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## The Sweetness and Bitterness of Sweet Flag [*Acorus calamus* L.] – A Review

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### ABSTRACT

Alternative and complementary medicines have gained an increase in popularity in the recent years. In various countries, a large number of individuals are adapting these medicines to complement conventional allopathic medicines. These complementary medicines include Ayurvedic, Homeopathic, Unani and other traditional medicinal practices. Medicinal plants are being used from times immemorial to treat various diseases. Active principle compounds have been isolated and characterized from these plants. An ethno-pharmacological based method has provided new potentials of identifying new drugs from plants related to many disorders. A large number of drugs currently available in allopathic medicine were originally isolated from plants, or have originated from compounds isolated from plants. Phyto-chemical studies help to understand the applications of medicinal plants. An attempt has been made in this review to understand the applications of an Indian medicinal and aromatic plant *Acorus calamus* L., [sweet flag]. The rhizome, roots and leaves of the plant have been used for insecticidal, antifungal, antibacterial and allelopathic properties.

**Keywords:** *Acorus calamus* L., Sweet flag, medicinal plant, Phytochemistry,  $\beta$ -asarone

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## INTRODUCTION

Sweet flag, *Acorus calamus* L., a semi-aquatic herbaceous plant growing in temperate to sub temperate regions. The plant has long, erect, narrow, aromatic leaves ascending from a branched, underground rhizome. The visibly seen large numbers of plants in a population probably arise from a single plant connected by an extensive underground rhizome. The inflorescence consists of a leaf-like spathe and a spike-like spadix that is densely covered with yellow and green flowers. *Acorus* was considered a member of Araceae for a long time [1]. Based on its morphological and anatomical characteristics that are different from other members of the Araceae, it has now been treated as their own family Acoraceae [2]. Molecular phylogenetic analyses also revealed that *Acorus* is the basal lineage of the monocots [3, 4].

Many morphological, anatomical studies have been conducted on this small genus to understand the evolutionary patterns. [5]. *Acorus calamus* is commonly known as “bach” or “ugragandha” in India. Roots, rhizomes and leaves have been used in the Indian systems of traditional medicine for hundreds of years. The rhizome contains active ingredients possessing insecticidal [6,7,8], antifungal [9], antibacterial [10] and allelopathic [11] properties [12]. Rhizomes contain the essential oil which is used in the production of alcoholic beverages and beer [8, 13]. Pharmacological studies on sweet flag essential oils have put into evidence, besides their beneficial effects, their toxicity too [14]. Among the essential oil constituents, the most characteristic component is  $\beta$ -asarone [[Z]-1,2,4-trimethoxy-5-prop-1-enyl-benzene][15,8].

The essential oil composition of sweet flag rhizomes depends on ploidy. Diploid cytotypes are characterized by the absence of  $\beta$ -asarone, European and North American triploid cytotypes contain 3–19% of  $\beta$ -asarone, whereas the Indian, Indonesian and Taiwan tetraploid cytotypes contain up to 96% of  $\beta$ -asarone [16, 8].

## TAXONOMY

Kingdom: *Plantae*; Division: *Magnoliophyta*; Class: *Liliopsida*; Order: *Acorales*; Family : *Acoraceae*; Genus : *Acorus*; Species: *calamus*/ *A. aromaticus* / *A. calamus* var. *americanus* and *Acorus gramineus*

## BOTANICAL DESCRIPTION

*Acorus calamus* is a perennial herb with long, cylindrical rhizomes which are creeping and extensively branched which are up to 2.5 cm thick, which is white internally and brownish externally. The plant has long leaves which are about 1cm long and have a single prominent mid vein and on both sides slightly raised secondary and tertiary veins. The margin is curly edged or undulate. Plants very rarely flower or set fruit, but when they do, it consists of a leaf-like spathe and a spike-like spadix that is densely covered with yellow and green flowers which are 3 to 8 cm long, cylindrical in shape. The spadix, at the time of expansion, can reach a length between 4.9 and 8.9 cm. the inflorescence starts 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. From a karyotypic point of view, sweet flag includes four cytotypes: diploid [ $2x = 24$ ], triploid [ $3x = 36$ ], tetraploid [ $4x = 48$ ] and hexaploid [ $6x = 72$ ].

