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Review Article

AN INSIDE REVIEW OF *CISSAMPELOS PAREIRA* LINN: A POTENTIAL MEDICINAL PLANT OF INDIA

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ABSTRACT

Cissampelos pareira which is commonly known as velvetleaf belongs to the family Menispermaceae. Numbers of species are available all over the world but only one species is found in India. It is found in tropical and subtropical parts of India. This plant is a climbing shrub with green leaves, orange to red drupe berries, horseshoe shaped seeds and brown to yellowish roots. Its aerial parts contain number of secondary plant metabolites like flavonoids, alkaloids, tannins, volatile oils, glycosides. Our data describes phytochemical investigation and healthcare properties of *Cissampelos pareira*.

Keywords: *Cissampelos pareira*, Menispermaceae, Ice vine, Cissampelos, Velvetleaf.

INTRODUCTION

Cissampelos pareira Linn. Belongs to the family Menispermaceae is a sub-erect or climbing herb, known as ambastha or laghupatha in Indian traditional medicine[1]. There are 37 plant species summarized under this botanical name[2]. All these species are found in all over the world but only one species occur in India. The plant is common in orchards, hedges, parks and gardens on moist soils distributed throughout tropical and subtropical India, ascending up to an altitude of 2000 m, either creeping or twining around other plants. It is also common on the hilly tracts along watercourses[3]. It is also found in Asia, East Africa and America[2]. The plant is a climbing shrub, 2 - 5m high with a thickened root. When not climbing, *C. arvensis* can form thick mats up to 5cm off the ground. Leaves are green, have an orbicular shape 7-14 cm in diameter. The petiole is flattened, and grooved on the upper side. The first true leaves are dull green and may be covered with fine granules on the upper surface. The most common leaf type is hastate or sagittate, which means they have distinctive arrowhead shapes with pointed lobes at the bases. Some leaves are round, ovate or oblong, and some may even be linear. These deviations from the typical leaf types may be found on plants growing in disturbed conditions[4]. The stems of field bindweed are slender vines that run along the ground or climb any available object. Stem length ranges from one to six feet (0.3-1.8 m), they are normally hairless but can be pubescent[5].

Flowers are green and unisexual; pedicel up to 2mm long; male flowers 10 – 12, with 4-5 sepals. These sepals are greenish or yellowish, ovate to obovate, 1.5mm X 0.5mm, keeled hairy outside, corolla cup shaped, 1mm long, filaments of stamens completely fused; females in pendulous spikes, 7 - 10cm long, with a little round leaflet at the base of every flower, 1 obtraingular to kidney- shaped petal 1.5mm x 2 mm, ovary superior, hairy, 1-celled, style thick with spreading, 3-lobed stigma[6,7]. The flowers are probably pollinated by small insects. It produces inedible grape sized berries. Fruit a short hairy, orange to red drupe, 5mm long, curved with style-scar near base; stone with two rows of very prominent transverse ridges, 1- seeded. Seed horseshoe-shaped; embryo elongate, narrow, embedded in endosperm, cotyledons flattened[8]. Roots, cylindrical, 1-1.5 cm in diameter, light brown to yellowish in colour, surface rough and at places rugged due to transverse wrinkles, cracks and fissures, fracture short and splintery, odour, faint aromatic, taste, bitter.

Synonyms / Common Names / Related Terms

Abuta fluminum, *Abuta grandifolia*, *Abuta grisebachii*, *Abuta panurensis*, ice vine, Menispermaceae, pareira, pareira brava, velvetleaf.

Taxonomic Position[9]

Kingdom	**:**	**Plantae**
Subkingdom	:	Tracheobionta
Super division	:	Spermatophyta
Division	:	Magnoliophyta
Class	:	Magnoliopsida
Subclass	:	Asteridae
Order	:	Solanales
Family	:	Convolvulaceae
Genus	:	*Convolvulus*
Species	:	*arvensis*

