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"PHARMACOLOGICAL INSIGHTS AND BOTANICAL OVERVIEW OF *AYAPANA TRIPLINERVIS:* A COMPREHENSIVE REVIEW"

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ABSTRACT

Ayapana triplinervis also known as Ayapana, is a medicinal plant widely used in healing processes and in mystical-religious rituals by traditional communities in South America, Africa, and Asia. It is a perennial shrub native to the Amazon rainforests of South America. Ayapana has three different Latin names (*Ayapana triplinervis*, *Eupatorium ayapana*, and *Eupatorium triplinerve*), but all three names refer to the same plant. The flowers are pale pink, and the stem is reddish, hairless and thin. Traditional medicinal practices have long utilized various parts of the plant for treating a wide range of ailments, including digestive disorders, respiratory ailments and skin conditions. Chemical constituents like 7-ethoxy coumarin (ayapanin), 6,7-dimethoxy coumarin (ayapin), hydrangetin, daphnetin, daphnetin dimethyl ether, 7-methyl daphnetin ether, umbelliferone, carotene, vitamin C and stigmasterol have been isolated from the plant. Furthermore, recent scientific investigations have highlighted the therapeutic potential of *Ayapana triplinervis* in the management of various health conditions such as antioxidant, antimicrobial, anti-inflammatory, antitumorous, hepatoprotective, antiulcerous, gastroprotective and antinociceptive activity. This review aims to provide a comprehensive overview of *Ayapana triplinervis*, covering its botanical characteristics, phytochemical composition and pharmacological activities. Overall, *Ayapana triplinervis* emerges as a valuable botanical resource with significant therapeutic potential, deserving further exploration for its diverse health benefits.

KEYWORDS: *Ayapana triplinervis*, traditional medicine, anti-oxidant, hepatoprotective, botanical characteristics, phytochemicals, antiulcerous, antitumorous.

INTRODUCTION

Ayapana triplinervis (Vahl) R.M. King & H. Robinson (*Ayapana triplinervis*), also known as ayapana, ayapana tea, ayapan, belongs to the asteraceae family. It is an elegant, upright and perennial herb with scented leaves. It is native to South America and can be found in the Mascarene Islands, China, India, Java, Vietnam, and the Philippines. Synonyms of the plant are *Ayapana officinalis* Spach, *Eupatorium ayapana* Vent, *Eupatorium luzoniense* Llanos, *Eupatorium triplinerve* Blume and *Eupatorium triplinerve* Vahl. *Ayapana triplinervis* has traditionally been employed in folk medicine to cure a number of illnesses. Its traditional uses include antibacterial, antitussive, antiulcerous, laxative, sedative, stimulant, stomachic, tonic, hepatoprotective, astringent, cardiotonic, antitussive, hemostatic and other purposes. This herb can be used as a diuretic, expectorant, emetic, tonic, antiperiodic, and cardiac stimulant in medicine. Additionally, it treats hemorrhage, wounds, ulcers, and snakebite injuries. From prehistoric times, people have utilized medicinal plants to heal a variety of ailments. The World Health Organization estimates that traditional medicine is the primary source of care for 80% of the world's population. It deals with plant extracts and their active ingredients; many plants have long been utilized in folk medicine to treat a wide range of illnesses.[1] Herbal remedies are essential for both health treatment and illness prevention. They include phytochemical constituents that aid in the healing process and are a major source of molecules with therapeutic properties.[2] Terpenoids, phenolics, flavonoids, tannins, alkaloids, and glycosides are among the most significant secondary metabolites and are a significant source of individual bioactive components.[3] The use of medications derived from plants is growing globally.[4] It was discovered that several plant parts, including the roots, stems, leaves, fruits, and flowers, have secondary metabolites that possess bioactivity.[5]

In traditional cultures in South America, Asia, and Africa, *Ayapana triplinervis* is widely utilized in folk medicine and mystical-religious ceremonies. It is found in two morphotypes: morphotype A, also known as

"Japana-branca," and morphotype B, also known as "Japana-roxa." Plants defend themselves against herbivores and phytopathogens in a variety of ways, one of which is through the intricate chemical process of secondary metabolites. *Ayapana triplinervis* is one of the species that produces a wide range of compounds in different tissues both above and below ground. These chemicals are used by humans as medications, food and beverage flavourings, fragrances, textile dyes, hygiene products, and insect control, in addition to being used as a defence against biotic or abiotic stressors.[6]

