

ACORUS CALAMUS: AN OVERVIEW

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This article is available online at www.ssjournals.com

ABSTRACT

In recent times, focus on plant research has increased all over the world. *Acorus calamus* is an important medicinal herb that is widely used. B asarone primary constituents *Acorus calamus* are mainly believed to be responsible for its wide therapeutic actions. (*Acorus calamus* L., Araceae) is an aromatic herb, indigenous to Central Asia and Eastern Europe. The fragrant oils obtained by alcoholic extraction of the rhizome are mainly used in the pharmaceutical and oenological industries. Different parts of the plant showed the presence of large number of phenyl propanoids, sesquiterpenes and monoterpenes as well as xanthone glycosides, flavones, lignin lignans, steroids and inorganic constituents. Alcoholic extracts of the triploid *A. calamus* were characterized by a higher percentage of b-asarone (11%), which was the main compound, followed by higher percentages of camphene (2.27%), E-b-ocimene (3.28%), camphor (1.54%), calarene (1.42%), a-selinene (5.02%) and s-cadinol (2.00%), when compared to the diploid *A. calamus*. The latter had higher percentages of isoshyobunone (8.62%), b-sesquiphellandrene (3.28%), preiso calamendiol (22.81%) and acorone (26.33%), and completely lacked of b-asarone. It is also reported to possess insecticidal, lucicidal, anti-inflammatory, antibacterial, antiulcer radioprotective, antispasmodic, bronchodilatory, glucosidase inhibitory, insulin sensitizing, antiepileptic, anticholinestrase, larvicidal, antibacterial, mutagenic, anticonvulsant, neuroleptic, smooth muscle relaxant and smooth muscle stimulant activity.

KEY WORDS: *Acorus calamus*, Pharmacological activity, Morphology.

1. INTRODUCTION

The sweet flag *Acorus calamus* L (vernacular: Bach) is a perennial herb belonging to the family Araceae. It is found in marshy land, shallow water and pond edges of the northern temperate, subtropical and warm regions of Indian subcontinent. It contains 1.5 to 3.5% of volatile oil, starch, resin (2.5%) and tannins (1.5%). The main constituents of calamus oil is asarone, β -asarone and it has been successfully employed for the

preparation of perfume, flavors and medicine. Traditionally it was used to treat the diseases such as dyspepsia, flatulence, cough, fever piles and asthma. The leaves and rhizome of *Acorus calamus* is reported to possess antimicrobial and antifungal activity. Due to varied uses, there has been demand for the plant. The herb rarely produces seeds and is mainly propagated by vegetative means. *Invitro* method of vegetative multiplication of *Acorus calamus* would

have considerable benefits for the medicinal trade and germplasm conservation. ¹It has been long known for its medicinal value, it is wild or cultivated throughout Himalayas at an altitude ascending up to 6000 ft ⁴. The rhizomes of *Acorus calamus* contain aromatic oil that has been used medicinally since ancient times and has been harvested commercially. The rhizomes are considered to possess anti-spasmodic, carminative and anthelmintic, aromatic, expectorant, nauseate, nervine, sedative, stimulant and properties and also used for the treatment of epilepsy, mental ailments, chronic diarrhea, dysentery, bronchial catarrh, intermittent fevers and glandular and abdominal tumors. In Ayurvedic system of medicine the powder of this drug is being used to produce therapeutic emesis i.e. Vamana, one of the Panchakarma specialized therapeutic procedures of Ayurveda. The use of paste of the rhizomes in children (chanting) to improve / rectify the speech defect and improving the memory power is in vogue in most of the rural areas of southern India. They are also employed for kidney and liver troubles, rheumatism, sinusitis, and eczema. This medicine is also being used in Unani, Sowa-rigpa and Siddha systems of medicine in various disease conditions. Some of the Ayurvedic formulations with this drug are Vachadi, taila, Vachalasanadi, taila, Sarasvata, churna, Sarsvatarishta, Chandraprabha, vati, Khadiradivati drug in dry form and control the adulterants Hinguvachadichurna etc It is used in the Philippines for rheumatism and memory

problems also. In Korea, it is an ingredient in a type of moonshine called Immortals' Booze. Research in China has shown the essential oil in this rhizome to be sedative and neuroprotectant.² Other virtues of this plant include its mature leaves, which act as an insect repellent when cut up and stored in dry foods. *Acorus calamus* Linn has threats due to harvest for medicines loss of habitat and trade Crude methanolic extract of *Acorus calamus* rhizomes possesses antimicrobial activity against bacteria, fungi and yeast. It shows strong effect against filamentous fungi like *Trichophyllum rubrum* and *Microsporium gypseum*, moderate inhibitory effect against yeast and low against bacteria₂ethanolic extract traditionally used for antidiabetis, immunosuppressive, antiproliferative, hypolipidemic and antidiarrhoeal. In Ayurvedic in insomnia, melancholia, hysteria, epilepsy loss of memory remembrance fever, neurosis. in recently *acorus calamus* possesses antioxidant activity main constituent of *acorus calamus* terpene, sesquiterpene, phenylpropanoid, quinine. rhizome contain active constituent possessing antifungal, antiulcer, insecticidal, antibacterial, and mitogenic activity against human lymphocyte essential oil from this plant *asarone* possess immunosuppressive, anticarcinogenic antiproliferative besides sedative hypothermic effect.³

