

Original Research

Beyond Tradition: A Contemporary Perspective on *Cissampelos pareira* Linn's Medicinal Attributes

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Abstract

Cissampelos pareira Linn, an herbal medicine deeply rooted in traditional healing practices, has garnered renewed interest in contemporary pharmacological research. This detailed review explores the phytochemical richness and pharmacological potentials of *Cissampelos pareira* Linn, shedding light on its multifaceted therapeutic attributes. The paper synthesizes current scientific insights into the plant's anti-oxidant, anti-inflammatory, anti-venom, anti-fertility, anti-malarial, anti-insecticide, anti-microbial, and anti-cancer properties, providing a bridge between age-old traditional uses and modern evidence-based medicine. The main bioactive compounds present in this species are alkaloids, particularly isoquinoline alkaloids. Emphasizing the phytochemical diversity of *Cissampelos pareira* Linn the review navigates through its bioactive compounds, unraveling the intricate tapestry of its medicinal efficacy and also as an agent for making country liquor. The present study aims at exploration of phytochemical, ethno medicinal, ecological, pharmacological as well as medicinal practices of *Cissampelos pareira* Linn for better understanding of medicinal activities and sustainable use of this plant. The importance of bioactive compounds of *Cissampelos pareira* Linn in the pharmaceutical industry as well as livelihood of natives is highlighted. *Cissampelos pareira* L. is widely distributed throughout the world and has its utility in treatment of a large number of diseases and ailments.

Keywords: *Cissampelos pareira* Linn, Phytochemicals, Antioxidant activity, Alkaloids, Antimicrobial, Anti-inflammatory.

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Introduction

The optimal functioning of primary health care systems is contingent upon the discerning use and uninterrupted availability of appropriate drugs and medicines. Traditional medicine has emerged as a paramount and cost-effective treatment modality, representing a readily accessible option for addressing numerous ailments within the realm of primary health care. Notably, the World Health Organization estimates that a substantial portion of the world's population uses traditional medicine to satisfy their basic medical requirements, indicating the practice's broad acceptability and adoption. The use of the herbs in the formulation of traditional medicine to cure disease is known as Local Health Tradition [1].

Velvet leaf, a plant widely utilized in traditional medicine across tropical regions, has garnered attention in modern research for its alignment with various traditional medicinal applications. The plant is rich in alkaloids, some of which demonstrate potent

antileukemic properties. Recent investigations on rhizome extracts revealed their dose-dependent reduction of the growth and multiplication rate of stomach tumors. Furthermore, ethanolic rhizome extracts displayed noteworthy anti-inflammatory characteristics without causing stomach lesions or carcinogenic consequences in tests measuring acute, subacute, and chronic inflammation. These extracts also exhibited antihistaminic, hypotensive, antispasmodic, and anticonvulsant properties [2].

Velvet leaf demonstrates curare-like activity, impacting the central nervous system and smooth muscles, along with hypotensive and hypoglycemic actions. Specifically, individuals traditionally consume an infusion of the bitter rhizome, leaves, and stems to address gastrointestinal issues such as diarrhea, dysentery, ulcers, colic, intestinal worms, and digestive complaints. Additionally, it is employed for urogenital problems such as menstrual disorders, venereal diseases, infertility, uterine bleeding, and

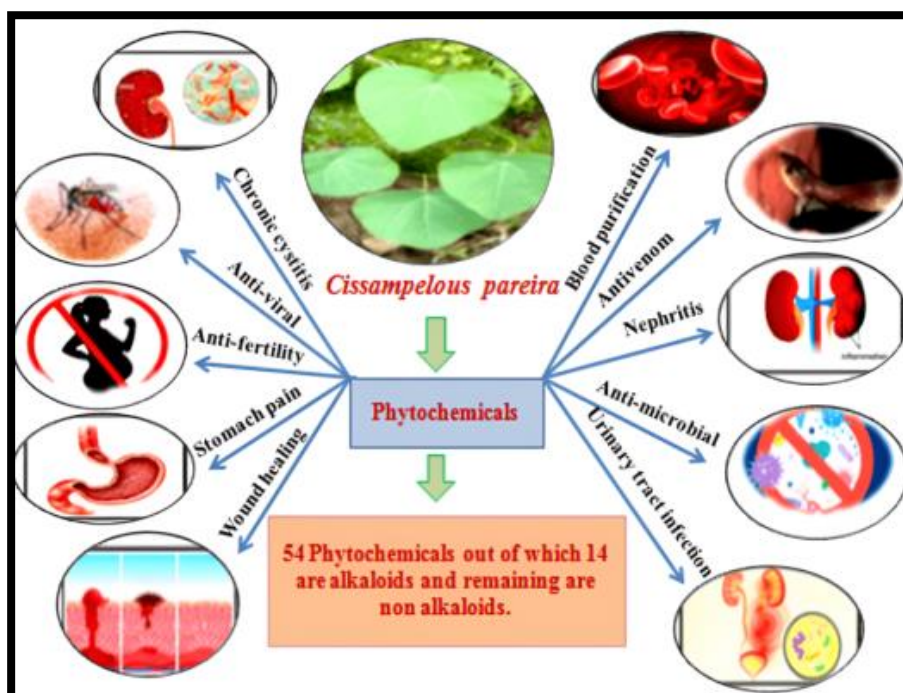
threatened miscarriage. The roots, either decocted or pounded, is commonly used as a febrifuge and stomachic agent, addressing conditions like cough, heart trouble, rheumatism, jaundice, snake bites, and skin infections such as sores, boils, scabies, and childhood eczema. Specifically, the rhizome serves as a diuretic, addressing acute and chronic bladder inflammation, dissolving urinary calcifications, and functioning as an emmenagogue [2].

