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Review Article

Current status on biological activities of *calamus aromaticus* (the healing plant): a review

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ABSTRACT

Calamus aromaticus is the synonym of *Acorus Calamus* (Sweet flag).It is a perennial, grass-like monocot plant with creeping rhizomes and scented leaves belonging to the family Acoraceae. Chemical analysis of sweet flag shows that it contains phenyl propanoids, sesquiterpenes and monoterpenes, xanthone glycosides, flavones, steroids, α- and β-asarone and various other constituents. Several, recently published reports have revealed many newer useful bioactivities of leaves and rhizome extracts, essential oils and isolated chemical constituents such as anti-inflammatory, immunosuppressive, anti-adipogenic, antimicrobial, fungicidal, insulin sensitizing/Antidiabetic, neuroprotective, mitogenic, insecticidal, anthelmintic, allelopathic, antiepileptic, insecticidal, larvicidal. This review presents a pragmatic description that deals with chemical constituents, toxicology, ethno botany and pharmacological properties of *A. calamus* for easy and better understanding of the outstanding medicinal potential of this very special plant and sirens for its conservation.

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INTRODUCTION

Mother earth has bestowed upon the mankind and various plants with healing ability for curing the ailments of the human being (Balakumbahan et al., 2010). The earliest description of the curative properties of medicinal plants are found in the Rig-Veda, Charaka Samhita and Sushrusha Samhita give an extensive description on various medicinal herbs (Kirtikar et al., 1989). The worldwide use of herbal therapies and healthcare preparations that are prescribed in ancient books like Vedas and the bibles were given away for discovering of natural products with medicinal values (Bhuvaneswari et al., 2009). *Acorus calamus* is a semi-aquatic perennial, aromatic herb with creeping rhizomes (Givya et al., 2011) which has been used traditionally as a medicine and also the powder of rhizome has a spicy flavor in it (Balakumbahan et al., 2010). The word '*Acorus*' is originated from the Greek word 'acoron' used by the Dioscorides which in turn derived from the 'coreon' word means 'pupil' because it is used in the treatment of eyes diseases and its inflammation (Johnson, 2017). Vacha powder mixed with ghee is given ritually in India to improve the intellect and speech development. In China it is used in a similar way, to improve speech and aid recovery from stroke. When powdered, it can be of avail for depressed psychosis and dementia. Further indications include the loss of consciousness, confusion of the mind, forgetfulness, anorexia and epilepsy and as a traditional Ayurvedic medicine to treat memory loss (Howes and Houghton, 2003). There are several polypoid varieties to be found, some of which do not contain the toxic constituents. Ayurveda has described *Acorus calamus* for prevention and treatment of a wide number of diseases (Kumar Amit et al., 2013).

Taxonomical classification

Kingdom	: Plantae
Subkingdom	: Tracheobionta
Super division	: Spermatophyta
Division	: Magnoliophyta
Class	: Liliopsida
Subclass	: Arecida
Order	: Arales
Family	: Acoraceae
Genus	: *Acorus*
Species	: *Calamus*

Vernacular names

English	: Sweet Flag
Ayurvedic	: Vacha
Unani	: Bacch
Hindi	: Bajai, Gora-bach, Vasa Bach
Marathi	: Vekhand
Tamil	: Vashambu
Telugu	: Vadaja, Vasa

Distribution: *Acorus calamus* is a native of eastern countries and also it is indigenous to the marshes of the mountains of India. It is cultivated throughout India, ascending to an altitude of about 2200 meters. It is also found in marshy tracts of Kashmir, Shirmaur (Himachal Pradesh), Manipur and in Naga Hills. It is regularly cultivated in the Koratagere Taluka of Karnataka state in peninsular India.

Description of buch plant

Acorus calamus Linn. is an herbaceous perennial with a long indefinite branched cylindrical rhizome which is about 3/4 inch in diameter, smooth, pinkish or pale green, Its leaf scars are brown, white and spongy. It possesses slender roots. Its leaves are few and distichously alternate.

Rhizome: A. *calamus* is a perennial plant with creeping and extensively branched, aromatic rhizome, cylindrical, up to2.5 cm thick, purplish-brown to light brown externally and white internally. At the rhizome forming, perennial that can grow to 2 meters resembling an iris.

Root: It consists of long creeping roots which spread out just below the surface of the soil.

Leaves: The leaves are thick, erect and are very similar in appearance to the iris but edges are crimped. 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 the average of 1 cm. The sympodial leaf of *A. calamus* is somewhat shorter than the vegetative leaves.

