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A Review of the Phytochemistry, Pharmacology, and Traditional Applications of Cissampelos Pareira

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Abstract: In Indian traditional medicine, Cissampelos pareira, is a perennial climbing herb that is a member of the Menispermaceae family and is referred to as Ambastha or Laghu Patha. A review of the literature shows that C. pareira's phytochemistry and pharmacology have advanced significantly, indicating the plant's enormous therapeutic potential. Numerous pharmacological effects, including antipyretic, anti-inflammatory, antiarthritic, antiulcer, antidiabetic, anticancer, antifertility, antibacterial, antioxidant, antivenom, antimalarial, and immunomodulatory properties, have been demonstrated by the crude extracts of C. pareira.

Fatty acids, flavonoid glycosides, and alkaloids (isoquinoline alkaloids) were detected by HPTLC, HPLC, UPLC, LC-MS, and GC-MS. Only a limited amount of research has been done on the toxicological evaluation of C. pareira; more thorough research is needed. Pharmacological investigations of C. pareira through pre-clinical and clinical trials require greater focus in future studies.

Furthermore, before being used in therapeutic settings, traditional knowledge of C. pareira must be scientifically validated to guarantee safety, effectiveness, and mechanism of action.

Keywords: Traditional Medicine, Cissampelos pareira, Menispermaceae, Therapeutic Potential

I. INTRODUCTION

The World Health Organization (WHO) recognizes that hundreds of different traditional medical practices are in use worldwide. Acupuncture in China, magnetic treatment in France, Heilpraxis in Germany, herbalism in Sweden, shiatsu in Japan, and sowa rig-pa in Tibet and Bhutan are only a few instances of the global continuity of traditional medical systems. The Indian subcontinent has developed several ancient, mostly plant-based health care systems, some of which, like naturopathy, Siddha, and Ayurveda, are still quite effective in treating acute and chronic illnesses.

People also own, choose, and favor different healthcare systems based on cultural and familial customs. In India, medicinal plants have considerable acceptability in religious activities, where the plants are revered in the shape of numerous gods, goddesses, and local deities. Medicinal plants that are widely utilized for both religious and medical purposes include *Ficus religiosa, Saussurea obvallata, Ocimum sanctum, Ficus benghalensis, and Zanthoxylum armatum*. Across all habitats, from the southern Indian coast to the high Himalayan altitudes, 4,635 ethnic tribes employ plants as medicine for both human and veterinary health. Numerous plant species are used as the main source of healthcare in animal husbandry, aside from human usage. One strategy to fight biopiracy is to document traditional knowledge.

To avoid biopiracy, preserve the sovereignty of traditional herbal knowledge, and guard against the exploitation of traditional knowledge in patenting non-original findings, the Indian government endeavors to document traditional knowledge in the public domain.

By compiling data from the body of existing literature into a digital format known as the Traditional Knowledge Digital Library (TKDL), this pioneering move has led to the documentation of 202,500 pharmaceutical formulas. After seeing its value in avoiding the theft of the wealth of traditional knowledge and in promoting cutting-edge research, this digital library has been influenced on a global scale. (1)

II. TAXONOMY

Kingdom Plantae
Division Tracheophyta
Class Magnoliopsida
Order Ranunculales
Family Menispermaceae
Genus Cissampelos
Species *pareira* (2)

A. Vernacular Names

English - Velvet leaf
Hindi - Patha, Padh, Akanadi
Marathi - Pashadvel, Paharrel, Pahadavel, Padali
Bengali - Akanadi, Patha
Kannada - Pahadavela, Agalushunthi
Gujrati - Kalipath, Karondhium, Karondium, Venivel, Karedhium
Assamese – Tuprilata. (2)

B. Synonyms

Cebatha orbiculate, Cissampelos acuminata, Cissampelos argentea, Cissampelos auriculata, Cissampelos australis, Cissampelos benthamiana. (3)

C. Description

The plant has enlarged roots and grows to a height of 2 to 5 meters as a climbing shrub. The leaves are 7–14 cm in diameter and have an oval shape. They have veins, are glabrous to thickly pilose, and are either membrane-like or leathery. Each flower has a little circular leaflet at the base, and the men are in short umbels that are 10 to 12 cm long, while the females are in pendulous spikes that are 7 to 10 cm long. (4)

D. Distribution

Subtropical regions of America, Asia, East Africa, and India are inhabited by it. India is home to Patha, particularly in Assam, the Konkan, Matheran, and Mahabaleshwar. (2,4)