In combination with a hot water extract of the roots and leaves of *Launaea cornuta*, it is administered orally to treat epilepsy. Moreover, the extract from macerated leaves and stems, when mixed with water, is utilized as an anti-conjunctivitis treatment or for

sore eyes. This juice is also applied as an anti-inflammatory agent. When leaves and stems are macerated in water, they serve as an anti-infective agent. Notably, tribal communities in India employ the plant to prevent pregnancy [2].

Taxonomic position

Cissampelos pareira L., a perennial climbing herb in the Menispermaceae family (Table 1), is commonly referred to in South America as "*parreira*" and in Indian traditional medicine as "Ambastha" or "Laghu Patha" [3]. It is commonly known as "Patha" in India.



Graphical abstract

Table No.1:- Table showing the Taxonomic Classification of *Cissampelos pareira* Linn.

Scientific Classification	
kingdom	Plantae
Division	Tracheophyta
Subdivision	Spermatophytina
Infradivision	Angiospermae
Class	Magnoliopsida
Superorder	Ranunculanae
Series	Thalamiflorae
Order	Ranunculales
Family	Menispermaceae
Genus	<i>Cissampelos</i>
Species	<i>pareira</i> L.

Botanical Description

Macroscopic

The roots are cylindrical, frequently twisted, and have a diameter of 1 to 1.5 cm. They are colored light brown to yellowish, with a rough surface caused by transverse wrinkles, cracks, and fissures. The fractures

are short and splintery, and they have a faintly aromatic smell and a bitter taste. It is a highly erratic, tall, thin, dioecious, perennial climber that can reach 2000 meters in altitude (Fig. 1(a)) [4]. In addition to producing fruits in the winter, the plant blooms in the autumn and during the period of rainfall. It is a thin

climber with velvety hair, leaves are peltate, obtuse, mucronate, base cordate or truncate, triangularly broad-ovate or orbicular. Covered with fluffy hairs on both surfaces, the leaves have dimensions ranging from 2.5–12 cm in length and 2.5–11.5 cm in width. The petiole is hairy, small flowers (Fig. 1(b)) with filiform pedicels are present. Male flowers are clustered in the axil of a small leaf. The four petals unite to form a four-toothed cup, while there are four stamens with a short column, and connate anthers encircle the apex of the column. The sepals are four, obovate-oblong and covered with hairs on the exterior. Small, roundish fruits with a flattened shape, covered in fine hairs. The fruit appears bright red when it's fresh and turns black as it dries. Its dimensions are 4-6 mm in length and 3.4 mm in width. The roots are light brownish in colour and are cylindrical rough surface [4].

3.2. Microscopic

The transverse section of the root reveals 6-10 layers of thin-walled, rectangular cork cells and 1-3 layers of oval to tangentially elongated cells forming the secondary cortex. A discontinuous ring consisting of 2-3 rows of stone cells and groups of phloem fibers is present, with stone cells exhibiting variable shapes and simple pits. The phloem, located just below the ring of stone cells, consists of small strands of sieve elements and parenchyma. The xylem includes vessels, tracheids, fibers, and parenchyma, with vessels and tracheids featuring simple pits on their walls. Typically, the xylem parenchyma is thick-walled and lignified, but due to delignification, patches of thin-walled parenchyma appear in the xylem region [5].



Fig. 1: (a) Showing the leaves of *Cissampelos pareira* L., (b) flower of *Cissampelos pareira* L.

3.3. Vernacular names of *C. pareria* L.

The botanical name of Patha is *Cissampelos pareira* Linn. List of different names of *C. pareria* L. in different regions of the world is given in table 2.

Table 2. Shows the vernacular names of *C. pareria* L. with the language of their origin.

Language	Names	References
Sassamese	Tubukilota	[6]
Rajasthani	Kalipar	
Khasi	Jyrmi Salla	
Hindi	Padh, Bhatvel, Harjori	[6,7]
Bengali	Venivel	[6]
Konkni	Pahadvel	
Kannada	Parera Beru	
Marathi	Padaval, Pahadmul, Lahan, Pahdbel, kuruphad, tahadvel, tannivel	[7]
Malayalam	Malathaanti, Paataththali	[6]
Tamil	Abuta, laghu patha	
Oriya	Godaku, Akanbindi, okanbindu, paru, pitusing, shantimul, Ghodakuri, Duapar	[7]
Chinese	xí shēng téng , yà hū nú	[8]
Spanish	Butua, Pareira brave	
Brazil	Abutua, Pareira brave	
Portuguese	Abutua,	
Others	Abuta, Barbasco, Barel-panrhe, False Pareira Brava, False Pareira Root, Ice Vine, Midwife's Herb, Pereira Root, Sulara, Velvet Leaf.	