Flower: The flower is very rarely grown in this plant if grown than it is 3- 8cm long, cylindrical in shape, greenish-brown in color and covered with the multitude of rounded spikes. The flowers are small, sessile and densely packed and 5-10 cm of the spadix. 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.

Fruit: The fruits are small and berrylike c-diglucoside; chemical constituents vary in ecotypes and containing few seeds. Flowering and Fruiting occurs in July The other species in this genus is *Acorus gramineus* native to eastern Asia commonly called as Japanese sweet flag, Japanese rush, grassy-leaved sweet flag, the dwarf sweet flag is an aquatic or wetland perennial with semi-evergreen grass-like foliage. It has narrow, 6 to 14 in (15 - 35.6 cm) glossy leaves and looks like thick, lush grass. The leaves are carried in two ranks, like opposing fans. They are flat, about a 0.5 in (1.3 cm) wide and tend to flop over. The insignificant flowers, shaped like little horns, are produced in midsummer on erect hollow stems. Usually, only plants grown in water produce flowers (Ralakumbahan et al., 2010).

Figure1. Rhizome

Figure 2. Root

Figure 3. Flower

Figure4. Leave

Uses

Parts used: The parts used are leaves, root (rhizome) and stem. In Asia, the Sweet flag has been used for at least the last 2000 years. The ancient peoples of China used it to lessen swelling and for constipation. In Ayurvedic medicinal practice India, the rhizomes have been used to cure several diseases like fever, asthma and bronchitis, and as a sedative. Native tribes used it to treat a cough, made a decoction as a carminative and as an infusion for cholic. In Western herbal medicine, the herb is chiefly employed for digestive problems such as gas, bloating, cholic, and poor digestive function. *Calamus* helps distended and uncomfortable stomachs and headaches associated with weak digestion. Small amounts are thought to reduce

stomach acidity, while larger doses increase deficient acid production, it is a good sedative so that the extract is used for epilepsy, insanity and as a tranquilizer along with Valeriana jatamansi and nardostacys Grandiflora. It is an ingredient of any Ayurvedic preparation "Brahmi Bati" (Budhivardhar) which is indicated in epilepsy, coma, and hysteria and in cases of mental retardation; the same uses are prescribed for an *Acorus* containing Unani drug Ma′jun Baladur" (Balakumbahan et al., 2010).

Phytochemical constituents: Phytochemical studies have reported the presence of glycosides, flavonoids, saponins, tannins, polyphenolic compounds, mucilage, volatile oil and bitter principle. The plant has been reported for the presence of glucoside, alkaloid and essential oil containing calamen, clamenol, calameon, asarone, and sesquiterpenes. It also contains a bitter glycoside named acorine along with eugenol, pinene, and camphene (Paithankar et al., 2011). The plant has been extensively investigated and a number of chemical constituents from the rhizomes, leave and roots of the plant have previously reported which includes β asarone, α asarone, elemicine, cisisoelemicine, cis and trans isoeugenol and their methyl ethers, camphene, P-cymene, α-selinene, bgurjunene, β-cadinene, camphor, terpinen 4 ol, aterpineol and a calacorene, acorone, acrenone, acoragermacrone, 2 deca -4, 7 dienol, shyobunones, linalool and preisocalamendiol are also present. Acoradin, galangin, 2, 4, 5 trimethoxy benzaldehyde, 2, 5 dimethoxy benzoquinone, calamendiol, spathulenol, and sitosterol have been isolated from *Acorus calamus* (Raja AE et al., 2009). Alcoholic extracts of the triploid A. *calamus* were characterized by a higher percentage of β-asarone (11%), which was the main compound, followed by higher percentages of camphene (2.27%), enriched (E) β-ocimene (3.28%), camphor (1.54%), calarene (1.42%), α-selinene (5.02%) and s-cadinol (2.00%), when compared to the diploid A. *calamus*. The latter had higher percentages of isoshyobunone (8.62%), bsesquiphellandrene (3.28%), preiso calamendiol (22.81%) and acorone (26.33%)11,12.Dong W et al., isolated three new sesquiterpenes, 1β, 7α(H) cadinane 4α, 6α,10α triol (1), 1α, 5 β guaiane 10α O ethyl 4β,6 β-diol (2), and 6β,7β(H)cadinane 1α, 4α, 10α triol (3), together with 25 known ones, from the rhizome of *Acorus calamus* L. Their chemical structures were established on the basis of interpretation of spectroscopic data and comparison with those of the related known compounds (Lokesh et al., 2004).

