Medicinal Marvels of Cissampelos pariera Linn: Pharmacognosy Phytochemistry and Pharmacological Activities

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Abstract: Cissampelos pareira Linn, as it is most commonly as velvetleaf, is a medicinal plant with diverse pharmacological properties. This abstract provides a concise overview of its botanical characteristics, traditional uses in various cultures, and the scientific investigations into its bioactive compounds. The plant has Anti-microbial, anti-inflammatory, and anti-cancer properties in preclinical studies. As interest in natural remedies grows, exploring the therapeutic potential of Cissampelos pareira Linn may contribute to the creation of novel medications and increased comprehension of conventional medicine.

Keywords: Cissampelos pareira, Menispermaceae, Cissampeloflavone, Antinociceptive, Cardiac Hypertrophy

INTRODUCTION

Although Cissampelos pareira is found across the tropics, it was initially identified in Latin America.[1] Cissampelos Pareira Linn. In Indian traditional medicine, this sub-erect or climbing herb is also called laghupatha or ambastha, is a member of the Menispermaceae family. This botanical name is a summary of 37 plant species. While all of these species are worldwide, only one species is found in India. Throughout tropical and subtropical India, the plant can be found in gardens, parks, hedges, and orchards on damp soils. It can grow as high as 2000 metres and twine or creep over other plants. It is also widespread in the mountainous areas near watercourses..[2-4] C. In Ayurvedic writings, pareira is sometimes referred to as Patha (Charaka and Sushruta). The plant is used for both its poisonous and medicinal properties in a variety of traditional applications..[5] Traditionally, C-pareira has been used as a medicinal plant to treat a wide range of illnesses, including diabetes, ulcers, inflammation, pain, haemorrhage, gastrotoxicity, cancer, and diarrhoea. It is also utilised as a hepatoprotective agent.[6]

Botanical name: Cissampelos pareira L. var. hirsuta (DC.)

Synonyms: Hirsute Buch. Ham ex DC; C pareira (pro parte)

Family: Menispermaceae

Fig 1 :Climbing herb of Cissampelospareira

PHARMACOGNOSY

- Geographical Occurrence:

found in Himachal Pradesh and other tropical and subtropical regions of India. Nagpur Chota. Bihar. Bengal Occidental. Punjab. Rajasthan. especially in the Marathwada Konkan's eastern Aravalli steep woods. Deccan. Hills of Bababuden in Mysore, Tamilnadu. It is said to be under danger in India's northeastern region.[7]

- Botanical description:

C. pareira is a perennial shrub that grows 2 to 5 metres tall and climbs trees for support..[8] The stem is thin, flexible, and has a maximum diameter of one centimetre. The simple, alternating, membrane-based

leaves have four to eight palmate nerves. The petiole is inserted somewhat out from the edge of the blade. Lamina is also called a "velvet leaf" because of its dark green exterior, greyish underside, and silky, hairy top. The lamina is 2–12 cm by 4.5–12 cm and is broadly oval with a notched apex. The tiny, dioecious, unisexual, green-colored flowers have pulvinated tips on their 4–7 cm long petiole..[9,10] The fruits are hairy, somewhat spherical, reddish-orange drupes with a circular bract covering them. The seeds resemble a horseshoe. [11].

- Scientific Classification [12]

Kingdom: Plantae
Subkingdom: Tracheobionta
Super division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Asteridae
Order: Ranunculales
Family: Menispermaceae
Genus: Cissampelos
Species: C.pareira

- Ayurvedic Properties :

The plant is associated with various activities in Vedic scriptures, including Rasayana, Medya, Kamya, Rakshoghni, Viryavathi, and Garbhastapana.[13] Patha falls under the Charak Samhita's Jwarahara Mahakashya and Stanyashodhana Mahakashya[14], and the Sushruta Samhita's Mustadi, Aragvadhadi, Pippalyadi, Bruhatyadi, and Patoladi Gana. [15].