Phytochemical Review

Two novel tropoloisoquinoline alkaloids, Pareirubrines A and B, had been isolated as antileukemic substances from *Cissampelos pareira*, together with the same skeleton alkaloids, grandirubrine and isoimerubrine. Their structures were elucidated by nuclear magnetic resonance (NMR) studies, and their solid state tautomeric forms were examined by X-ray crystallographic analysis[10,11]. Cissampelosine was reported from *C. pariera* which was later on shortened as pelosine. Pelosine was an amorphous white alkaloid, studied in association with an indifferent body, Deyamittin. Cissamine and cycleanine have been reported from the roots. Root was also reported to contain *l*-curine. Root bark was reported to contain menismine, pareirine and hayatinine. Chemical investigation on the roots from Kashmir, reported 0.33 % of alkaloids, mainly hayatine and bebeerines, 0.2 % essential oils, 3.4 % fixed oils and a sterol. Tetrandrine has been reported from the roots of *C. pareira* growing in Thailand. Dicentrine, dihydrodicentrine, cycleanine, insularine and isochondrodendrine have been reported from roots of the plant growing in Ghana. *Cissamplos pareira* contains a number of alkaloids, especially bisbenzylisoquinoline alkaloids. The rhizomes contain hayatine, hayatidine, d-4''o-methylbebeerine, L-bebeerine,

isochondrodendrine, dicentrine, dehydrodicentrine, insularine. The rhizomes and leaves contain cycloanine while cissampareine has been isolated from the whole plant[8,12,13]. A Chalcone dimer named Cissampeloflavone was isolated and was identified by spectroscopic techniques. It was proved to be 2-(4-hydroxy-3-methoxyphenyl)-7-(4-methoxyphenyl)-6-(2-hydroxy-4,6-dimethoxybenzoyl)-furano [3,2 g]benzopyran-4-one. The compound has good activity against Trypanosoma cruzi and T. brucei rhodesiense and has a low toxicity to the human KB cell line[14]. Aerial parts of the plant contains Polyphenolic compounds flavonoids and tannins[15]. Thirteen saponins were isolated and identified from *C. Arvensis*[16]. Flavonoid glycosides were obtained the leaves: Kaempferol3-mono- glycosides and Quercetin 3-mono or di-glycosides[17].

Ethnobotanical Uses

In the traditional folk medicine the extracts of roots were used against a lot of ailments. They had a bitter taste and possess diuretic, purgative and antiperiodic properties. Furthermore they were judged to be good against dyspepsia, diarrhoea, dropsy, cough, urinary difficulties like cystitis, dysentery, asthma and heart diseases[18]. In the simplest cases leaves were good as an antiseptic against inflammation and can be put on wounds in order to heal sores[19].In Assam, India was some discussion about family planning with C. pareira. It is applied together with other indigenous plants[20]. In a new report on screening, it was find to treat malaria, fever, sexually transmitted diseases, snake bites and conjunctivitis[21].

Biological Review

Although this plant has been widely used in various symptoms and diseases, however few pharmacological studies have been reported.

Anti-diarrhoeal activity

The antidiarrhoeal activity of the Ethanolic extract of *Cissampelos pareira* roots was assessed on experimental animals. The hydroethanolic extract (25-100 mg dry extract kg (-1) body mass, p.o.) exhibited a dose dependent decrease in the total number of faecal droppings (control 65, reduced to 26-46) and 29.2-60.0% inhibition in castor oil-induced diarrhoea. Further, C. pareira produced a significant ($p < 0.01$) and dose dependent reduction in intestinal fluids accumulation (26.0-59.0%). The extract showed a greater inhibitory effect on the concentration of Na+ (20.0 and 34.5%) than on the concentration of K+ (6.7 and 9.4%)[22].

Anti-protozoal effect

A chalcone-flavone dimer has been isolated from the aerial parts of *Cissampelos pareira* L. which has been assigned the trivial name Cissampeloflavone. The compound has good activity against Trypanosoma cruzi and T. brucei rhodesiense and has a low toxicity to the human KB cell line[14].

Antileukemic activity

Two novel tropoloisoquinoline alkaloids, Pareirubrines A and B, have been isolated as antileukemic substances from *Cissampelos pareira* , together with the same skeleton alkaloids, grandirubrine and isoimerubrine. These alkaloids shows effect as antileukemic agent[10].

Curariform activity:

An alkaloid *hayatinin methochloride* from *C.Pareira* shows curare like activity [23,24,25].

