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Acorus calamus Linn.: A herbal tonic for central nervous system

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Abstract

Ayurveda, Unani, Siddha and Homeopathy medicines are the major systems of indigenous medicines. Among these systems, Ayurveda is most trusted and widely practiced in India. *Acorus calamus* Roots and rhizomes have been used in Indian system of traditional medicine for hundreds of years and it is highly valued as a rejuvenator for the brain and nervous system and as a remedy for digestive disorders. *Acorus calamus* rhizome constituents, particularly α and β-asarone, possess a wide range of pharmacological activities such as sedative, CNS depressant, behavior modifying, anticonvulsant, acetyl cholinesterase inhibitory & memory enhancing. The aim of the present article is different uses of *Acorus calamus* in CNS disorders.

Keywords: Anticholinergic activity, α & β-asarone, Anticonvulsant.

Introduction

In Ayurveda *Acorus calamus* Linn. (Family Araceae) is known as VACHA and publically known as "sweet flag" or Bacha. This is a species of semiaquatic, perennial, aromatic herb with creeping rhizomes. The plant is found in the northern temperate and subtropical regions of Asia, North America, and Europe. The plant prefers swampy or marshy habitats. It is plentiful in the marshy tracts of Kashmir, Himachal Pradesh, Manipur, and Naga hills, and is regularly cultivated in Karnataka. The plant exhibits polyploidy and three karyotypes. The diploid karyotype (2n ¼ 24) grows in North America and in parts of Asia (Siberia); the triploid karyotype (3n ¼ 36) is present in Central Europe and Kashmir, India; the tetraploid karyotype (4n ¼ 48) is found in India, East Asia, and Japan. In India, the plant is found growing wild as well as cultivated up to an altitude of 2200m in the Himalayas.[1]

Along with other therapeutic applications, The Ayurvedic Pharmacopoeia of India[2] indicates the use of the dried rhizomes as a brain tonic in weak memory, psychoneurosis and epilepsy. Four types of Calamus are used in herbal medicine: type I—*Acorus calamus* L. var. americanus, a diploid American var.; type II—var. vulgaris L. (var. calamus), a European triploid; type III and type IV—var. augustatus Bess. and var. versus L., subtropical tetraploids. Beta-asarone is carcinogenic in animals. The volatile oil of types II, III and IV—major constituent is usually beta-asarone (isoasarone), up to 96%. Indian calamus oil contains asarone up to 82% and its beta-isomer. In type I, beta-asarone and other phenylpropanoids are absent. It is superior in spasmolytic activity to the other types (Indian medicinal plants).[3]

Medicinal Uses

The extracts of *A. calamus* have been found to possess an antibacterial activity.[4-6] β-asarone in *A. calamus* rhizomes were demonstrated to have antibacterial activity5. However, β-asarone concentrations vary markedly among the oil from *A. calamus* varieties. The tetraploid plant oil is high in β- asarone (90-96%). The triploid plants contain a small portion of β-asarone (5%) in their oil and the diploid plants lack β-asarone.[7]

Uses ascribed in traditional medicine In the Ayurvedic system of medicine, the rhizomes of AC are considered to possess aromatic, stimulant, bitter tonic, emetic, expectorant, emmenagogue, aphrodisiac, laxative, diuretic, antispasmodic, carminative, and anthelmintic properties. They are used for the treatment of a host of diseases such as mental ailments like epilepsy, schizophrenia, and memory disorders, chronic diarrhea and dysentery, bronchial catarrh, intermittent fevers, tympanitis, colic, otitis media, cough, asthma, and glandular and abdominal tumors8, 9 . They are also used traditionally for flatulent colic and chronic dyspepsia. They are also employed for kidney and liver troubles, rheumatism, and eczema. The skin of the rhizomes is said to be hemostatic. The rhizomes are used in the form of powder, balms, enemas, and pills and also in ghee preparations.[8, 9]

Chemical constituents

A wide variety of chemical constituents have been reported from the rhizomes of AC. The oil of AC rhizomes has been analyzed by various workers for their chemical constituents.[10, 11] The oil was found to contain varying concentrations of a-asarone (1), b-asarone (2), c-asarone (3), calamene, calamenenol, calameone (4), a-pinene (5), b-pinene (6), camphene, p-cymene, eugenyl acetate, eugenol (7), isoeugenol (8), methyl isoeugenol (9), calamol, azulene (10), eugenol methyl ether, dipentene (11), methyleugenol, asaronaldehyde (12), terpinolene (13), 1,8-cineole (14), camphor (15), a-caryophyllene (16), and hydrocarbons[12-14] The oil also contains fatty acids such as palmitic acid and its ester, heptylic acid, an ester of butyric acid.[15]

Pharmacological Activities

AC has been screened for various pharmacological activities. It has significant CNS actions such as anticonvulsant, sedative, hypnotic, tranquilizing, and memory enhancing, which justifies its use in some CNS diseases in the Ayurvedic system of medicine. It also has acetylcholinesterase inhibitor, antispasmodic, antimicrobial, anti-inflammatory, anthelmintic, and insecticidal effects.

