Abstract

The plant *Cissampelos pareira* is a sub-erect or climbing herb, belongs to the family Menispermaceae. It is commonly known as Bhatindupat in Punjab and laghupatha or ambastha in Indian traditional medicine. There are around 30 plant species summarized under this botanical name “*Cissampelos pareira*”, found in all over the world. Only one species is found in tropical and subtropical parts of India. The plant is commonly found on the hilly tracts along watercourses, orchards, parks, hedges and gardens of moist soils, either twining or creeping around other plants. This plant mainly occurs in Asia, East Africa and America. It 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 alkaloids, flavonoids, tannins, volatile oils and glycosides. In the last two decades of the century the scientists are trying to evaluate many plant drugs used in traditional system of medicine. The pharmacognostical study is one of the major criteria for identification of plant drugs. The present review on *C. pareira* provides useful information for its correct identity. Studies on pharmacology and phytochemical screening serve as a valuable source of information and provide suitable standards to determine the quality of this plant material in future investigations.

**Keywords:** Ayurvedic; *Cissampelos pareira*; Extracts; Medicine

Introduction

*Cissampelos pareira* was first described from Latin America, but actually occurs throughout the tropics [1]. It is a dioecious climbing plant which belongs to the family Menispermaceae of tribe Cocculeae [2]. *Cissampelos* consist of approximately 30 species, spreadall over tropical and subtropical forests of Asia, America, East Africa and India [3,4]. The genus “*Cissampelos*” is derived from the Greek words “kissos” meaning “Ivy” and “ampelos” meaning “vine”[5]. The name refers to the ivy-like resemblance of the growth of this plant in green rambling branches and the grape-like racemes of fruits [6]. The species “pareira” is derived from the Portuguesename given to the roots of some wild vine [7].
C. pareira is generally known as Patha in Ayurveda in classical texts of (Charaka and Sushruta). The plant has various traditional uses, being applied for its therapeutic as well as toxic effects [8]. It has been used for the treatment of urinary problems, fever and skin infections. In the rainforests of South America, C. pareira is known as Abuta, commonly known as the “Midwife’sherb” [9]. The root of this plant has a rich history, being used by resident peoples of South America, for centuries to treat many women’s ailments i.e. menstrual cramps, to stop uterine hemorrhages after childbirth, prevents threatened miscarriage, ease childbirth and postpartum, because of its intense relaxant effect on smooth muscle [10,11]. C. pareira is frequently prescribed to treat diseases of cough, abdominal pain, heart, kidney stones, asthma, arthritis, diarrhea, dysentery kidney infections and fever according to Ayurvedic Pharmacopeia of India [12,13]. However, at the same time it was traditionally used in the preparation of curares, the famous South American arrow poison used in hunting to cause death by asphyxiation. With greater potency and less toxicity, the root of this plant is used as a promising muscle relaxing agent, neuromuscular blocking agent and a substitute for tubocurarine.

The genus “Cissampelos” contain alkaloids mainly bisbenzylisoquinolines, morphines, berberines, and aporphines [14]. Since ancient times, it has been used in Indian Ayurvedic medicine for preparing Pathadi kwath, Mahayograj guggulu, Pusyanug churn and Agnimukh churn. C. pareira has been used to treat coughs, delirium, fever-cerrado habitants, madness, epilepsy and convulsions [15]. It is also used as a stimulant, sedative, analgesic, febrifuge, anti-oxidant, tonic and narcotic in various parts of the world. It is used to treat snake bites in Mexico and Central America. C. pareira, in combination with Mimosa pudica L., Piper nigrum L., and Hibiscus rosa-sinensis L., is used for birth control in different parts of India [16,17].