Anti-inflammatory activity

50% Ethanolic extract of *Cissampelos pareira* roots (CPE) in acute, subacute and chronic models of inflammation was assessed in rats by administration of dose (200, 400 mg/kg) exhibited significant anti-inflammatory activity. In acute inflammation as produced by carrageenin 59.55% and 64.04%, by histamine 15.38% and 30.77%, by 5-hydroxytryptamine 17.78% and 31.11% and by prostaglandin E(2)-induced hind paw edema 19.23% and 30.77% protection was observed. While in subacute anti-inflammatory models using formaldehyde-induced hind paw edema (after 1.5 h) 38.36% and 47.95% and in chronic anti-inflammatory model using cotton pellet granuloma 15.02% and 19.19% protection from inflammation was observed[26].

Anti-fertility activity

Methanolic leaf extract, when administered orally, altered the estrous cycle pattern in female mice, prolonged the length of estrous cycle with significant increase in the duration of diestrus stage and reduced significantly the number of litters in albino mice. The analysis of the principal hormones involved in estrous cycle regulation showed that the plant extract altered gonadotropin release (LH, FSH and prolactin) and estradiol secretion. The results indicated the antifertility effect of *Cissampelos pareira* leaf extract (7.3 g/kg) in female albino mice[27].

Anthelmintic activity

The extract of *Cissampelos pareira* not only demonstrated paralysis, but also caused death of worms especially at higher concentration of 50 mg/ml in shorter time as compared to reference drug Piperazine citrate. The standard drug Piperazine citrate shows paralysis at 18.50 min and death at 60.29 min at 15 mg/ml concentration. The two concentrations (50, 100 mg/ml) of this plant show good antihelmintic activity as compared to standard drug[28].

Antinociceptive and Antiarthritic activity

A 50% aqueous Ethanolic extract of *Cissampelos pareira* roots at the dose levels of 100-400mg/kg once daily for 3 days exhibited significant ($P<0.001$) resistance against mechanical pain after 30 min. In analgesy meter induced pain in mice. Further *Cissampelos pareira* showed the dose dependent significant protective effect against arthritis[29].

Anti ulcer activity:

A flavonoid Quercetin, isolated from *C. pareira*, showed significant antiulcer property against 100% ethanol- ($P < 0.05$), aspirin- ($P < 0.001$), cold-restraint stress- ($P < 0.01$) and pylorus ligation- ($P < 0.001$) induced acute gastric ulcers in rats at dose of 25–100 mg/kg[30].

Anti-oxidant activity:

C. Pareira extract was found to significantly scavenge superoxide, hydrogen peroxide, hydroxyl radicals, and nitric oxide at a dose regimen of 50 to 400 µg/kg *in vitro*. *C. pareira* extract also inhibited hydroxyl radical-induced oxidation of proteins *in vitro*. *C. pareira* extract exhibit a potent protective activity in an acute oxidative tissue injury animal model: benzo (a) pyreneinduced gastric toxicity in mice in vivo[31].

Anti-hemorrhagic effects

To establish the antihemorrhagic activity of aqueous extract from leaves of *C. pareira*, the skin of mice was injected with a mixture of extract and venom, and it as found that extract produced a total inhibition of this activity[32].

Hepatoprotective activity

In vitro hepatoprotective activity of the extract was evaluated at 20, 40, 60, 80 and 100 µg/ml concentration against CCl_4 (1%) induced toxicity in freshly isolated rat hepatocytes Administration of hydroalcoholic extract of *Cissampelos pareira* roots and standard drug Silymarin in rats showed significant hepatoprotective action against CCl_4 induced Hepatotoxicity. Elevated serum marker enzymes of AST, ALT, ALP and serum bilirubin were significantly reduced to

near normal level in extract treated rats. Lipid per oxidation level was decreased significantly at 100, 200, 400 mg/kg doses treatment groups. In case of antioxidant enzymes SOD, catalase levels were increased significantly after 200, 400 mg/kg doses, similarly it increased the enzyme levels of GST, GPx, and GSH. 200, 400 mg/kg decreased cholesterol level, and increased triglyceride level[33].

Memory enhancing activity

The effects of *Cissampelos pariera* on learning and memory in mice. Elevated plus maze and passive avoidance paradigm were employed to test learning and memory. Three doses (100, 200 and 400 mg/kg, p.o.) of hydroalcoholic extract were administered for 7 successive days in separate group of animals. The dose of 400-mg/kg p.o. of extract significantly improved learning and memory of mice. Furthermore, this dose significantly reversed the amnesia induced by scopolamine (0.4 mg/kg, p.o.) and ageing induced amnesia[34].