BOTANICAL DESCRIPTION

Ayapana triplinervis is an ornamental perennial herb grows up to 30 to 60 centimetres in height. This plant roots and creeps at its base, where it is partially woody. The stem is hairless and has a reddish-brown colour. The leaves are lanceolate, acuminate, 3-nerved, smooth, opposite, subsessile, and glabrous inflorescence. Leaves are 5 to 8 cm long and is a small herb that has a strong smell. The fruits are achenes, narrowly oblong, 5-angled and about 2 mm length.[7] Each flowering head has pink flowers and measures 6–13 mm in length. Flowers have slender reddish stems with slaty blue or pale pink petals.[8]

Figure: Leaves and flower of *Ayapana triplinervis.*

TAXONOMICAL CLASSIFICATION

Kingdom	**Plantae**
Division	**Phanerogamae**
Class	**Eudicots**
Sub class	**Gamopetalae**
Order	**Asterales**
Family	**Asteraceae**
Genus	**Eupatorium**
Species	**Eupatorium triplinerve vahl**

DISTRIBUTION

Ayapana triplinervis is indigenous to South America and can be found there as well as in the Mascarene Islands (Reunion, Mauritius, and Rodrigues), China, India, Philippines, Java, Bangladesh, Vietnam, and Indonesia. It is found in Brazil, Puerto Rico, Guyana, Ecuador, Peru, South America, and Hawaii.[1]

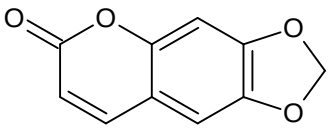
VERNACULAR NAMES

Sl.No	Language	Common names
1.	Hindi	Ayapana, Ayaparna
2.	Malayalam	Aiyappana, Mrithasanjeevani
3.	Tamil	Ayapani
4.	Telugu	Gurivinda, Guriginja
5.	Sanskrit	Vishalyakarni, Ayaparnah
6.	Latin	*Eupatorium triplinerve*
7.	English	Ayapana tea, Water hemp

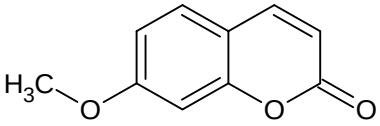
CHEMICAL CONSTITUENTS

The aqueous extract of *Ayapana triplinervis* leaves contained the coumarins Ayapin, Ayapina, thymoquinol dimethyl ether, thymoquinone, and methylthymyl ether. Galvin-Bialecke and Marodon reported the presence of seven distinct categories of coumarins: ayapanin, ayapina, daphnetin, daphnetin dimethyl ether, 7-methyl-daphnetin ether, hydrangetin and umbelliferone. Furthermore, the authors found that dimethyl ether

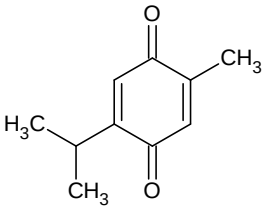
thymohydroquinone (89.9 - 92.8%) was present in Reunion Island plant species.[6]