3.4. Geographical distribution of *C. pareria* L.

The plant is widely distributed across tropical and subtropical regions of Nepal and India, from Sind and Punjab to South India and Sri Lanka. Locally, it can be found in Arunachal Pradesh, Andhra Pradesh, Assam, Bihar, Gujarat, Haryana, Himachal Pradesh, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Manipur, Meghalaya, Mizoram, Nagaland, Odisha, Punjab, Rajasthan, Sikkim, Tamil Nadu, Tripura, Uttar Pradesh, and West Bengal (Table 3). Globally, it is found in various parts of Asia, including Bangladesh, Bhutan, India, Malaysia, Nepal, and Pakistan.

Table 3. Table shows the local distribution of *C. pariera* L. in Indian regions.

Area	Region	Reference
Andhra Pradesh	Anantapur, Chittoor, Kadapa, East Godavari, Guntur, Krishna, Kurnool, Nellore, Prakasam, Srikakulam, Visakhapatnam, Vizianagaram, and West Godavari districts.	[7]
Telangana	Nalgonda, Khammam, Mehboobnagar	
Karnataka	Ballari, Chamarajanagar, Kolar	
Maharashtra	Nagpur, Akola, Ganpatipule (Ratnagiri),	
Odisha	Sundergarh, Angul, Balasore, Bargarh, Bolangir, Boudh, Cuttack, Deogarh, Dhenkanal, Gajapati, Ganjam, Kalhandi, Kandhamal, Kendrapara, Keonjhar, Khurda, Koraput, Malkangiri, Mayurbhanj, Puri, Rayagada district, Sambalpur	
Tamil Nadu	Coimbatore, Dindigul, Dharmapuri, Kanchipuram (Changalpattu-CGP), Karur, Krishnagiri, Madurai, Namakkal, Pudukkottai, Sivaganga, Salem. Tiruchirapalli, Tiruvannamalai, Villipuram, Vellore	
Kerala	All districts of Kerala	
Gujarat	All districts of Gujarat	
West Bengal	West Bengal	
Arunachal Pradesh	Changlang, west kameng, siang, lohit	

Cissampelos pareira L., a member of the Menispermaceae family, is found in tropical and subtropical areas of Africa, Asia, and the Americas. Its distribution is global. The genus *Cissampelos* is widely distributed throughout the world, including five continents and numerous islands. The only species with a pan tropical range is *Cissampelos pareira* L., which spans the tropical regions of the three main continents: Asia, Africa, and the Americas (Fig.2). It is commonly found in Africa (Sierra Leone east to Congo, Rwanda, Tanzania, south to northern Angola, Zambia), America (Brazil, Argentina, Peru, Mexico, Colombia, and Florida), Australia, the West Indies, Comores, Mauritius, Seychelles, and Madagascar, and Asia (Indo-China, Southern China, Malaysia, Thailand, India, and Pakistan) [9].

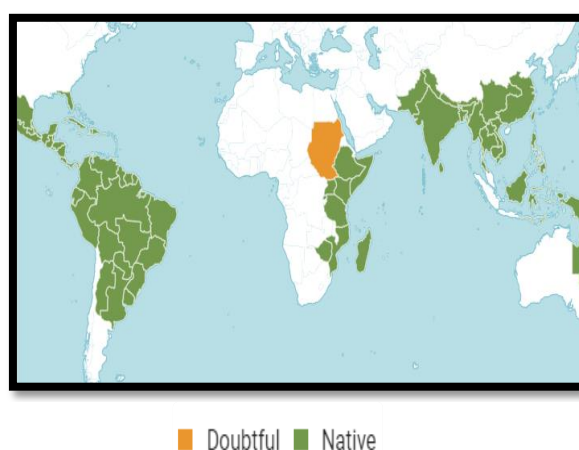


Fig.2. Showing global distribution of *C. pareria* L. (Source: [9].)

4. Traditional and Ethnomedicinal uses

According to Ayurveda there are 2 types of patha

- Raj patha
- Laghu patha

In Sanskrit, it is said, "नास्ति मूलमनौषधम्", which translates to "There is no root that is not a medicine." Similarly, Patha is also considered a highly beneficial medicinal herb. This plant is commonly used to cure a

wide range of ailments in Western herbalism, traditional Chinese medicine, and Ayurveda. It has a rich history of traditional uses. Roots of *C. pareira* are acrid and stinging, with carminative, sharp, anthelmintic, stomachic, digestive, diuretic, antispasmodic, and anti-inflammatory properties [10]. In Malawi, the tubers of *C. pareira* L. are utilized for pseudo-pregnancy. In addition to its medical use, this plant is known to have other qualities that increase milk production in dairy cows and food systems for varied uses, such as gel-forming agents, thickening agents stabilizing substances, and texture modifiers in Asia [11].

