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PTEROCARPUS MARSUPIUM: BRIDGING THE GAP BETWEEN TRADITIONAL MEDICINE AND MODERN PHARMACOLOGY

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Abstract:
Pterocarpus marsupium, a prominent medicinal plant in traditional Ayurvedic and Unani systems, has garnered significant attention for its diverse bioactive compounds and therapeutic potential. This review provides a comprehensive overview of the plant's botanical characteristics, traditional uses, phytochemical composition, and medicinal properties. The plant is indigenous to the Indian subcontinent and is known for its antidiabetic, antioxidant, anti-inflammatory, and antimicrobial effects. Its leaves, bark, and heartwood contain a variety of bioactive compounds, including flavonoids, tannins, saponins, and terpenoids. These compounds have been shown to exhibit therapeutic properties in both in vitro and in vivo studies. This review highlights Pterocarpus marsupium's historical and cultural significance, its traditional applications in treating diabetes, digestive disorders, and skin conditions, and the scientific evidence supporting its medicinal claims. Additionally, the review discusses the safety profile of the plant and identifies areas for future research to further elucidate its therapeutic potential. In conclusion, Pterocarpus marsupium is a promising medicinal plant with a rich history and a promising future in natural medicine. Its bioactive compounds offer a wide range of therapeutic benefits, making it a valuable resource for the development of novel treatments for various chronic diseases.

Keywords: Indian Kino Tree, Herbal remedy, Bioactive compounds, Clinical trials, Toxicity.

1. Introduction:

Pterocarpus marsupium, commonly known as the Indian Kino Tree or Malabar Kino, is a notable species within the Fabaceae family. This evergreen tree is indigenous to the Indian subcontinent and is widely distributed across Southeast Asia. Thriving in tropical and subtropical climates, it is often found in mixed deciduous and tropical moist forests. Characterized by its distinctive dark brown to reddish-brown bark and pinnately compound leaves, Pterocarpus marsupium produces yellow to orange flowers arranged in axillary clusters. The tree's wood is valued for its durability and is used in construction and furniture making. However, it is the leaf and bark extracts that have garnered significant attention for their medicinal properties. Traditionally, Pterocarpus marsupium has been an integral part of various indigenous medical systems, particularly Ayurvedic and Unani medicine. The leaves, bark, and seeds have been used for centuries to treat a range of ailments, reflecting its deep-rooted significance in traditional healing practices. In Ayurvedic medicine, the plant is often prescribed for diabetes, digestive issues, and wounds. In recent times, interest in Pterocarpus marsupium has surged due to the growing focus on natural and alternative medicines. Scientific research has begun to validate many of the traditional uses of the plant, uncovering its diverse

bioactive compounds and their potential therapeutic benefits. The plant's extracts are now being investigated for their antioxidant, anti-inflammatory, antimicrobial, and anticancer properties, aligning with contemporary trends in pharmacognosy and phytotherapy. The increasing prevalence of chronic diseases, such as diabetes and cardiovascular disorders, has further amplified the relevance of this plant in modern medicinal research.

The primary objective of this review is to provide a comprehensive and updated account of the medicinal and bioactive properties of Pterocarpus marsupium leaves. By synthesizing existing research, this review seeks to elucidate the various therapeutic potentials of the plant, as well as its underlying mechanisms of action. The review will focus on several key areas: the phytochemical composition of the leaves, their traditional and contemporary medicinal uses, and the scientific evidence supporting these uses. Additionally, the review will explore the safety profile of Pterocarpus marsupium and identify gaps in the current knowledge base that warrant further investigation. This review will serve as a valuable resource for researchers, practitioners, and policymakers interested in the field of natural medicine and pharmacology. By integrating traditional knowledge with modern scientific findings, it aims to bridge the gap between ancient practices and contemporary health solutions. Furthermore, the review will highlight potential areas for future research, offering insights into how Pterocarpus marsupium can be leveraged in the development of new therapeutic agents and treatments.

2. Literature Review:

2.1 Botanical Description of *Pterocarpus marsupium*

Pterocarpus marsupium is a member of the Fabaceae family, which is commonly referred to as the legume, pea, or bean family. This family is one of the largest in the plant kingdom and plays a significant role in agriculture and medicine due to its nitrogen-fixing abilities and wide range of bioactive compounds. The genus *Pterocarpus* includes several species known for their medicinal properties, valuable timber, and ornamental uses.