## ETYMOLOGY OF CALAMUS

Cognates of the Latin word *calamus* [meaning "cane"] are found in both Greek [*kalamos*, meaning "reed"] and Sanskrit [*kalama*, meaning "reed" and "pen" as well as a sort of rice] - strong evidence that the word is older than all three languages and exists in their parent language, Proto-Indo European. The Arabic word *Qalam* [meaning "pen"] is likely to have been borrowed from one of these languages in antiquity, or directly from Indo-European itself [17].

## TRADITIONAL MEDICAL USES OF THE PLANT

Traditionally *Acorus calamus* is used to treat appetite loss, bronchitis, chest pain, colic, cramps, diarrhea, digestive disorders, flatulence, gas, indigestion, nervous disorders, rheumatism, sedative, and vascular disorders. The plant has a long history from various countries and has been in use for at least around 2000 years in China and India. Many native American tribes used it as an anesthetic for toothache and headaches. The ancient Chinese used it to lessen swelling and for constipation. In India; to cure fevers, for asthma and bronchitis, and as a sedative. The root was also believed to be used by the ancient Greeks and included in the traditional remedies of many other European cultures. *Acorus calamus* was also known to many early American settlers and used for a number of folk remedies.

*Acorus calamus* was also widely used by Canadian trappers working for the Hudson Bay Company, using it as a stimulant, chewing a small piece whenever they feel tired [18]. The unpeeled, dried rhizome was listed in the U.S. Pharmacopoeia until 1916 and in the National Formulary until 1950, for medicinal use of humans. Both the leaves and rhizome are apparently psychoactive, due to the presence of asarones, which have mescaline-like hallucinogenic properties if taken in sufficient quantities. In lesser amounts it has stimulating and tonic effects. According to Arabic, Roman and later European folk botany, the plant is also an aphrodisiac. The plant is mentioned by many of the great classical writers on medicine, from Hippocrates [460-377 BC] and Theophrastus [371-287 BC] onwards. According to Dioscorides, the smoke of *Acorus calamus*, if taken orally through a funnel, relieves a cough, Celsus records that the plant was readily available in the markets of India almost 2,000 years ago [19,20].

There is strong evidence that certain tribes, including the Pawnee and the Sioux, planted it, as it is commonly found at old Indian village sites and camping grounds. This planting was probably undertaken not only to maintain a supply of it for medical use but also to provide the muskrat with its favorite food and thereby profit from a steady supply of furs.

## PHYTO CHEMISTRY

The plant has a characteristic essential oil called as the asarone oil. The composition of each chemical compound in the oil varies according to the ploidy level of the plant. It is believed that tetraploid plant has the highest beta asarone content [90-96%], triploid contains a small portion and diploid lacks it [12]. Individual plants also show variation in the percentage of chemical components depending on the part of the plant from which the oil was extracted [21]. Various compounds observed in different parts of *Acorus calamus* plant are listed out (Table.1). Chemical isolation studies have led to the discovery that the two stereoisomers,  $\alpha$  and  $\beta$  asarone (fig.1), have psychoactive effects. It has been described as "the root induces an experience similar to LSD (Lysergic acid diethylamide). The pale yellow to pale brown volatile calamus oil has an odour described as "woody-spicy with increasingly sweet after notes and great tenacity"[22]. This characteristic aroma is derived from the chemical compound [Z,Z]-4, 7-decadienal which is present in the oil at about 100,000 times its odour threshold value [22]. This oil and  $\beta$ -asarone have a relaxing effect on smooth muscle tissue. Tannins, starches, mucin, soft gums, and resins are also found in sweet flag [23].

