



## A REVIEW ON PHARMACOLOGY OF ACORUS CALAMUS – AN ENDANGERED MEDICINAL PLANT

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### ABSTRACT

In Ayurveda many medicinal plants are described and are widely used by traditional practitioners for curing and controlling various diseases. *Acorus calamus* is one of the important herbs known for its medicinal properties. It is a perennial, aromatic herb with creeping rhizomes commonly known as sweet flag and contains a wide variety of phytoconstituents having different medicinal properties. The active constituents such as phenyl propanoids, sesquiterpenes and monoterpenes as well as xanthone glycosides, flavones, lignans, steroids obtained from the plant has been proved to show various pharmacological activities such as insecticidal, larvicidal, antibacterial, mutagenic, cytotoxic, hepatoprotective, anticonvulsant, neuroleptic, smooth muscle relaxant and smooth muscle stimulant activity. This review is done to reveal the scope and application of *Acorus calamus* in the pharmaceutical and agricultural field to bring out more drugs and natural products out of it and also deals with various marketed product of *Acorus calamus*.

**KEYWORDS:** *Acorus calamus*, Sweet flag, medicinal plants, Pharmacological action.



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## INTRODUCTION

Mother earth has gifted the mankind with lots of plants which have the ability for curing the health disorders of human being<sup>1</sup>. Plants have been the major source of drugs in Indian system of medicine and other ancient systems in the world. The earliest description of the curative properties of medicinal plants is found in the Rig-Veda. Charaka Samhita and Sushruta Samhita give an extensive description on various medicinal herbs<sup>2</sup>. These feature has been identified in the pre-historic times<sup>1</sup> and the worldwide use of herbal therapies and health care preparations that are prescribed in ancient books like vedas and the bibles given away for discovering of natural products with medicinal values<sup>3</sup>. 80% of the world populations meet their primarily health care through traditional medicines which is estimated by WHO. Medicinal plants possess secondary metabolites which are the main sources of medicinal drugs having curative nature. 7500 species are being used as medicinal plants in India<sup>1</sup>. From those, *Acorus calamus*, is a semi aquatic perennial, aromatic herb with creeping rhizomes<sup>4</sup> which has been used traditionally as a medicine and also the powder of rhizome has

a spicy flavor in it<sup>1</sup>. In Ayurvedic science the use of sweet flag is effective against wide varieties of illnesses. The word 'acorus' is originated from the Greek word 'acoron' used by the Dioscorids which in turn derived from the 'coreon' word means 'pupil' because it is used in the treatment of eyes diseases and its inflammation<sup>7</sup>. Sweet flag has been known for its medicinal value. It originated in Europe, but extensively used in Ayurveda, particularly to enhance memory. 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)<sup>6</sup>. There are several polyploid 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.<sup>5</sup>

Description of Buch Plant<sup>5, 8, 27</sup> :

Kingdom : Plantae

Subkingdom : Tracheobionta (Vascular plant)

Superdivision : Spermatophyta (Seed plants)

Division : Magnoliophyta (Flowering plants)

Class : Liliopsida (Monocotyledons)

Subclass : Arecidae

Order : Arales

Family : Acoraceae

Genus : *Acorus* L.

Species: *calamus*

Syn : *Acorus griffithii* Schott. *A. belangeii* Schott, *A. casia* Bertol

English Name : The sweet flag, sweet sedge, myrtle flag.

Indian Name : Bach

Botanical description:

Sweet flag or buch plant is a grass-like, rhizome forming, perennial that can grow to 2 meters high, resembling an iris. This plant found in the wet areas like ponds, lakes and ditches<sup>11</sup>. *Acorus calamus* Linn. is a herbaceous perennial with a long indefinite branched cylindrical

rhizome which is about  $\frac{3}{4}$  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<sup>9</sup>. These are longitudinally fissured with nodes, somewhat vertically compressed and

spongy internally. Flowers small, fragrant, pale green in a spadix, fruit are a three-celled fleshy capsule. In India it grows in marshy and humid land in many places. The root is about 1 cm thick, spreads within the soil and has distinct nodes and internodes. Numerous root fibres arise all over the internodes. During collection, the roots are removed from the soil, cut into 5 cm long pieces and dried. When powdered they produce a sweet and very pleasant aroma<sup>10</sup>.

### **Rhizome**

*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. 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 average of 1 cm. The sympodial leaf of *A. calamus* is somewhat shorter than the vegetative leaves. The leaves are free, alternate, green and wavy. 1-3 in

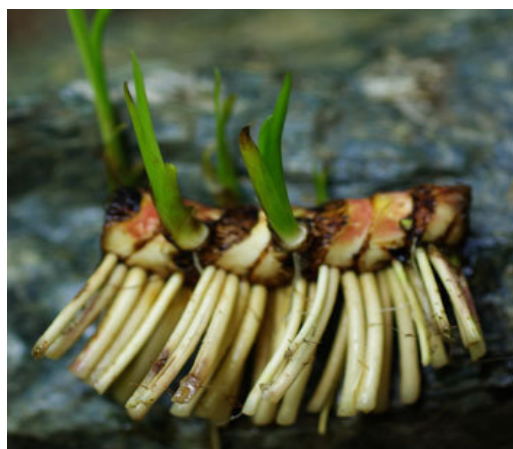
seeded having a thin testa which is cylindrical in shape and green in colour.

