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CISSAMPELOS PAREIRA: AN INTEGRATIVE REVIEW OF ITS ETHNOBOTANY, PHYTOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY, AND THERAPEUTIC POTENTIAL

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ABSTRACT

Background: Medicinal plants are vital for safe and compatible healthcare. The liver, central to detoxification, is vulnerable to drug-induced damage. Herbal compounds treat liver disorders, with growing evidence supporting their hepatoprotective effects**. Objectives:** This review bridges traditional ethnobotany with modern phytochemical and pharmacological evidence for *Cissampelos pareira L.*, highlighting its hepatoprotective and antioxidant activities, other preclinical bioactivities, safety profile, and key research gaps. **Methods:** A structured literature review synthesized ethnobotanical records, phytochemical data, and preclinical pharmacological studies from scientific databases. Traditional uses, morphology, phytochemistry, antioxidant and hepatoprotective assays, other bioactivities (immunomodulatory, antidiabetic, anti-asthmatic), and toxicology data were extracted and analyzed. **Findings*:*** *C.pareira* contains alkaloids, phenolics, and volatile oils. It shows strong antioxidant activity and hepatoprotection against CCl_4 and drug-induced liver injury. Additional effects include immunomodulatory, antidiabetic, anti-asthmatic, antiprotozoal, and cardioprotective activities. Acute toxicity suggests a wide safety margin, but anti-fertility and hormone-altering effects warrant caution. **Conclusion:** *C.pareira* is supported by ethnopharmacological and preclinical evidence as a promising hepatoprotective, multipotent bioactive source. Key gaps include alkaloid isolation, chemotype and quality-control validation, mechanism studies, ADME/PK and drug–herb interactions, chronic/reproductive toxicity, and early clinical trials. Filling these will clarify its liver disorder potential and enable evidence-based development.

KEYWORDS: Medicinal plants, Herbal remedies, Traditional medicine, Phytotherapy, Ethnobotony.

INTRODUCTION

Medicinal plants are essential to global healthcare, used both for treating illness and promoting wellness. Their extensive use in primary care is driven by cultural acceptance, biological suitability, and a lower risk of side effects. These plants have played an important historical role and continue to serve as a source of numerous compounds used in modern medicine.[1] Plants have served as medicines since antiquity; India's diverse aromatic and medicinal flora underpins traditional therapeutics. Secondary plant metabolites distinct from universal primary metabolites are especially valued for their pharmacological activity.[2]

The liver maintains metabolic homeostasis and mediates biotransformation, detoxification, and elimination of endogenous and exogenous substances, including drugs and environmental chemicals. Drug-induced hepatotoxicity is an important iatrogenic problem, responsible for approximately 1 in 600 to 1 in 3,500 hospital admissions.[3] Reliable hepatoprotective agents are urgently needed in modern medicine. Plants and natural products have long been used globally to prevent and treat liver disorders, and substantial research has confirmed the hepatoprotective effects of several herbal compounds.[4]

The term "hepatic disease" covers a wide range of disorders affecting the liver's tissues, structures, and cells. Because the liver carries out many vital functions, it is susceptible to various injuries. Liver disease is frequently associated with inflammation resulting from factors such as alcohol abuse, poor nutrition, and inadequate dietary intake.[5] Drug-induced liver injury is a major healthcare and regulatory challenge. According to the U.S. Acute Liver Failure Study Group, drugs cause over half of acute liver failure cases, driven largely by acetaminophen overdoses (39%) and idiosyncratic reactions to other medications.[6] Hepatocellular damage can result from toxic chemicals (some antibiotics, chemotherapeutics, carbon tetrachloride, thioacetamide), excessive alcohol intake, and infectious agents.[7]

Cissampelos pareira (*Menispermaceae*) is India's only *Cissampelos* species, a perennial climber up to 2000 m. Known as Patha or Ambastha, its bitter root is traditionally used for fever, diarrhea, wounds, respiratory and urinary disorders, snakebite, malaria, and female reproductive complaints. Modern research reports antipyretic, antidiarrheal, cardioprotective, immunomodulatory, antioxidant, anthelmintic, antiviral, antiprotozoal, and antileukemic activities, attributed mainly to benzyl- and bisbenzylisoquinoline alkaloids. This review connects traditional use with pharmacological and phytochemical evidence to highlight active compounds and research needs.[8]

Cissampelos has a pantropical distribution. The name combines Greek kissos (ivy) and ampelos (vine); pareira reflects a Portuguese term for wild-vine roots. *Cissampelos pareira* L., traditionally recognized as Patha in Ayurveda, is frequently used together with *Stephania japonica* and *Cyclea peltata*, is also called the "midwife's herb" in South America, where its root treats menstrual pain, threatened miscarriage, postpartum hemorrhage, and childbirth discomfort.[9]

Cissampelos pareira Linn (Menispermaceae) is a climbing shrub (2–5 m) with a thickened root, orbicular leaves (7–14 cm), and variable indumentum from glabrous to densely pilose. Male flowers form short umbels (10–12 cm) and females appear in pendulous spikes (7–10 cm), each with a small rounded bract at the flower base. The taxonomy is unsettled, with about 37 names allied to *Cissampelos* and frequent use of *C. pareira* or "pareira" as an umbrella designation; the species occurs across subtropical India, Asia, East Africa, and the America.[10]