Below is the scientific classification of *Pterocarpus marsupium*:

- **Kingdom**: Plantae
- **Clade**: Angiosperms (flowering plants)
- **Clade**: Eudicots
- **Clade**: Rosids
- **Order**: Fabales
- **Family**: Fabaceae
- **Subfamily**: Faboideae
- **Tribe**: Dalbergieae
- **Genus**: *Pterocarpus*
- **Species**: *Pterocarpus marsupium*

The species name, *marsupium*, is derived from the Latin word “marsupium,” meaning pouch or bag, which refers to the winged fruits (pods) produced by the plant. *Pterocarpus marsupium* is closely related to other species within the genus, such as *Pterocarpus santalinus* (Red Sandalwood) and *Pterocarpus angolensis* (African Teak). While these species share similarities in appearance and use, *Pterocarpus marsupium* stands out for its unique medicinal properties, especially its anti-diabetic effects.

2.2 Pterocarpus marsupium: A Botanical Profile

Pterocarpus marsupium, commonly known as the Indian kino tree or Malabar kino, is a deciduous tree native to India, Nepal, and Sri Lanka. It is renowned for its medicinal properties and its valuable timber. This majestic tree can reach heights of up to 30 meters, with a broad, spreading crown and a trunk that can attain a diameter of 1.5 meters.

Root System and Soil Preference: The tree boasts a deep and well-developed root system, particularly a strong taproot, allowing it to thrive in various soil types, including sandy and loamy soils. This adaptation enables it to access deep water sources, making it resilient to dry spells.
Stem and Bark: The stem of Pterocarpus marsupium is robust, with a thick, dark brown to reddish-brown bark. The outer surface is rough and scaly, while the inner layer is smooth and red. This bark contains a wealth of bioactive compounds, including flavonoids, tannins, and saponins, contributing to its therapeutic properties. One of the tree's most distinctive features is the reddish exudate known as "kino gum," which is rich in tannins and has been used in traditional medicine for centuries.
Leaves: The leaves of Pterocarpus marsupium are pinnately compound, consisting of several leaflets arranged along a central axis. Each compound leaf typically has 5 to 7 leaflets, which are oval or elliptical in shape with smooth margins. The leaflets exhibit reticulate venation, a characteristic feature of dicotyledonous plants. The leaves are deciduous, shedding seasonally in response to dry conditions or temperature changes.
Flowers and Fruit: The tree produces small, yellow to orange flowers arranged in axillary racemes. These flowers are bisexual and can self-pollinate or be cross-pollinated by insects. The fruit is a flat, disc-shaped pod containing one or two seeds. The pod has a winged margin that aids in wind dispersal.
Seeds: The seeds of Pterocarpus marsupium are kidney-shaped and encased within the pod. They are hard and woody and contain bioactive compounds, including oils with potential medicinal properties. The seeds can remain viable for extended periods, allowing them to germinate under favourable conditions.
Kino Gum: This reddish-brown resin, exuded when the bark is cut or injured, is a valuable byproduct of Pterocarpus marsupium. Rich in tannins, kino gum has been used in traditional medicine for centuries to treat various ailments, including diarrhoea, dysentery, and wounds. It is also valued for its antidiabetic properties.
Wood: The wood of Pterocarpus marsupium is highly prized for its durability and resistance to decay. It is used in the construction of furniture, flooring, and other woodworking applications. The wood's density, reddish-brown colour, and fine texture make it a desirable material for various purposes. Pterocarpus marsupium is a versatile and valuable plant species. Its medicinal properties, high-quality timber, and ecological significance have made it an important component of many ecosystems and traditional practices.

2.3. Pterocarpus marsupium: A Historical and Phytochemical Overview

Pterocarpus marsupium, a prominent tree in traditional Indian medicine, has been revered for centuries for its therapeutic properties. Its rich history, coupled with modern scientific research, has solidified its status as a valuable medicinal plant.

2.3.1. Historical Context: Pterocarpus marsupium in Traditional Medicine:

The use of Pterocarpus marsupium in ancient Ayurvedic and Unani systems of healing dates back centuries. The tree's bark, leaves, heartwood, and resin (kino gum) were all employed to treat various ailments. In Ayurveda, it was known as "Vijayasar" and was particularly celebrated for its anti-diabetic properties. The Charaka Samhita and Sushruta Samhita, ancient Ayurvedic texts, reference its use in treating diabetes. Beyond diabetes, the plant was also used to treat digestive disorders like diarrhoea and dysentery due to its astringent properties. Unani medicine, rooted in Greco-Arabic traditions, also recognized the plant's value. It was used for diabetes and skin conditions like eczema and psoriasis. The cooling, astringent, and anti-inflammatory properties of the tree were employed in formulations to reduce skin irritation and promote wound healing. During the British colonial era, European physicians and botanists became acquainted with Pterocarpus marsupium, particularly its kino gum. Its astringent properties were recognized as effective in controlling internal bleeding and diarrhoea, leading to its incorporation into Western pharmacopoeias.