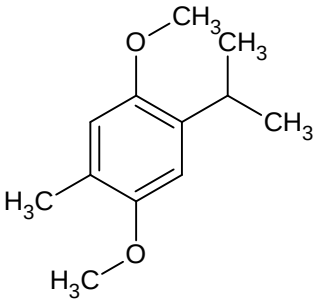
Ayapin



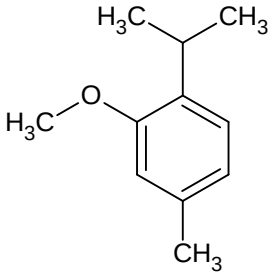
Ayapina



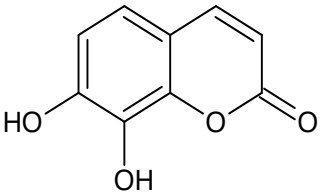
Thymoquinone



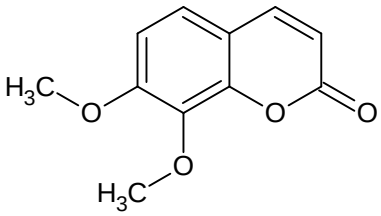
Thymoquinol dimethyl



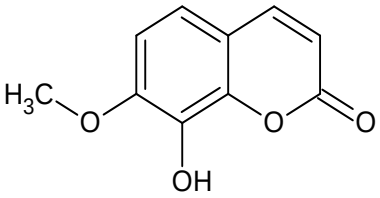
Methylthyml ether



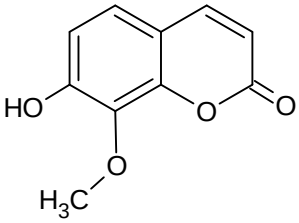
Daphnetin



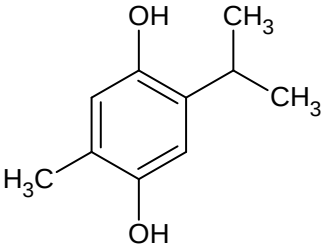
Daphnetin dimethyl



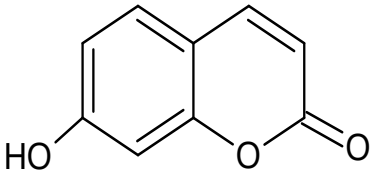
7-methyl-daphnetin



Hydrangetin

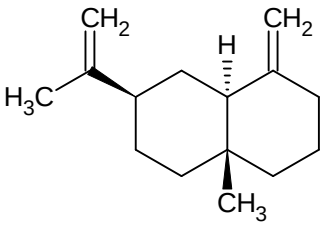


Thymohydroquinone

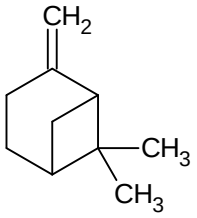


Umbelliferone

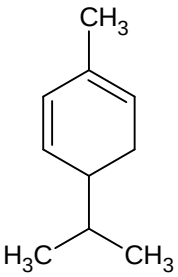
GC-MS was used to evaluate the essential oil from the aerial parts of *Eupatorium triplinerve*. The oil yield was 1.10%. GC-MS analysis was used to identify thirty compounds, with b-selinene (8.59%) and 2-tert-butyl-1,4-methoxbenzene (74.27%) as the two main compounds. Additional noteworthy chemicals include b–pinene (1.51%), b-pinene (2.19%), a–phellandrene (2.2%), thymolmethyl ether (2.03%), b–selinene (1.28%) and 6-isopropenyl-4, 8adimethyl-1, 2, 3, 5, 6, 7, 8, 8a-octahydronaphthalene-2-ol (2.63%).[8]



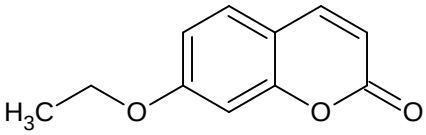
β-selinene



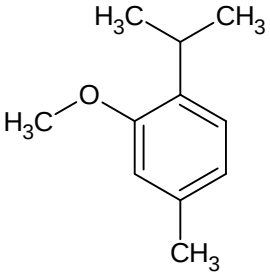
β-pinene



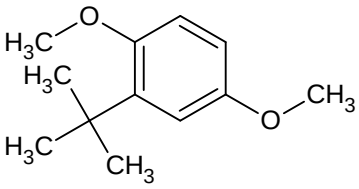
α-phellandrene



Ayapanin

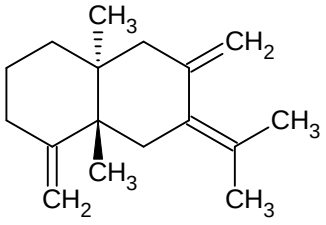


Thymol methyl ether

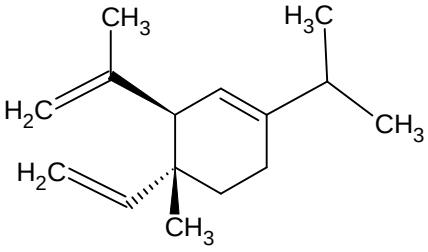


2-tert-butyl-1,4-dimethoxybenzene

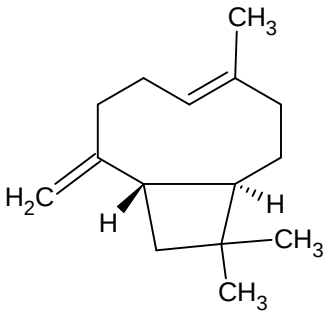
Gupta, Charles and Garg, had examined essential oil from the leaves of the species collected in Lucknow, which reported the presence of the principal components such as selin-4(15),7-dien-8-one with 36.6%, β-caryophyllene with 14.7% and δ-elemene with 5.9%.[9]