### **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 spadix. The spadix, at the time of expansion, can reach a length between 4.9 and 8.9 cm. 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-digluco-side; 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, 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<sup>1,14</sup>.



**Regeneration of plantlets**



**Leaves**



**Flower**



**Roots**

**Figure 1**  
***Acorus calamus* Regeneration of planlets, leaves, Fruiting and roots of plant.**

### **Origin and Distribution**

*Acorus calamus* is a native of Central Asia and Eastern Europe<sup>11</sup> 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 metres. 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<sup>9</sup>.

### **Area and production in India**

Sweet flag is a popular medicinal plant used in several Ayurvedic formulations in India. Due to its growing medicinal use, it is being rapidly extacted from wild. At present, it is listed as endangered species. Taking cue from physical and economic scarcity farmers in Karnataka have planned for the cultivation of this annual crop in Tumkur district. This plant is available both under wild and under cultivated condition. It has been estimated that 77 percent of the sweet flag is cultivated with an area of 80 ha and 23 percent is gathered from the wild in India. About 70 percent of total cultivated area is in Karnataka. The total production of sweet flag in the country is 5725qt/annum<sup>12</sup>.

### **ADULTERANTS**

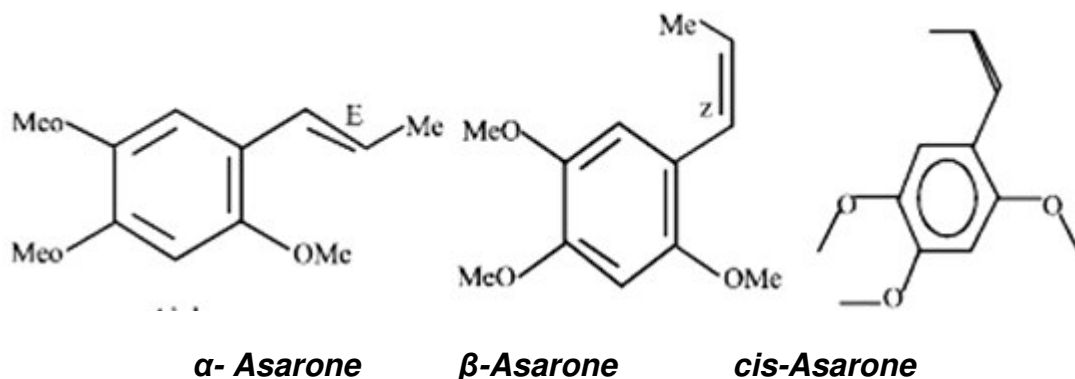
The rhizomes of *Althae officinalis* and common yellow flag *Iris pseudo corus* Linn. are reported to be important adulterants which are mixed with that of the sweet flag rhizome. The powdered drug is reported to be adulterated with siliceous earth and cereal flours. However sweet flag is readily distinguished from its adulterants due to its darker, different structure and want of aromatic odour and taste<sup>9, 14</sup>.

### **Major chemical constituents**

Studies revealed that the volatile constituents of *Acorus calamus* obtained in gas chromatography and mass spectrometry has 184 compounds in the oil of the triploid European *A. calamus* var. *calamus* and 93 compounds in the oil of the tetraploid Indian *A. calamus* var. *angustatus*, with f-asarone as the major constituent. The chemical constituents are of 67 hydrocarbons, 35 carbonyl compounds, 56 alcohols, eight phenols, two furans and four oxido compounds also detected, in an alcohol extract of *A. calamus* var. *calamus*, 243 volatile components, 45 of which were new records from sweet flag. Based on the oil the chemical compound varies in *A. Calamus* based on ploidy level of the taxon<sup>23</sup>.  $\beta$ -Asarone (isoasarone) is usually the major constituent<sup>13</sup>. And its concentrations vary markedly among the

oils from the three varieties.  $\beta$ -asarone (90-96%) is highly present in tetraploid plants and also contains  $\alpha$ -asarone. In triploid plants,  $\beta$ -asarone (5%) in their oil and the diploid plants lack  $\beta$ -asarone, but it has high amount of geranylacetate. The percentage of chemical components varies depending on the part of the plant from which the oil extracted<sup>23</sup>.  $\alpha$ -Asarone, elemicine, cis-isoelemicine, cis and trans isoeugenol and their methyl ethers, camphene, P-cymene,  $\beta$ -gurjunene,  $\alpha$ -selinene,  $\beta$ -

cadinene, camphor, terpinen-4-ol,  $\alpha$ -terpineol and  $\alpha$ -calacorene, acorone, acorenone, acoragermacrone, 2-deca-4,7-dienol, shyobunones, isohyobunones, calamusenone, linalool and pre isocalamendiol are also present.<sup>14</sup> *Calamus* has the constituent such as alkaloids, flavanoids, gums, lecithins mucilage, phenols, quinine, saponins, sugars, tannins and triterpenes<sup>24</sup>. Sugars composition were indicated by densitometer as maltose (0.2%), glucose (20.7%) and fructose (79.1%)<sup>1</sup>