E. Traditional Uses

The leaves are used to cure diarrhea and indolent ulcers in the Ayurvedic medical system. The plant is used to treat urinary tract infections since it is thought to have antiseptic properties. *C. pareira's* expressed juice is used to treat migraines. For many years, C. pariera has been used to treat menstruation issues, rheumatism, muscular soreness, snakebite, and diarrhea. It has been used to treat a wide range of female illnesses. In tropical nations, the root is used to reduce uterine hemorrhages following childbirth and to avert a threatening miscarriage. (4)

F. Phytochemistry

The isolated and described phytomolecules from *C. pareira* include mostly isoquinoline alkaloids, with a small amount of flavonoids, flavonoid glycosides, and fatty acids. (5)

Magnoflorine, magnocurarine, cissamine, curine, hayatinine, and cycleanine are isoquinoline alkaloids that have been isolated due to the phytochemical and biological analysis of *Cissampelos pareira*. (6) Cissampeline, (−)-curine, (−)-cyclanoline, (+)-tetrandrine, (+)-obaberine, (+)-obamegine, (−)-oblongine, (+)-homoaromoline, (−)-nor-Nγ-chondrocurine, trans-N-feruloyltyramine, and (+)-coclaurine were isolated through phytochemical analysis of the roots of *Cissampelos pareira* (7).

Root- Deyamittin, Cissamine, isochondrodendrine, l-curine, menismine,, pareirine, hayatinine, berbeerines, essential oils, fixed oils, sterols, tetrandine, cycleanine, dihydrodicentrine, insularine, , bisbenzylisoquinoline, dicentrine.

Rhizomes- hayatine, hayatidine, d-4''o-methylberbeerine, L- bebeerines, isochondrodendrine, dicentrine, dehydrodicentrine, insularine.

Aerial parts- polyphenolic compounds like flavonoids and tannins

Leaves- Kaempferol-3-mono-glycosides, Quercetin-3-mono or di- glucosides, cycloanine.

Whole plant- tropoloisoquinoline alkaloids like pareirubrines A and B, grandirubrine, isoimerubrine, Pelosine, cissampareine. (2)

III. PHARMACOLOGY

According to the arachidonic acid test, oral administration of an ethanolic extract of the aerial parts of *Cissampelos pareira* demonstrated considerable and dose-dependent anti-inflammatory action in the carrageenin test, which was based on interference with prostaglandin formation. While the optimal dose for the hot-plate test was 100 mg/kg, a greater dose of the plant extract exhibited the strongest analgesic effect in the acetic acid-induced abdominal writhing test. According to the LD50, the extract (2000 mg/kg) exhibited little toxicity. (8)

The experimental study examines the scavenging capacity of *C. pareira* pectin from leaves at varying concentrations of nitric oxide (NO) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radicals, as well as the anti-inflammatory effect on RAW264.7 macrophage cells stimulated by lipopolysaccharide (LPS) and cell viability. With comparable half maximum inhibitory concentrations (IC50) of 0.54 and 0.52 mg/ml, the experimental results demonstrate a favorable correlation between the pectin concentrations and the DPPH and NO scavenging capabilities of *C. pareira* pectin. In the meantime, there is an inverse relationship between the concentrations of pectin and the NO generation in the LPS-stimulated macrophage cells. Because the extract component is not cytotoxic, there is a positive correlation between the quantities of *C. pareira* pectin and the cell viability in the LPS-stimulated macrophage cells. (9)

The methanol extract of *C. pareira* leaves has antibacterial activity that is equivalent to chloramphenicol against tested strains of *S. aureus* and *E. coli*. With a rise in extract concentration, the zone of inhibition becomes more visible. The methanol extract also showed the highest level of free radical scavenging activity, measuring 35.84 ± 0.05 at a concentration of 100 µg/ml. In contrast, the aqueous extract of *C. pareira* showed a lower level of free radical scavenging effectiveness, measuring 33.84 ± 0.05 at the same concentration. Additionally documented is the preventive impact of leaf on cisplatin on oxidative damage and nephrotoxicity, which has been shown to improve the oxidative stress parameters. (10)

The roots of the *C. pareira* plant were extracted using ethanol, methanol, acetone, hexane, and chloroform. Using the disc diffusion experiment, the antibacterial properties of the crude extracts at several doses were assessed. A two-fold broth dilution procedure was used to assess the crude extracts' minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). The lowest inhibition zone, measuring 7.0±0.1 mm against the pathogenic bacterial strain *E. coli*, was observed with the chloroform extract at 6.25µg, while the maximum inhibition zone, measuring 10.0±0.8 mm at 100µg extract, was observed with *E. faecalis*. The hexane extract exhibited the maximum zone of inhibition against *P. mirabilis* (10.8±0.2 at 100µg), whilst the lowest zone of inhibition (7.0±0.8 mm at 6.25 µg) towards *E. coli*. The acetone extract exhibited the greatest inhibition zone of 15.0±0.8 mm at 100 µg, and the lowest inhibition zone of 7.0±0.3 mm at 6.25 µg against *E. faecalis* and *S. saprophyticus*, respectively.