2.3.2. Cultural Significance: Regional Applications and Practices

Pterocarpus marsupium is deeply intertwined with the cultural practices of the regions where it grows. In India, it is often associated with longevity, health, and resilience. In certain regions, parts of the tree are used during religious rituals, with its gum employed as a sacred offering. In Sri Lanka, the tree is known as "Gammalu" and is used by traditional healers to treat diabetes, inflammation, and skin diseases. In Nepal, it is known as "Bijaysar" and is traditionally used to treat diabetes and gastrointestinal issues. Throughout its native range, Pterocarpus marsupium is valued for its role in maintaining environmental balance. It provides shelter and food for various animal species, contributing to the ecosystem's health.

2.3.3. Phytochemical Composition of Pterocarpus marsupium

The therapeutic potential of *Pterocarpus marsupium* is largely attributed to its rich phytochemical profile, which includes a variety of primary and secondary metabolites with significant bioactive properties. These compounds are responsible for the plant's anti-diabetic, antioxidant, anti-inflammatory, and antimicrobial effects, making it a valuable resource in traditional and modern medicine. Below is an overview of the major classes of metabolites found in *Pterocarpus marsupium*, as well as the common extraction methods used to isolate these bioactive compounds.

A. Primary Metabolites

1. Flavonoids

Flavonoids are one of the most important classes of phytochemicals in *Pterocarpus marsupium*, known for their strong antioxidant properties. These compounds help protect cells from oxidative damage and have been linked to the plant's anti-diabetic and anti-inflammatory effects.

Epicatechin: One of the key flavonoids found in *Pterocarpus marsupium* is epicatechin. It is primarily responsible for the plant's anti-diabetic action by enhancing insulin activity and improving glucose metabolism. Epicatechin also acts as a potent antioxidant, protecting pancreatic beta cells from oxidative stress, which is a common factor in the progression of diabetes.

Pterosupin and **Pterostilbene**: These are other notable flavonoid compounds that contribute to the plant's anti-inflammatory and cardioprotective effects. Pterostilbene, in particular, has been shown to reduce blood glucose levels, improve lipid profiles, and exhibit anti-cancer properties, which broadens the medicinal value of *Pterocarpus marsupium*.

2. Saponins

Saponins are another class of bioactive compounds present in *Pterocarpus marsupium*, contributing to its therapeutic properties, particularly in reducing cholesterol and exhibiting anti-microbial activities. These compounds are known for their ability to lower blood cholesterol by binding with bile acids and preventing their reabsorption in the intestine.

Glycosides: Saponins are glycosidic in nature, meaning they consist of a sugar moiety attached to a triterpenoid or steroid aglycone. This structure allows them to interact with various biological systems, including acting as immune system modulators and exhibiting antifungal and antibacterial properties. In *Pterocarpus marsupium*, saponins enhance the plant's ability to heal wounds and treat skin infections.

3. Tannins

Tannins are polyphenolic compounds that give *Pterocarpus marsupium* its astringent properties, making it effective in treating gastrointestinal disorders such as diarrhoea and dysentery. The high tannin content in the bark, heartwood, and leaves of the plant contributes to its ability to reduce inflammation and protect tissues from oxidative damage.

Catechol tannins: These are the primary types of tannins found in *Pterocarpus marsupium*. They are known for their strong antioxidant properties, which play a critical role in neutralizing free radicals and protecting against cellular damage. Tannins also contribute to the plant's anti-microbial effects, making it useful in treating infections.

Gallic acid derivatives: These are another form of tannins present in the plant, which exhibit potent anti-inflammatory and antioxidant effects. Gallic acid and its derivatives help in the management of chronic conditions like diabetes by modulating glucose metabolism and reducing oxidative stress in tissues.

B. Secondary Metabolites

Secondary metabolites, while not directly involved in the growth and reproduction of the plant, play a crucial role in its defence mechanisms and bioactive properties. These lesser-known compounds contribute to *Pterocarpus marsupium*'s pharmacological effects, though they are not as abundant as primary metabolites.

1. Terpenoids

Terpenoids, also known as isoprenoids, are a diverse class of secondary metabolites with a wide range of biological activities, including anti-inflammatory, antimicrobial, and anticancer properties.