Figure 1: Two stereoisomers of *Acorus calamus.L*

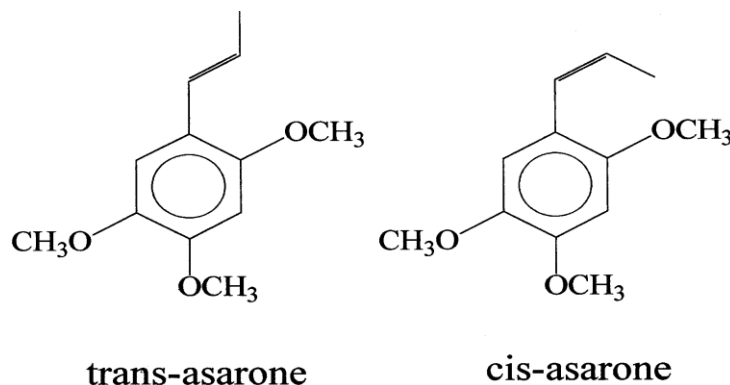


Table 1: Various compounds observed in the *Acorus calamus* plant

S.no	Compound name	Leaves	Roots	Rhizomes	References
1.	Calamenone	-	+	+	[24]
2.	$\alpha$ -pinene	-	-	+	[24]
3.	Calamine and Calamol, Azulene, Isoeugenol and camphor	-	+	-	[24]
4.	Palmitic and butyric acids	-	+	+	[25]
5.	Asaronic acid, Eugenol, eugenol methyl-ether	-	-	+	[25]
6.	Asarylic acid, calamine, Calamenol,calamenone	-	-	+	[25]
7.	Heptylic acid	-	+	+	[26]
8.	Iso-calamendiol,pre-isocalamendiol	-	-	+	[26]
9.	Aliphatic and oxygenated mono terpenes	+	-	-	[26]
10.	n-heptanic acid	-	-	+	[27]
11.	Dehydroabietic acid, acetic acid,linolenic	-	-	+	[28]

	acid				
12.	nonanoic acid, a-Ursolic acid	-	-	+	[28]
13.	Furylethylketone, galagravin, retusin,	-	-	+	[28]
14.	Dehydrodiisoeugenol, sakuranin	-	-	+	[28]
15.	Elimicin, epidesmin lysidine	-	-	+	[28]
16.	Borneol, borynl acetate	-	-	+	[29]
17.	Methyl-eugenol, cis-methyl eugenol, geranyl acetate	-	-	+	[29]
18.	Shyobunone, iso shyobunone and epi isoshyobunone	-	-	+	[15]
19.	Asoraldehyde, acorenone, calamendiol	-	-	+	[15]
20.	Z-3-[2-.4,5-trimethoxy phenyl]-2 propenal	-	-	+	[30]
21.	Phenyl indane	-	-	+	[30]
22.	Phenyl propane, carbonyls, phenols.	-	-	+	[30]
23.	aliphatic compounds, alkaloids, carbohydrates and resins.	-	-	+	[30]
24.	Calamusenone and its isomer	-	-	+	[31]
25.	Asarone and its isomer	+	+	+	[26],[12]
26.	Acorgaeracrone	-	-	+	[30]
27.	Elemene, caryophyllene, cadalene, calamenene	-	-	+	[31]
28.	Acolamone and isoacolamone	-	-	+	[32]

Note: - [+ ] showing presence and [- ] showing absence of particular compound.

## BIOLOGICAL ACTIVITIES EXHIBITED BY THE PLANT

*Acorus calamus* is well known from ancient times for its various pathogenic properties such as anti-bacterial, anti-fungal, insecticidal, nematocidal and bio-pesticidal activities. These activities have been listed in table 2.

**Table 2: Biological activity of *Acorus* sps. on various types of organisms**

Antifungal Activity Against Pathogens	Reference
<i>Candida albicans</i> and <i>Cryptococcus neoformans</i>	[33]
<i>Epidermophyton floccosum</i> , <i>Microsporium gypseum</i> , <i>Trichophyton mentagrophytes</i> and <i>T.rubrum</i>	[34]
<i>Ascosphaera apis</i>	[35]
<i>Aspergillus oryzae</i> , <i>A.nidulans</i> , <i>A.fumigates</i> , <i>Penicillium aculactum</i> , <i>Phomopsis destuctum</i>	[36]
<i>Curvularia lunata</i> and <i>Alternaria alternata</i>	[37]
<i>Macrophomina phaseolina</i>	[38]
<i>Fusarium moniliforme</i> , <i>Trichosporium vesiculosum</i> <i>Helminthosporium oryzae</i>	[39]
Anti-bacterial Activity Against Pathogenic bacteria	
<i>Aeromonas hydrophila</i>	[40]
<i>Shigella dysenteriae</i> , <i>Shigella flexneri</i> , <i>Vibrio cholera</i> , <i>Salmonella paratyphi</i> , <i>Bacillus cereus</i> , <i>Pseudomonas - pseudoalcaligenes</i> , <i>Bacillus proteus</i> , Aerobic spore bearers, <i>Staphylococcus pyogens</i> and the <i>Shigella shiga</i> <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> and <i>Klebsiella pneumonia</i>	[41]