The methanol extract's highest inhibitory zone was seen against *E. coli* (18.0±1.0 mm at 100 µg), whereas the minimum was observed against *P. aeruginosa* (7.0±0.3 mm at 6.25 µg). The ethanol extract exhibited the least growth inhibition zone (7.0±0.1 mm at 6.25 µg) against the *K. pneumoniae* strain and the largest inhibition zone (20.8±1.0 mm at 100 µg) against the *P. mirabilis* strain. The acetone extract exhibited the greatest inhibition zone of 15.0±0.8 mm at 100 µg, and the lowest inhibition zone of 7.0±0.3 mm at 6.25 µg against *E. faecalis* and *S. saprophyticus*, respectively. The methanol extract's highest inhibitory zone was seen against *E. coli* (18.0±1.0 mm at 100 µg), whereas the minimum was observed against *P. aeruginosa* (7.0±0.3 mm at 6.25 µg). The ethanol extract exhibited the least growth inhibition zone (7.0±0.1 mm at 6.25 µg) against the *K. pneumoniae* strain and the largest inhibition zone (20.8±1.0 mm at 100 µg) against the *P. mirabilis* strain. (11)

The current study sought to assess the aqueous-ethanolic extract of *C. pareira* roots' antidiabetic impact in diabetic rats produced by streptozotocin-nicotinamide (STZ-NAM) by focusing on SGLT2 inhibition. Epoch Microplate Spectrophotometer has been used to perform in vitro α-amylase and α-glucosidase inhibitory experiments. Western blot and MTT assays were used for the SGLT2 protein expression investigation and the viability test of A-498 cells, respectively. Rats with STZ-NAM-induced diabetes were used as a model to assess the extract's antidiabetic potential. The extract IC50 values for α-amylase and α-glucosidase were 18.0 ± 1.01 and 4.87 ± 0.54 mg/mL, respectively, indicating that they were inhibitory effects. The viability assay for A-498 cells revealed a CC50 value of 0.8 mg/mL. The expression of the SGLT2 protein was significantly impacted by the extract. In a 28-day in vivo investigation, the extract significantly decreased the rats blood glucose levels at a dosage of 500 mg/kg. With docking scores of -10 and -9.9 kcal mol−1, respectively, insulanoline and warifteine were identified as the most active compounds in the molecular docking investigations. (12)

The purpose of this study was to examine the preventive effect of *C. pareira* hydroalcoholic extract against hepatotoxicity brought on by anti-tuberculosis medications. For 28 days, Wister albino rats received intraperitoneal injections of silymarin (200 mg/kg), isoniazid and rifampicin (50 mg/kg), and a hydroalcoholic extract of *C. pareira* (100, 200, and 400 mg/kg), in that order. To show that the hydroalcoholic extract of *C. pareira* and silymarin protects the liver from anti-tuberculosis medications, serum biochemical tests for liver functions and histological evaluation of livers were conducted. Hepatotoxicity was averted in a dosage-related manner in the groups that received 50% ethanol extracts of *C. pareira* once daily for 28 days at a dose of 100–400 mg/kg. SGPT (82.33±5.61 – 52.63±4.99), SGOT (376.4±8.55 – 193.96±6.96), SALP (389.78±8.24 –248.64±12.49), total protein (3.48±0.50–7.64±0.38), albumin (0.71±0.07-1.18±0.12), and total bilirubin (1.71±0.21–0.61±0.11) were the ranges of protection in the serum marker. For SGPT (82.33±5.61 – 46.80±4.14, $p<0.001$), SGOT (376.4±8.55 – 168.36±7.01), SALP (389.78 ± 8.24 – 239.22±7.50), Total protein (3.48±0.50–7.23±0.28), Albumin (0.71±0.07-1.29±0.07), Total bilirubin (1.71±0.21 – 1.03±0.10), and Direct bilirubin (0.93 – 0.26), the protection of silymarin varied accordingly. (13)