Pharmacological activities of the plant

Anti-inflammatory activity

A large number of medicinal plants are known to be showing anti-inflammatory activities. Studies have been carried about the anti-inflammatory potential of *Acorus* spp. A study by has revealed that ethanolic extract of A.*calamus* rhizome display anticellular and immunomodulatory properties. The ethanolic extracts of A.*calamus* inhibit proliferation of mitogen (phytohaemagglutinin; PHA) and antigen (purified protein derivative; PPD)-stimulated human Peripheral Blood Mononuclear Cells (PBMCs). The anti-inflammatory properties of the extract have been studied using RT-PCR. ELISA. Immuno-blotting and immunofluorescence staining techniques revealed that A.*calamus* leaf extract inhibits the production of pro-inflammatory cytokines through multiple mechanisms (Parab et al., 2002). This study indicated that "*Acorus calamus* prevented chronic constriction injury-induced behavioral, bio-chemical and histo-pathological changes in rats which may be attributed to its multiple actions including antioxidative, anti-inflammatory, neuro-protective and calcium inhibitory actions.

Anti-adipogenic activity

Acorus calamus demonstrates hypo-lipidemic activity in rats (Wu et al., 2009). The major anti-adipogenic component of *calamus* oil was purified and identified as α-asarone (Lee et al., 2004). α-asarone present in the essential oil of A. *calamus* has the inhibitory effect on adipogenesis in 3T3-LJ cells (Si et al., 2010). It has been suggested that α-asarone might have suppressed the expression of adipogenic transcription factors. Earlier, the same group of researchers had reported that asarones have properties of inhibiting adipogenesis and stimulating lipolysis in 3T3-LJ adipocytes (Lee et al., 2004). Asarone tends to reduce intracellular triglyceride levels by stimulating the phosphorylation of hormone-sensitive lipase which triggers lipolysis in adipocytes. These results suggest that β-asarone exerts anti-adipogenic activity, in part by suppressing the expression of adipogenic transcription factors."

Anti-diabetic activity

The radix of *A. calamus* is widely used in the therapy of diabetes in traditional folk medicine of America and Indonesia. Si et al. (2010) reported the insulin-releasing and alpha-glucosidase inhibitory activity of A. *calamus* extract In vitro using HTT-T15 cell line and in vivo in fasted and glucose/amylum challenged normal mice. A. *calamus* improves postprandial hyperglycemia and cardiovascular complications (Si et al., 2010). The hypoglycemic effects of A. *calamus* extract could be via mechanisms of insulin-releasing and alpha-glucosidase inhibition. Wu et al. have studied the insulin sensitizing activity of ethyl acetate fraction of A. *calamus* in vitro and in vivo. Owing to the ability of insulin sensitizing,

ACE has the potential to be useful for the treatment of diabetes and cardiovascular complications without body weight gain (Wu et al., 2009). An anti-diabetic study reported that oral administration of the methanolic extract of A. *calamus* showed a significant restoration of the levels of blood glucose in streptozotocin induced diabetic rats. After 21 days of extract treatment to the streptozotocin induced diabetic rats the biological parameters like blood glucose, LDL and HDL cholesterol, glucose 6 phosphatase, fructose 1,6 bis phosphatase, levels and hepatic marker enzymes were decreased whereas plasma insulin, tissue glycogen, and glucose 6 phosphate dehydrogenase levels were increased significantly when compared with diabetic control. Their study concludes the anti-hyperglycemic activity of A. *calamus* in streptozotocin-induced diabetic rats (Prisilla et al., 2012).

Immuno-modulatory

"Modulation of immune response to alleviate disease has been of interest since long. Plant extracts have been widely investigated for possible immune-modulatory properties. For a long time, the radix of A. *calamus* is being used in the therapy of diabetes in traditional folk medicine of America and Indonesia. A recent study investigated that A. *calamus* improves postprandial hyperglycemia and cardiovascular complications (Wu et al., 2009). It revealed that ethyl acetate fraction of A. *calamus* had insulin releasing and α-glucosidase inhibitory activities in vitro HTT-T15 cell line and in vivo glucose challenged normal mice (Wu et al., 2009). The hypoglycemic effects are due to insulin releasing and a-glucosidase inhibitory properties of A. *calamus* extract.

Neuroprotective activity

The study based on the receptor-ligand binding using a dependent NMDA receptor-channel blocker ['HlMK-801] revealed that asarone inhibited the specific bindings in a concentration-dependent fashion (Shukla et al., 2006). Asarone exhibited neuroprotective action against the NMDA or Glu-induced toxicity through the blockade of NMDA receptor function. *Acorus calamus* rhizome extract prepared with ethanol: water (1: 1) has demonstrated neuroprotective effects in the middle cerebral artery occlusion-induced ischemia in rats (Sandeep et al., 2010). Application of A. *calamus* rhizome extract has resulted in a significant improvement in neuro-behavioral performances such as Rota-rod performance and grid walking in the experimental rats. Free radicals and other ROS have been recognized as an important causative factor in the development of neurodegenerative disorders.