selin-4(15),7-dien-8-one



δ-elemene



β-caryophyllene

PHARMACOLOGICAL ACTIVITY

Antimicrobial activity

Phytochemical screening of hydroalcoholic extract from all parts of *Eupatorium triplinerve* identified mainly steroids, coumarins, alkaloids, saponins, tannins, depsides and absence of polysaccharides and flavonoids. The leaf methanol extract had the largest coumarin content and the lowest minimum inhibitory concentration (MIC) values (62 and 75 mg/mL) against *Staphylococcus aureus* and *Enterococcus faecalis*, respectively. The antibacterial activity of its non-polar components was shown against Gram-negative bacteria, primarily *Escherichia coli*, with MIC values ranging from 16 to 125 mg/ml. The non-polar fractions of *Eupatorium triplinerve* methanolic extract has better antimicrobial activity.[10] Using the leaf extract, *Ayapana triplinervis* conjugated silver nanoparticles were synthesized. The FTIR, SEM, and UV-Visible spectrophotometer was used to examine the produced silver nanoparticles. The well diffusion method was used to assess the antibacterial activity against common microorganisms. Highly effective antibacterial action against *Salmonella*, *Bacillus* and *Pseudomonas*.[11] The essential oil demonstrated a moderate level of antibacterial activity against every pathogen tested. At a concentration of 20 µl/disc, the greatest antibacterial activity was observed against *Salmonella typhi* (21 mm), followed by *Shigella sonnei* (18 mm).[8]

Antifungal activity

GC-MS was used to evaluate the essential oil from the aerial portions of *Eupatorium triplinerve*. GC-MS analysis was used to identify thirty chemicals, with b-selinene (8.59%) and 2-tert-butyl-1,4-methoxbenzene (74.27%) as the two main constituents. A few other important constituents are 6-isopropenyl-4, 8adimethyl-1, 2, 3, 5, 6, 7, 8, 8a-octahydronaphthalene-2-ol (2.63%), b-pinene (2.19%), b-pinene (1.51%), a-phellandrene (2.2%), thymolmethyl ether (2.03%), and b-selinene (1.28%). The essential oil showed better antifungal activity in comparison to the conventional antibiotic, Nystain. The MIC value of the essential oil was found between 6000-9000 ppm against the test fungi. The lowest MIC value (6000 ppm) was recorded against *Macrophomina phaseoline* and *Colletrotrichum corchori*. MFC value of the essential oil were found between 8000-12000 ppm. The oil exhibited the lowest MFC value (8000 ppm) against *Macrophomina phaseoline* and *Botryodiplodia theobromae.*[8]

Anti-inflammatory activity

The antibiofilm and anti-inflammatory properties of Ayapana leaves were assessed through extraction using solvents such as hexane, dichloromethane and ethyl acetate. The CH_2Cl_2 and EtOAc extracts exhibited moderate anti-inflammatory activity against nitric oxide in RAW264.7 cells with IC_{50} values of 65.7 and 66.9 µg/ml.[12]

Anti-oxidant activity

Antioxidant activity was done based on the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay using a UV–visible spectrophotometer and based on ferric reducing antioxidant power (FRAP) assay using a microplate reader. Various solvents such as n-hexane, ethyl acetate, and methanol were used. According to the DPPH assay conducted using a UV-visible spectrophotometer, n-hexane, ethyl acetate, and methanol extracts at a final concentration of 25 µg/mL reduced DPPH radical generation by 38.91, 51.03 and 54.06%. The extracts of ethyl acetate and methanol had IC50 values of 26.71% and 23.472 µg/mL, respectively, based on the percent inhibition. Using a microplate reader, the ferrous equivalent antioxidant capacity values of n-hexane, ethyl acetate, and methanol extracts were determined using the FRAP test, yielding values of 460, 828.99, and 940.22 µmol/g. The methanol extract had the greatest antioxidant activity.[13] The antioxidant activity of the Kupchan fractions of the methanolic extract of *Eupatorium triplinerve* was examined. The Kupchan technique was used to partition the crude extract using methanol, petroleum ether, chloroform, carbon tetrachloride and water-soluble components. The proportion soluble in petroleum ether exhibited the highest level of antioxidant activity (IC50 = 1.67 µg/ml).[14] The antioxidant activity of the plant was evaluated using extracts of hexane, CH_2Cl_2 and EtOAc as solvent. With a half inhibition concentration (IC50) value of 22.7 µg/ml, the EtOAc extract demonstrated remarkable efficacy against DPPH radicals.[12]

Antidiabetic activity

The following 10 compounds were extracted from the methanol leaf extract used in the study of antidiabetic compounds from *Eupatorium triplinerve* leaves by using ESI-MS, 1D, and 2D NMR techniques: β-sitosterol (1), stigmasterol (2), β-sitosterol 3-O-β-D-glucopyranoside (3), ayapanin (4), ayapin (5), thymoquinol 5-O-β-D-glucopyranoside (6), thyrsifloside (8), (E)-4-methoxymelilotoside (9), and kaempferol 3,7-di-O-β-D-glucopyranoside (10) were studied. Compounds 4–9, compound 5 and compound 7 demonstrated enzymatic inhibition of 40%, 46%, and 81% at 256 µg/mL in the in vitro test for α-glucosidase inhibition.[15]