Plant profile

- **Kingdom** : *Plantae*
- **Phylum** : *Magnoliophyta*
- **Class** : *Magnoliopsida*
- **Order** : *Ranunculales*
- **Family** : *Menispermaceae*
- **Genus** : *Cissampelos L.*
- **Species** : *C. pareira*

Geographical distribution

Cissampelos has a broad pantropical distribution. *Cissampelos pareira* occurs across Africa, Asia, the Americas and numerous islands (including Brazil, Mexico, Peru, Argentina, Indo-China, Southern China, Malaysia, Thailand, India, Pakistan, much of sub-Saharan Africa, Australia, the West Indies, Comoros, Mauritius, Seychelles, and Madagascar) and is reported from Indian states such as Himachal Pradesh, Punjab, Rajasthan, West Bengal, Bihar, and Tamil Nadu.[8]

Morphological description

Habit: *Cissampelos pareira* is a perennial, climbing shrub with twining stems that can extend up to 2–5 meters along the ground, often supported by trees or their canopies.

Stem: Its stems are slender, flexible, and twining for support, reaching a maximum diameter of 1 cm.

Leaves: The leaves are simple, membranous, and alternate, with an oblong to cordate or truncate base. They feature 4–7 palmate nerves, are somewhat peltate, and have petioles inserted slightly inward from the blade margin. Fully mature leaves display a thickly velvety pubescent or silky-hairy lamina dark green above, lighter green below earning it the common name "velvet leaf," with sparse silky hairs on both surfaces.

Flower: The flowers are small, dioecious, unisexual, and greenish, borne in tiny inflorescences in the leaf axils. Male inflorescences measure 10–12 cm long and consist of small umbels, typically grouped in 1–3.

Fruit: The fruits are round, red-orange, hairy drupes, measuring 4–5 mm in diameter, single-seeded, and partially enclosed by a rounded bract. The seeds exhibit a distinctive horseshoe shape.

Root: The roots are cylindrical, often tortuous, measuring 1–1.5 cm in diameter, and light brown externally. Their surface appears rough and sometimes rugged due to transverse wrinkles, cracks, and fissures; they break with a short, splintery fracture, emit a faint aromatic odour, and have a distinctly bitter taste.[8]

Phytochemistry

Qualitative phytochemical screening: [11-15]

Chemical tests were performed using solvents including methanol, ethyl acetate, acetone, water, and hexane to detect various phytochemical constituents.

Alkaloids

Plant extracts were treated with Mayer's reagent, prepared by dissolving 1.36 g mercuric chloride and 5 g potassium iodide in 100 mL distilled water. Formation of a yellow-cream precipitate indicates the presence of alkaloids

Carbohydrates

Molisch Test: Plant extracts were mixed with 2 drops of alcoholic α-naphthol solution in a test tube, followed by careful addition of 2 mL concentrated H_2SO_4 along the tube's sides. A dull violet or crimson ring at the interface confirms the presence of carbohydrates.

Tannin Detection: To 1 mL of plant extract, a few drops of 1% $FeCl_3$ solution were added. Development of a blue, black, green, or bluish-green precipitate indicates tannins.

Protein and amino acid test

Ninhydrin Test: Plant extract was treated with 0.25% ninhydrin reagent and gently boiled. Formation of a purple or bluish color indicates the presence of amino acids.

Detection of phenols

Ferric Chloride Test: One mL of plant extract was diluted with 3 mL distilled water, then a few drops of neutral 5% $FeCl_3$ solution were added. A dark green color signals the presence of phenolic compounds.

Volatile Oils Detection: One mL plant extract was combined with 1 mL 90% ethanol, followed by a few drops of $FeCl_3$. A green coloration confirms the presence of volatile oils.

Detection of reducing sugar

Benedict's Test: Plant extracts were mixed with Benedict's reagent and heated in a water bath. An orange-red precipitate indicates the presence of reducing sugars.

Detection of Steriods

Salkowski Test: To 0.5 g of ethanol extract, 2 mL acetic anhydride and 2 mL H_2SO_4 were added. A color change from violet to blue or green confirms steroids.

Pharmacology [16-21]

Hepatoprotective Effects

Hydroalcoholic extracts from the plant exhibited protective activity against hepatotoxicity in Wistar albino rats induced by anti-tuberculosis drugs. Similarly, the root hydroalcoholic extract showed significant hepatoprotection against carbon tetrachloride (CCl4)-induced liver damage.[16]

Anti-infertility

Oral administration of *Cissampelos pareira* leaf extract altered the estrous cycle in female albino mice, resulting in an increased overall cycle duration, a significant prolongation of the diestrus phase, and a marked reduction in litter size.