Rats given a hydroalcoholic extract of *Cissampelos pareira* roots (CPRE) plus silymarin had a strong hepatoprotective effect against CCl4-induced hepatotoxicity. Rats treated with CPRE showed a substantial reduction in elevated blood marker enzymes, including AST, ALT, ALP, and serum bilirubin, to levels close to normal. The treatment groups treated with 100, 200, and 400 mg/kg of CPRE also showed a substantial reduction in lipid peroxidation levels. After receiving 200 and 400 mg/kg dosages of CPRE, the levels of the antioxidant enzymes SOD and catalase rose noticeably, and the levels of GST, GPx, and GSH also increased. Triglyceride levels rose and cholesterol levels dropped when CPRE 200 and 400 mg/kg were administered. When HepG2 cells were treated to CPRE at dosages of 20, 40, 60, 80, and 100 microg/ml, their percentage viability significantly increased in comparison to HepG2 cells exposed to CCl4. The study's findings clearly show that Cissampelos pariera has high hepatoprotective potential. (14)

The study sought to determine if *Cissampelos pareira* root extract might protect rats' hearts from isoproterenol-induced cardiac failure. Each of the eight groups of Male albinos wistar rats was randomly assigned to receive either normal saline (0.5 ml/kg intraperitoneally), isoproterenol (5 mg/kg intraperitoneally), *C. pareira* (100 and 200 mg/kg, by gavage, respectively), amlodipine (9 mg/kg, by gavage) alone, *C. pareira* (100 and 200 mg/kg, respectively) + isoproterenol, or amlodipine (9 mg/kg) + isoproterenol once daily for 30 days. The heart weight/body weight ratio, serum calcineurin, nitric oxide, lactate dehydrogenase, and thiobarbituric acid reactive substance levels significantly increased in isoproterenol-induced cardiac dysfunction, while serum-reduced glutathione, cardiac glutathione peroxidase, glutathione reductase, and glutathione-S-transferase levels significantly decreased which the *C. pareira* therapy considerably improved. When comparing the group treated with *C. pareira* alone to the control, no discernible changes were seen. The histological alterations seen in rats given isoproterenol were likewise reversed by *C. pareira* therapy. In this trial, amlodipine is the conventional medication. These findings imply that the reduction of isoproterenol-induced cardiac dysfunction by the use of *C. pareira* ethanolic root extract may be the consequence of increased antioxidant enzyme activity, a reduction in calcineurin activity, and a reduction in the production of free radicals. (15)

Using the Lipschitz technique, the diuretic effect of an alcoholic extract of *Cissampelos pareira* roots was examined in albino rats. Using metabolic cages, the diuretic effect of an alcoholic extract was assessed in five groups of Albino rats. 2% CMC in normal saline is used as the usual control vehicle in group I. Furosemide (10 mg/kg, p.o.) is used in group II. Low (100 mg/kg), medium (200 mg/kg), and high (400 mg/kg) dosages of alcoholic extract of *Cissampelos pareira* roots are used in groups III, IV, and V, respectively. All rats were immediately hydrated with saline (15 ml/kg, p.o.) following the alcoholic extract treatment, and two rats were put in each metabolic cage, which was maintained at 21°C±0.5°C. The animals were denied food and water for five hours. After five hours, the total amount of urine collected with each metabolic cage was assessed. Numerous characteristics were examined, including the total volume of urine and the levels of sodium, potassium, and chloride. , groups treated with alcoholic extract at varying dose levels (100, 200, and 400 mg/kg) showed a substantial increase in urine volume and a significant increase in the excretion of sodium, potassium, and chloride ions in urine as compared to the control group. (16)

Middle cerebral artery occlusion (MCAO) was applied permanently to male Sprague-Dawley rats. Five groups were created from the animals: control, MCAO, and MCAO + *Cissampelos pareira* (50 mg/kg) extracts of n-hexane, ethyl acetate (EtOAc), and methanol (MeOH). Immunohistochemistry and the enzyme-linked immunosorbent assay were used to identify the expression of several inflammatory factors and enzymes in response to disease and extracts, such as cyclooxygenase (COX-2), c-Jun N-terminal Kinase (p-JNK), and nuclear factor kappa-light-chain-enhancer of activated B cells (p-NF-κB). Neurobehavioral impairments were alleviated, neuronal death was reversed, and the infarction area was decreased by the n-hexane extract (LD50 > 5.0 g/kg). In contrast, the n-hexane extract markedly increased the decreased levels of GST, GSH, CAT, SOD, and GPx. GCMS revealed that 1,2-benzene dicarboxylic acid was the main constituent of the n-hexane extract. Additional research is necessary to clarify the neuroprotective benefits of n-hexane extract since it may have therapeutic utility for stroke patients. (17)