Ethnomedical Considerations

The C. pareira roots are bitter and pungent and exhibited carminative, astringent, anthminthic, and stomachin, digestive, diuretic, expectorant and anti-inflammatory activity [18]. The plant has been used in cough, leprosy, sensation, asthma, bronchitis, cystitis, dysuria and lactation disorders in various parts of the earth [19]. It is also used in skin disorders, scabies, non-healing ulcers, leprosy, migraine, leucorrhoea and gonorrhea. Its leaves are used in skin ailments, burns, eye trouble, wounds, fever and cold. The root decoction of C. pareira is used in malaria and pneumonia in India. The leaves of C. pareira are used in Pakistan to treat abscesses and wounds [20]. The tubers of C. pareira are used in pseudo-pregnancy in Malawi. The other species of Cissampelos such as C. glaberrima and C. ovalifolia are used for delirium, madness, stimulant, convulsions, coughs, epilepsy, sedative, analgesic and as a tonic and narcotic. Apart from the medicinal uses, this plant is reported for other different properties such as augmenting milk production in dairy cows and food systems for various purposes i.e. thickeners, texture modifiers, gelling agents and stabilizers in Asia [21].

Pharmacognosy

C. pareira is a 2-5 m twinning, perennial and a climbing shrub, supported on trees [22]. The stem is flexible, slender and reaches a maximum diameter of 1 cm. The leaves are simple, alternate, and membranous and palmately 4-8 nerved. Insertion of petiole is slightly away from the margin of the blade. Lamina is dark green outside and grayish underneath with silky-hairy above, hence known as “velvet leaf”. Lamina is cordate, apex notched and broadly ovate, 2-12 cm × 4.5-12 cm. The petiole (4-7 cm long) is pulvinate at both the ends; flowers are dioecious, small, unisexual and green in color [23,24]. The fruits are red-orange hairy drupes, partially rounded and covered by a rounded bract. The seeds have horseshoe shape [25].
**Microscopic evaluation of leaves**

The leaf of *Cissampelos* is microphyll, consisting of an average length of 4.5 cm and width of 5.2 cm. Leaves have no characteristic odor and taste. Histo-anatomical characteristics of leaf have dorsi-ventral differentiation with adaxial and abaxial epidermis. Lamina is flat and reduced in dimension having slender uniseriate clothing trichomes [26]. Midrib region is slightly raised on the adaxial side and composed of epidemics, collenchyma, mesophyll and vascular bundle. Just below the epidermis of the mid rib lies a patch of sub epidermal collenchymas (3-4 cells wide). A chlorenchyma zone consists of 1-2 layers, located beneath the collenchymas. Parenchymatous ground tissues (6-7 layers) occupy the large area. Collateral vascular bundle lies in the middle of the parenchymatous ground tissue with the xylem in the adaxial and phloem on abaxial side. Patches of 3-5 cells of sclerenchyma are distributed around the vascular strand. Epidermis at both surfaces is uniseriate, composed of rectangular cells. Cells of the lower epidermis are very small. Epidermal cell of the midrib are moderately smaller in size than those of the lamina. Starch grains are distributed in epidermal as well as in mesophyll [27].

**Microscopic evaluation of stem**

In microscopic view, the transverse section of young stem has a circular out line with an undulate and smooth surface. Epidermis is single layered composed of rectangular cells, outer wall of cells are cuticularised (< 3.2 μm) [28]. Some of the epidermal cells have bicellular trichomes (182.1-333.8 μm in length and 13.2–14.5 μm in width). A chlorenchyma zone consists of 2 layers, beneath the epidermis, followed by 2-3 layered parenchymatous layers. Cortex is composed of thin-walled parenchyma cells enclosing the secondary phloem. Transverse section of the mature stem has eight vascular bundles arranged in a ring. Adjacent vascular bundles are divided by wide bands of parenchymatous vascular rays [29]. The vascular bundles are dispersed around the parenchymatous ground tissues. Xylem occupies a small portion of the stem. Vessels are mostly circular and solitary in shape. Vessels with a diameter of 40.2-54.3 μm are co-occurred with vessels bearing narrow lumen (19.5-32.5 μm) [30].