Anti-oxidant property

The properties of scavenging free radical of A. *calamus* has been found to be useful to overcome excess production of oxygen free radicals generated due to continuous exposure to loud noise which pose a serious health problem (Manikandan et al., 2007). Protective effect of ethyl acetate and methanolic extract of A.*calamus* against noise stress-induced changes in the rat brain have also been reported. These extracts have shown to protect most of the changes induced by noise-stress in the rat brain. The protective effects were substantiated by measurement of the activities of enzymes super oxide dismutase, catalase, glutathione peroxidase, reduced glutathione as well as the level of vitamin C, E, protein thiols and lipid peroxidation (Manikandan et al., 2007). The antioxidant property of β-asarone found in A. *calamus* is believed to be responsible for counteracting the stress in the rat brain due to continuous exposure to noise. Another study has revealed that A. *calamus* helped to prevent the development of ferric chloride-induced epileptogenesis in rats by modulating antioxidant enzymes (Mishra et al., 2003).

Bronchodilatory activity

Acorus calamus has been long used for the treatment of bronchial diseases. A study on isolated guinea-pig tracheal segments was performed using crude extracts of the plant. It was found to be more effective than carbacholin which causes relaxation of high K+ pre contractions, similar to verapamil, suggesting blockade of calcium channels. Pretreatment of tracheal preparations with ethyl acetate fraction caused a rightward parallel shift in carbacholin response curve at the lower concentration similar to atropine and a non-parallel shift at higher concentrations, with reduction of maximum response, similar to rolipram. These results indicate the presence of unique combination of airways relaxant constituents in crude extract of *Acorus calamus*, a papaverine-like dual inhibitor of calcium channels and phosphor di-esterase in n-hexane fraction and a novel combination of anticholinergic, rolipram-like phosphodiesterase 4 inhibitor in ethyl acetate fraction and associated cardiac depressant effect, provide a pharmacological basis for traditional use of *Acorus calamus* in disorders of airways .

Anti-fungal activity

The β-asarone compound fraction obtained from the crude methanolic extract of *Acorus Calamus* rhizomes has been reported to possess the antifungal activity against the yeast strain of Candida Albicans, Cryptococcus Neoformans, and Saccharomyces Cerevisae (S. Phongpaichit et al., 2005)and also against Aspergillus Niger (Divya et al., 2011). The α- and β-asarone compound which was isolated from the

different extracts of *Acorus calamus* has been found to show the inhibition on the fungi strains of Penicillium Chrysogenum, Aspergillus Niger, Aspergillus Flavus, Microsporum Canis and yeast strain of Cryptococcus Gastricus and Candida Albicans(Devi and Ganjewala et al., 2011).

Antibacterial activity

The growth of cultured Gram-negative organism was inhibited significantly by an extract of the rhizome. A standard cultured of staphylococcus aureus, Escherichia coli, and Shigella flexneri was observed after treatment with the essential oil, the leaf and rhizome part of *Acorus Calamus* is found to possess the antibacterial activity. The methanolic extract of *Acorus Calamus* showed the inhibitory action against the bacterial strains of Salmonella typhi, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Staphylococcus aureus (Aqil et al., 2007). The third fraction of the crude methanolic extracts has been found to show the highest inhibition of S. aureus, E.coli, and the fraction is confirmed as β-asarone (Phongpaichit et al., 2005). β-asarone compound of *Acorus Calamus* has the highest inhibitory effect against E.coli strain at various concentration (G (Divya et al., 2011). The ethanolic and aqueous extract of *Acorus Calamus* also showed the inhibitory effect against the above organisms (Manikandan et al., 2010).

Antiulcer activity

The ethanolic extract of *Acorus* rhizome is used as the antiulcer agent as they were found to inhibit the gastric secretion and also shows the protection against the gastro duodenal mucosa injuries that were caused by the pyloric ligation in the rat (Raja et al., 2009).

Antispasmodic and anti-diarrhoeal

Effect In the isolated rabbit jejunum preparation the crude extract (Ac. Cr), which tested positive for the presence of alkaloid, saponins and tannins, caused inhibition of spontaneous and high K+ (80 mm) induced contractions, with respective EC50 values of 0.42 ± 0.06 and 0.13 ± 0.04 mg/ml, thus showing spasmolytic activity, mediated possibly through calcium channel blockade (CCB). These results suggest that the spasmolytic effect of the plant extract is mediated through the presence of CCB-like constituent(s) which is concentrated in the n-hexane fraction and this study provides a strong mechanistic base for its traditional use in gastrointestinal disorders such as colic pain and diarrhea (Gilani et al., 2006).