**Figure 2**  
**Three important chemical constituents of *Acorus Calamus* Other chemical constituents**

Acoradin, galagin, 2,4,5-trimethoxy benzaldehyde, 2,5-dimethoxybenzoquinone, calamendiol, spathulenol and sitosterol have been isolated from *Acorus calamus*.<sup>5</sup> Other compounds that are identified in *A. calamus* were 4-Terpineol, 2-Allyl-5-ethoxy-4-methoxyphenol, Epieudesmin, Lysidine, Spathulenol, Borneol, Furylethyl ketone, Nonanoic Acid, 2,2,5,5-Tetramethyl-3-hexanol, Bornyl acetate, Galgravin, Retusin, (9E,12E,15E)-9,12,15-Octadecatrien-1-ol, Butyl Butanoate, Geranylacetate, Sakuranin, Acetic acid, Camphor, Isoelemicin,  $\alpha$ -Ursolic acid, Acetophenone, Dehydroabietic acid, Isoeugenol methylether, Apigenin 4',7-dimethyl ether, dehydrodiisoeugenol, Linalool, Elemicin, Linolenic acid<sup>1</sup>. Lectins present in plant have mitogenic action on mononuclear cells of human cells (macrophages of murine spleen). Lectins have inhibitory effect on the growth of some neoplastic cell lines from mice. Saponins showed effects against hyperlipidemia in rats<sup>23</sup>. Especially  $\alpha$  and  $\beta$ -asarone are highly active in

antioxidant, antilipidemic, antimicrobial, anticancer, immunosuppressive, antidiabetes activities.

#### **Parts used**

The parts used in most of the experimental studies are the leaves, roots and stem of the plant. The dry rhizome contains some of the yellow aromatic oil<sup>1</sup>, calamus oil that are responsible for their medicinal and insecticidal properties<sup>9</sup>. Studies were also done on their rhizome part and in its oils in order to identify the active constituents and its medicinal values<sup>22</sup>.

#### **Medicinal uses**

*Calamus* is a herb used for the appetite and as an aid to the digestion. It is used for fevers, stomach cramps and cholera. Their rhizomes were used for toothache and powdered rhizome for congestion. The rhizome part is also used to treat several diseases like asthma and bronchitis and as sedative. Native tribes treated

cough by making a decoction of the plant as a carminative and also for cholera<sup>1</sup>.

It is a main medhya drug, which has the property of improving the memory power and intellect. *Acorus calamus* is used in the conditions of vata and kapha, stomatopathy, hoarseness, flatulence, dyspepsia, helminthiasis, amenorrhoea, dysmenorrhoea, nephropathy, calculi, stragury<sup>15</sup>. *Acorus calamus* leaves, rhizomes and its essential oil has many biological activities<sup>16</sup> like antispasmodic, carminative and also used for treatment of epilepsy, mental ailments, chronic diarrhea, dysentery, bronchial catarrh, intermittent and tumors. It also has the insecticidal, antifungal, antibacterial<sup>17</sup>, tranquilizing, antidiarrhoeal, antidyslipidemic, neuroprotective, antioxidant, anticholinesterase, spasmolytic, vascular modulator activities<sup>18</sup>. The various extract of *Acorus calamus* is traditionally used for the antidiabetes, antiproliferative, immunosuppressive, hypolipidemic, mitogenic and anticarcinogenic activity towards human lymphocytes. The different extract forms possess the antispasmodic, anthelmintic, antifungal, antibacterial, fish toxin, insecticidal, anti diabetes, anti proliferative, immunosuppressant, antidiarrhoeal, antioxidant and hypolipidemic activities. The rhizomes and leaf part were found to possess the mitogenic and anticarcinogenic activity towards human lymphocytes<sup>15</sup>. The rhizomes are also used for treatment of epilepsy, mental ailments, chronic diarrhea, dysentery, bronchial catarrh, intermittent fevers, cough, throat irritations, bronchitis, as expectorant, and tumors<sup>16, 17</sup>. The extract were used in the traditional Chinese prescription and its beneficial effects on memory disorders, on learning performance, lipid peroxidase content and anti-aging effect in senescence have been reported<sup>19</sup>. *Acorus calamus* is also combined with *Polygala* root to help maintain mental and intellectual health of the elderly (Hou and Jin, 2005). 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). *Acorus calamus* is registered in the Pakistani Materia Medica where both the roots and rhizomes are used for nervous diseases and disorders, whereas the rhizome is especially indicated in cases of neurological symptoms of the brain (Said and Ahmad, 1986)<sup>6,10,13</sup>. *Acorus calamus* shows neuroprotective effect against stroke and chemically induced neurodegeneration in rats. Specifically, it has protective effect against acrylamide induced neurotoxicity<sup>20</sup>. *Acorus calamus* extract is also used in traditional Chinese prescription and its beneficial effects on memory disorder and learning performance, by decreasing brain lipid peroxide content have been reported<sup>21</sup>

## PHARMACOLOGICAL ACTION

### Antibacterial activity

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<sup>24</sup>. 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*, *Staphylococcus aureus*<sup>25</sup>. The third fraction of the crude methanolic extracts has been found to show the highest inhibition against *S. aureus*, *E.coli* and the fraction is confirmed as  $\beta$ -asarone<sup>17</sup>.  $\beta$ -asarone compound of *Acorus Calamus* has the highest inhibitory effect against *E.coli* strain at various concentration<sup>4</sup>. The ethanolic and aqueous extract of *Acorus Calamus* also showed the inhibitory effect against the above organisms<sup>26</sup>.