Anthelmintic activity

At 50 mg/ml and 100 mg/ml, the ethanolic extracts from the leaves of *Eupatorium triplinerve* shown a dose-dependent anthelmintic activity in the invitro models *Pheritima posthuma* and *Ascardia galli*, thus indicating a broad spectrum of action.[16]

Anticancer activity

The study assessed the anticancer activity of ethanolic and aqueous extracts of *Eupatorium ayapana* leaf in Swiss albino mice having Ehrlich's Ascites Carcinoma (EAC). It was assessed by evaluating tumor volume, viable cell count, increase in body weight, mean survival time and hematological parameters of the EAC bearing host. The findings showed that both extracts, at 150 mg/kg body weight, had strong antitumor activity, with the ethanolic extract being significantly more effective than the water extract.[17]

Antinociceptic activity

Swiss male and female mice as well as two-month-old male Wistar rats were used to test the anti-nociceptic properties of the hydroalcoholic extracts of *Eupatorium triplinerve*. Both thermal and chemical (formalin and acetic acid) nociception models were applied. It showed that antinociceptive effects was not related to opioid system.[18]

Thrombolytic and Membrane stabilizing activity

The thrombolytic and membrane stabilizing properties of the Kupchan fractions of the methanolic extract of *Eupatorium triplinerve* were assessed. The Kupchan technique was used to partition the crude extract using methanol, petroleum ether, chloroform, carbon tetrachloride and aqueous soluble materials. Significant thrombolytic activity was found in the petroleum ether and chloroform soluble partition, with 15.75% and 10.41% clot lyses, respectively. The carbon tetrachloride soluble fraction showed the highest percentage inhibition of hemolysis for membrane stabilizing activities.[14]

Gastroprotective effect

The hydromethanolic extract was used to assess the gastroprotective effect of *Ayapana triplinervis* leaves against indomethacin-induced gastric ulcer in male albino rats. The active ingredients present in the *Ayapana triplinervis* shows gastroprotective properties that prevent the indomethacin-induced gastric ulcer.[19]

Hepatoprotective effect

The hepatoprotective activity of methanol extract of *Eupatorium triplinerve* was evaluated in wistar albino rats. Superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and protein levels were significantly ($p < 0.05$) elevated in response to the extract, while the activity of serum enzymes, bilirubin, uric acid, and lipid peroxidation was significantly ($p < 0.05$) decreased. Strong hepatoprotective properties are present in the methanol extract of *Eupatorium triplinerve*.[20]

Hemostatic effect

Based on the ethanomedical survey, the hemostatic effect of *Eupatorium ayapana* was examined in rat model by measuring the tail bleeding time and blood clotting time in fresh juice and methanolic extract. The study validated the traditional usage of *Eupatorium ayapana* in stopping blood bleeding by showing that both fresh juice and methanolic extract significantly reduced the bleeding and clotting times at doses of 200 mg/kg and 50 mg/kg, respectively.[21]

DISCUSSION

The exploration of *Ayapana triplinervis* encompasses a diverse range of traditional applications, phytochemical constituents, and pharmacological effects. This plant, widely utilized in traditional medicine across various cultures, has garnered significant attention from researchers globally. Analyses of the phytochemistry of *Ayapana triplinervis* have revealed the presence of a wide array of compounds, including coumarins, essential oils, and various secondary metabolites. These chemical components serve as the foundation for its medicinal attributes, highlighting its importance as a potential reservoir for drug discovery and advancement. Studies have unveiled numerous pharmacological activities including anti-inflammatory, antioxidant, antimicrobial, antidiabetic, anticancer, wound healing, hepatoprotective, analgesic, antiulcerative and gastroprotective properties.

CONCLUSION

Ayapana triplinervis emerges as a reservoir of botanical significance, revered for generations in traditional medicinal practices and increasingly acknowledged by contemporary scientific endeavors for its pharmacological promise. Its diverse phytochemical composition, alongside its multifaceted pharmacological attributes, positions it as a promising avenue for further exploration and application in pharmaceutical and nutraceutical domains. Ongoing investigation into *Ayapana triplinervis* holds the potential to unveil novel therapeutic modalities, addressing unmet healthcare needs and promoting the welfare of individuals on a global scale.

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