Anti-inflammatory activity

Human Keratinocyte (HaCaT) cells treated with polyinosinic: Polycytidylic acid (polyI: C) and peptidoglycan (PGN) induced the inflammatory reactions. The anti-inflammatory activities of ACL were investigated using RT PCR, ELISA assay, immunoblotting, and immunofluorescence staining. The result shows that the 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 (nuclear factor kappa light chain enhancer of activated B cells) and IRF3 (Interferon regulatory factor 3) after poly I: C treatment. ACL also inhibited expression of IL 8 and activation of NF-κB following PGN induction (Kim et al., 2009).

Anticonvulsant activity

Acorus oil investigated for its ant analeptic 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 (Khare et al., 1982). 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 (Sharma JD et al., 1961). In a study using electro convulsions, α-asarone increased the percentage mortality of animals treated with chlorpromazine but not of those treated with reserpine (Dandiya et al., 1962; Dandiya et al., 1961). 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 (Manis et al., 1991).The essential oil showed a protective effect against electroshock seizures in rats (Bret al., 1960).

Antimutagenic activity

Anticancer Activity Gaidhani et al., Evaluated anticancer activity of *Acorus calamus* rhizomes. They prepared the hydro alcoholic extract of Terminalia chebula, the rhizome of *Acorus calamus* and the root of Glycyrrhiza glabra and further studied their anti-proliferative activity on the anti-cancer cell. Results predict the fact that all of these plant materials have significant anti proliferative activity (Gaidhani et al., 2009).

Anti-HIV activity

40 traditional Asian medicinal plants were screened against HIV 1 reverse transcriptase. The results showed that the crude extracts from plants Cinnamomum loureiroi (stem bark), Quercus infectoria (fruit), Plumbago indica L. (root), and *Acorus calamus* L. (rhizomes) showed strong HIV 1 reverse transcriptase inhibition effects. The efficiency of anti-HIV 1RT activity was reported as 50% inhibitory concentrations (IC50). This showed that the hexane crude extracts from

Acorus calamus L. and A. heterophyllus Lam. contained potent activity against HIV 1 RT (Silprasit et al., 2011).

Antidepressant activity

In a clinical study in fifty cases of depression at OPD of S.S. Hospital BHU, Varanasi, *Acorus calamus* (500 mg in a dose of 2 tablets three times a day after meal with water) given for six weeks showed the reduction in the degree of severity of depression and better rehabilitation. There was also a significant improvement in assessment based on the rating of symptoms on Hamilton depression rating scale. The rate of improvement before and after treatment was significant ($P < 0.001$) (Tripathi et al., 1995).

Important formulations

Vachadi churna, Vachadi ghritta, Vachavleha, Vachadi taila, Vachalashunadi taila, Saraswata churna, Saraswatarishta, Manasmitra vataka, Chandraprabha vati, Khadiradi vati, Hinguvachadi churna, Lakshmivilasa rasa, Medhya rasayana (Sastry, 2001; Lucas, 2013).

CONCLUSION

The above-collected information regarding the use of Sweet flag (*Acorus calamus*) in the world is matched with available literature. The sweet flag was included in many of the early herbals and has a rich history in the Chinese and Indian cultures. Very few plants have gained such widespread use in diverse cultures. In the present era, herbs are being rediscovered, as people around the world seek a healthier and more natural life style and Vacha is one of the important herbal drugs. *Acorus calamus* is a versatile medicinal plant used for the treatment of various diseases and possesses the property of improving the memory power and enhancing the intellect. γ- asarone, sesquiterpenes, and acorenone showed many biological activities. The compounds were found to be highly active in antimicrobial, anti-inflammatory, antioxidant, ant diarrheal, antiulcer, antispasmodic, and immunosuppressant and mitogen inhibitor activity. The rhizome part of *Acorus calamus* is also used to treat several diseases like asthma and as a sedative and can also be used in the form of a tincture or infusion. Regular intake of Vacha with Ghritta or Taila or milk serves the purpose of Rasayana and boosts the immunity. So this plant *Acorus calamus* helps in treating different ailments involving various systems and enhances the immunity and improves hoarseness of voice. So further studies must be carried out to explore some other benefits of Vacha and this plant species has to be properly identified and conserved to avoid the extinct condition.

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