The current work used an animal model of age-related cognitive impairment to assess the acute toxicity, protective effect, and underlying mechanism of PM52, a combination extract of *Cissampelos pareira* and Anethum graveolens, against age-related cognitive impairment. The OECD guideline classified PM52 as acute toxicity. Male Wistar rats weighing 180–220 g were administered oral doses of PM52 at 2, 10, and 50 mg/kg 14 days prior to and 7 days following the bilateral intracerebroventricular infusion of AF64A. Spatial memory, neuron density, MDA level, and the activities of SOD, CAT, GSH-Px, and the AChEI impact in the hippocampus were evaluated for each animal. It was discovered that all PM52 dosages might reduce hippocampal neurodegeneration and memory loss. The inhibition of AChE and the reduction of oxidative stress in the hippocampus may be the processes. Our findings thus imply that PM52 may be used as a dietary supplement to guard against age-related cognitive decline, including early-stage Alzheimer's disease and moderate cognitive impairment (MCI). However, further study is still necessary. (18)

A hydro-alcoholic solvent was used to extract *Cissampelos pareira* leaves. The open field test, locomotor test, despair swim test, and tail suspension test were used to assess the antidepressant activity. The rotarod, grip strength, chimney, and inclined plane tests were used to measure the skeletal muscle relaxant action, while the elevated plus maze and hole board tests were used to measure the anxiolytic activity. Experimental mice administered up to 2000 mg/kg of hydro-alcoholic extract (CPHE) showed no signs of death or moribund condition. Mice treated with CPHE 200 and 400 mg/kg showed a substantial reduction in ambulation, number of central squares traversed, and total locomotion in the open field and actophotometer tests and depicted less coordinated movements, and in despair swim and tail suspension tests, CPHE 400 mg/kg treated mice significantly decreased duration of immobility and increased number of climbing, confirming its anti-depressant effect. In an elevated plus-maze test, CPHE 200 and 400 mg/kg increased the open arm exploration, while in the hole board test, CPHE 400 mg/kg treated rats augmented the number of head dips, depicting its anxiolytic effect. In rotarod, grip strength, and inclined plane test, CPHE 400 mg/kg treated mice decreased the fall-off time on a rotating rod, suspended wire, or inclined plane. Furthermore, in the chimney test, treatment with CPHE 400 depicted less coordinated movements in mice; the mice of this group took more time to leave the cylinder, depicting its skeletal muscle relaxant effect. (19)

Rats were tested for anxiolytic action utilizing the elevated plus maze test (EPM), light dark (LandD) model, and forced swim test (FS) models. In the EPM, LandD, and FS models, the effectiveness of the extract (100, 200, and 400 mg/kg) was contrasted with that of the control and conventional diazepam (DZ; 2 mg/kg, p.o.) and imipramine (IM; 2.5 mg/kg, p.o.). According to the findings, DZ and extract considerably reduced the fecal count in EPM while increasing the number of entrances, time spent in open arms, head dip counts, and rearing time. In addition, DZ and extract considerably extended the period of immobility in the L and D model while increasing the number of crossings and time spent in the light compartment. For the FS model, mobility and swimming time were greatly enhanced by IM and extract. Accordingly, the findings support the possibility of using a 200–400 mg/kg hydroethanolic extract of *C. pareira* to treat anxiety-like behavior. To investigate the plant and its components for anxiolytic potential, more research is necessary. (20)