Lupeol: One of the key terpenoids found in *Pterocarpus marsupium*, lupeol has strong anti-inflammatory properties, making it effective in reducing swelling and pain associated with conditions like arthritis. Additionally, lupeol has been studied for its potential in cancer prevention and treatment, as it can inhibit the growth of cancer cells.

2. Alkaloids

Alkaloids are nitrogen-containing secondary metabolites known for their pharmacological activity, including analgesic and antimicrobial properties. Although *Pterocarpus marsupium* is not primarily known for its alkaloid content, minor alkaloid compounds present in the plant may contribute to its overall therapeutic effects.

Isoflavones: Isoflavones are a specific type of flavonoid with estrogenic properties, and they are present in small quantities in *Pterocarpus marsupium*. These compounds may play a role in promoting cardiovascular health and protecting against hormone-related diseases.

3. Sterols

Plant sterols, or phytosterols, are structurally similar to cholesterol and have been linked to cardiovascular health. They help reduce cholesterol absorption in the intestines, contributing to the hypocholesterolemic effect of *Pterocarpus marsupium*.

Beta-sitosterol: This is the most common phytosterol found in *Pterocarpus marsupium*. It has been shown to reduce cholesterol levels, support prostate health, and exhibit anti-cancer properties. Beta-sitosterol is also known to possess anti-inflammatory properties, which enhance the overall medicinal potential of the plant.

4. Lignans

Lignans are another group of secondary metabolites present in small amounts in *Pterocarpus marsupium*. These compounds have been shown to possess anti-cancer, anti-inflammatory, and antioxidant properties. They work by scavenging free radicals and protecting cells from oxidative damage, which is particularly useful in treating chronic diseases such as cancer and cardiovascular disorders.

Pinoresinol: One of the lignans found in *Pterocarpus marsupium*, pinoresinol, has demonstrated anti-cancer properties, particularly in inhibiting the proliferation of cancer cells and inducing apoptosis (programmed cell death) in tumour cells.

2.5 Medicinal Properties of *Pterocarpus marsupium*

Pterocarpus marsupium has been extensively studied for its medicinal properties, which are attributed to the bioactive compounds found in its bark, heartwood, leaves, and resin. This plant has demonstrated therapeutic effects in various areas of health, ranging from antioxidant and anti-inflammatory activities to antidiabetic and antimicrobial properties. Below is a detailed overview of the key medicinal properties of *Pterocarpus marsupium* based on scientific evidence and traditional uses.

2.5.1 Antioxidant Activity

Evidence and Mechanisms:

The antioxidant activity of *Pterocarpus marsupium* is one of its most well-documented medicinal properties, primarily attributed to the presence of flavonoids (such as epicatechin), tannins, and phenolic compounds. These compounds help neutralize reactive oxygen species (ROS) and prevent oxidative damage to cells, which is a key factor in the development of chronic diseases such as diabetes, cardiovascular disease, and cancer.

Mechanism of Action: Flavonoids and tannins scavenge free radicals, stabilize cell membranes, and inhibit lipid peroxidation, which is the oxidative degradation of lipids that leads to cell damage. The antioxidant activity of *Pterocarpus marsupium* also involves enhancing the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase, which play a crucial role in maintaining cellular homeostasis. Research has demonstrated that extracts from *Pterocarpus marsupium* exhibit significant antioxidant activity in both in vitro and in vivo studies. For instance, a study showed that the methanolic extract of *Pterocarpus marsupium* heartwood significantly reduced oxidative stress in diabetic rats by decreasing malondialdehyde (MDA) levels and enhancing the activity of antioxidant enzymes.

2.5.2 Anti-inflammatory Activity

Findings from Studies:

The anti-inflammatory properties of *Pterocarpus marsupium* are closely linked to its flavonoid content, especially epicatechin and pterostilbene. These compounds have been shown to reduce inflammation by inhibiting the production of pro-inflammatory cytokines and enzymes such as cyclooxygenase (COX) and lipoxygenase (LOX).

Mechanism of Action: The anti-inflammatory action of *Pterocarpus marsupium* is mediated through the inhibition of nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) signalling pathways, which are responsible for the expression of pro-inflammatory cytokines like tumour necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). By downregulating these pathways, *Pterocarpus marsupium* reduces the inflammatory response in tissues. Several animal studies have confirmed the anti-inflammatory effects of *Pterocarpus marsupium*. In one study, an extract of the plant significantly reduced paw edema in rats induced by carrageenan, a substance commonly used to simulate inflammation in experimental models. This effect was comparable to standard anti-inflammatory drugs such as indomethacin.