<b>Insecticidal Activity</b>	
<i>Culex quinquefasciatus</i> and <i>Callosobruchus chinensis</i>	[42]
<i>Musca domestica</i> L.	[43]
<i>Sitotroga cerealella</i> Oliv.	[26]
<i>Callosobruchus phaseoli</i> [Gyllenhal]	[45]
<i>Nilaparvata lugens</i> Stal	[46]
Diamondback moth, <i>Plutella xylostella</i> [L.]	[47]
<i>Callosobruchus maculatus</i> [F.]	[48]
Tobacco caterpillar <i>Spilarctia oblique</i> Walker	[49]
<i>Attagenus unicolor japonicus</i>	[50]
<i>Caryedon serratus</i> [Olivier]	[51]
<i>Trialeurodes vaporariorum</i>	[52]
<i>Spodoptera litura</i> [Fab.]	[53]
Rice bug <i>Leptocoris acuta</i>	[54]
<i>Tribolium castaneum</i>	[55]
<i>Trogoderma granarium</i>	[56]
<i>Dysdercus konenigii</i> F	[57]
<i>Callosobruchus chinensis</i>	[58]
<i>Bactrocera cucurbitae</i> [COQ]	[59]
<b>Nematicidal activity</b>	
<i>Meloidogyne incognita</i>	[60]
<b>Miticidal Activity</b>	
Ear canker caused by <i>Psoroptes cuniculi</i> in White Giant rabbits	[62]
<b>Bio-pesticidal Activity</b>	
Maize borer [ <i>Prostephanus truncates</i> Horn.] Rice weevil [ <i>Sitophilus oryzae</i> ], <i>Spodoptera litura</i> <i>F. attagenus</i> , <i>Unicolor japonicus</i>	[51]

## PHARMACOLOGICAL ACTIVITIES OF THE PLANT

### ANTI-INFLAMMATORY ACTIVITY

A large number of medicinal plants are known to be showing anti-inflammatory activities. Most plants and their products have the potential to alleviate diseases *via* modulation of immune responses. 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 [62]. The ethanolic extracts of *A. calamus* inhibits proliferation of mitogen (phytohaemagglutinin; PHA) and antigen (purified protein derivative; PPD)-stimulated human Peripheral Blood Mononuclear Cells (PBMCs).

A study was conducted by using *A. calamus* leaf extract and mechanism of action of the extract was elucidated using human keratinocyte HaCaT cells. The anti-inflammatory properties of the extract have been studied using RT-PCR. ELISA. Immuno-blotting and immuno-fluorescence staining techniques revealed that *A. calamus* leaf extract inhibits the production

of pro-inflammatory cytokines through multiple mechanisms [63]. This study indicated that “*Acorus calamus* prevented chronic constriction injury induced behavioural, bio-chemical and histo-pathological changes in rats which may be attributed to its multiple actions including anti-oxidative, anti-inflammatory, neuro-protective and calcium inhibitory actions. It may be used as a novel and effective anti-inflammatory agent for the treatment of skin diseases” [63].

### ANTI-ADIPOGENIC ACTIVITY

Research on anti-adipogenic properties of *Acorus* spp. for past few years have found that *A. calamus* demonstrate hypo-lipidemic activity in rats [64]. The saponins found in ethanolic extract of *A. calamus* are found to have hypo-lipidemic properties. The water extracts at high concentration have also demonstrated hypo-lipidemic activity.

Ethanol extract devoid of  $\alpha$ -asarone has been reported to enhance differentiation in adipocytes in mouse [65]. The property of *A. calamus* to enhance differentiations in adipocytes is most likely very useful in the treatment of type 2 diabetes. The major anti-adipogenic component of calamus oil was purified and identified as  $\alpha$ -asarone [66].  $\alpha$ -asarone present in the essential oil of *A. calamus* has inhibitory effect on adipogenesis in 3T3-LJ cells [67]. It has been suggested that  $\alpha$ -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 [66]. Asarone tend to reduces intracellular triglyceride levels by stimulating the phosphorylation of hormone-sensitive lipase which triggers lipolysis in adipocytes. these results suggest that  $\beta$ -asarone exerts anti-adipogenic activity, in part by suppressing the expression of adipogenic transcription factors.”