**Microscopic evaluation of root**

Root is slightly curved, long, cylindrical, narrow and highly bitter in taste. Bark is dark grey in color, surface rough, longitudinally striated with furrows and ridges. Different 10-14 radiating vascular stripes with broad medullary rays in the cross section of root resemble a wagon wheel with spokes appearance [31]. The cork zone has a strand of thick walled sclerenchyma, which forms a broken ring on the outside of each vascular strand. Stone cells are pentagonal in shape; walls are striated and pitted with wide lumen. Vascular rays are very prominent which occupy the major portion of the root. Vessels are circular and polygonal in shape [32,33]. The Diameter of lumen ranges from 18.6 μm to 60.3 μm with a mean diameter of 40.2 μm. Xylem vessels contain prismatic crystals of calcium oxalate, ranges from 7.4×11.6 μm to 24.7×42.2 μm. Secondary xylem tissues contain plenty of simple and compound starch grains. The root decoction of *C. pareira* is used in malaria, pneumonia, and dog and snake bite (antidote) in India [34].

**Powder microscopy**

Leaf powder is dark green in color and has no characteristic taste and odor. Fragments of leaf epidermis showed uniseriate trichomes. Stem powder is light brown, and has no characteristic taste and odor. Root powder is brown colored and highly bitter in taste. Stem and root power contain rich pyramidal calcium [26].

**Phytochemistry**

Alkaloids are the chief constituents reported from the genus “*Cissampelos*” along with moderate levels of non-alkaloids.
Alkaloid constituents

Wiggers (1840) reported an amorphous bisbenzyliso-quinoline alkaloid, “pelosine” (Figure 1) from the roots of *C. pareira* which was later found to be identical to hayatine [35]. During the 1950s, three bisbenzylisoquinoline alkaloids, hayatine (Figure 2), hayatinine (Figure 3) and hayatidine (Figure 4) were reported from the Indian species and their stereochemistry and chemical structure were described in the 1960s [36]. The stereo-chemistry of this plant was confirmed by its methylation with diazomethane, which afforded O-methylcissampareine and by reduction with sodium borohydride, which yielded dihydrocis-sampareine [37]. Boissier et al., in 1965 reported two bisbenzylisoquinoline alkaloids, hayatine or bebeerine and (þ)-isochondo-dendrine (Figure 5) [38]. Anwer et al., in 1968 isolated cissamine (Figure 6) as chloride from the roots of *C. pareira* [39]. Dwuma-Badu et al., in 1975 reported isochondodendrine, dehydrodicentrine (Figure 7), dicentrine (Figure 8) and insularine (Figure 9) from the roots [40]. Bhakuni et al., in 1987 reported the biosynthetic pathway for hayatidine, (R,R)-bebeerine, (R,R)-cycleanine, (R,R)-isochondodendrine. He also revealed that hayatidine is biosynthesised by intermolecular oxidative coupling of (R)- and (S)-N-methylcoclaurine, stereo-specifically while (R,R)-cycleanine, (R,R)-bebeerine and (R,R)-isochondodendrine are formed by oxidative dimerisation of (R)-N-methylcoclaurine [41].
Figure 6: Cissamine.

Figure 7: Dehydrodicentrine.

Figure 8: Dicentrine.
Figure 9: Insularine.

Figure 10: Nuciferine.

Figure 11: Bulbocarpine.
Figure 12: Corytuberine.

Figure 13: Laudanosine.

Figure 14: Magniflorine.
Figure 15: Pareirubrine.

Figure 16: Normeluteine: R=OCH₃.
Figure 17: Norruffscine: R=H.

Figure 18: Reserpine.
Ahmad et al., in 1992 observed five alkaloids, nuciferine (Figure 10), bulbo-carpine (Figure 11), corytuberine (Figure 12), laudanosine (Figure 13) and magniflorine (Figure 14) (as hydro-chloride) from the leaves and stems of *C. pareira* [42]. Morita et al., in 1993 determined two tropoloisoquinoline alkaloids, pareirubrines A and B (Figure 15) as antileukemic substances. The conformation of tropolone ring in their structures was confirmed by NMR studies, whereas their solid-state tautomeric forms were illucidated by XRD analysis. In addition an azafluoranthene alkaloid “norimeluteine” (Figure 16), as a cytotoxic substance together with norruffscine (Figure 17) was reported in *C. pareira* [43]. The plant roots contain reserpine (Figure 18) and berberine (Figure 19) similar to that of pelosine (a principle marker compoundl-bebeerine (Sharma et al., 2004) [44]. To establish the quality control parameters of *C. pareira* roots, Hullatti et al., in 2010 isolated l-bebeerine in pure form for the authentication of *C. pareira* [45].