The goal of the current study is to determine how a hydroalcoholic (50% ethanol) extract of *Cissampelos pareira* (CPE) roots affects antioxidant enzymes, phase I and phase II enzymes that metabolize carcinogens, and forestomach cancer. Glutathione S. transferase (GST), DT-diaphorase (DTD), and superoxide dismutase (SOD) all showed considerable and dose-dependent increases in activity in the forestomach. In mice with benzo(a.)pyrene [B(a.)P]-induced gastric cancer, the protective effect of CPE was investigated; tumor incidence, mean number of tumors, and tumor multiplicity were all substantially and dose-dependently decreased. CPE's modulatory influence on antioxidant enzymes, glutathione levels, lactate dehydrogenase, lipid peroxidation in the liver, and carcinogen-metabolizing phase I and phase II enzymes was also investigated. Despite a decrease in malondialdehyde (MDA), there were notable increases in the levels of acid-soluble sulfhydryl (–SH) and cytochrome P450 contents as well as in the activities of the enzymes cytochrome P450 reductase, cytochrome b5 reductase, GST, DTD, SOD, catalase, glutathione (GSH) peroxidase, and GSH reductase. GSH concentration, cytochrome b5, DTD, GST, glutathione reductase (GR), and catalase were all up in the liver when butylated hydroxyanisole (BHA) was present, but MDA production was markedly suppressed. Additionally, BHA revealed markedly elevated DTD, GST, and SOD levels in the forestomach. *Cissampelos pareira's* chemopreventive effectiveness against chemotoxicity, including carcinogenicity, is suggested by the increased GSH level and enzyme activities involved in xenobiotic processing and preserving the antioxidant state of cells. (21)

With the use of NMR and many spectrophotometer techniques, including U.V., I.R., and other chemical assays, the substance that was obtained from the bioassay-guided fractionation of the CPE was identified as 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one (quercetin). Mice were used to test the preventive effects of ethanolic extract of *Cissampelos pareira* (CPE) at doses of 50 and 100 mg/kg body weight against B(a)P-induced gastric cancer. When comparing the CPE-treated groups to the B(a) P-treated groups, there was a dose-dependent and notable increase in body weight. The body weight dosages of CPE at 50 and 100 mg/kg demonstrated a protective effect against gastric cancer caused by B(a)P. In addition to a considerable and dose-dependent decrease in the mean number of tumors, the tumor incidence also decreased. Additionally, the tumor multiplicity was considerably decreased at 100 mg/kg. the antigenotoxic effects of CPE on the incidence of chromosomal abnormalities and MnPCEs caused by B(a)P. When compared to the control group, the B(a)P-treated mice showed a much higher incidence of MnPCEs and chromosomal abnormalities. Animals treated with B(a)P and CPE showed a dose-dependent reduction in the incidence of chromosomal abnormalities and MnPCEs at 100 mg/kg when compared to the B(a)P-treated group. In comparison to the control group, B(a)P administration markedly raised SOD and LPO while lowering CAT. The catalase level was dramatically and dose-dependently raised whereas the LPO and SOD were significantly and dose-dependently lowered with further CPE treatment. When comparing B(a)P-treated animals to control, there was a substantial decrease in GSH levels as well as GPx and GST activity. Animals treated with CPE showed a substantial and dose-dependent increase in GSH, GPx, and GST. (22)

The current study used the axillary bud of *Cissampelos pareira* to examine the effects of several carbon sources, including sucrose, fructose, maltose, and glucose, on in vitro shoot regeneration. The kind and concentration of carbon sources utilized had a significant impact on the frequency, development, and rate of multiplication. The MS medium supplemented with 2% fructose, BAP 1.0 mg/l, NAA 0.5 mg/l, and a 95% regeneration frequency produced the greatest number of shoots (8.06±0.11). The MS medium supplemented with 4% maltose produced the fewest shoots (3.4±0.10) and glucose (3.26±0.11). For repeated shoot regeneration from axillary bud explants of *Cissampelos pareira*, fructose 2% outperformed the other carbon sources employed in this study. Sucrose, maltose, and glucose came next. Following their removal from the shoot clumps, in vitro shoots were moved to the rooting medium, including NAA and IBA (0.5–3.0 mg/l). After removing the culture tubes, the firmly established plantlets were placed in sterile soil and vermiculate (1:1) in the greenhouse. Lastly, for maximum survival, the hardened plants were moved to the field setting. (23)

To assess *Cissampelos pareira* anticancer efficacy and in vitro cytotoxicity against Swiss mice's Dalton's lymphoma ascites (DLA) cells. It was extracted in stages using several solvents. The MTT test was used to measure in vitro cytotoxicity. The methanol extract of C. pariera (MECP) was given to mice at 200 and 400 mg/kg body weight for 14 days in a row, 24 hours after the DLA cells were intraperitoneally inoculated. Six mice were killed on day 14, while the remaining animals were kept alive to gauge any gain in lifespan. By measuring the packed cell volume, viable tumor cell count, increase in body weight, and increase in life span, the anticancer impact was evaluated. With an IC50 value of 95.5 mg/ml and a notable reduction in packed cell volume, viable cell count, and longevity (54 and 72%), Methanol Extract of Cissampelos Pariera (MECP) demonstrated strong cytotoxic action. Mice treated with MECP showed normal hematological and serum biochemical profiles. SOD, CAT, and lipid peroxidation were all markedly reduced to normal in the MECP-treated group. This study showed that C. pariera has strong anti-tumor effects both in vitro and in vivo, which might be attributed to its growing endogenous antioxidant system. (24)