(The Ayurvedic Pharmacopeia of India)

Rasa: Tikta
Guna: Laughu Tikshna
Veery: Ushna
Vipak: Katu
Dosshaghnata: Tridoshamaka
Karma: Veana ropana

Colloquial Names:

(The wealth of India Raw Material, 1952)

Hindi: Akanadi
Sanskrit: Patha
English: Velvet leaf
Kanad : Kodupalli
Malyalum: Katuvlli
Tamil: Appatta
Telgu: Adavibankateega
Marathi : Pahadmud
Bengal: Akaleja
Punjabi: Baphbel
Oriya: Akarnamini
Urdu: Pahata
Kashmiri: Butter bail
Gujrati: Karemdhiu

- Microscopic evaluation

Microscopic examination of the foliage :

The typical size of a Cissampelos leaf is 5.2 cm in width and 4.5 cm in length, making it a microphyll. Leaves don't taste or smell particular. Adaxial and abaxial epidermis are distinguished by dorsi-ventral differentiation in the histo-anatomical features of leaves. Lamina has narrow, uniform clothing trichomes that are slender and decreased in dimension..[16] The midrib area consists of the vascular bundle, mesophyll, collenchyma, and epidemics. It is slightly elevated on the adaxial side. The mid rib has a patch of subdermal collenchymas, which is 3–4 cells broad, located just below the epidermis. Underneath the collenchymas lies a zone of chlorenchyma, which is made up of one or two layers. The bulk of the area is made up of 6-7 layers of parenchymatous ground tissues. The xylem is on the adaxial side and the phloem is on the abaxal side of the collateral vascular bundle, which is located in the centre of the parenchymatous ground tissue. Patches of three to five sclerenchyma cells are scattered all throughout the vascular strand. The epidermis consists of rectangular cells and is uniseriate on both surfaces. The lower epidermis has little cells. The midrib's epidermal cells have a somewhat smaller size than the lamina's. Starch.[17]

Microscopic assessment of the stem:

The young stem's transverse portion displays a smooth, undulating, round outlining when viewed in microscopic detail. The epidermis consists of a single layer of rectangular cells with cuticularized (less than 3.2 pm) outer walls.[18] Below the epidermis, a chollenchyma zone is made up of two layers, which are followed by two to three parenchymatous layers. The secondary phloem is surrounded by thin-walled parenchyma cells, which make up the cortex. The mature stem's transverse section contains eight vascular bundles arranged in a circle. Parenchymatous vasculal rays form broad bands that split adjacent vascular bundles..[19] The xylem makes up a tiny percentage of the stem, and the vascular bundles are scattered throughout the parenchymatous ground tissues. Most vessels have a singular, circular shape.

Vessels having a narrow lumen (19. 5-32. 5 Hm) coexist with vessels with a diameter of 40.2–54.3 pm.)[20]

Microscopic analysis of the root:

The root is tall, thin, and cylindrical, and slightly curved. Its flavour is extremely bitter. The bark has a rough, dark grey colour and is longitudinally striated with ridges and furrows. In the cross section of the root, various 10–14 radiating vascular stripes with wide medullary rays resemble a spoked waggon wheel. [21] A strand of thick-walled sclerenchyma exists in the cork zone, and it forms a fractured ring around each vascular thread. Stone cells have a pentagonal shape, with pitted and striated walls and a large lumen. Vascular rays are quite noticeable and take up most of the root. The shape of vessels is polygonal and round..[22,23]