**Non-alkaloid constituents**

Apart from alkaloids as essential constituents of *Cissampelos* species, some non-alkaloidal constituents were determined. The roots of *C. pareira* contain sterols, fixed oil, d -quercitol (Figure 20) and essential oil, which contains thymol (Figure 21) as a major constituent (Chowdury, 1972) [46]. Rosario et al., 1996 reported a chalcone-flavone dimer, cissampeloflavone (Figure 22) from the aerial parts of *C. pareira* [47].

![Figure 19: Berberine.](image1)

![Figure 20: d-Quercitol.](image2)
Singthong et al., in 2005 extracted pectin from *C. pareira* leaves that consist mainly of 70-75% of uronic (galacturonic) acid (Figure 23) and a very little amount of neutral sugars [48]. This pectin showed shear thinning flow behavior, when studied for its rheological properties. Additionally, a well known flavonoid named 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one (quercetin) (Figure 24) and a saturated fatty acid, eicosanoic acid (Figure 25) were reported from *C. pareira* [49]. Vardhanabhuti and Ikeda in 2006 reported that the leaves of *C. pareira* produce polysaccharides and pectins mainly composed of galacturonic acid with trace amounts of neutral sugars [50].
Pharmacology

Anti-inflammatory activity

*C. pareira* extract and its polyherbal formulation in combination with *Pongamia pinnata* (L.) Pierre and *Vitex negundo* L., exhibited *in vitro* anti-inflammatory activity at a dose of 600 mg/kg on carrageenan-induced hind paw oedema by 0.16 mL, respectively (Batista-Lima, 2001) [51]. Amresh et al., in 2007 reported that ethanolic extract of the aerial parts of *C. pareira* at a dose of 100 mg/kg, (p.o) showed anti-inflammatory and analgesic activity (abdominal writhes and hot plate) in mice and rat respectively. He also showed that the ethanolic root extract of the same plant exhibited anti-inflammatory activity on acute, subacute and chronic rat models at a dose of 400 mg/kg, p.o [52].

Analgesic and antipyretic activity

Amresh et al., in 2007 reported that the hydroalcoholic root extract from *C. pareira* showed resistance against mechanical pain in analgesiometer-induced pain in mice. The hydroalcoholic root extract reduced the writhing episodes in acetic acid-induced writhing (0.6%; i.p.) by protection of 51.63% at dose of 400 mg/kg, body weight, respectively. The extract also showed protective effects against complete Freund’s adjuvant-induced arthritis by 71.52% at similar dose. *C. pareira* in combination with *Pongamia pinnata* (L.) Pierre exhibited 600 mg/kg, respectively [53,54].

Immunomodulatory activity

Moreira et al., in 2003 determined that the hydroalcoholic extract of *Cissampelos sympodialis* leaves showed an immunomodulatory effect on B -lymphocyte function. It has been reported that the methanolic root extract of *C. pareira* at a dose of 200-800 mg/kg hasan immunomodulatory activity in mice. Higher doses of this extract also obtained protection against cyclophosphamide-induced myelosuppression by raising the total WBC count significantly. The berberine-containing alkaloidal fraction of *C. pareira* roots showed an immunosuppressive effect at a dose of 50 mg/kg, (p.o.) [55].

Neuroprotective activity

Hage et al., in 2010 observed that, *C. pareira* in combination with *Anethum graveolens* (1:5) showed protection against age-related cognitive impairment in rats at doses of 10 and 50 mg/kg. He reported that this extract can be used as a food supplement for protection in mild cognitive impairment and Alzheimer’s disease [56].
Antivenom activity

The aqueous leaf extract of *C. pareira* has shown to neutralize the proteolytic and haemorrhagic effect of the venom of venomous pit viper (*Bothrops asper*) [57].