Female rats in various groups were given an oral ethanolic extract of *C. pareira* for 14 days. Before receiving additional treatments, certain rat groups were given levonorgestrel (0.14 mg/g) orally for seven days to cause temporary infertility. At the close of each oral delivery method, the rats were killed. Heart punctures were used to obtain blood samples for lipid and hormone profiles, which were then examined using a commercially available ELISA kit. Organs were removed to measure the oxidative parameters. The extract contains alkaloids, saponins, glycosides, tannins, steroids, and flavonoids, according to phytochemical screening. Prolactin and estradiol concentrations were raised, testosterone was dramatically decreased, and progesterone was not significantly affected by the extract. There was no discernible hormonal difference between the groups before levonorgestrel was given. Even in individuals who had previously received levonorgestrel, the extract dramatically decreased cholesterol levels while increasing serum triglycerides. The extract considerably decreased the kidney's and ovary's H2O2 and SOD activity. The extract dramatically decreased H2O2 and GSH in the liver and kidney after levonorgestrel pre-administration, and it increased SOD activities in the brain, ovary, and liver. This study showed that the ethanolic extract of *Cissampelos pareira* has antifertility qualities based on its impact on the lipid profile and hormones, along with a mild antioxidant effect. (25)

Ethanolic extract of *Cissampelos pareira* roots has been examined in various acute and chronic ulcers in validated experimental models in rats. *C. pareira* extract of 25–100 mg/kg administered orally, twice daily for 5 days showed a dose-dependent, ulcer-protective effect. The extract demonstrated significant protection against 100% ethanol, aspirin, cold-restraint stress, and pylorus ligation-induced acute gastric ulcers in rats. A flavonoid Quercetin, isolated from *C. pareira*, showed significant antiulcer properties against gastric ulcers in different acute models. In chronic ulcers induced by 50% acetic acid, *C. pareira* significantly ($P < 0.001$) reduced the ulcer index with decreased perforations after 5- and 10-day treatment. *C. pareira* significantly enhanced the defense factors as total hexose and sialic acid while significantly reducing the ulcer index in the lipid peroxidase product malondialdehyde in ethanol-induced ulcers. (26)

An aqueous extract from *Cissampelos pareira* leaves was tested for its ability to counteract the hemorrhagic and proteolytic effects of Bothrops asper venom. The extract from *C. pareira* had a dose-dependent action, fully stopping the bleeding (ED50 = 25.1 mg). The absorbance at 280 nm was the same for all extract-venom and venom control solutions. The studied extract quantity was insufficient to neutralize 1.4 mg of the minimal proteolytic dosage. The venom's proteolytic activity could not be inhibited by any quantity of extract. (27)

Mice were used to test the alkaloidal fraction (AFCP) of *Cissampelos pareira* Linn. roots for immunomodulatory and antioxidant properties in vitro. To identify AFCP, an HPTLC fingerprint profile was also created, and it was discovered to contain 0.176 percent berberine. The capacity of AFCP to scavenge the stable free radicals DPPH and superoxide ion as well as to prevent lipid peroxidation in rat liver homogenate caused by the iron/ADP/Ascorbate complex demonstrated its potent antioxidant activity. At lower dosages (25 and 50 mg/kg), AFCP was shown to have a strong immunosuppressive effect; at larger doses (75 and 100 mg/kg), no activity was seen. At dosages of 25 and 50 mg/kg, AFCP substantially ($p<0.01$) reduced the titer of humoral antibodies. At a dosage of 75 mg/kg, the AFCP also markedly reduced the delayed type hypersensitivity reaction. Consequently, the current investigation demonstrated the antioxidant and immunosuppressive properties of the alkaloidal fraction of *C. pareira* roots. (28)

IV. CONCLUSION

Cissampelos pareira, sometimes referred to as velvet leaf. Horseshoe-shaped seeds, brownish roots, red drupe berries, and green leaves characterize this climbing plant. Ancient writings such as the Nighantus and Bruhatrayee (Charaka Samhita, Sushruta Samhita, and Ashtang Hridya) indicate several applications of *C. pareira* in Atisara, Prameha, Arsha, Bastivikara, and other places. Research on *C. pareira* also demonstrates its pharmacological properties, which include antioxidant, hepatoprotective, diuretic, antidiabetic, antiasthmatic, and anti-inflammatory properties. The purpose of this review is to increase our understanding of *C. pareira* by gathering all available data on its pharmacognosy, phytochemical ingredients, pharmacological properties, and different traditional applications. It will undoubtedly provide a fresh approach for scientists and the pharmaceutical sector to create a new medication.