Analysis of key regulatory hormones revealed that the extract altered gonadotropin secretion (including LH, FSH, and prolactin) as well as estradiol levels. Additionally, the oral LD50 of the extract in mice was determined to be 7.3 g/kg.[17]

Anti-oxidant activity

The 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay demonstrated substantial antioxidant potential in the *C. pareira* extract. The extract demonstrated potent in vitro antioxidant activity by effectively scavenging nitric oxide, hydrogen peroxide, superoxide, and hydroxyl radicals at concentrations ranging from 50 to 400 μg/mL. Moreover, it inhibited hydroxyl radical-mediated protein oxidation *in vitro*. *In vivo*, *C. pareira* extract provided robust protection against acute oxidative damage, as evidenced by its ability to mitigate benzo[a]pyrene-induced gastrointestinal toxicity in a mouse model.[18]

Immunomodulatory activity

Isoquinoline alkaloids have gained significant attention in recent studies for their diverse pharmacological effects, including antibacterial, anticancer, neuroprotective, and immunosuppressive activities. Given that certain members of this class are already employed in clinical therapies, exploring their influence on immune function holds considerable promise.[19]

Anti-diabetic activity

The aqueous leaf extract of *C. pareira* demonstrated notable anti-diabetic effects. Male albino mice received oral doses of 250 mg/kg or 500 mg/kg body weight daily for 14 days. Throughout the experiment, researchers periodically tracked body weight and blood glucose levels, alongside other biochemical parameters such as liver glycogen content.[20]

Anti-asthmatic activity

In various animal models of asthma, the aqueous fraction derived from the ethanolic leaf extract of *C. pareira* exhibits immunomodulatory activity. This fraction elevates anti-inflammatory cytokine levels, suppresses antigen-specific immunoglobulin production, and attenuates mucus secretion and accumulation in the airways.[21]

Toxicology studies

Acute toxicity: Throughout the 14-day study period, no mortality was observed in male or female animals administered 2 g/kg of the 50% aqueous ethanolic extract of *Cissampelos pareira* orally. During the observation period, the animals exhibited no changes in general appearance or behavior.

General signs: In this study, no mortality was observed, and no clinically significant changes were noted in general behavior or other physiological parameters.[22]

Traditional Uses

Ethnobotanical studies identify *C. pareira* as one of the most commonly used *Cissampelos* species with longstanding traditional applications. In Ayurveda it is known as Patha and features in formulations such as Brhatgangadhara churna, Pusyanuga churna, Pradarantaka lauha, and Sarasvata ghrita. According to the Ayurvedic Pharmacopoeia of India (API), this plant is traditionally used for the management of pain, diarrhoea, vomiting, fever, itching, skin ailments, cough, blood purification, and disorders associated with lactation.[8]

India: In Ayurveda, *C. pareira* leaves are utilized to treat chronic (indolent) ulcers and diarrhoea. The plant is regarded as antiseptic and traditionally employed for urinary tract infections. Fresh leaf juice is traditionally used as a remedy for migraine.[10]

Brazil: *C. pareira* is widely used in herbal medicine as a diuretic and general tonic, and for reducing fever and pain. It is commonly prescribed for menstrual cramps, dysmenorrhea, excessive uterine bleeding, fibroids, pre- and postnatal pain, colic, constipation, indigestion, and dyspepsia.[10]

South America: *C. pareira*, called the "midwife's herb," is traditionally used for a wide range of women's reproductive complaints. Its root is employed to relieve menstrual cramps, manage excessive bleeding, prevent threatened miscarriage, and arrest postpartum uterine hemorrhage; Amazonian midwives still used for pre- and postnatal pain.[10]

Thailand: The leaf extracts are processed into a dark green gel and used locally to treat fever. The plant is also employed as a diuretic and for various conditions, including asthma and trauma.[10]

Mexico: *C. pareira* has long been used to treat muscle inflammation, snakebite, rheumatism, diarrhoea, dysentery, and menstrual disorders.[10]

CONCLUSION

Cissampelos pareira L. (Menispermaceae) is a pantropical medicinal climber with well-documented ethnobotanical uses and promising preclinical pharmacology. Its benzyl- and bisbenzylisoquinoline alkaloids, phenolics, and volatile compounds have strong antioxidant and hepatoprotective effects against CCl_4- and drug-induced liver injury, alongwith immunomodulatory, antidiabetic, anti-asthmatic, and antiprotozoal activities. Acute toxicity indicates a relatively wide safety margin, but observed anti-fertility and hormone-altering effects warrant caution. While this review bridges traditional knowledge with phytochemical and pharmacological evidence, future researchers should prioritize isolating and quantifying major alkaloids, establishing chemotypes and validated quality-control markers, elucidating hepatoprotective and immunomodulatory mechanisms, conducting ADME/PK and drug–herb interaction studies, performing comprehensive toxicity assessments (subchronic/chronic, reproductive, genotoxicity), defining dose–response ranges and developing stable formulations, executing phase I/II clinical trials in liver disorders, applying network pharmacology for lead prioritization, and documenting regional practices while promoting sustainable cultivation to conserve wild populations. Addressing these priorities will clarify *C. pareira*'s therapeutic potential and enable its development into evidence-based hepatoprotective agents.

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