Memory-enhancing activity

Kulkarni et al., 2011 reported that, hydroalcoholic extract of *C. pareira* at 400 mg/kg significantly improved learning and memory of mice and considerably reversed amnesia, induced by scopolamine at a dose of 0.4 mg/kg, (p.o). This extract also lowered whole brain acetylcholinesterase activity when compared to piracetam at a dose of 200 mg/kg [58].

Antifertility activity

Ganguly et al., 2007 reported that the leaf extract of *C. pareira* has antifertility effect. He also observed that it altered the oestrous cycle in female mice and extended the length of the oestrous cycle with significant increase in the duration of dioestrus stage [59].

Antidiarrhoeal activity

The ethanolic root extract of *C. pareira* has got antidiarrhoeal activity at a dose of 25 and 100 mg/kg, (p.o.) [60].

Antidiabetic activity

The hydroalcoholic leaf extract of *C. pareira* at a dose of 200 and 400 mg/kg, (p.o.) has been evaluated to exhibit antidiabetic activity on streptozotocin-induced diabetic rats. It significantly reduced fasting blood glucose and improved the body weight of rats compared to glibenclamide (5 mg/kg). The study also demonstrated decrease in the gluconeogenesis and increase in glucose metabolism as evidenced by increase in serum lipids, liver glycogen and creatinine levels [61].

Hepatoprotective activity

Surendran et al., in 2011 reported that hydroalcoholic root extract of *C. pareira* exhibit significant hepatoprotective effect against CCl₄-induced hepatotoxicity in rats at doses of 100, 200 and 400 mg/kg. The levels for anti-oxidant Superoxide Dismutase (SOD) enzymes were enhanced at doses of 200 and 400 mg/kg. At the same doses, it has shown to decrease cholesterol levels and increased triglyceride levels when compared to silymarin [62].

Muscle-relaxant activity

Kupchan et al., in 1960 reported that hayatin methiodide in combination with hayatin methochloride from *Cissampelos pareira*, showed muscle-relaxant properties and were recognised as curariform drugs. The aqueous leaf extracts from *Cissampelos mucronata* exhibit anti-abortifacient and uterine relaxant properties. The extract was found to have toxic effects on the blood vessels of the kidneys of wistar rats. The ethanolic root extract of *Cissampelos mucronata* showed significant in vitro relaxant activity on isolated non-gravid rat uterine smooth muscles [63].

Anti urolithic activity

Urolithiasis is the third most common disease of the urinary tract. It is defined as the formation of sediment in the urinary tract consisting of poorly soluble crystalloids of urine. Ramesh C in 2010 reported that alcoholic extract of roots of *C. pareira* at (200 mg/kg and 400 mg/kg) doses showed curative effect in urolithiasis induced rats by preventing the formation, reducing number and disruption of calcium oxalate calculi formed in the kidneys. Phytoconstituent like berberine, present in *C. pareira* is responsible for antiurolithic activity. It is therapeutically effective for curative aspect of calcium oxalate urolithiasis [64].
Cardiovascular activity

Singh et al., in 2013 reported that the ethanolic leaf extract from C. pareira has cardioprotective activity on isoproterenol-induced cardiac dysfunction in rats. It improved the heart weight/body weight ratio, nitric oxide, lactate dehydrogenase, and serum calcineurin and thiobarbituric acid reactive substance levels. The hydroalcoholic extract of Cissampelos sympodialis showed contractions (EC50 value of 76.6 μg/mL) in the presence of functional endothelium. Leaves from Cissampelos sympodialis has shown to regulate intracellular Ca2+ as a mechanism of spasmolytic activity in the rabbit aorta [65].

Anti-oxidant activity

Hussain et al., in 2010 proved that, ethanolic root extract of C. pareira (containing polyphenols) exhibited anti-oxidant activity in the 2, 2-Diphenyl-1-Picrylhydrazyl (DPPH) assay at doses ranging between 50 and 300 μg/kg in vitro. He also reported that the extract exhibited effective protective effects in an acute oxidative tissue injury on benzo(a)pyrene-induced gastric toxicity in mice at a dose of 100 mg/kg [66]. The alkaloidal fraction from C. pareira roots showed strong anti-oxidant activity by scavenging the superoxide ion, stable free radical DPPH and by inhibiting lipid peroxidation in rat liver homogenate induced by iron/ADP/ascorbate complex [67].