2.5.3 Antidiabetic Effects

Impact on Blood Glucose Levels and Insulin Sensitivity:

One of the most well-known medicinal uses of *Pterocarpus marsupium* is in the treatment of diabetes. The plant has been traditionally used to manage blood glucose levels, and scientific studies have confirmed its efficacy in lowering blood sugar and improving insulin sensitivity.

Mechanism of Action: The anti-diabetic effects of *Pterocarpus marsupium* are primarily attributed to the flavonoid epicatechin, which enhances insulin secretion, improves glucose uptake, and increases insulin sensitivity in peripheral tissues. Additionally, the plant's compounds inhibit alpha-glucosidase and alpha-amylase enzymes, which are responsible for the breakdown of carbohydrates into glucose, thereby reducing postprandial blood sugar spikes. Research has shown that extracts of *Pterocarpus marsupium* significantly lower blood glucose levels in both diabetic and non-diabetic animal models. In one study, diabetic rats treated with the plant extract showed a marked improvement in insulin sensitivity and a reduction in fasting blood glucose levels. Another clinical study in humans demonstrated that water stored in cups made from *Pterocarpus marsupium* heartwood significantly lowered blood glucose levels in individuals with type 2 diabetes.

2.5.4 Antimicrobial Properties

Efficacy Against Bacteria and Fungi:

Pterocarpus marsupium has demonstrated antimicrobial activity against a range of pathogenic bacteria and fungi, making it a valuable natural remedy for treating infections. The antimicrobial effects are primarily due to the presence of tannins, flavonoids, and phenolic compounds in the plant.

Mechanism of Action: The antimicrobial activity of *Pterocarpus marsupium* is believed to involve disrupting the cell membranes of bacteria and fungi, leading to cell death. Tannins, in particular, can precipitate microbial proteins, rendering them inactive. Additionally, phenolic compounds inhibit the growth of microbes by interfering with their enzymatic processes and metabolism. In vitro studies have shown that extracts of *Pterocarpus marsupium* exhibit strong antibacterial activity against both Gram-positive bacteria (such as *Staphylococcus aureus* and *Bacillus subtilis*) and Gram-negative bacteria (such as *Escherichia coli* and *Pseudomonas aeruginosa*). The plant has also shown antifungal activity against species like *Candida albicans*, which causes infections in humans.

2.5.5 Anticancer Potential

Research on Cancer Cell Lines and Mechanisms of Action:

The anticancer potential of *Pterocarpus marsupium* is an emerging area of research, with studies showing that certain bioactive compounds in the plant, such as pterostilbene and epicatechin, exhibit anti-cancer properties by inhibiting the growth and proliferation of cancer cells.

Mechanism of Action: The anticancer effects of *Pterocarpus marsupium* are mediated through several mechanisms, including the induction of apoptosis (programmed cell death) in cancer cells, inhibition of angiogenesis (formation of new blood vessels that support tumour growth), and cell cycle arrest. Pterostilbene, in particular, has been shown to activate pro-apoptotic proteins such as caspases, which play a crucial role in the apoptosis pathway. Research on cancer cell lines has demonstrated that *Pterocarpus marsupium* extracts can inhibit the proliferation of various cancer cells, including breast, colon, and lung cancer cells. In one study, pterostilbene was shown to induce apoptosis in human colon cancer cells by activating the mitochondrial pathway of cell death.

2.5.6 Cardiovascular Health: Effects on Blood Pressure, Cholesterol, etc.:

Pterocarpus marsupium has been shown to have a beneficial effect on cardiovascular health by regulating blood pressure, improving lipid profiles, and reducing the risk of atherosclerosis.

Mechanism of Action: The cardiovascular benefits of *Pterocarpus marsupium* are due to its antioxidant, anti-inflammatory, and hypolipidemic effects. Flavonoids like epicatechin improve endothelial function by increasing nitric oxide (NO) production, which helps relax blood vessels and lower blood pressure. Additionally, beta-sitosterol, a phytosterol present in the plant, reduces cholesterol absorption in the intestines, leading to lower LDL cholesterol levels. Animal studies have demonstrated that *Pterocarpus marsupium* extracts can reduce systolic blood pressure in hypertensive rats. Moreover, studies in diabetic and hyper lipidemic animals have shown that the plant reduces

total cholesterol, triglycerides, and LDL cholesterol while increasing HDL cholesterol, which is protective against heart disease.

2.5.7 Other Therapeutic Effects

1. Hepatoprotective Effects:

Pterocarpus marsupium has shown hepatoprotective properties, protecting the liver from damage caused by toxins and oxidative stress. The antioxidant compounds in the plant help neutralize free radicals and prevent lipid peroxidation, which is a key factor in liver damage. Animal studies have demonstrated that *Pterocarpus marsupium* extracts can reduce liver enzyme levels (such as ALT and AST), which are markers of liver damage, in rats exposed to toxic chemicals like carbon tetrachloride.

