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An Overview on Various Properties and Pharmacological Studies of *Acorus Calamus*

Dhruti Bhatt*, Gaurav Kumar Sharma, Ronak Soni, Ashok Dashora
Geetanjali Institute of Pharmacy, Geetanjali University, Udaipur-313002, India

Review Article

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*For Correspondence

Dhruti Bhatt, Geetanjali Institute of Pharmacy, Geetanjali University, Udaipur-313002, Rajasthan India

E-mail: Dhruti.bhatt008@gmail.com

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ABSTRACT

Acorus calamus (Araceae), commonly, known as "sweet flag" is a semiaquatic, perennial, aromatic herb with creeping rhizome. It is used in Ayurveda, Siddha, Unani and Homeopathy for domestic consumption and export purposes. It comprises many Pharmacological activities such as anti-inflammatory activity, anticonvulsant, analgesic, anti-cellular, immunosuppressive, anti-diabetic and many more. Sweet flag is constituted and made up of various chemical constituents such as α-asarone, β-asarone, calameone, eugenol methyl ether, dipentene etc. Also toxic substances are present which result into various genotoxicity and mutagenecity.

INTRODUCTION

Mother earth has bestowed to the mankind and various plants with healing ability for curing the ailments of human being. This unique feature has been identified since pre historic times. The WHO has also estimated that 80% of the world population meets their primary health care needs through traditional medicine only. Medicinal plants are those plants possessing secondary metabolites and are potential sources of curative drugs with the very long list of chemicals and its curative nature. India is the eighth largest country having rich plant diversity with a total of around 47,000 species, of which more than 7500 species are being used as medicinal plants. Plant products are used as main source of medicine throughout the world for treating various human ailments. About 50% of the present day medicines in the United States of America are derived from natural sources especially from various plants [1]. There is a growing demand for medicines of Ayurveda, Siddha, Unani and Homeopathy for domestic consumption and export purposes. The world trade in plant based drugs and its products are many fold expanding continuously; because the general awareness of the wide spread toxicity and harmful after effects associated with the long-term use of synthetic drugs and antibiotics **(Figure 1).**

Figure 1. Dig *Acorus calamus*.

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Taxonomy

Kingdom: Plantae

Division: Magnoliophyta

Class: Liliopsida

Order: Acorales

Family : Acoraceae

Genus : *Acorus*

Species: *calamus/ A. aromaticus / A. calamus var. americanus*

Other species: *Acorus gramineus* [2]

Vernacular names

English- Sweet Flag

Ayurvedic- Vacha

Unani- Bacch

Hindi- Bajai, Gora-bach, Vasa Bach

Marathi- Vekhand

Tamil- Vashambu

Telugu- Vadaja, Vasa

Kannada-Baje

Malayalam-Vayambu

Sanskrit- Bhutanashini, Jatila1

Botany

A. calamus is a perennial plant with creeping and extensively branched, aromatic rhizome, cylindrical, up to 2.5 cm thick, purplish-brown to light brown externally and white internally. The leaves of *A. calamus* has a single prominent mid vein and then on both sides slightly raised secondary veins and many, fine tertiary veins. This makes it clearly distinct from *Acorus americanus.* The leaves are between 0.7 and 1.7 cm wide, with average of 1 cm. The sympodial leaf of *A. calamus* is somewhat shorter than the vegetative leaves. The margin is curly-edged or undulate. Plants are very rarely flower or set fruit, but when they do, the flowers are 3 to 8 cm long, cylindrical in shape, greenish brown and covered in a multitude of rounded spikes. The spadix, at the time of expansion, can reach a length between 4.9 and 8.9 cm. The fruits are small and berry-like, containing few seeds. Flowers from early to late summer depending on the latitude, grows wild in marshy places up to 2000 m altitude in the Himalayas, Manipur, Naga Hills and in some parts of South India [3].

Ethanobotany

The rhizome has been regarded as an emmenagogue, an excitant, a stomachic, a diaphoretic, a diuretic, an incisive, and an aid for flatulence, vertigo, and headaches arising from dyspepsia [4] Sweet flag, or in Arabic, *vash* or *vaj* was an ancient remedy for "burning water" rising from the stomach to the throat. The Spanish names for the plant are acoro and acoro verdadero [5] Women are given the rhizome for painful menstruation [6]. Medicinally sweet flag has been used as an Anthelmintic [7].