CNS depressant activities

Tripathi and Singh[16] performed a clinical study in 50 cases of depression. AC given for 6 weeks showed reduction in the degree of severity of depression and better rehabilitation and also a significant improvement in assessment based on the rating of symptoms on the Hamilton depression rating scale. The effect of the ethanol extract of AC was studied (experimental study on rats) on spontaneous electrical activity and monoamine levels of the brain. Thus, AC showed its depressive action by changing electrical activity and by differently altering brain monoamine levels in different brain regions.[17]

α-Asarone and β-asarone showed many pharmacodynamic actions similar to some well established tranquilizers. The mechanism of tranquilizing action of α-asarone was also studied. It was found that the sedative effect of α-asarone was dependent on the depression of the ergotropic division of the hypothalamus.[18] α-Asarone reduced spontaneous motor activity and caused a reduction in anxiety without dulling the perception in rats. It produced a prolonged calming effect in monkeys.[19]

Anticonvulsant activity

Acorus oil investigated for its antianaleptic activity was used as a saline suspension, given 1 h prior to production of convulsions in adult albino mice. It successfully prevented seizures in maximal electroshock seizures test.[20] β-Asarone caused generalized convulsion and potentiated metrazol seizures in rats, while α-asarone showed a tendency to protect against metrazol convulsions and modified electroshocks.[21] In a study using electroconvulsions, α-asarone increased the percentage mortality of animals treated with chlorpromazine but not of those treated with reserpine.[22, 23] The aqueous and alcohol extracts were found to reduce the severity of maximum electric shock–induced seizure in rats. Further, the extracts significantly increased the pentylenetetrazole-induced seizure latency.[24] The essential oil showed a protective effect against electroshock seizures in rats.[25]

Behavioral changes

The in vitro studies of the oil on the respiration of rat brain revealed that it inhibited the oxygen uptake of brain tissues.[26] The oil affects the 5-HT and noradrenaline

contents of the brain similar to reserpine.[27] Estimation of the brain 5-HT content of rat revealed that neither the oil nor its active principles liberated 5-HT. These compounds also did not cause an additional decrease of the brain 5-HT content in reserpine-treated animals.[22, 23] The effect of α-asarone was studied on experimentally induced conflict neurosis in rats, and it was found to increase the number of shocks accepted by the animals.[28] Intraperitoneal administration of flavones isolated from the chloroform extract of the rhizome produced profound behavioral changes in the rhesus monkey. This flavone also produced a calming effect on conscious animals, viz., mice, rats, and rabbits. The flavone showed an activity similar to Cannabis indica.[29] A study was conducted with crude powder administered for 60 days to investigate the effects of the plant on escape avoidance conditioning and general motor activity of rats. It enhanced learning performance, especially in the females, whereas the effect of the plant on general activity was not significant.[30] In one study, the essential oil of AC was tested for its effect on motor activity, the position of the eyelids, and the general state. General depression without ataxia was observed.[31] In one study, exposure of rats to acrylamide caused hind limb paralysis in 58% of the animals on day 10 and decreased behavioral parameters, namely distance traveled, ambulatory time, stereotypic time, and basal stereotypic movements compared with the control group. Treatment with the ethanol: water (1:1) extract of the rhizomes of AC increased the GSH content and GST activity in the corpus striatum where as insignificant changes were observed in other parameters. The rats also showed a partial recovery in other behavioral parameters. The levels of GSH content and GST activity increased in the corpus striatum, whereas the dopamine receptors decreased compared with the AC-treated rats. The results proved that the neurobehavioral change produced by acrylamide was prevented by the treatment by AC rhizomes.[32] The neuroprotective potential of ethanol: water (1:1) extract of rhizomes of AC was reported in middle cerebral artery occlusion (MCAO) - induced ischemia in rats. Ischemic rats treated with AC exhibited a significant improvement in neurobehavioral performance, viz., rota-rod performance and grid walking. Extract treatment significantly decreased malonaldialdehyde levels in cortex, increased reduced glutathione levels and SOD activity in both cortex and corpus striatum, and neurologic function score was also improved in the AC-treated rats.[33]

Acetylcholinesterase-inhibitory and memory-enhancing effect

In Ayurveda, herbal medicines with Rasayanas effects are believed to be restorative, to attain longevity, intelligence, and freedom from age-related disorders. *Acorus calamus* (VACHA) is regarded in Ayurvedic medicine as promoting Rasayana effects and has been used to treat memory loss.[34, 34] *Acorus calamus* used in Ayurvedic medicine on a regular basis for the treatment of memory loss and other mental disorders.[34, 36] *Acorus Calamus* extract has also been used as traditional Chinese prescribed, and its beneficial effects on memory disorder, on learning performance, lipid peroxide content, and anti-aging effects in senescence have been reported.[37, 38] The in vitro acetylcholinesterase (AChE) inhibitory effect of hydroalcohol extract and essential oil of AC rhizomes was reported based on Ellman's method in 96-well Microplates are using bovine erythrocytes. The essential oil showed stronger inhibition than the hydro-alcohol extract.[39] Methanol extracts of AC showed significant acetylcholinesterase enzyme inhibition at a concentration 200 mg/mL.[40] The AChE-inhibitory activity of the oil can be ascribed to b-asarone. Because cognitive performance and memory are related to acetylcholine levels, the AChE-inhibitory effect of the plant may account for its traditional use.[41]

Conclusions

At present, the current modalities for treating CNS disorders are symptomatic and have not been shown to either block or reverse the progressive disorders. This has resulted in heightened interest in the use of alternative therapies. *Acorus Calamus* has been used in many traditional therapies for many years, the plant exhibits polyploidy, and the composition of the essential oil obtained from the plant rhizome depends on the karyotype of the phytoconstituents reported from Acorus rhizomes, a-asarone and b-asarone is the predominant bioactive constituents. Together with this, some untoward effects of AC rhizome and its constituents a-asarone and b-asarone such as genotoxicity and mutagenicity have also been reported, which limits its therapeutic usage. Thus, this rhizome is well-known as a CNS active herb from Ayurvedic tradition and requires further research to establish the molecular mechanisms of evaluating its activity. Comparatively lesser side effects of this herbal remedy can make the CNS treatment more rational and patient friendly.

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