Anticancer activity

De Wet et al., 2009 observed that the hydroalcoholic root extract of C. pareira exhibited activity against carcinogen metabolising phase I and phase II enzymes along with anti-oxidant enzymes. The extract improved, the mean number of tumor, tumor incidence and the tumor multiplicity on benzo(a)pyrene-induced gastric cancer in mice. The ethanolic extract of C. pareira (containing quercetin) exhibited protective property on tumor multiplicity, benzo(a)pyrene induced gastric cancer and micronucleus polychromatic erythrocytes in mice. The other species of Cissampelos such as Cissampelos mucronata, Cissampelos hirta and Cissampelos torulosa showed cytotoxicity against TK10 (renal) cancer cell lines, MCF7 (breast) and UACC62 (melanoma) [68]. Gessler et al., 1995 reported that, ethanolic extract of Cissampelos mucronata exhibited cytotoxic activity in human carcinoma cell lines in vitro, whereas cissampelo flavone had less toxicity to the human KB cell line. When administered orally, the extract mainly polysaccharides and proteins inhibit the tumor growth in a dose dependent fashion. Tumor growth was inhibited by seventy percent at a dose of 200 mg/kg/day. Intraperitoneal or subcutaneous administration at a dose of 50 mg/kg/day also improved the tumor growth [69].

Anti-ulcer activity

Nwafor and Okoye in 2005 observed that ethanolic root extract of C. mucronata, showed an anti-ulcer effect on histamine, indomethacin and stress-induced ulcer models in rats. Ethanolic root extract of C. pareira and its constituent quercetin, exhibited protective effects against ulceration at doses of 25-100 mg/kg (p.o.) in various acute and chronic ulcers in rats. The extract also improved the ulcer index with decreased perforations in acetic acid-induced chronic ulcers [70].

Antiparasitic activity

The alkaloidal extract from the leaves of Cissampelos ovalifolia showed an in vitro antiparasitic effect against Trypanosoma cruzi and Leishmania chagasi parasites with an EC50 value of 64.88 μg/mL [71]. The aqueous fraction of the ethanolic leaf extract of Cissampelos sympodialis showed anti-inflammatory effects by increased cAMP levels in intact smooth cell cultures and inhibiting cyclic nucleotide phosphodiesterase activity. Cissampelo flavone isolated from C. pareira exhibited admirable activity against Trypanosoma brucei rhodesiense.
The methanolic extract from *Cissampelos torulosa* exhibited *in vitro* anti amoebic activity against *Entamoeba histolytica* with IC$_{90}$ values of 410 mg/mL [72].

**Antimalarial activity**

Fischer et al., in 2004 reported that ethanolic extracts of *Cissampelos ovalifolia* exhibited *in vitro* antimalarial activity with IC$_{50}$ values of 165.6 and 34.8 mg/mL against a chloroquine-sensitive strain of *Plasmodium falciparum* and IC$_{50}$ values of 103.1 and 37.4 mg/mL against a chloroquine-resistant strain [73]. Jannu et al., in 2011 showed that ethanolic root extract of *C. pareira* repressed the propagation of the rodent parasite *Plasmodium berghei* *in vitro* on BALB/c mice [74]. Rukunga et al., in 2009 reported that hydromethanolic extract of *C. pareira* revealed significant anti-plasmodial activity against chloroquine-resistant (ENT30) *Plasmodium falciparum* strains *in vitro*. Singh and Banyal in 2011 reported that an ethanolic root extract of *C. pareira* revealed potent inhibition of *Plasmodium berghei* with an oral dose of 500 mg/kg in mice [75].

**Antimicrobial activity**

Kumar et al., in 2006 reported that an extract from the whole plant of *C. pareira* showed antifungal activity against *Saccharomyces cerevisiae* and *Aspergillus niger* via complete inhibition at concentrations of 1000 mg/mL in comparison to the positive controls amphotericin B at a concentration of 3 mg/mL. Moreover, Dichloromethane extracts from aerial parts of *Cissampelos mucronata* showed activity against bacteria including *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus faecalis* and *Vibrio cholera* [76].