Powdered, the rhizome is used to treat buboes, car-buncles, deaf ears, sore eyes, anorexia, and abdominal and chest congestion. The powdered rhizome is said to act as a diaphoretic, an expectorant, and, due to the presence of coumarins, as a cure for tuberculosis [8]. In the treatment of children an infusion of the rhizome is given to aid in the relief of choleric diarrhea, dysentery, bronchitis, cough, fever, dyspepsia, epilepsy, and intestinal worms. The burnt rhizome is given to infants for diarrhea, teething, colic, and as an emetic, and that the oil is used as an expectorant and relieves asthma, dysentery, loss of appetite, catarrh, ague, and hysteria [9].

USES

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

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abdominal tumors [10]. 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 [11].

Chemical constituents

The oil was found to contain varying concentrations of

1. a-asarone
2. b-asarone
3. c-asarone
4. calamene, calamenenol, calameone
5. a-pinene
6. b-pinene
7. camphene, p-cymene, eugenyl acetate, eugenol
8. isoeugenol
9. methyl isoeugenol
10. calamol, azulene
11. eugenolmethylether,dipentene
12. methyleugenol
13. asaronaldehyde
14. terpinolene
15. 1,8-cineole
16. camphor
17. a-caryophyllene [12]

The oil also contains fatty acids such as palmitic acid and its ester, heptylic acid, an ester of butyric acid [13]. Fractionation from the volatile oil by gas chromatography resulted in the isolation of a-asarone and b-asarone, which are the trans- and cis-isomers, respectively, of 2,4,5-trimethoxy-l-propenylbenzene [14]. Other constituents identified in the rhizome were cyclobutanolignan acoradin, 2,4,5-trimethoxybenzaldehyde, 2,5-dimethoxybenzoquinone, galangin (5,7-dihydroxytlavanol), along with sitosterol and acoramone [15].

PHARMACOLOGICAL STUDIES

Inhibitory role in ferric chloride induced-epileptogenesis in rat

Of the various methods used for inducing experimental epileptic models, the intracortical administration of ferric chloride ($FeCl_3$) into sensorimotor cortex induces recurrent seizures and epileptic discharge similar to human post-traumatic epilepsy through the generation of free radicals. The study focuses on the effect of *Acorus calamus* on the behavioral, electroencephalographic, and antioxidant changes in $FeCl_3$-induced rat epileptogenesis. Topical administration of $FeCl_{3\ n}$(5 µL; 100 mM) into the sensorimotor cortex of rats showed an increase in the wet dog shake behavior, spike wave discharges together with an significant increase in antioxidant enzyme activity, such as superoxide dismutase and catalase, resulting in an increase in the level of lipid peroxidation in cerebral cortex. Pretreatment with *Acorus calamus* (200 mg/kg b.w., p.o. for 14 days) and also diazepam (DZ, 20 mg/kg b.w., i.p.) decreased the WDS behavior, spike wave discharges with single isolated positive waves, and a significant decrease in activity of superoxide dismutase and level of lipid peroxidation was observed in cerebral cortex with respect to those observed in $FeCl_3$-induced epileptic group. This in turn exhibits the potentiality of *Acorus calamus* to be developed as an effective anti-epileptic drug [16].

Analgesic and anti-convulsant studies on mice

The analgesic effects of methanolic extract of *Acorus calamus* roots (MEAC) have been evaluated using acetic acid induced Writhing response and Rat caudal immersion method. Whereas the anticonvulsant effect were investigated by utilizing pentylenetetrazol induced convulsion methods. MEAC administered orally at the doses of 100 and 200 mg/kg, exhibited protective effect against the pain models in mice. Also the methanolic extract of *Acorus calamus* roots significantly increased the latency period in seizures induced by PTZ in mice. These obtained results indicate the analgesic as well as anticonvulsant effect *Acorus calamus* roots [17].

Protection of DNA and membrane from gamma radiation induced damage

The *in vitro* free radical scavenging activity of the extract (water:ethanol, 1:1) of *A. calamus* was studied by parameters viz DPPH (1,1-diphenyl-2-picryl-hydrazyl) radical scavenging activity,hydroxyl radical scavenging activity,and superoxide radicalscavenging activity. Membrane damage due to radiation exposure was measured as the peroxidation of lipids in terms of thiobarbituric acid reacting substance (TBARS). The *in vitro* DNA damage was monitored by assessing the radiation induced relaxation of supercoiled plasmid DNA (pBR322). Damage to cellular DNA induced by gamma radiation (6Gy) was monitored by alkaline single cell gel electrophoresis or comet assay in murine cells and human peripheral blood leukocytes [18].