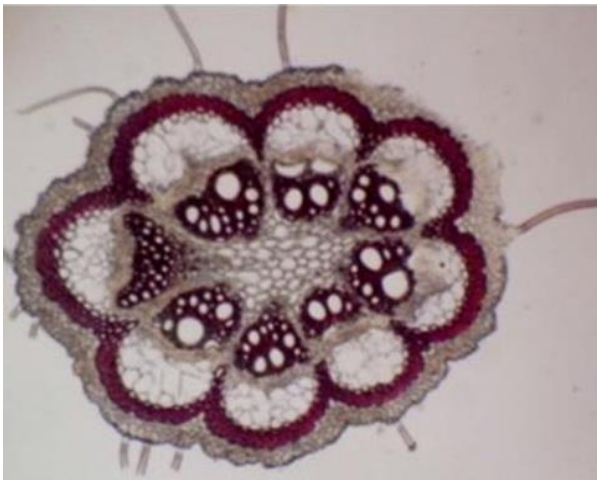

Fig.2. Transverse section of the stem Cissampelos pareira

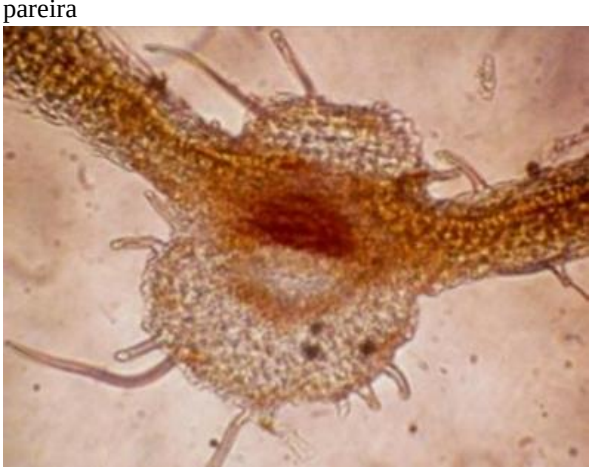

Fig.3. Transverse section of the leaf Cissampelos pareira

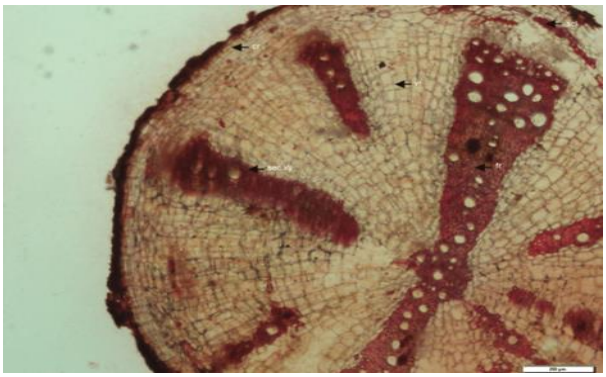

Fig.4. Transverse section of the root Cissampelos pareira

Powder microscopy:

Leaf powder has a dark green hue and is odourless and tasteless. Uniserinate trichomes were visible in leaf epidermis fragments. The powdered stem is pale brown in colour and lacks any distinct flavour or aroma. The powdered root has a dark hue and a strong bitter flavour. Rhizome and root strength have abundant pyramidal calcium.[16]

- **Fluorescence analysis:**

By treating the powdered roots independently with various chemicals and exposing them to visible, ultraviolet light, the fluorescence and overall behaviour of the material were investigated. Since the methanol's evaporation might cause the colour to shift, the colour that appeared was noticed within a minute.[24,25]

- **Physicochemical analysis:**

A variety of physicochemical characteristics were evaluated, including foaming index, moisture content, total solid content, total phenolic content, total flavonoid content, and ash values (total ash, acid insoluble ash, and water soluble ash) are among the solvent extractive values.[26-31]

PHYTOCHEMISTRY

- **Chemical constituents:**

Reza and colleagues discovered that Cissampelos pareira extract Numerous phytochemical substances, such as saponins, gums, and carbohydrates, lowering sugars, were present throughout the entire plant.[32] As of now, Kumari et al. have shown that about 54 phytomolecules, mostly isoquinoline alkaloids, a small number of flavonoids, flavonoid glycosides,

terpenoids, and fatty acids have been identified from Cissampelos pareira.[33]

Three bisbenzylisoquinoline alkaloids—hayatine, hayatinine, and hayatidine—from an Indian plant were identified in the 1950s; In the 1960s, their stereochemistry and chemical structure were described.[34]

A few non-alkaloidal components were identified in addition to alkaloids, which are crucial components of the Cissampelos species. Sterols, fixed oil, d-quercitol, and essential oil—of which thymol is a primary constituent—are all present in the roots of C. pareira.[35]

This plant has been shown to have unique chemical components such as cissamperine and cissampeloflavone.[36]