2. Wound Healing:

The tannins and flavonoids present in *Pterocarpus marsupium* contribute to its wound-healing properties. These compounds promote tissue repair, reduce inflammation, and exhibit antimicrobial effects that help prevent infections in wounds. Research on wound healing has shown that topical application of *Pterocarpus marsupium* extract accelerates the closure of wounds in animal models by promoting collagen synthesis and reducing inflammation.

3. Gastroprotective Effects:

The plant has also been used traditionally to treat gastrointestinal disorders, such as ulcers and diarrhoea. The tannins and saponins in *Pterocarpus marsupium* exert a protective effect on the gastric mucosa, preventing ulcer formation and promoting healing. Studies have shown that *Pterocarpus marsupium* extracts reduce the severity of gastric ulcers in animal models, possibly by enhancing mucus production and reducing acid secretion.

3. Result and Discussion:

3.1 Mechanisms of Action of *Pterocarpus marsupium* Bioactive Compounds

The medicinal properties of *Pterocarpus marsupium* are primarily attributed to the diverse array of bioactive compounds it contains, such as flavonoids, tannins, terpenoids, and phenolic compounds. These compounds interact with various molecular targets and cellular pathways, modulating physiological processes that contribute to its antioxidant, anti-inflammatory, antidiabetic, antimicrobial, anticancer, and cardiovascular benefits. Understanding these mechanisms at the molecular and cellular levels is key to appreciating the therapeutic potential of the plant.

3.2 Molecular Targets: Key Pathways and Targets Influenced by Bioactive Compounds

3.2.1 Nuclear Factor-kappa B (NF-κB) Pathway

The NF-κB pathway plays a central role in regulating the immune response, inflammation, and cell survival. Chronic activation of NF-κB is linked to several diseases, including cancer, diabetes, and inflammatory disorders. Flavonoids like epicatechin and pterostilbene found in *Pterocarpus marsupium* inhibit the activation of NF-κB, reducing the expression of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β. By blocking this pathway, these compounds help mitigate inflammation and prevent the progression of inflammatory diseases like arthritis and inflammatory bowel disease. Inhibition of the NF-κB pathway results in reduced inflammation, less tissue damage, and a lower risk of chronic diseases associated with prolonged inflammation.

3.2.2 Mitogen-Activated Protein Kinase (MAPK) Pathway

The MAPK signalling pathway regulates cell proliferation, differentiation, and apoptosis. Dysregulation of this pathway can lead to cancer, diabetes, and neurodegenerative diseases. Pterostilbene, a potent stilbenoid found in *Pterocarpus marsupium*, has been shown to inhibit MAPK signalling, particularly in cancer cells. By disrupting this pathway, pterostilbene induces apoptosis (programmed cell death) in cancer cells and prevents their uncontrolled growth. Inhibition of the

MAPK pathway triggers apoptosis in cancerous cells while sparing healthy cells, contributing to the plant's anticancer potential.

3.2.3 Peroxisome Proliferator-Activated Receptors (PPARs)

PPARs are nuclear receptors that regulate glucose and lipid metabolism, making them critical targets in the management of metabolic diseases such as diabetes and dyslipidemia. Epicatechin and pterostilbene modulate PPARγ activity, which plays a key role in enhancing insulin sensitivity and reducing blood glucose levels. By activating PPARγ, these compounds improve glucose uptake in skeletal muscle and adipose tissue and increase insulin sensitivity, which is particularly beneficial for individuals with type 2 diabetes. Activation of PPARγ enhances insulin sensitivity and helps control blood glucose levels, reducing the severity of diabetes and preventing diabetic complications.

3.2.4 Adenosine Monophosphate-Activated Protein Kinase (AMPK) Pathway

AMPK is an energy-sensing enzyme that regulates cellular energy homeostasis. Activation of AMPK leads to improved glucose uptake, fatty acid oxidation, and mitochondrial biogenesis, making it a key therapeutic target for metabolic disorders. Flavonoids such as epicatechin activate AMPK in liver and muscle cells, leading to increased glucose uptake and reduced hepatic glucose production. This mechanism contributes to the antidiabetic effects of *Pterocarpus marsupium* by lowering blood sugar and improving insulin sensitivity. AMPK activation promotes glucose uptake and fatty acid oxidation, which helps regulate blood sugar levels and enhances metabolic health.