Anti-cellular and immunosuppressive properties

Modulation of immune response to alleviate disease has been of interest since long. Plant extracts have been widely investigated for possible immunomodulatory properties. The anti-cellular and immunomodulatory property of ethanolic extract of *Acorus calamus* rhizome has been evaluated. This extract inhibited proliferation of mitogen (phytohaemagglutinin; PHA) and antigen (purified protein derivative; PPD)-stimulated human peripheral blood mononuclear cells (PBMCs). In addition, *A.calamus* extract inhibited growth of several cell lines of mouse and human origin. It also inhibited production of nitric oxide (NO), interleukin-2 (IL-2) and tumor necrosis factor-a (TNF-a). Intra cytoplasmic interferon-gamma (IFN-gamma) and expression of cell surface markers, CD16 and HLA-DR, on human PBMC, were not affected on treatment with *A. calamus* extract but CD25 expression was down regulates [19].

Insulin releasing and alpha-glucosidase inhibitory activity of ethyl acetate fraction

AC and ACE increased insulin secretion in HIT-T15 cells as gliclazide did. As *in vivo* results, ACE (400 and 800 mg/kg) significantly decreased fasting serum glucose, and suppressed the increase of blood glucose levels after 2 g/kg glucose loading in normal mice. In addition, ACE as a mixed-type inhibitor inhibited alpha-glucosidase activity invitro with an IC_{50} of 0.41 µg/ml, and 100 mg/kg of it clearly reduced the increase of blood glucose levels after 5 g/kg amylum loading in normal mice. Apart from its insulin sensitizing effect, ACE may have hypoglycemic effects via mechanisms of insulin releasing and alpha glucosidase inhibition, and thus improves postprandial hyperglycemia and cardiovascular complications [20].

Anti-inflammatory activity on keratinocyte hacat cells

HaCaT cells induced the pro-inflammatory cytokines, interleukin-8 (IL-8) and/or interleukin-6 (IL-6) expressions after treatment with polyI:C or PGN. ACL inhibited the expression of IL-8 and IL-6 RNA and protein levels, and attenuated the activation of NF-κB and IRF3 after polyI:C treatment. ACL also inhibited expression of IL-8 and activation of NF-κB following PGN induction. ACL inhibits the production of pro-inflammatory cytokines through multiple mechanisms and may be a novel and effective anti-inflammatory agent for the treatment of skin diseases [21].

TOXICOLOGY

Acorus calamus is poisonous under certain conditions, causing disturbed digestion, gastroenteritis, persistent constipation, followed by diarrhea and passage of blood into the feces In 1968 the U.S. Food and Drug Administration reported that the use of sweet flag was unsafe, based upon cancerous tumors found in laboratory animals treated with the plant [22]. AC is a mild co-carcinogen and may interfere with normal pregnancy inter-reactions. The effects of β-asarone on chromosomes were studied in human lymphocyte cultures. A very strong effect on the induction of structural chromosome aberrations was found after metabolic activation and cellular damage occurred. The results demonstrate clearly the Genotoxic potency of β-asarone and suggested that only Acorus with low content of β-asarone should be used. α-Asarone was mutagenic to Salmonella typhimurium in a concentration-dependent fashion. α-Asarone–induced mutagenicity required a promutagen mixture containing liver S-9 fraction and NADPH. The mutagenicity of α-asarone was comparable with that induced by aflatoxin. Apparently, α-asarone is a positive mutagen. In another study, β-asarone showed mutagenic activity in the *Salmonella* mammalian microsome assay, and the results of the study suggested that only commercial drugs free from or with a low content of β-asarone should be used in human phytotherapy [23].

CONCLUSION

Acorus calamus (Sweet flag) is a wetland perennial monocot plant, in which the scented leaves and rhizomes have been traditionally used medicinally against different ailments like, fever, asthma, bronchitis, and cough and mainly for digestive problems such as gas, bloating, colic, and poor digestive function. Number of active constituents and essential oil were identified and characterized from the leaves and rhizomes. It contains many pharmacological activities amongst which some are highlighted in this article along with its toxic effects.

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