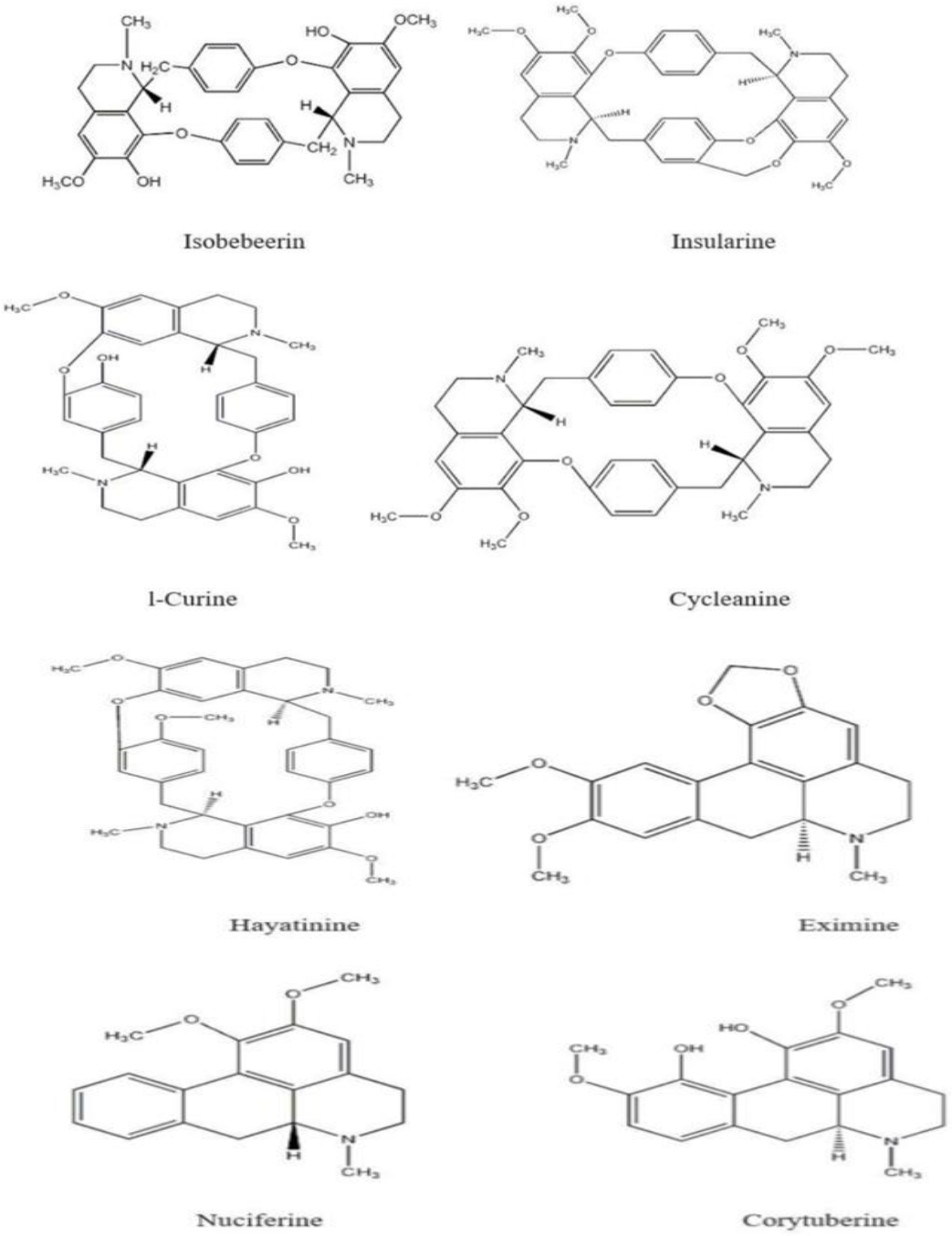

Fig.5. Some chemical structure isolated from C.pareira

- Qualitative phytochemical screening:

To identify different ingredients, chemical tests were conducted utilising solvents such as methanol, ethyl acetate, acetone, aqueous, and hexane. Standard techniques of Sofowora, Trease & Evans, Kokate, Harbone, and Raman were employed.[37-41]

Identifying Alkaloids:

Mayer's Examination: Mayer's reagent (1.36 mercuric chloride and 5 grammes of potassium iodide dissolved in 100 millilitres of distilled water) was used to treat plant extracts. Yellow cream precipitate's appearance suggests the existence of alkaloids .

Identifying Carbohydrates :

The Molisch Test : In a test tube containing two drops of an alcoholic α-napthol solution, two millilitres of conc. H_2So_4 were carefully applied along the test tube's sides to treat the plant extracts. Carbohydrates are present when a dull violet or crimson ring forms during the interphase.

Tannin Detection:

A couple of drops of 1% $FeCl_3$ solution were added to the 1 millilitre of plant extract. Precipitate that appears blue, black, green, or blue green suggests the existence of tannins.

Protein and Amino Acid Detection:

Ninhydrin Test: After adding 0.25% Ninhydrin reagent to the plant extract, it was brought to a boil for a short while. Amino acid content is shown by the formation of blue colour.