4.1. Historical review in India:

Patha, also referred to as Pata in Vedic literature, was discovered by Garuda and Shukara. According to mythology, Indra used this drug to defeat the Asuras. Historical texts cite various synonyms for Patha, including Uttanaparna, Devajuta, and Sahamaanasahayas. Vedic texts highlight its properties as Viryavathi, Vishagni, Rakshagni, Medya, Kamyā, and Garbha Sthapana. The Rig Veda describes it as Saphaneebhadana and Vasekarana, while the Atharvaveda mentions its use for enhancing intelligence and prevailing in debates. The Indian subcontinent has been using Ayurveda, an ancient medical system, since 6000 BCE [11]. This herb is

recommended for blood cleansing, fever, coughing, and abdominal pain, per the Ayurvedic Pharmacopoeia of India (API). Disorders pertaining to the secretion of breast milk are also treated with patha. Patha is mentioned in an old Charaka Samhita poem for the therapy for heart problems, poisoning, worm infection, fever, asthma, vomiting, diarrhea, burning feeling, itching, leprosy, and stomach tumors (Fig. 3).

C. pareira L. has been utilized in Ayurvedic preparations like Agnimukh churn, Pusanug churn, Mahayograj guggulu, and Pathadi kwath since ancient times. The root portion is mostly used for medicinal purposes in India. Therefore, in many states of India, dried roots are sold for medicinal purposes, with notable activity observed in Haridwar, Uttarakhand [12].

Sanskrit verse on patha: In a verse (fig. 3) from the Charaka Samhita, *C. pareira* L. (Patha) is mentioned as a remedy for a diverse range of ailments. These include temperature, breathing problem, nausea, diarrhea, heat sensations, itching, leprosy, heart problems, poisoning, worm infestations, and stomach tumors [11].

पाठाऽम्बष्ठऽम्बष्ठकी च प्राचीनापापचेलिका।
एकाष्ठीला रसा प्रोत्का पाठिका वरतत्किका॥१९१॥
पाठोष्णा कटुका तीक्ष्णा वातश्लेष्महरी लघुः ।
हन्ति शूलज्वरच्छर्दक्षिष्ठातीसारहृद्दूरजः।
दाहकण्ड्विश्वासकृमिगुल्मगरव्रणान्॥१९२॥
चरक संहिता, सूत्रस्थान ४।१२, ४।१६

Fig. 3: Sanskrit verse on patha from *Charaka Samhita* (Source: Samhita, 1949 [11]).

Explanation: This herb, known by various names such as Patha, ambhashtha, ambhash thika, prachina, papchellika, ekashthila, rasa, pathika, and vartitika, has a bitter taste and possesses hot potency. It is considered a lightweight herb that helps balance vata and kapha doshas in the body. Its effectiveness extends to treating a wide range of ailments including stomach pain, fever, nausea, leprosy, diarrhea, heart problems, stomach burning, itching, poisoning, breathing problems, worm infestations, and stomach tumors.

4.2. Other countries:

In other Asian countries *C. pareira* L. roots have various applications, including treating diarrhea,

stomach pain, dyspepsia, headaches, ulcers, wound healing, anorexia, skin problems, abdominal discomfort, constipation, indigestion, blood purification, and chronic cystitis, nephritis, fever, urinary infections, cough, sores, and gastrointestinal problems (Fig.4). In African countries *C. pareira* L.'s roots and leaves are traditionally used to cure coughs, sore throats, colds, pregnancy pain, diarrhea, stomach ache, wounds, diabetes, malaria, and anti-helminthiasis for veterinary purposes. It is also referred to as Midwives herb in South America because the roots are in use for menstrual cramps and excessive bleeding [13].