### Anti-fungal activity

$\beta$ -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*, *Saccharomyces Cerevisiae*<sup>17</sup> and also against *Aspergillus Niger*<sup>4</sup>. The  $\alpha$ - and  $\beta$ -asarone compound which were 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*<sup>16</sup>.

#### **Antiulcer and cytoprotective activity**

The ethanolic extract of the rhizome was studied in rats, for protection of the gastroduodenal mucosa against injuries caused by indomethacin, reserpine and cysteamine, and also in a pyloric ligation model. The extract produced a marked reduction in the volume and acidity of basal gastric secretions and ulcer index and helped to protect against chemically induced lesions<sup>27, 9</sup>.

#### **Antispasmodic activity**

Experiments on the ileum, uterus, bronchial muscles, tracheal chain and blood vasculature showed the relaxant and antispasmodic activity of  $\beta$ -asarone and essential oil of the rhizomes. The rhizomes are useful in the treatment of diarrhea and dysentery, combined with ginger for relief in flatulent colic<sup>28</sup>. In vitro antispasmodic action has been proved in the preparation of rabbit isolated jejunum in which the crude extract of calamus has inhibited the contractions that has occurred either spontaneously or through the induction with potassium. The antispasmodic effect occurs through the blockade of calcium channels in particular with n-hexane fraction. This fraction has been found to contain at least one constituent that can block calcium channels which results in the antispasmodic action<sup>23</sup>.

#### **Antitumour**

It was reported to be a potent antitumour agent against Daltons Ascites Lymphoma in mice by evaluating the tumour growth, toxicity and haematological parameters<sup>27</sup>.

#### **Anti-inflammatory activity**

An extract of the rhizome was studied in acute, chronic and immunological model of inflammation; including carrageenan-induced rat paw edema, and compared with the activity of the hydrocortisone. The extract showed

significant anti-inflammatory activity with the reduction of 44%. The essential oil is also an effective anti-inflammatory agent and coconut oil extract of the rhizomes produced a 45% inhibition of carrageenan-induced rat paw edema and 61% inhibition using the granuloma pouch method<sup>19, 30</sup>. *Acorus calamus* is a traditional remedy for the inflammation problems but their biological function in the human skin cells not well characterized. *Acorus calamus* has been found to inhibit the expression of poly: C-induced IL-6 and IL-8 which indicates their inhibitory effect on the expression of the cytokines which were likely to be in association with the suppression of NF- $\kappa$ B activation and phosphorylation of IRF3 that shows the *Acorus calamus L.* may be used as a promising immunomodulatory agent in the inflammatory skin diseases<sup>30</sup>. *Acorus calamus* have been found to show the inflammatory activity in the tested rat model of vincristine induced painful neuropathy and chronic constriction injury induced neuropathic pain in rats<sup>30, 31</sup>.

#### **Anticonvulsant activity**

A polyherbal compound containing rhizome of *Acorus calamus* as one of the ingredients has been reported clinically to reduce epilepsy attacks in patients by up to 50%. Treatment continued for 6 months resultant in cure in 66 out of 88 patients and no repeat in episodes was reported after 2 years of treatment. The isolated constituted of the rhizomes, asarone and  $\beta$ -asarone, showed anticonvulsant activity in experimental models. There was a decrease in sociability scores with a reduction in anticholinergic action. Experiment on animal model also revealed the depression action of the essential oils and the crude extract of the rhizomes<sup>32, 33</sup>.

#### **Anti-oxidant activity**

Phenolic compounds present in the plants is well known for their ability of scavenging free radical which shows antioxidant activity<sup>16</sup>. The *Acorus calamus* extract showed a remarkable increased and decreased levels of certain parameters due to the exposure to noise-stress which ultimately proves their antioxidant activity