Biuret Test: After being cooked, 1 millilitre of a 10% NaOH solution was added to the plant extracts. A drop of 0.7% CuSO4 solution was added to this. The development of a violet-purple hue signifies the existence of proteins.

Detection of Quinones:

One millilitre of concentrated H_2So_4 was added to millilitres of plant extract. The presence of quinones is indicated by the formation of red colour.

Finding Reducing Sugars

Benedict's examination: Benedict's adjuvant was applied to the plant extracts, and they were then heated in a a bath in water. When there is an orange-red precipitate, reducing sugars are present. forms.

Finding fixed fats and oils :

Test for Stains: Plant-based extracts in small amounts were squeezed between two filter sheets. The presence of fixed oils and fats is indicated by an oily stain on filter paper.

Saponification Test: A little amount of crude extract was cooked in a water bath for an hour after a few drops of a 0.5N alcoholic potassium hydroxide solution were added. Additionally, a few drops of phenolphthalein were added separately. The presence of fixed oils and fats is indicated by the soap's formulation.

Detection of Flavonoids:

Ferric chloride Test: A blackish red colour formed in the test solution upon treatment with The presence of flavonoids is shown by a few drops of $FeCl_3$.

Detection of Steroids:

To each sample's 0.5g ethanol extract, 2ml of acetic anhydride and 2ml of H2SO4 were added. When steroids are present, the violet hue shifts to either blue or green.

Detection of Glycosides in the Heart:

Test Kella-Killani: An excerpt of the plant was dissolved in acid found in glaciers. that contained $FeCl_3$ remnants. After that, The tube was grasped at a 45° angle, and 1 ml of the conc. H_2SO_4 was introduced along the side. The interface's A purple ring indicates that cardiac glycosides are present.

Finding of Saponins:

Foam Examine: One millilitre of botanical extract and two millilitres of distilled H2O were combined and violently shaken. Saponins are present when there is a steady, sustained forth.

Detection of Phenols:

Ferric Chloride Test: Add 3 millilitres of distilled water to one millilitre of plant extracts. A small amount a neutral 5% $FeCl_3$ solution was added to this. Phenolics are indicated by a dark green hue.

Detection of Terpenoids:

Salkowski Test: Two millilitres of chloroform were added to one millilitre of plant extract. Next, a layer was carefully formed by carefully adding 3ml of conc. H_2SO_4. The interface's reddish-brown colouring suggests terpenoids' existence.

Finding of Starch:

Saturated NaCl solution (10 ml) was added to 1 ml of plant extract and heated. The starch reagent was added after heating. Starch is shown by the creation of a blue-purplish colour.

Detection of volatile oils:

One millilitre of plant extract was mixed with one millilitre of 90% ethanol, and then a few drops of FeCl3 were added. The presence of volatile oils in the

sample is indicated by the production of a green colour.

Finding Anthroquinones:

The Borntrager Test: A Just a tiny portion of the plant extract was thoroughly 10 millilitres of benzene were added, shaken, and then 5 millilitres of a 10% ammonia solution were added and agitated with the filtrate. The development of a violet, crimson, or pink hue suggests the existence of free anthroquinones.

Detection of Coumarins:

On a filter paper, a few drops of ammonia were applied. After adding a drop of plant extract, fluorescence was seen. This suggests that coumarins are present.

Test	Aqueous	Hexane	Ethyl acetate	Acetone	Methanol
Alkaloids	-	-	-	+	+
Carbohydrates	-	+	-	-	-
Tannins	-	-	+	+	+
Protein & amino acids	+	-	-	-	-
Quinones	-	-	-	+	+
Reducing sugars	-	-	-	-	-
Fixed oil and fats	+	-	-	-	-
Flavonoid	+	-	-	-	-
Steroids	-	-	+	+	+
Cardiac glycosides	-	-	-	+	+
Saponins	-	-	-	-	-
Phenols	-	-	+	-	-
Terpenoids	+	-	-	-	-
Starch	-	+	-	-	-
Volatile oils	-	-	+	+	+
Antraquinons	-	-	-	-	-
Coumarins	-	+	+	+	+

(+) presence (-) absence

Table: phytochemical investigation of Cissampelos pareira leaf extracts in various solvent systems, conducted qualitatively.