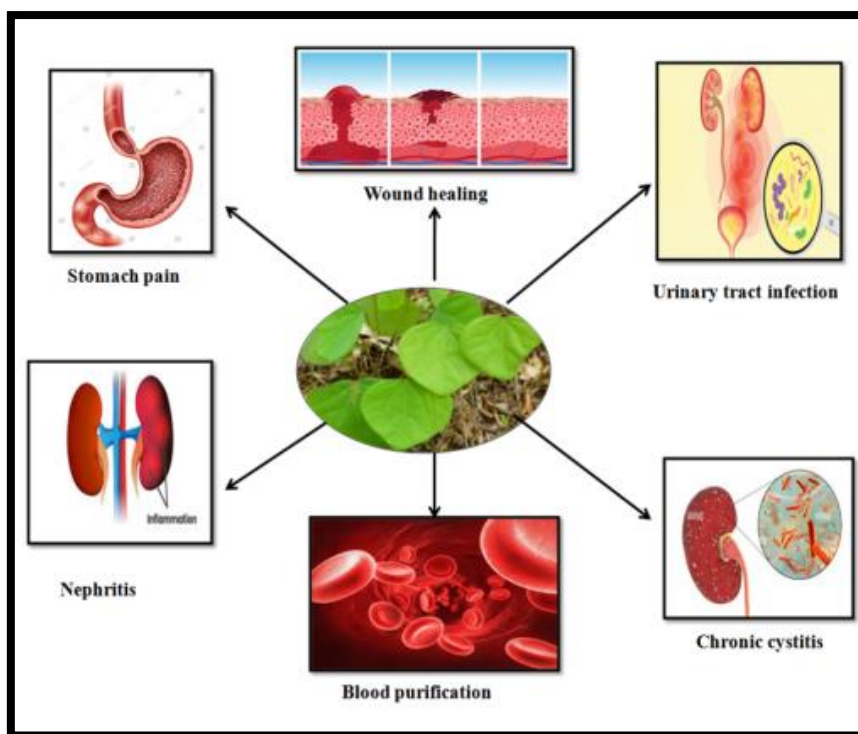


Fig. 4: Showing the traditional uses of *C. pareira* L.

4.3. Ethnomedical consideration:

The rhizome of *C. pareira* L. have a strong, bitter flavor and have been shown to have anti-inflammatory, stomach-inducing, diuretic, carminative, astringent, and anthminthic properties. The herb's applications include treating dysuria, asthma, leprosy, cough, and sensation. The aerial part is used for skin conditions, burns, eye problems, wounds, fever, and colds.

Medicinal plant *C. pareira* L. is highly valued for its therapeutic properties. In scriptures of Ayurveda, patha has been frequently cited by Charaka and

Sushruta for a number of potent ayurvedic indications such as Guna (qualities), Teekshan (penetrating deeply into the tissues), Laghu (light to digest), and Tikta (bitter flavor); while it contains Katu (pungent), Veerya (hot potency), and Vipaka (taste conversion after digestion). Pitta and Kapha doshas are known to be balanced by it. In Ayurveda, it is classified as a "Tridoshic," meaning it balances all three doshas: Vata, Pitta, and Kapha. Here are some functions (Table 4) of *C. pareira* L. describe in Ayurveda [14].

Table 4: Functions of *C. pareira* L. used in Ayurveda (Source: Singh, 2017) [35].

In Sanskrit	In English
Vrushya	Acts as an aphrodisiac.
Vishaghni, Vishahara	Detoxifies the body.
Kushta, Kandunut	Relieves skin diseases characterized by itching.
Chardijit	Alleviates vomiting.
Hrudroga	Eases heart diseases.
Jwara	Relieves fever.
Tridoshashamani	Balances Tridosha, particularly Vata and Kapha.
Atisara	Relieves diarrhea.
Shulaghni	Eases abdominal colic pain.
Kaphapitta jwara	Relieves fever caused by an imbalance of Kapha and Pitta, with symptoms like heaviness and burning sensation.
Krumi	Relieves intestinal worms.
Gulma, Gara	Relieves abdominal mass or bloating, and chronic toxicity.
Vrana	Promotes wound healing.

5. Phytochemistry:

Literature research indicates that alkaloids, particularly isoquinoline alkaloids, represent the

primary constituents of *C. pareira* L.. Various types of isoquinoline alkaloids; including bisbenzylisoquinoline; benzylisoquinoline;

tropolisoquinoline; aporphine; azafluoranthene; and protoberberine have been identified in *C. pareira* L.. Additionally, several non-alkaloid constituents have been extracted from this herb [15]. The phytochemicals Hayatidine; Hayatine; Hayatinine; d-Isochondrodendrine; Cissampareine, Tetrandrine; Cycleanine; Insularine; Sepeperine, (+)-Obaberine; (+)-Obamegine; (+)-Homoaromoline; (-)-nor-N'-chondrocurine; 1-(4-(formyloxy)-3-methoxybenzyl)-6,7-dimethoxy-2,2-dimethyl-1,2,3,4-tetrahydroisoquinolin-2-ium; Magnocurarine; (-)-Oblongine; (+)-Coclaurine; Pareirarine; Dicentrine; Dehydrodicentrine, Magnoflorine; Pareirubrine A; Pareirubrine B; Isoimerubrine; Grandirubrine; Pareitropone; Cissamine; Berberine; Norimeluteine; Norruffscine; Reserpine; Cissampeline; trans-N-feruloyltyramine; Salutaridine; Laudanosine; Nuciferine; Corytuberine; Bulbocarpine; nor-N-magnoflorine; Pelosinare alkaloids and the rest are non alkaloids.

6. Pharmacology:

C. pareira, commonly known as Velvetleaf, has been subjected to extraction using solvents of increasing polarity, ranging from water to chloroform. Phytochemical screening of the resulting extracts revealed the presence of alkaloids (hayatine, hayatinine), flavonoids, steroid tri-terpenoids, saponins, tannins, and essential oils. The traditional medicinal uses of *C. pareira* have prompted numerous scientific investigations to validate its efficacy. These studies have confirmed several pharmacological activities attributed to the plant, supporting its traditional claims. *C. pareira* has been studied for various pharmacological activities, showcasing its potential therapeutic benefits. Some of the pharmacological activities (Fig. 5) of *C. pareira* that have been investigated include.

