 the DNA, formation of apoptotic bodies and distortion of the cell membrane. They highlighted that mechanism behind of its apoptosis effect is by preventing the cell proliferating factors such as Akt, Bcl-2 and improved apoptotic signals like Bax and caspases in mitochondria. In addition, it prevents the two metastasis inducers such as Matrix metalloproteinase 9 (MMP9) and a-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 different cell lines like A431, HeLa, REN and PC-3 and compared with Imatinib mesylate as positive control. The observed results concluded that aqueous extract of *P. marsupium* heartwood has anticancer activity against all the cell line with the IC_{50} value of 8.7, 9.8, 12.5 and 13.4 µg/mL for A431, HeLa, REN and PC-3 cell line respectively [57].

5.5. Anti-inflammatory activity

Londonkar *et al*., performed a comparative anti-inflammatory activity study by protein denaturation method between aqueous and methanol extract of *P.marsupium* bark using diclofenac sodium as standard. The study results revealed that both extracts have distinct anti-inflammatory activity which was comparable with standard. The IC_{50} values were found to be 45±1.6, 45±0.94 and 55±0.24 µg/mL for methanol extract, aqueous extract and diclofenac sodium respectively [58]. Pant *et al.,* investigated the acetone: isopropyl alcohol (1:1) extract of*P. marsupium* stem wood for its anti-inflammatory activity in Swiss albino mice at 200 and 400 mg/kg/oral and compared with indomethacin as 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 activity with the inhibition activity at 5 h is 52.96%, 45.18% and 47.03% for standard, 200 and 400 mg/kg respectively [26].

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

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

Elevated inflammatory cytokines were observed during hyperglycemic condition. A study performed by Halagappa and team examined the anti-inflammatory effect of aqueous extract of heart wood of *P. marsupium* at a dose of 100 and 200 mg/kg in Type 2 diabetes rats for 4 weeks. Diabetes was induced in a neonatal rat by administering streptozotocin (90 mg/kg, i.p). The results exposed that the extract decreased the elevated TNF-α level in serum significantly ($P<0.001$). Also, they highlighted that presence of flavonoids in the extract might be responsible for its anti-inflammatory activity. In addition, they evaluated bioactive fraction (2.5% and 5%) of *P. marsupium* extract for its anti-inflammatory activity by measuring TNF-α and Interleukin-6 (IL-6) in diabetic rats for 45 days at 50, 100, and 200 mg/kg body. The study results demonstrated that bioactive fraction at 5% in the dose of 200 mg/kg body weight showed significant anti-inflammatory activity by reducing the oxidative stress, TNF-α and IL-6 as inflammatory cytokines [35].

Rageeb *et al*., examined the methanol and aqueous extract of *P.marsupium* stem bark for its anti-inflammatory activity at 100 mg/kg and compared with Ibuprofen 60 mg/kg as standard. Paw oedema was induced in albino rats by carrageenan. The result revealed that both the extract showed significant anti-inflammatory activity and outlined that 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 mental disorder which leads to deterioration in the intellectual ability and involves in the impairment of memory. It is considered as 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* for its memory enhancing activity in albino mice at 25 and 50 mg/kg p.o by elevated plus-maze and Morri's water maze test. In elevated pulse-maze model, administration of extract significantly increased inflexion ratio and reduction in transfer latency whereas in Morri's water maze models enhanced the impairment in learning and memory. The study outlined that the extract showed the memory enhancing potential by facilitation of cholinergic transmission [62].

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

5.7. Hepatoprotective activity

Mankani and team investigated on CCl_4 induced hepatotoxicity in rats with methanol and aqueous extract of*P. marsupium* stem bark as hepatoprotective agent at 25 mg/kg/day based on its liver function biochemical parameters such as total bilirubin, serum protein, alanine aminotransaminase, aspartate aminotransaminase, 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 function biochemical parameters and showed the normal hepatic cords, absence of necrosis and lesser fatty infiltration. However, among these two extracts methanol extract showed more potent activity than the aqueous extract. In addition, they concluded that presence of higher content of flavonoids could be the responsible for its hepatoprotective activity [23].

Saidurrahman and team evaluated the hepatoprotective effect of ethanol leaf extract of*P. marsupium* against paracetamol-induced liver damage in rats at 200mg/kg/day and 400 mg/kg/day by measuring the 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 extract showed potent hepatoprotective activity by inhibiting the oxidative stress and altered the biochemical markers [64].

Devipriya *et al.,* conducted a study on the hepatoprotective activity of the*P.marsupium* extracts at 100 mg/kg orally against the CCl_4 induced hepatotoxicity model and measured the various marker enzymes like ALT, AST, ALP, lactate dehydrogenase (LDH) and bilirubin. The study results revealed that the extract significantly increased the marker enzyme levels in CCl_4 induced hepatotoxicity model [65].

Gupta and team examined the hepatoprotective activity in streptozotocin induced diabetes rats at 100 and 300 mg/per/kg-b.wt for 21 days and assessed the hepatic LPO, glutathione (GSH), Septo-optic dysplasia (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 hepatoprotective effect in diabetes rats [66].