<sup>34</sup>. *Acorus calamus* has been found to render the protection against  $\gamma$ -radiation induced oxidative stress <sup>35</sup>. Exposure of rats to acrylamide caused hind limb paralysis in 58% of the animals on day 10 and decreased behavioural parameters, namely distance travelled, ambulatory time, stereotypic time and basal stereotypic movements compared with the control group. These rats also had a decrease in the reduced glutathione (GSH) content and glutathione-S-transferase (GST) activity in the corpus striatum and an increase in striatal dopamine receptors, as evident by an increase in the binding of 3Hspiperone to striatal membranes. Treatment with the ethanol: water (1:1) extract of the rhizomes of *A. calamus* increased the glutathione content and glutathione-S-transferase activity in the corpus striatum while insignificant changes were observed in other parameters. Rats treated with acrylamide and *A. calamus* extract in combination had a lower incidence of paralysis (18%) compared with those treated with ACR alone on day 10 of the experiment. The rats also showed a partial recovery in other behavioural parameters. The levels of GSH content and GST activity increased in the corpus striatum, while the dopamine receptors decreased compared with the ACR treated rats. The results suggest that the neurobehavioural changes produced by ACR may be prevented in the following treatment with *A. calamus* rhizomes (Pradeep et al., 2002). Epieudesmin has been shown to have antineoplastic activity against the murine P388 lymphocytic leukemia cell line and several human cancer cell lines (BXPC-3, MCF-7, SF268, NCI-H460, KM20L2, and DU-145) <sup>1</sup>. Galgravin has demonstrated activity in preventing neuronal death and stimulating neurite growth. Structurally, similar lignans have also shown neuroprotective activity in *in vitro* models for Alzheimer's and Parkinson's disease<sup>2</sup>. Both epieudesmin and galgravin were identified in the methanolic extracts of *A. calamus* leaves by liquid chromatography electron impact mass spectrometry (George et al., 2004). The steam volatile fraction of the roots and rhizomes of *A. calamus* prolongs the sleeping time of mice when used with pentobarbital, hexobarbital and

ethanol. It reduces body temperature of mice. The maximum reduction of body temperature and the potentiation of the hypnotic activity are observed 1 h after its administration. It exacerbates tonic seizures provoked by convulsive doses of Metrazol in rats and potentiates of the action of reserpine in reducing amphetamine toxicity in aggregated mice. The fall produced in the blood pressure of anesthetized rats is not prevented by vagal, adrenergic or ganglionic blockade and does not appear to be due to any nervous mechanism. It causes dilatation of the blood vessels of the splanchnic area in cats and constricts the blood vessels of the frog's hind limbs. It prevents the action of acetylcholine, histamine and barium chloride on the isolated guinea pig's ileum<sup>1</sup>.

### **Bronchodilatory effect**

*Acorus calamus* has been found to be a famous remedy for the respiratory disorders due to the unique combination of airways relaxant constituents that were found in the crude extract of *Acorus calamus* such as papaverine-like dual inhibitor of calcium channels and phosphodiesterase in the hexane fraction and anticholinergic, rolipram-like phosphodiesterase-4 inhibitor in the ethylacetate fraction and finally the associated cardiac depressant effect that has provided a pharmacological basis for the traditional use of *Acorus calamus* in the treatment of the disorders of airways such as asthma<sup>18</sup>. Treatment of tracheal preparation with ethyl acetate fraction caused a rightward parallel shift in carbachol response curve at lower concentration (0.003mg/mL) similar to atropine and anon-parallel shift at higher concentrations (0.01mg/mL), with reduction of maximum response, similar to rolipram<sup>37</sup>.

### **Antidiabetic activity**

*Acorus calamus*, is widely used in the treatment of diabetes in the traditional folk medicine of America and Indonesia. Four fractions obtained from the radix of *Acorus calamus* were used for insulin releasing or alpha-glucosidase inhibitory action <sup>37</sup>. The ethyl acetate fraction of *Acorus calamus L.* has been found to possess hypoglycemic, hypolipidemia and other



beneficial effects through the mechanism of insulin sensitizing and hence possess the great potential for the treatment of diabetes and other cardiovascular complications without any body weight gain<sup>38</sup>.

#### **Antihepatotoxic activity**

The antihepatotoxic activity of the ethanolic extract of the plant is due to the increase in the level of the serum level of hepatic enzymes such as glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase (ALP) and total bilirubin levels in the tested models which in turn showed their hepatocellular damage in the hepatotoxicity induced animal model. This indicates that the ethanol extract brings the anti-lipid peroxidation and / or adaptive nature of the systems against the free radicals damaging effect. *Acorus calamus* at two dose level 250mg/kg and 500mg/kg show hepatoprotective activities on acetoaminophen induced hepatotoxicity in rat. ethanol extract of *A.C* confers hepatoprotective activities. activities of *acorus calamus* compare to standard drug silymarin<sup>39</sup>.

#### **Antimutagenic activity**

The antimutagenic property of methanolic extract of *Acorus calamus* has been proved by using AMES salmonella test assay against the two direct acting mutagens which has finally showed the decrease in the number of revertants colonies in all the tested strains against NaN<sub>3</sub> induced mutagenicity. The plant possesses significant antimutagenic activity that provides a scientific validation for the traditional use of the plant<sup>40</sup>.