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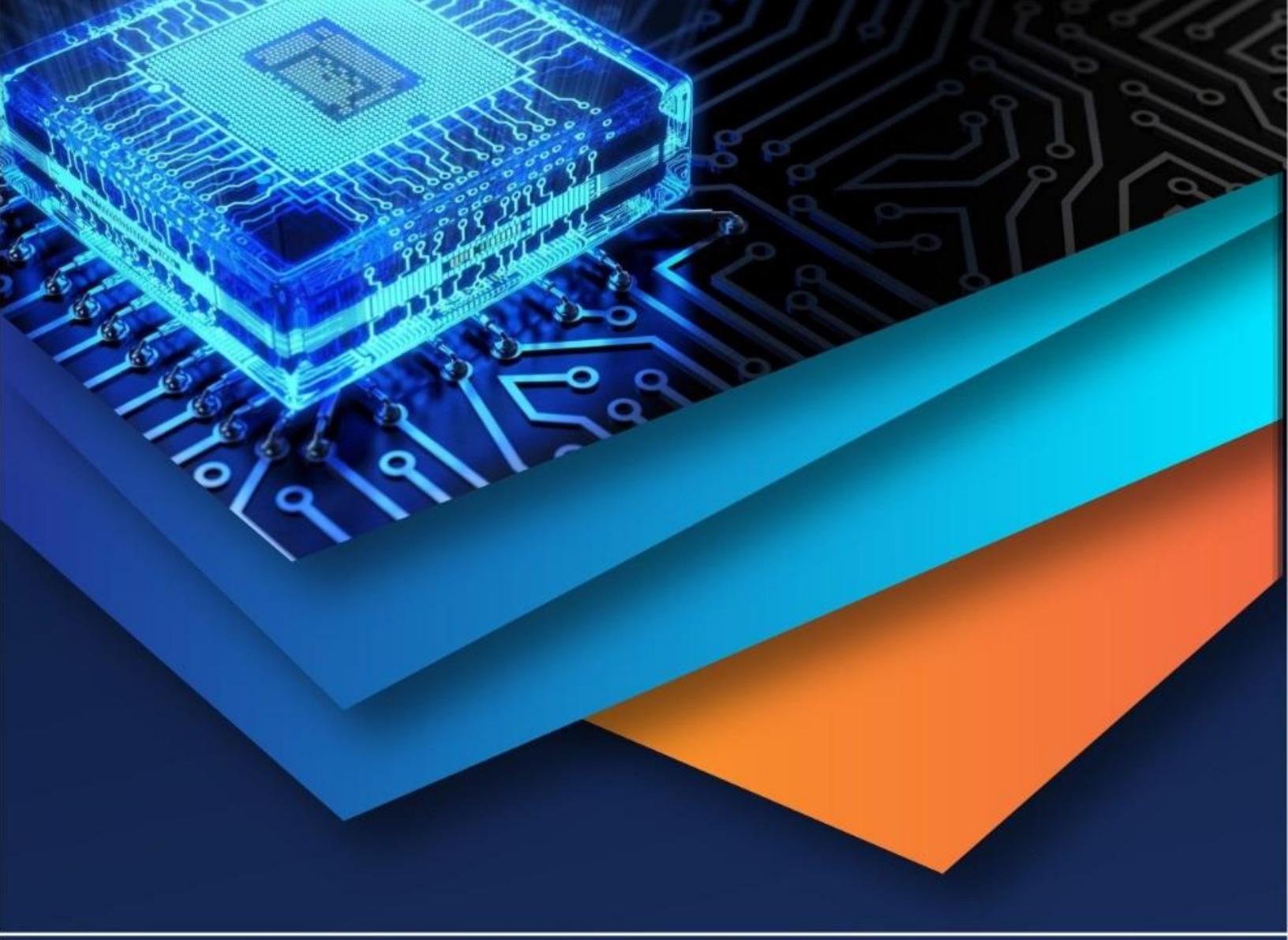

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