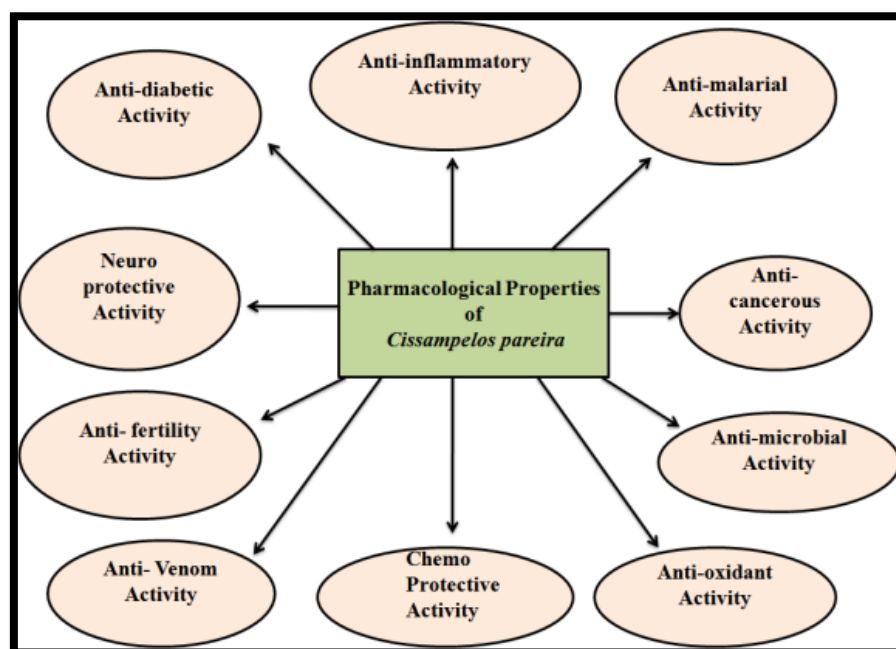


Fig. 5: Showing the Pharmacological properties of *C. pareira*.

6.1. Anti-inflammatory activity.

In 2001, Batista-Lima [16] found that *C. pareira* extract, as well as a polyherbal formulation containing *C. pareira* along with *Pongamiapinnata* (L.) Pierre and *Vitex negundo* L., demonstrated in vitro anti-inflammatory activity at a dosage of 600 mg/kg in carrageenan-induced hind paw edema, with a reduction of 0.16 mL, the ethanolic extract of *C. pareira* aerial parts, administered orally at 100 mg/kg, exhibited anti-inflammatory and analgesic effects in mice (abdominal writhes) and rats (hot plate test).

6.2. Anti-diabetic.

Various studies have investigated the antidiabetic properties of extracts derived from *C. pareira* roots and leaves. In one study, the aqueous extract from *C.*

pareira leaves demonstrated significant anti-diabetic effects in male albino mice, with doses of 250 mg/kg and 500 mg/kg over 14 days. This extract effectively reduced random blood glucose levels and showed promise in increasing body weight [17].

6.3. Antifertility activity:

The methanolic extract from *C. pareira* leaves was evaluated for its antifertility effects in mice, with doses of 250 and 450 mg/kg/day. The extract altered the pattern of the oestrous cycle in female mice, prolonging its length and increasing the duration of the dioestrus stage, consequently reducing the number of litters. Additionally, changes in hormone levels, including follicle-stimulating hormones, luteinizing

hormones, prolactin, and oestradiol secretion, were observed, with an LD₅₀ of 7.3 g/kg [18].

6.4. Anti-parasitic activities.

The ancient Sanskrit text Charak Samhita mentions *C. pareira*'s effectiveness against parasitic worm infections, which modern research has supported. Studies have isolated Cissampeloflavone from the plant's aerial parts, showing efficacy against parasites like *Trypanosoma cruzi* and *Trypanosoma brucei rhodesiense* [19].

6.5. Gastro-protective activity

The ethanolic root extract of *C. pareira* shows promising protective effects against both acute and chronic ulcers in rats, shielding against various ulcer-inducing factors including ethanol, aspirin, stress, and pylorus ligation. Quercetin from *C. pareira* roots also exhibits significant antiulcer properties. Additionally, the extract demonstrates notable hepatoprotective activity against CCl₄-induced hepatotoxicity, enhancing liver antioxidant enzymes and mitigating biochemical abnormalities. It also safeguards against liver damage induced by anti-tuberculosis drugs [20].

6.6. Antioxidant activity

Antioxidants are necessary for combating oxidative processes and neutralizing free radicals; which helps to overcome various diseases. *C. pareira* has shown promising antioxidant properties, particularly its 50% aqueous-ethanolic root extract, which scavenges radicals like DPPH; superoxide; hydrogen peroxide; nitric oxide and hydroxyl with significant effectiveness. These findings suggest that while *C. pareira* constituents, including flavonoids, may not directly target specific diseases, their antioxidant effects play a crucial role in preventing oxidative damage-related conditions such as Alzheimer's disease, cancer, cardiovascular issues, and muscular degeneration [21].