### INSULIN SENSITIZATION

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. It revealed that ethyl acetate fraction of *A. calamus* had insulin releasing and  $\alpha$ -glucosidase inhibitory activities in vitro HTT-T15 cell line and in vivo glucose challenged normal mice [68]. The hypoglycemic effects are due to insulin releasing and  $\alpha$ -glucosidase inhibitory properties of *A. calamus* extract. Previously, a study had reported similar insulin sensitizing properties of ethyl acetate fraction of *A. calamus* in vitro and in vivo [65]. Although these preliminary reports have clearly indicated the potential of the plant for its application in the treatment of diabetes and cardiovascular complications, more research efforts needed for the investigation of other members of the species for their anti-diabetic or insulin sensitizing properties and elucidation of exact mechanism of action.



## 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 [68]. It revealed that ethyl acetate fraction of *A. calamus* had insulin releasing and  $\alpha$ -glucosidase inhibitory activities in vitro HTT-T15 cell line and in vivo glucose challenged normal mice [68]. The hypoglycemic effects are due to insulin releasing and  $\alpha$ -glucosidase inhibitory properties of *A. calamus* extract. There are reports on similar insulin sensitizing properties of ethyl acetate fraction of *A. calamus* in vitro and in vivo [69]. Evaluation of the anti-cellular and immuno-modulatory properties of ethanolic extract of the plant’s rhizome extract inhibited proliferation of mitogen [phyto-haemagglutinin; PHA] and antigen [purified protein derivative; PPD]-stimulated human peripheral blood mononuclear cells [PBMCs]”. Although these preliminary reports have clearly indicated the potential of *A. calamus* for its application in the treatment of diabetes and cardiovascular complications, more research efforts needed for the investigation of other members of the species for their anti-diabetic or insulin sensitizing properties and elucidation of exact mechanism of action.

## DNA PROTECTION

The study carried out by *in vitro* has showed that extract of *A. calamus* safeguarded DNA and membrane damages in murine cells and human peripheral blood leukocytes caused due to  $\gamma$  –radiation [69]. Presence of *A. calamus* extract during irradiation prevented peroxidation of membrane lipids in mouse liver homogenate. The radio protective effects were evaluated by measuring the degree of lipid peroxidation caused using thiobarbituric acid reacting substances. In vitro DNA damage was measured by assessing the radiation induced relaxation of supercoiled plasmid DNA ( $P^{BR322}$ ) whereas alkaline single cell gel electrophoresis or comet assay was used to monitor any damage to cellular DNA induced by gamma-radiation [69]. The properties of *A. calamus* extract scavenging free radicals have been attributed for radio protective effects studied.

## NEURO-PROTECTIVE ACTIVITY

Asarones isolated from *A. gramineus* have been evaluated for their neuro-protective properties and their mechanism of action in the primary cultured rat cortical cells [70]. Commercially obtained  $\alpha$  and  $\beta$  asarone and asarone isolated have been found to inhibit the toxicity induced by the N-Methyl-D-Aspartate (NMDA) in primary cortical cultures but the commercial  $\alpha$  and  $\beta$ -asarone exhibited more potent inhibitions of the NMDA-induced toxicity. Furthermore, the toxicity induced by glutamate has also been inhibited, but with much less potency than the toxicity induced by NMDA. The study based on the receptor-ligand binding using a dependent NMDA receptor-channel blocker [HIMK-801] revealed that asarone inhibited the specific bindings in a concentration-dependent fashion [70]. Asarone exhibited



neuro-protective 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 neuro-protective effects in the middle cerebral artery occlusion-induced ischaemia in rats [71]. Application of *A. calamus* rhizome extract has resulted in a significant improvement in neuro-behavioural 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.