3.2.5 Phosphoinositide 3-Kinase (PI3K)/Akt Pathway

The PI3K/Akt pathway plays a critical role in cell survival, proliferation, and glucose metabolism. It is often dysregulated in cancer and diabetes. Epicatechin and other flavonoids from *Pterocarpus marsupium* activate the PI3K/Akt pathway, leading to improved glucose transport into cells by increasing the translocation of glucose transporter type 4 (GLUT4) to the cell membrane. This action improves glucose uptake and utilization, enhancing insulin sensitivity. Activation of the PI3K/Akt pathway improves glucose metabolism and contributes to the antidiabetic effects of *Pterocarpus marsupium*, while also supporting cell survival and reducing apoptosis in non-cancerous tissues.

3.3 Safety and Toxicity of *Pterocarpus marsupium*

While *Pterocarpus marsupium* is recognized for its significant medicinal properties, understanding its safety profile and potential toxicity is crucial for ensuring its safe use. This includes evaluating any known side effects, assessing toxicological data, and establishing appropriate dosage ranges.

3.3.1 Toxicological Data: Known Side Effects and Safety Profile

1. General Safety Profile

Pterocarpus marsupium is generally considered safe when used appropriately, particularly in traditional medicine practices. However, like any medicinal plant, it can have adverse effects if used improperly or in excessive amounts.

- **Adverse Effects**: In clinical and animal studies, *Pterocarpus marsupium* extracts have been reported to cause mild gastrointestinal disturbances, such as nausea and diarrhea, in some individuals. These side effects are usually transient and resolve once the dosage is adjusted or the treatment is discontinued.
- **Hypoglycemic Effects**: The plant's strong antidiabetic properties, while beneficial for managing blood glucose levels, can lead to hypoglycemia (abnormally low blood sugar) if not monitored carefully. This is particularly important for diabetic patients who are already on hypoglycemic medications. Symptoms of hypoglycemia include dizziness, sweating, and shakiness.
- **Allergic Reactions**: Although rare, some individuals may experience allergic reactions to *Pterocarpus marsupium* extracts, which can include skin rashes, itching, or swelling. These reactions are usually dose-dependent and may be mitigated by reducing the dosage or discontinuing use.

2. Toxicological Studies

- **Acute Toxicity**: Studies assessing the acute toxicity of *Pterocarpus marsupium* have shown that the plant extracts have a relatively low acute toxicity profile. In animal studies, high doses of *Pterocarpus marsupium* extracts did not result in severe toxicity or mortality, suggesting a wide safety margin. However, it is always important to follow recommended dosages to avoid potential adverse effects.
- **Chronic Toxicity**: Long-term studies on the chronic toxicity of *Pterocarpus marsupium* are limited. Preliminary studies indicate that long-term use at recommended doses does not cause significant adverse effects or organ damage. However, comprehensive studies are needed to fully understand the long-term safety profile, especially for chronic conditions requiring extended use of the plant.
- **Interaction with Medications**: *Pterocarpus marsupium* may interact with certain medications, particularly those used for diabetes and hypertension. The plant's hypoglycemic effects could potentially enhance the effects of antidiabetic drugs, leading to an increased risk of hypoglycemia. Similarly, its effects on blood pressure and lipid levels may interact with antihypertensive and lipid-lowering medications. Patients should consult healthcare providers before combining *Pterocarpus marsupium* with other medications.

3.3.2 Dosage and Administration: Effective and Safe Dosage Ranges

1. Traditional Dosages

In traditional medicine, *Pterocarpus marsupium* is used in various forms, including decoctions, powders, and extracts. The dosages typically depend on the preparation and the condition being treated.

- **Decoctions**: Traditional preparations often involve boiling the plant's bark or leaves in water. Commonly, 1-2 grams of dried plant material is used per cup of water, consumed 1-2 times daily.
- **Powdered Form**: The powdered form of the plant is usually taken in doses of 500 mg to 1 gram per day. This form is often used in combination with other herbs in traditional formulations.

2. Clinical Dosages

Clinical studies on *Pterocarpus marsupium* have provided more standardized dosage recommendations based on its bioactivity and safety profile.

- **Extracts**: In clinical settings, standardized extracts of *Pterocarpus marsupium* are commonly used. Effective doses of standardized extracts range from 200 mg to 500 mg daily, depending on the concentration of the active compounds and the condition being treated.
- **Tablets/Capsules**: Commercially available tablets or capsules containing *Pterocarpus marsupium* extract typically provide doses of 250 mg to 500 mg per tablet or capsule. The usual recommendation is 1-2 tablets or capsules taken 1-2 times daily, depending on the product's specific formulation and the condition being treated.
- **Safety Margin**: While *Pterocarpus marsupium* is generally safe at recommended dosages, it is important to start with the lowest effective dose and gradually increase it as needed. This approach helps minimize the risk of adverse effects and allows for monitoring of any potential reactions.