PHARMACOLOGY:

Antifertility activity:

When given orally, C. pareira leaf extract changed the pattern of the estrous cycle in female mice, lengthened the estrous cycle with a significant increase in the diestrus stage duration, and dramatically decreased the number of litters in albino mice. The plant extract changed gonadotropin release (LH, FSH, and prolactin) and estradiol secretion, according to an examination of the main hormones regulating the estrous cycle. It was discovered that the extract's oral LD50 in mice was 7.3 g/kg. [42]

Antioxidant activity:

The 1,1-diphenyl-2-picrylhydrazyl test revealed a noteworthy antioxidant activity in the C. pareira extract. At doses ranging from 50 to 400 µg/kg, C. pareira extract was seen to significantly scavenge nitric oxide, hydrogen peroxide, superoxide, and hydroxyl radicals in vitro. Additionally, in vitro hydroxyl radical-induced protein oxidation was reduced by C. pareira extract. In an animal model of acute oxidative tissue damage, benzo (a) pyrene-induced gastrointestinal toxicity in mice, C. pareira extract shows strong protective effects. [43]

Chemo preventive effects:

The study examined the preventive effect of C. pareira extract against benzo (a) pyrene [B(a)P]-induced gastric cancer in mice. The results showed a significant and dose-dependent reduction in tumour incidence, mean number of tumours, and tumour multiplicity. The study also investigated the modulatory effect of C. pareira extract on antioxidant enzymes, glutathione concentration, lactate dehydrogenase, and lipid peroxidation in the liver, as well as carcinogen metabolising phase I and phase II enzymes. Acid-soluble sulfhydryl (-SH) and cytochrome P450 contents were found to be significantly elevated, along with the activities of enzymes such as cytochrome P450 reductase, cytochrome b5 reductase, GST, DTD, SOD, catalase, glutathione (GSH) peroxidase, and GSH reductase, but

malondialdehyde (MDA) was found to be decreased. [44]

Anti-hemorrhagic effects:

Mice's skin was injected with a mixture of extract and venom to test the anti-hemorrhagic activity of the aqueous extract from C. pareira leaves. The results showed that the extract completely inhibited this activity. Conversely, studies on the anti-proteolytic activity were carried out by monitoring the impact on casein in a test tube or on microplates containing biotinylated casein. Both techniques failed to demonstrate any inhibitory activity. [45]

Immunomodulatory activity:

Numerous isoquinoline alkaloids have recently been the subject of extensive research due to their antibacterial, antitumor, neuropharmacological, and immunosuppressive properties. It would be interesting to look at their potential effects on the immune system because some of them are already being used in therapeutic settings.[46]

Antinociceptive and anti-arthritic activity:

In mice given an analgesymeter to produce pain, a 50% aqueous ethanolic extract of the roots of C. pareira showed substantial resistance to mechanical pain at dose ranges of 100–400 mg/kg. Additionally, the study indicated that plants had a strong protective effect against arthritis produced by Freund's adjuvant in a dose-dependent manner. [47]

Gastroprotective effects:

Root ethanol extract demonstrated a dose-dependent protective effect against ulcers, both chronic and acute. In ethanol-induced ulcers, C. pareira dramatically reduced the ulcer index in the lipid peroxidase product malondialdehyde while also greatly improving the defence variables total hexose and sialic acid. [48]

Cardioprotective effect:

The cardiac dysfunction caused by isoproterenol was lessened by the ethanolic extract of C. pareira roots. This effect may have been caused by an increase in antioxidant enzyme activities, a reduction in free radical production, and an improvement in calcineurin activity. [49]

Anti-diarrhoeal activity:

The total quantity of stool droppings decreased in a dose-dependent manner in the hydro-ethanolic extract of C. pareira, and castor oil-induced diarrhoea was inhibited in a 29.2–60.0% range. It decreased gastrointestinal transit and intestinal fluid buildup (26.0–59.0%). [50]

Hepato-protective effect:

In wistar albino rats, hydro alcoholic extract demonstrated protective effect against hepatotoxicity induced by anti-tuberculosis medications (20). The roots' hydro-alcoholic extract demonstrated a notable hepatoprotective effect against the hepatotoxicity caused by CCl4. [51,52]

Memory enhancing activity:

A mouse study using the elevated plus maze and passive avoidance paradigm revealed that C. pariera had memory-enhancing properties. [53]

Anti-diabetic activity:

The C. pareira leaf aqueosextract exhibited anti-diabetic properties. Male albino mice were administered a dose of 250 mg/kg and 500 mg/kg body of C. pareira extract over a period of 14 days. In this study, body weight and blood glucose levels were randomly monitored on a regular basis. The study also measured other biochemical indicators, including the amount of liver glycogen. [54]

Anti-anxiety activity:

The leaves of C. pareira were extracted with 70% hydroethanol, revealing the presence of steroids, terpenoids, alkaloids, and flavanoids. In the Elevated Plus Maze test (EPM), Light Dark (Land D) model, and Forced Swim test (FS) conducted on rats, the extract exhibited noteworthy anti-anxiety properties. [55,56]

Anti-asthmatic activity:

In many animal models of asthma, the aqueous portion of the ethanolic extract from the leaves of C. pareira has immunomodulatory effects. This work demonstrates that the aqueous fraction of C. pareira increases the levels of anti-inflammatory cytokines, reduces the generation of immunoglobulin specific to a particular antigen, and reduces the creation and deposition of mucus in the airways. [57]

Anti-cancer activity:

Pareitropone, a stropone-isoquinoline alkaloid found in C. pareira, had strong cytotoxic effects. A novel alkaloid called cissampareine, which is derived from Cpareira, exhibits consistent inhibitory effects on human nasopharyngeal cancer cells cultured in vitro. [58]

Anti-inflammatory activity:

Rats with acute, subacute, and chronic inflammation models respond favourably to a 50% ethanolic extract of C. pareira roots. [59]

Anti-ulceractivity:

At dosages of 25–100 mg/kg, the flavonoid Qurectein, which is present in C. pareira, shown anti-ulcer properties against rats that developed acute stomach ulcers due to pylorus ligation, 100% ethanol, aspirin, and cold-resistant stress. [57]

Antileukemic activity:

Pareirubrins A and B, which are tropoisoqunoline alkaloids found in C. pareira, exhibited antileukemic action. [60]

Anti Dengue Activity:

Dengue is turning into a major health threat. If dengue becomes a daily problem. If treatment is delayed, the viral titer can decrease, which can also decrease dengue virus infection. It has been discovered that the alcoholic extract of C. pareira works well as an anti-dengue agent by lowering the virus titer. [53]. In experiments involving cells, it suppresses dengue viruses (DENNVs). In the AG129 mouse model, the extract demonstrated strong anti-dengue effects. This extract inhibits the production of TNF-a cytokine [54]. The plant exhibits antiviral activity against all strains of dengue virus, as demonstrated by the traditional assay, with PRNT50 values ranging from 1.2-11.1 pg/mL.[61-63]

Anthelmintic activity:

The entire plant of C. pareira was tested for anthelmintic activity using earthworms in an in vitro setting. The paralysis and death of earthworms were investigated using alcoholic and aqueous extracts at different doses. Significant activity was seen in the extract, with aqueous extract being proven to be more effective in killing earthworms. [64]

Cardiac Hypertrophy:

The hyperthyroid-induced cardiotoxicity was reported to relapse in response to the C. pareira extract. The ratio of body weight to heart weight significantly decreased. By increasing the activities of antioxidant enzymes and improving calcineurin activity, the extract counteracts the effects of cardiotoxicity. [65]

Evaluation of toxicity:

The toxicity of C. arvensis in mice has been studied for a long time42. It is somewhat harmful to certain grazing animals. Nonetheless, grazing has been employed in the past to try and manage the weed. It is unknown how much field bindweed sheep, cattle and goats can safely eat. It is said to upset hogs when they consume it. [66,67] Oral administration of C. pareira did not alter the behaviour or physiological activity of experimental animals in the acute or subacute toxicity test. Haematological and biochemical analyses revealed no alterations. [68]

CONCLUSION

Cissampelos Pareira Linn. is a possible herb that is a member of the Menispermaceae family. There are many species on the planet, but only one of them is found in India. The plant can be used to cure a number of illnesses and may have therapeutic properties. The plant has the following medicinal uses: diuretic; anti-inflammatory; anti-cancer; anti-ulcer; antioxidant; antifertility; anti-anxiety; anti-arthritis; antidengue; antibacterial; anthelmenthic; antidiarrheal; and antihemorrhagic. Researchers are always trying to figure out new applications for it. Additionally, a variety of phytoconstituents found in plants have been discovered; these need to be further investigated. in order to carry out the activity connected to the single ingredient.

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