### **RADIO-PROTECTING ACTIVITY**

A study carried out by *in vitro* has showed that extract of *A. calamus* safeguarded DNA and membrane damages in murine cells and human peripheral blood leukocytes caused due to  $\gamma$ -radiation. The radio-protective effects were evaluated by measuring the degree of lipid peroxidation caused using thiobarbituric acid reacting substances. *In vitro* DNA damage was measured by assessing the radiation induced relaxation of supercoiled plasmid DNA ( $P^{BR322}$ ) whereas alkaline single cell gel electrophoresis or comet assay was used to monitor any damage to cellular DNA induced by  $\gamma$ -radiation [72]. The properties of *A. calamus* extract scavenging free radicals have been attributed for radio protective effects studied.

### **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 [73].

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 [73]. The antioxidant property of  $\beta$ -asarone found in *A. calamus* is believed to be responsible for counteracting the stress in the rat brain due to continuous exposure to noise. Though these studies have favored implication of  $\alpha$ -asarone against noise-stress induced changes perhaps further studies involving clinical trials would be required for validation of efficacy of  $\alpha$ -asarone in noisy environment in human subjects. Another study has revealed that *A. calamus* helped preventing the development of ferric chloride-induced epileptogenesis in rats by modulating antioxidant enzymes [74].

### **ANTI-PROLIFERATIVE ACTIVITY**

"*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- $\alpha$  [TNF- $\alpha$ ]. Intra cytoplasmic interferon-g [IFN-g] 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 regulated. Our study demonstrates the anti-proliferative and immunosuppressive potential of ethanolic extract of *A. calamus* rhizome *in vitro* [62].

### **BRONCHO-DILATORY EFFECT**

*Acorus calamus* has been long used for 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  $K^+$  precontractions, 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 lower concentration similar to a tropine 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 [76].

### **GUIDELINES ON USE OF ACORUS CALAMUS**

The FDA interdicted the utilization of sweet flag owing to the potential carcinogenic effects of its essential oil, with particular reference to  $\beta$ -asarone [FDA, 1974].  $\beta$ -Asarone has been demonstrated to be responsible for carcinogenic effects involving duodenal tumour induction [77], unscheduled DNA synthesis in hepatocytes [78] as well as anti-proliferative and immunosuppressive [75], central nervous system inhibitory [79], sedative and hypothermic effects [80]. Wichtl says "It is not clear whether the observed carcinogenic effects in rats are relevant to the human organism" [81]. However, most sources advise caution in ingesting strains other than the diploid strain. In reality  $\beta$ -asarone is not actually a carcinogen but it is a pro-carcinogen that is neither hepatotoxic nor directly hepato-carcinogenic. It must first undergo metabolic l'-hydroxylation in the liver before achieving toxicity. Cytochrome P450 in the hepatocytes is responsible for secreting the hydrolyzing enzymes that convert  $\beta$ -asarone into genotoxic epoxide structure [4]. Even with the activation of these metabolites, the carcinogenic potency is very low due to the rapid breakdown of epoxide residues with hydrolase which leaves these compounds inert. Additionally, the major metabolite of  $\beta$ -asarone is 2,4,5-trimethoxyninnamic acid, a derivative which is not a carcinogen [78].

### **CONCLUSION AND SUMMARY**

This review gives a brief insight on to the pharmaceutical, phytochemical, medicinal and antimicrobial properties of *Acorus calamus*. The plant has had a history dated to a very long period. The essential oil of the plant has widespread uses. It can be utilized in different fields of biotechnology by evaluation of desired germplasm and using different DNA based techniques.

*Acorus calamus* has a very long history and also numerous traditional, economic and ethno-botanical applications. Indian and Chinese cultures sweet flag has been included in preparations of many herbal formulations. Very few plants have gained such widespread use in diverse cultures. This can be attributed to the aromatic constituents and medicinal properties due to which the plant has surpassed all cultural barriers and has gained widespread use. Some of the uses involve the alkaloids and oils produced by the rhizomes. These have been used to check pathogenicity against various micro-organisms and the plant has been used to treat various other conditions which indicate the plant has applications for some ailments with a historic record.

Even though FDA interdicted the utilization of sweet flag owing to the potential carcinogenic effects of its essential oil, with particular reference to  $\beta$ -asarone. In reality  $\beta$ -asarone is not actually a carcinogen, but it is a pro-carcinogen that is neither hepatotoxic nor directly hepato-carcinogenic. Based on these evidences further studies can be carried out so that the plant has beneficial applications in modern medicine.

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