6.7. Neuro-protective activity

Research suggests that a combined extract of *C. pareira* and *Anethum graveolens* (PM52) exhibits a dose-dependent protective effect against age-related cognitive decline in Wistar rats. It reduces memory impairment and neuro degeneration, indicating potential as a food supplement to prevent age-related cognitive decline and premature Alzheimer's disease [22].

6.8. Chemopreventive

C. pareira is traditionally used for abdominal tumor treatment, exhibits chemo-protective actions. Studies by Bala et al. 2017 [23] found hydro-alcoholic extract fractions and pure molecules to be cytotoxic against KB, SiHa, and A549 cells. Notably, cycleanine and hayatinine displayed significant efficacy.

6.9. Antivenom

The aqueous leaf extract of *C. pareira* was checked for its ability to counteract *Bothrops asper* venom's hemorrhagic and proteolytic effects. While it did not inhibit the venom's proteolytic activity in vitro, it completely neutralized its hemorrhagic effects when injected simultaneously into the skin of experimental mice. In another study, the ethanolic extracts of *C. pareira* roots and aerial parts were examined for their antivenom activity against *Bothrops diporus* venom [24].

6.10. Analgesic and antipyretic activity

C. pareira has been traditionally used for pain and fever relief, supported by in vivo studies evaluating its analgesic and antipyretic properties. Moreover, the methanolic root extract exhibited antipyretic effects in yeast-induced pyrexia. Additionally, the whole plant extract displayed dose-dependent analgesic and antipyretic properties. Dose selection varied across studies, with some based on animal body surface area ratios or acute toxicity studies. An acute toxicology study suggested a safe dose of 2g /kg [25].

6.11. Anti-cancerous

In their study, De Wet et al. 2009 [26] highlighted the significant anti-cancer properties of the hydroalcoholic root extract of *C. pareira*. This extract not only targeted carcinogen-metabolizing enzymes but also showed effectiveness against antioxidant enzymes. It notably reduced tumor incidence, multiplicity, and the average number of tumors in mice with benzo(a)pyrene-induced gastric cancer. Additionally, the ethanolic extract of *C. pareira*, enriched with quercetin, exhibited protective effects against cancer development and micronucleus formation in the same model.

6.12. Anti-anxiety

The 70% aqueous ethanolic extract derived from *C. pareira* leaves consist of alkaloids, flavonoids, steroids; terpenoids. This extract demonstrated notable anti-anxiety effects in rats according to Elevated Plus Maze test (EPM), Light Dark (Land D) model, and Forced Swim test (FS) experiments [27].

6.13. Anti-microbial

In 2006, Kumar et al. [28] found that an extract from the whole plant of *C. pareira* displayed potent antifungal effects against *Aspergillus niger*; *Saccharomyces cerevisiae* completely inhibiting their growth at concentrations of 1g/ml, surpassing the efficacy of the positive control, amphotericin B, at 3 mg/ml. Furthermore, dichloromethane extracts derived from the aerial parts of *Cissampelos mucronata* exhibited antibacterial activity against a range of bacteria, including *Vibrio cholerae*; *Salmonella typhi*; *Streptococcus faecalis*; *Staphylococcus aureus* and *Escherichia coli*.

6.14. Anti-insecticide

The study (Kumari et al., 2022) [29] sought to evaluate the insecticidal potential of various root and stem extracts, as well as fractions, derived from *C. pareira* against *A. craccivora*, with the aim of identifying promising leads for pest management. Among the root extracts and fractions examined, the n-hexane fraction exhibited the highest efficacy against *A. craccivora*, with an LC50 value of 1828.19 mg/L, followed by the parent extract at 2211.54 mg/L. These findings underscore the promising insecticidal activity of *C. pareira* parent extract and its fractions against aphids. However, further field bio-efficacy studies are warranted to validate these results and facilitate the development of botanical formulations for practical application in pest management strategies.

6.15. Antimalarial activity

In 2004, Fischer et al. [30] identified ethanolic extracts of *Cissampelos ovalifolia* as having noteworthy in vitro antimalarial effects. Their study demonstrated IC50 values of 165.6 and 34.8 mg/mL against a chloroquine-sensitive strain of *Plasmodium falciparum*, and IC50 values of 103.1 and 37.4 mg/mL against a chloroquine-resistant strain. Similarly, [88] observed significant anti-plasmodial activity in the hydromethanolic extract of *C. pareira* against chloroquine-resistant strains of *Plasmodium falciparum* in vitro. These studies collectively highlight the promising antimalarial potential of *Cissampelos* species, particularly *C. ovalifolia* and *C. pareira*, paving the way for further exploration of their therapeutic applications.