#### **Hypolipidemic activity**

The efficacy of the *A. calamus* extract in lowering serum cholesterol and triglycerides effects has been proved on the serum lipids of rats which already fed with an atherogenic diet. The alcoholic extract of *A. calamus* contains saponins which plays a role in hyperlipidemia. Saponins also found to prevent the cholesterol absorption and interferes with its enterohepatic circulation and also increase its fecal excretion<sup>41</sup>. The rhizomes of *Acorus calamus* are

empirically used in the treatment of a wide variety of human diseases. Administration of the 50% ethanolic extract (100 and 200 mg/kg) as well as saponins (10 mg/kg) isolated from the extract demonstrated significant hypolipidemic activity. On the contrary, the aqueous extract showed hypolipidemic activity only at a dose of 200 mg/kg<sup>42</sup>.

#### **Anticellular and immunosuppressive activity**

The ethanolic extract of *A. calamus* rhizome has been found to possess anticellular and immunosuppressive potential. *A. calamus* extract inhibits the proliferation of various cell lines such as monocytic, lymphoblastoid, fibroblast, erythroleukemic of mouse and human origin which demonstrates that the effect is not cell specific. Effect of *A. calamus* extract on the IL-2 production and their inhibition in the levels of TNF- $\alpha$  production also proved. The inhibition of mitogen and antigen-stimulated lymphocyte proliferation of *A. calamus* has been reported. *A. calamus* extract prevents the cell activation that proved their anticellular and immunosuppressive effect in it<sup>19</sup>.

#### **Adipogenesis activity**

$\alpha$  and  $\beta$ -asarone compounds were found to be the major constituents of calamus oil. 50% alcoholic extract of *A. calamus* rhizomes in combination with saponins has been found to produce hypolipidemic activity in the tested rats.  $\alpha$ -asarone exhibits the hypolipidemic activity in hypercholesterolaemic rats and  $\beta$ -asarone inhibit the differentiation of 3T3-L1 adipocytes and decreased the expression of PPAR $\gamma$ , C/EBP $\alpha$  and C/EBP $\beta$  and also the phosphorylation of p-ERK in 3T3-L1 cells.  $\beta$ -asarone which is isolated from the *calamus* oil has been found to inhibit the differentiation of adipocytes and hence possess the potential for the treatment of obesity and other obesity-associated insulin resistance<sup>43,44</sup>.

#### **Insecticidal activity**

Rhizomes of sweet flag possess the insecticidal properties against a variety of insect pests. The powder and extracted oil of rhizomes has been found to act as stomach / contact poison, anti-feedant and as the repellent. The observation of

the toxic and sterilizing effect of vapours of rhizome oil against certain insect pests has been proved<sup>45</sup>. Asarones (2,4,5-trimethoxypropenyl-benzenes) isolated from the essential oil of *A. calamus* L. rhizomes, are potent growth inhibitors and anti-feedants to the variegated cutworm. *cis*-Asarone added to artificial diet significantly inhibited growth and feeding by first-, third-, and fourth-instar larvae, whereas the *trans* isomer produced an anti-feedant effect alone. The insecticidal activities of compounds derived from the rhizomes of *A. gramineus* against four agricultural insect pests were examined using direct contact application method. The biologically active constituents of *A. gramineus* rhizomes were characterized as the phenylpropenes, *cis*- and *trans*-asarones by spectroscopic analyses. Potencies varied according to insect species, compound, and dose. In a test with female adults of *Nilaparvata lugens*, *cis*-asarone caused 100, 83 and 40% mortality at 1,000, 500 and 250 ppm, respectively, whereas 67% mortality was achieved at 1,000 ppm of *trans*-asarone. Against 3rd instar larvae of *Plutella xylostella*, *cis*-asarone gave 83 and 50% mortality at 1,000 and 500 ppm, respectively, whereas *trans*-asarone at 1,000 ppm showed 30% mortality. Against female adults of *Myzus persicae* and 3rd instar larvae of *Spodoptera litura*, *cis*- and *trans*-asarones both were almost ineffective at 2,000 ppm. The *A. gramineus* rhizome-derived materials merit further study as potential insect-control agents or as lead compounds against *N. lugens* and *P. xylostella*<sup>1</sup>.

#### **Larvicidal property**

Study indicated that *A. calamus* carries huge potential as a mosquito larvicide. This potential could be exploited for the development of safer and effective botanical mosquito larvicidal tool for the management of *Aedes aegypti*<sup>50</sup>.

#### **Licidal activity**

The licidal activity of different fractions of *A. calamus* rhizome obtained by the exhaustive sequential extraction method in the *in vitro* condition showed the chemical constituents that were responsible for their licidal property and

the constituents are found to be predominately soluble in n-Hexane and also in chloroform<sup>45</sup>.

#### **Antidiarrheal activity**

The mice which ingested with castor oil showed the rapid onset of diarrhea within the period of four hours. Meanwhile, the mice which were given the extract (methanol or water) of the rhizome showed the decreases in total number of feces, number of wet feces, and total weight of wet feces. When the large doses of the methanol extract were given, diarrhea is not found to occur<sup>23</sup>. *Acorus calamus* in dose 15mg, aqueous and methanolic extract in combination with other drug aqueous and methanolic plant extracts of *Acorus calamus* rhizome, *Pongamia glabra* leaves, *Aegle marmelos* unripe fruit and *Strychnos nuxvomica* root bark for their antidiarrhoeal potential against castor-oil induced diarrhoea in mice. The methanolic plant extracts were more effective than aqueous plant extracts against castor-oil induced diarrhoea. The methanolic plant extracts significantly reduced induction time of diarrhoea and total weight of the faeces. The result obtained establish the efficacy of these plant extracts as antidiarrhoeal agents<sup>46</sup>.