**Anti-diuretic activity**

Sayan SB et al., in 2014 observed that alcoholic extract of roots of *C. pareira* at a dose of 400 mg/kg has shown a potent diuretic activity by increasing urinary output and increased excretion of sodium, potassium, chloride. This effect was found to be dose dependent, i.e., among the three doses studied, higher dose produced significant effect. He made the comparison with the standard diuretic drug furosemide (10 mg/kg). Earlier Hullatti et al., 2011 reported the diuretic activity with methanolic extract of roots of *C. pareira* [77].

**Anti-dengue activity**

Dengue is a mosquito borne viral disease that majorly affects global public health risk [78]. In India, dengue outbreaks are correlated to the high prevalence of the mosquito vector, high population density and circulation of all four Dengue Viruses (DENVs). So, potent drugs for dengue are being progressively more needed for public health [79,80].

Pigili RK et al., in 2014 reported anti-dengue activity of extract of aerial parts of *C. pareira* [81]. Sood R et al., in 2015 reported that the alcoholic extract of *C. pariera* (Cipa extract) is an effective inhibitor of all four DENVs in cell-based assays, assessed in terms of viral replication, based on plaque assays and viral NS1 antigen secretion via ELISA. Cipa extract shows virucidal effect in a time and dose-dependent manner in the type-1 assay format. This extract exhibited statistically significant protection against dengue virus infection using the AG129 mouse model. A preliminary evaluation of Cipa extract exhibited no adverse effects on RBC viability and platelet counts. The effect of *C. pariera* extract on virus titers confirmed a >1 log reduction compared to untreated virus, that suggests its potent efficacy in altering the course of major dengue disease to a more favorable outcome [82].

**Miscellaneous activities**

Kupchan et al., in 1965 revealed that the methiodide of hayatine isolated from *C. pareira*, showed powerful neuromuscular blocking activity when compared to that of d-tubocurarine chloride. The aqueous and alcoholic extract of *C. pareira* exhibited anthelmintic activity against earthworms at doses of 5, 10, 25, 50 and 100 mg/mL. Adesina in 1982 reported that the extract from *C. pareira* has anticonvulsant activity *in vitro*/*in vivo* [83].
Toxicity Studies

Amresh et al., 2008 showed that the hydroalcoholic extract of C. pareira has acute and subacute toxicity and produced neither mortality, nor changes in behavior, in animals at a dose of 2 g/kg, (p.o.) for a period of 28 days. The ethanolic extract of the aerial parts of C. pareira was reported to be safe up to a dose of 2000 mg/kg (LD$_{50}$). Ganguly et al., 2007 revealed that the acute toxicity of the leaf extract of C. pareira was found at an LD$_{50}$ of 7.3 g/kg, (p.o.) in female mice [84].

Future Perspectives and Conclusions

C. pareira is potential herb belongs to the family Menispermaceae, used to treat a broad range of ailments in folk medicine across many countries, centuries, and continents. It is a rich source of many bioactive alkaloids including aporphines and bisbenzylisoquinolines. This plant is gaining popularity due to their promising antiplatelet, anticancer, vasodilator and antiprotozoal activities. The chemistry and biological activity of some species of this plant, including C. capensis, C. sympodialis, and C. glaberrima, are well known. However, many other species including C. friesiorum Diels, C. andromorpha DC and C. nigrescens Diels have not been pharmacologically and phytochemically explored. Consequently, a large field of future perspective is awaiting the researcher to discover purified fractions and lead molecules, which may have capable biological activity. Thus, there is an urgent need for proper documentation of traditional knowledge to lead to the selection of authentic medicines to provide a solid basis for further research. Some research groups attempted the polyherbal formulation concept with Cissampelos plant and found promising analgesic and antipyretic activities. A detailed study is required to clarify the structure-activity relationships and mechanism of action to determine the minimal side-effects and standard dose. This review concludes that C. 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.

References