7. Formulations

7.1. Available in market

Patha, a revered medicinal herb, boasts extensive therapeutic properties and has been employed since the Vedic period, featuring prominently in Ayurvedic literature. Its medicinal efficacy is underscored by its application in diverse disease conditions such as Atisara (diarrhea), Grahani (irritable bowel syndrome), Arsha (hemorrhoids), Jwara (fever), Kushtha (skin diseases), Shotha (edema), and more. An examination of data sourced from eight classical texts indicates that Patha is included as an ingredient in approximately 434 compound formulations. Among these, the highest proportion, totaling 409 formulations, is intended for internal administration. Conversely, 23 formulations are designated for external application, while 2 formulations are suitable for both internal and external use. Notably, it serves as an ingredient in 434 compound formulations utilized for treating 110 distinct diseases, encompassing 17 varied dosage forms. **IMPORTANT**

FORMULATIONS - *Bṛhatgaṅgādhara Churna*, *Puṇyānuga Churna*, *Pradarantaka Lauha*, *Śārsvata Ghrita*, *Stanyashodhana Kashaya Churna* [31].

7.2. Other formulations

In recent studies [32], pectin extracted from the leaves of *C. pareira* has been used to develop innovative biodegradable films. These films were formulated by combining *C. pareira* leaf pectin with polyvinyl alcohol (PVA) and crosslinking with varying concentrations of succinic acid (SA). The resulting pectin/PVA films exhibited desirable mechanical properties, antioxidant activity, and biodegradability, making them suitable for applications such as food packaging. Notably, the film containing 16% SA showed optimal performance, with high tensile strength and enhanced antioxidant release, especially in ethanol-rich environments.

Rastogi et al., [33] focuses on the formulation of herbal gels using extracts from *Cissampelos pareira* and *Bergenia ciliate* aimed at promoting wound healing. Soxhlet extraction was utilized to obtain a wide range of bioactive compounds by sequentially using solvents from nonpolar to polar. These extracts were then incorporated at a 1% concentration into gel formulations, with Carbomer 940 serving as the gelling agent at concentrations of 0.5%, 1%, and 1.5%. The findings indicate that the methanol extracts from these plants play a significant role in the wound healing process, positively affecting various components essential for tissue repair.

Seetharaman et al., [34] synthesized silver nanoparticles using *Cissampelos pareira* L. leaf extracts, demonstrating effective antioxidant activity and potential for biomedical applications. The nanoparticles, with sizes ranging from 10 to 30 nm, were produced through an eco-friendly method using biological reducing agents. Despite some challenges with uniformity, the results suggest a promising alternative to traditional chemical methods.

8. Economic value

C. pareira holds significant economic value beyond its medicinal applications. In India, other than treating irregular menstrual cycles, menstrual cramps, and stomach pain, its leaves are utilized in treating abscesses and wounds. Remarkably, local communities in Odisha craft a pill known as Ranu, comprising root powder and rice powder, which is instrumental in producing country liquor (Fig. 6) like Mahua or Mahula (derived from the flowers of *Madhuca longifolia*) and Handia (a fermented rice beer). These pills are a commodity traded in local markets [12].



Fig. 6: The making of Mahua with the fermenting agent Ranu. (Source: Sharma *et al.*, 2022 [12])

9. Toxicity

The toxicity of *C. pareira*, utilized extensively in traditional Indian medicine and by various tribal communities globally. Despite its widespread use, comprehensive scientific investigations into its toxicity profile have been lacking. The short-term and longer-term toxicity studies on the 50% aqueous ethanolic extract of *C. pareira* found no adverse effects at doses up to 2 g/kg in mice [35]. The safety of the ethanolic extract from the leaves and stems of *C. pareira* was found to be established up to a dosage of 2000mg/kg (LD₅₀) [36].

10. Conclusion and future perspectives

Recent studies on *C. pareira* highlight the presence of numerous plants in local regions with significant food, medicinal, and economic potential. However, these plants remain largely unexplored due to insufficient documentation and a lack of value-added processes. *C. pareira* itself is utilized for treating various ailments and its roots are employed in the production of traditional alcoholic beverages. There is an opportunity to develop formulations based on *C. pareira* for addressing community health concerns. Additionally, value addition through the fermentation of *C. pareira* could lead to the formation of a fermenting agent. The genus *Cissampelos*, to which *C. pareira* belongs, has a long history of use in folk medicine across different cultures and regions. It is particularly valued for its rich content of bioactive alkaloids, including bisbenzylisoquinolines; aporphines, which are gaining attention for their potential anticancer; antiplatelet; vasodilator and antiprotozoal activities. The concept of polyherbal formulations, which combine multiple plant extracts rather than isolated compounds, is gaining attention in herbal medicine due to its potent and synergistic biological activity. However, further research is needed in this area to fully understand the mechanisms of action and to determine standard dosages and minimize side effects. While isolated compounds and extracts from the genus have shown significant bioactivity, many of their mechanisms of action remain unclear. It is essential to translate traditional knowledge into scientific studies to assess

efficacy, safety through toxicity studies, isolate active compounds, establish biomarkers for quality control, and elucidate mechanisms of action before progressing to clinical trials for validation of traditional uses. This study showcases the efficacy of *C. pareira* in treating a spectrum of diseases; thereby integration of traditional wisdom with scientific validation is necessary to advance drug development for liver diseases. Conducting studies in this area is critical to finding more effective treatments.

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