#### **Anticancer activity**

Cancer is the major disease caused by the abnormal proliferation of the tumour cells.  $\alpha$ -asarone has been found to show the anticancerogenic activity against the human carcinoma cells<sup>13</sup>. Essential oil obtained from this plant is *b*-asarone which is also responsible for its anti carcinogenic activity<sup>15</sup>.

#### **CNS activity**

The methanol and acetone extract of the plant possess certain psychoactive substances that are found to be depressant in nature. The extract produced alterations in the general behavioral pattern and does not induce any disturbances in the motor co-ordination. The methanol and acetone extract of the leaves of the plant possess CNS depressant activity which can be further utilized for its anticonvulsant research. Most studies proved that the roots and rhizomes of the plant possess the most CNS depressant activities<sup>47</sup>.

**Murine cancer**

Two novel lectins were purified from rhizomes of two sweet flag species, namely *Acorus calamus* (Linn.) and *Acorus gramineus* by affinity chromatography on mannose linked epoxy-activated Sepharose. Acorus lectins readily agglutinated rabbit, rat and guinea pig erythrocytes. Both ACL and AGL also reacted with RBCs from sheep, goat and human ABO blood groups after neuraminidase treatment. ACL and AGL were inhibited by mannose/glucose and their derivatives. These lectins showed potent mitogenic activity towards mouse splenocytes and human lymphocytes. Both ACL and AGL also significantly inhibited the growth of J774, a murine macrophage cancer cell-line and to lesser extent WEHI-279, a B-cell lymphoma. D<sup>48</sup>.

**Insulin sensitizing**

Ethyl acetate fraction of *Acorus calamus* (12.5 and 25\_g/ml) increased glucose consumption mediated by insulin in L6 cells. ACE (100 mg/kg) significantly reduced serum glucose, triglyceride, reinforce the decrease of total cholesterol caused by rosiglitazone, and markedly reduced free fatty acid (FFA) levels and increased adiponectin levels as rosiglitazone did. Serum insulin was decreased but not significantly. In addition, ACE decreased the intake of food and water, and did not increase body weight gain whereas rosiglitazone did. Due to the insulin sensitizing ability, ACE has the potential to be useful for the treatment of diabetes and cardiovascular complications without body weight gain<sup>49</sup>.

**Antidepressant activity**

Research studies demonstrated that *Acorus calamus* had potential against depression. The mechanisms by which ACE produced antidepressant effect may be mediated by normalizing the overactivity of hypothalamic-pituitary-adrenal (HPA) axis system and due to its involvement with adrenergic and dopaminergic systems, thereby increasing the levels of biogenic amines. The antidepressant activity was comparable to standard drug Lofepamine<sup>50</sup>.

**Anti-itching**

Boiling water extract of *A. calamus* is used as bathing agent for skin diseases. *A. calamus* was used as one of the constituent in a poly herbal formulation namely, herbal multi action skin gel (AV/AAGD/14/), which was found to be effective against a variety of specific and nonspecific dermatitis and maggot wounds<sup>52, 53</sup>.

**Anti-anxiety**

Three drugs i.e. Brahmi, Vacha and Shankhapuspi used in combination as ratio 10:3.8:0.2 exhibits a significant anti-anxiety activity<sup>54</sup>. Both the poly herbal formulations having *A. calamus* as an ingredient namely, Prasham (100mg) and P-tabs significantly provides a good relief against insomnia, stress excitement and irritability<sup>55, 56</sup>.

**Anti-convulsant**

*A. calamus* oil (100mg/kg) was ineffective against metrazol and minimal electro shock induced seizures in albino mice<sup>57</sup>. Plant extract of *Acorus calamus* did not afford strychnine induced convulsion at 10-20mg/kg. It caused –ve ionotropic and chronotropic effects in frogs at 100\_/ml. It antagonized spontaneous motor activity and also amphetamine induced hyperactivity in mice<sup>58</sup>.

**Anti-rheumatitis**

Vachadi gana, which consists of six plants including *A. Calamus* was found to be effective in case of Rheumatoid arthritis with pain, swelling and functional disability<sup>59</sup>.

**Anti-schizophrenia**

GK022, an herbal mixture containing *A. calamus* (100mg) as a constituent was reported to be significant in cases of Schizophrenia<sup>60</sup>.

**Tranquilizer**

The aqueous extract was also supposed to counteract the effect of mental stress by tranquilizing action as mentioned in ayurvedic texts<sup>61</sup>.

**Anti-asthmatic**

Small pieces of rhizome (1kg) and an ayurvedic recipe namely Maduyashtyadi syrup in which

A. Calamus as an ingredient, after administration showed a significant relief in bronchospasm without any side effect<sup>62</sup>.