Jadhav and Dhikale developed a polyherbal formulation comprising the extracts of*Bauhinia variegate, Pterocarpus marsupium* and *Oxalis corniculate.* Subsequently they investigated its hepatoprotective activity in CCl_4 induced hepatotoxicity in female Albino Wistar strain rats for 4 days. Changes in histopathology of the liver and quantification of SGOT, SGPT, Alkaline phosphatase (ALP) and Serum bilirubin were considered as hepatoprotective assessment parameters and compared with marketed tablets Liv- 52 as standard. The study determined that polyherbal formulation to be a hepatoprotective agent by increasing the SGOT, SGPT, ALP and serum bilirubin also showed less hepatocytes cell damage [67].

5.8. Anthelmintic activity

Helminthic diseases are worm infections caused by the parasitic worms. Panda*et al.,* performed an investigation of various extracts such as ethanol, ethyl acetate, n-butanol and petroleum ether of leaves of *P. marsupium* at 20, 40 and 60 mg/mL and determined the paralysis and death time in Indian earthworms Pheretimepasthuma as test worm and

compared with albendazole 10 mg/mL as standard. The study determined that petroleum ether, ethanol and 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 extracts petroleum ether and ethanol showed substantial dose dependant and significant anthelmintic activity which was comparable with 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 the combination therapy with the methanol extract of *O. sanctum* leaves and *P. marsupium* heart wood against the 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) and revealed that *P. marsupium* heart wood exhibited a potential anti-lipidemic effect by maintaining the serum triglycerides, VLDL, HDL and hepatic cholesterol. The study results concluded that combination of these two-extracts showed greatest lipid lowering potential, which can be used as corrective measures on metabolic machinery responsible in diabetic dyslipidemia [40]. Jahromi and Ray investigated the antilipidemic effect of ethyl acetate from the heartwood of *P. marsupium* in Diet-indued and Triton-induced hyperlipidemic models rats for 14 days at 75mg/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 reduced all lipidemic parameters significantly in both animal models [69]. Mohire performed a comparative study between aqueous extract of 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 from heart perfusion technique. The study results showed that at low concentration (0.25 mg/mL) increased in height of force of contraction and decrease in heart rate, whereas in higher concentration significant increase in height of force of contraction and decrease in heart rate were observed. Also, they concluded that extract showed narrow therapeutic window, very good cardiotonic activity and wide margin of safety [70].

5.10. Neuroprotective activity

A study performed by Gunasekaran *et al*., observed the neuroprotective effect of aqueous extract of*P. marsupium* 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 formalin evoked pain model was followed and measured the parameters such as TNF-α, IL-1β, IL-6 and pain threshold response. The study results demonstrated that 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 neuroprotective effect due to its anti-inflammatory and neurogeneration mechanisms in STZ-induced neuropathic pain [71].

5.11. Nephroprotective activity

Gupta *et al*., examined the alcoholic extract of*P. marsupium* heartwood at (100, 200 and 400 mg/kg) for its Nephroprotective activity 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 dose the extract showed significant reduction of kidney weight, serum creatinine, blood urea nitrogen, uric acid, total protein, remarkably decreased the urine volume, urine protein, and increasing the urine creatinine and creatinine clearance; whereas significantly increased SOD, GSH and catalase. The histopathological results confirmed that the extract prevented the kidney damage, also they concluded that the extract showed dose dependent nephroprotective activity [72].

6. Conclusion

In recent years, ethno medicinal studies received much attention as this brings light on the numerous little known and unknown medicinal virtues especially of plant origin. *P. marsupium* can aid as an effective remedy for the detrimental effects posed by the synthetic derivatives and drugs prevalent in this modern age. Various investigational studies are carried out to shed light on the recent progress of plant's bioactive phytochemicals and diverse pharmacological effects. Presence of bioactive phytoconstituents in the extracts of *P. marsupium* is very well scrutinized and documented by various researchers, however there are very few clear information about its phytoconstituents and its related pharmacological activities. Our present review summarized its high biomedical activities such as antioxidant, antidiabetic, antimicrobial, anticancer, anti-inflammatory, memory enhancing activity, hepatoprotective, anthelmintic, antihyperlipidemic, neuroprotective and nephroprotective activities. Various pharmacological screenings of *P. marsupium* revealed its therapeutic potential and representing that it is a valuable pharmaceutical plant with several medicinal properties. As the pharmacologists are looking forward to develop new drugs from natural sources, development of modern drugs from *P. marsupium* can be emphasized for the control of various diseases. In the near future, further investigational studies are needed to isolate and characterize the bioactive compounds as lead molecules in the drug discovery research process. Also, a systemic research and development work should be undertaken for the conservation of *P. marsupium* and development of products for their better economic and therapeutic utilization.

Statements and Declarations

Conflicts of interest - The authors declare that they have no conflicts.

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