3. Recommendations for Use

- **Consultation**: Individuals considering the use of *Pterocarpus marsupium* should consult a healthcare provider, particularly if they have pre-existing conditions, are pregnant or breastfeeding, or are taking other medications.
- **Monitoring**: Regular monitoring of blood glucose levels is recommended for individuals with diabetes using *Pterocarpus marsupium* to avoid hypoglycemia. Similarly, monitoring of blood pressure and lipid levels may be necessary for those using the plant for cardiovascular health.
- **Avoiding Overuse**: Adhering to recommended dosages and avoiding excessive use are crucial to prevent potential side effects and interactions with other medications.

4. Conclusion:

1. Further Pharmacological Research

While current research highlights the significant medicinal properties of *Pterocarpus marsupium*, further pharmacological studies are essential to fully understand its mechanisms of action and therapeutic potential. Future research should focus on:

- **Mechanistic Studies**: Investigating the detailed molecular mechanisms underlying the plant's effects on various pathways, such as NF-κB, MAPK, PPARs, AMPK, and PI3K/Akt, will provide deeper insights into how its bioactive compounds exert their beneficial effects.
- **Bioavailability and Metabolism**: Understanding the bioavailability, metabolism, and pharmacokinetics of key compounds like pterostilbene and epicatechin will help optimize dosing regimens and improve therapeutic efficacy.
- **Long-Term Safety**: Conducting long-term safety studies to evaluate the chronic toxicity and potential side effects of prolonged use will ensure the plant's safety for extended therapeutic applications.

2. Clinical Trials and Standardization

To translate the promising preclinical findings into clinical practice, well-designed clinical trials are necessary. Future research should focus on:

- **Clinical Efficacy**: Conducting randomized controlled trials to confirm the efficacy of *Pterocarpus marsupium* in managing specific conditions, such as diabetes, cardiovascular diseases, and cancer, will validate its therapeutic benefits and establish evidence-based guidelines.
- **Standardization**: Developing standardized extracts with consistent concentrations of active compounds will enhance the reliability and reproducibility of clinical outcomes. Establishing quality control measures and dosage recommendations will ensure the safe and effective use of the plant in various formulations.

3. Exploring Synergistic Effects

Investigating the synergistic effects of *Pterocarpus marsupium* in combination with other medicinal plants or conventional treatments could enhance therapeutic outcomes. Research should focus on:

- **Combination Therapies**: Evaluating the potential of *Pterocarpus marsupium* in combination with other herbs or pharmaceuticals to improve efficacy, reduce side effects, and address complex health conditions.
- **Mechanistic Synergy**: Studying how the plant's bioactive compounds interact with other drugs or natural products at the molecular level can reveal potential synergistic effects and optimize treatment strategies.

4. Ethnobotanical and Environmental Research

Exploring the ethnobotanical uses and environmental factors affecting the plant's medicinal properties will provide valuable insights for sustainable utilization.

- **Ethnobotanical Surveys**: Conducting surveys to document traditional uses and practices related to *Pterocarpus marsupium* can uncover additional therapeutic applications and cultural significance.
- **Sustainable Cultivation**: Investigating cultivation practices, environmental conditions, and conservation strategies will ensure a sustainable supply of *Pterocarpus marsupium* and protect its natural habitats.

Pterocarpus marsupium is a remarkable medicinal plant with a wide range of therapeutic properties supported by both traditional knowledge and scientific research. Its bioactive compounds, including flavonoids, tannins, and terpenoids, have demonstrated significant antioxidant, anti-inflammatory, antidiabetic, antimicrobial, anticancer, and cardiovascular benefits. The plant's diverse medicinal applications highlight its potential as a valuable resource for improving human health.

Despite its promising therapeutic potential, further research is needed to fully understand the mechanisms of action, optimize dosage, and ensure long-term safety. Future studies should focus on

detailed pharmacological investigations, clinical trials, standardization of extracts, and exploration of synergistic effects to maximize the plant's benefits and establish evidence-based guidelines for its use.

In addition to its medicinal value, *Pterocarpus marsupium* offers opportunities for sustainable development and conservation. By integrating ethnobotanical knowledge with modern scientific research, we can enhance our understanding of this valuable plant and promote its responsible use for the benefit of global health.

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