#### **Anti-viral and Anti-anginal activity**

The alcoholic extract of *A. calamus* exhibited potent antiviral activity against herpes virus. i.e. HSV-1 and HSV-2<sup>63</sup>. *A. Calamus* in dose of 1.5-3gm/day was found effective

against ischaemic heart disease, improvement in chest pain, in stable angina, dyspnoea reduction of body weight, improving in ECG, decreasing serum cholesterol, decreasing SLDL and increasing SHDL<sup>64</sup>. *A. calamus* being a constituent in polyherbal drug namely Haritaki vati (HT), which reduced the anginal frequency and decreases the serum cholesterol and serum triglyceride Levels<sup>65</sup>.

**Table 1**  
**Marketed Formulations of Buch plant**  
**GUIDELINES ON USE OF ACORUS CALAMUS**

<b>Formulations</b>	<b>Company</b>
1. Scavon Vet cream <sup>66</sup>	Himalaya Drug Company, Makali, Bangalore, India.
2. Acorus calamus Herbal Extract <sup>67</sup>	Vidya Herbs Private Limited, Bangalore, Karnataka, India.
3. Ayurvedic and Herbal Chemicals of Acorus calamus <sup>68</sup>	Jenson Enterprises Private Limited, Chengalpattu, India.
4. Bulk Drugs of Acorus calamus <sup>69</sup>	Hindustan Pharmaceuticals, Amritsar, India.
5. Varch oil <sup>70</sup>	Herbotech Pharmaceuticals, Amritsar, India.
6. Ayurvedic tablets <sup>71</sup>	Krishna Herbal Company, Chandigarh, India.
7. Anxi-6 <sup>72</sup>	Kalhan Pharmaceuticals Private Limited, Jalandhar, Punjab, India.
8. Manufacturer and Exporter of Medicinal Herbs of Acorus calamus <sup>73</sup>	Karthik Enterprises, Arokiapura Shanmugapura, Chottaian Thoppu, Tuticorin, Tamil Nadu.
9. Herbal preparations of Acorus calamus <sup>74</sup>	Sydler Remedies Private Limited, Mumbai, India.
10. Ayurvedic Preparations of Acorus calamus <sup>75</sup>	Kebee Pharmachemie Private Limited andheri, Mumbai, India.
11. Perfumes, Vach oil, Alcoholic Drinks, toothpastes <sup>76</sup>	Ram Prakash Company, Khari Baoli, New Delhi.
12. Botanical Insecticide (Vasambu) <sup>77</sup>	Coimbatore, Tamil Nadu Agricultural University and Bhuvicare Private Limited, Tirunelveli.
13. Wholesale suppliers of Acorus calamus herbs <sup>78</sup>	Tripti Herbal and Plantation Services, Jabalpur, Madhya Pradesh.
14. Nervine tonic, Antispasmodic <sup>79</sup>	Salem Impex, Salem, Tamil Nadu.
15. Stresnil <sup>80</sup>	Universal Pharmaceuticals Limited, Chennai, TN
16. Calamus Oil <sup>81</sup>	Modern Natural Products, Mumbai.
17. Spices, Herbs, Essential oil and Natural products of Acorus calamus <sup>82</sup>	The Pioneer Enterprises, Raudat Tahera, Mumbai.
18. Natural oil of Vacha <sup>83</sup>	Bhagat Aromatics Limited, New Delhi.
19. Calamus Essential Oil <sup>84</sup>	Katyani Exports, Pitam Pura, New Delhi.
20. Insecticides <sup>85</sup>	Ajinkya Chemtech Private Limited, Pune.
21. Krush capsules <sup>86</sup>	Prakruti Remedies Pvt. Ltd Karnataka (India).
22. Brainokan <sup>87</sup>	Kangra Herb Private Limited, Kangra, HP
23. Mahavishgarba Oil <sup>88</sup>	Herbs forever, Los Angeles, California, U.S.A.0
24. Herbal Skin Cream <sup>89</sup>	EcoPure Naturals, Fairport Harbor, OH 44077.

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<sup>91</sup>,

unscheduled DNA synthesis in hepatocytes<sup>92</sup> as well as anti-proliferative and immunosuppressive<sup>18</sup>, central nervous system inhibitory<sup>93</sup>, sedative and hypothermic effects. Wichtl says "It is not clear whether the observed carcinogenic effects in rats are relevant to the human organism"<sup>94</sup>. 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 hepatocarcinogenic. 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<sup>95</sup>. 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<sup>94</sup>

## CONCLUSION

*A. calamus*, the versatile medicinal plant is the unique source of various types of compounds having diverse biological activities. Its phytochemical constituents such as  $\alpha$ -, $\beta$  and  $\gamma$ -asarone, sequesterpenes and acorenone showed many biological activities. The compounds were found to be highly active in antimicrobial, anti-inflammatory, antioxidant, antidiarrheal, antiulcer, antispasmodic, immunosuppressant and mitogen inhibitor activity. Hence it has been proved from the different literature reviewed that *Acorus calamus* can be explored successfully for various marketed formulation.

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