Antihyperglycemic activity

Antihyperglycemic activity was studied on rats. The rats of group 1 are served as control. These animals received orally 1% CMC only. The animals of groups 2 to 4 received 2000 mg/kg b.w of methanolic extract of *Cissampelos pareira* roots[35].

Cardioprotective effect

Cissampelos pareira root extract on isoproterenol-induced cardiac dysfunction in rats. Male albino Wistar rats were randomly divided into eight groups and received either normal saline (0.5 ml/kg, intraperitoneal), isoproterenol (5 mg/kg, intraperitoneal), C. pareira (100 and 200 mg/kg, by gavage, respectively) alone, amlodipine (9 mg/kg, by gavage) alone, C. pareira (100 and 200 mg/kg, respectively) + isoproterenol and amlodipine (9 mg/kg) + isoproterenol, once a day for 30 days, respectively. Isoproterenol-induced cardiac dysfunction was characterized by a significant ($P<0.001$) increase in the heart weigh/body weight ratio, serum calcineurin, nitric oxide, lactate dehydrogenase, and thiobarbituric acid reactive substance levels, as well as a significant decrease in serum-reduced glutathione, cardiac glutathione peroxidase, glutathione reductase, and glutathione-S transferase levels, which were significantly ($P < 0.05$ and $P < 0.01$) improved by *C. pareira* treatment[36].

Immunomodulatory activity

The effect of plant extract was tested on humoral and cell-mediated immunity by measuring haemagglutination antibody titre and DTH response respectively. The effect was tested at four different dose levels ranging from 25 to 100 mg/kg. Results obtained during present investigation showed significant ($p<0.01$) reduction in antibody production in response to SRBCs at doses 25 and 50 mg/kg. With further increase in dose AFCP had no suppressive effect on antibody production and values obtained were more or less equal to control animals[37].

Antidengue activity

Extract of *Cissampelos pareira* have antidengue activity. A bioassay guided fractionation approach for plant material leading to identification of active extracts and fraction is provided. Process including preparing different extracts of C*issampelos pareira*, subjecting extracts for bioactivity (primary screening- conventional plaque reduction neutralization test (PRNT/assay, secondary screening-modified plaque reduction neutralization test (PRNT) assay and tertiary screening- virus titer reduction assay. Active extracts were further subjected to fractionation by one or more of solvents and each fraction was evaluated for bioactivity[38].

Diuretic activity

The animals were divided into eight groups of six animals each. Animals were fasted overnight with water ad libitum and subjected to pharmacological studies. Before treatment, all animals received physiological saline (0.9% NaCl) at an oral dose of 25 ml/kg body weight (BW). The first group served as the control and the second group was treated with an oral dose of 20 mg/kg BW of furosemide. Third and fourth groups were treated with an oral dose of 100 mg/kg and 200mg/kg BW of methanolic extract of *Cissampelos pareira* respectively[39].

Antiplasmodial activity

Antiplasmodial activities of extracts of *Cissampelos pareira* are reported first time. Most active extracts were from *Cissampelos pareira* (menispermaceae) with 5.8 µg/ml. The extracts were tested against chloroquine sensitive (NF54) and resistant (ENT30) P. falciparum strains in vitro using hypoxanthine assay[40].

Anti-tumour activity

The extract (primarily proteins and polysaccharides) inhibited tumor growth in a dose dependent fashion when administered orally. At the highest dose tested, 200 mg/kg/day, tumor growth was inhibited by roughly seventy percent. Subcutaneous or intraperitoneal administration at 50 mg/kg/day also inhibited tumor growth by over seventy percent[41].

Evaluation of toxicity

Toxicity of *C. arvensis* in mice had been investigated many years ago[42]**.** It is mildly toxic to some grazing animals. However, grazing has been used in the past as an attempt to control the weed. The amount of field bindweed that can be safely eaten by sheep, cattle, and goats is not known. It is reported to cause distress in hogs that eat it[43]**.**

CONCLUSION

Cissampelos pareira is a potential herb belongs to the family Menispermaceae. Number of species is available throughout the world but only one species is available in India. From this review it is concluded that *Cissampelos pareira* have potential medicinal activity and can be used in the treatment of various diseases. By going through literature review, various pharmacological activities of this plant has been familiarized and it is also found that plant contains a wide range of phytoconstituents which needs to be explored more and more. So that the single constituent related activity can be performed.

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