2. 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 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.⁴

3. 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 taste⁴

4. DESCRIPTION OF BUCH PLANT

Acorus calamus Linn. is a 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 alternate⁴

Botanical Name : *Acorus calamus*

Common Name of Buch Plant: Calamus root, sweet flag, rat root, sweet sedge, flag root, sweet calomel, sweet cane, sweet rush, beewort, muskrat root, pine root, racha, vaca.⁵

4.1. Morphology: Sweet flag or buch plant is a grass-like, this crop is more suitable where water is not scarce. It consists of long creeping roots which

spread out just below the surface of the soil This plant found in the wet areas like ponds, lakes and ditches.

4.2. 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.

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

4.4. 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 thin testa which is cylindrical in shape and green in colour. (a)

4.5. 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. (b)

4.6. Fruit: The fruits are small and berry-like c-diglucoiside; 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 14in (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 mid summer on erect hollow stems. Usually, only plants grown in water produce flowers.^{5,6}

5. USES

5.1. Parts used: The parts used are leaves, root (rhizome) and stem. In Asia, Sweet flag has been used for at least the last 2000years. 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, colic, 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 tranquillizer 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”.⁶

6. CULTURAL ASPECTS

6.1. Soil and climate: It is a hardy plant found growing from tropical to subtropical climates. Plenty of sunshine should be available to the plant during its growth and after harvesting for drying the rhizomes. Temperature ranging from 10 to 38°C and annual rainfall between 70 and 250 cm are best suited. Cultivation should be avoided in places where there is no irrigation facility. This species comes up well in clayey loams, sandy loams and light alluvial soils of river banks.

6.2. Land Preparation: The land should be ploughed twice or thrice prior to the onset of rains. The land should be prepared like paddy fields.

6.3. Propagation: *Acorus* is Propagation *Acorus* is propagated through rhizomes. Rhizomes obtained from earlier planting are kept preserved in the soil and

constantly kept moist. After emergence, the 2742 J. Med. Plant. Res. rhizomes are cut into small pieces and planted. Sprouted rhizome pieces are planted at a spacing of 30 x 30 cm and depth of 4 cm in the month of July-August. The best time for planting is the second fortnight of June. Around 1, 11,000 plants can be planted per hectare. As the growth rate is very fast, sprouts are visible on the second day of planting.

6.4. Fertilizers: Compost/FYM @15 t per hectare along with nitrogen and phosphorus is applied. One third of N along with 50 kg of P and 25 kg of K is the basal requirement. The second dose of N should be given after one month of planting as broadcast and a third dose should be applied after two months of planting.

6.5. Irrigation: The river or canal banks where the land is saturated with water is very suitable for its growth. The initial level of water standing in the field should be 5 cm and later increased to 10 cm. Irrigation can be avoided in the rainy season, however, if there is prolonged dry spell it must be irrigated at an interval of 2 to 3 days.

6.6. Plant protection: Mealy bugs and caterpillar are the pests occurring on this crop. Spraying the shoots and drenching the roots of plants with 10 ml methyl parathion or 20 ml Quinol phos in 10 L of water can be effective in controlling the shoot and root mealy bugs. Major disease is leaf spot and a spray of Captan 10 g with Chloropyriphos 20 ml/10 L controls leaf spot as well as mealy bugs and

caterpillar. Harvesting and post harvest operations After 6 to 8 months, in December, the lower leaves turn yellow and dry indicating their maturity. The field should be partially dried only leaving sufficient moisture for uprooting the plant. In case of large scale cultivation rhizomes may be removed by passing the plough. The uprooted rhizome is cleaned after washing with water and cut into size of 5 to 7.5 cm length and fibrous roots removed. The cut rhizomes are dried by spreading under the shade so that the amount of oil present in it is not harmed. The yield is expected to be 4.22 t of dry rhizomes or 10 t fresh rhizomes per hectare.⁶

7. ACTIVE CONSTITUENTS

Phytochemically it has reported the presence of glycosides, flavonoids, saponins, tannins, polyphenolic compounds, mucilage, volatile oil and bitter principle⁷ 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 better glycoside named a corine along with eugenol, pinene and camphene⁸ 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, b-gurjunene, α -selinene, β -cadinene, camphor, terpinen-4-ol, α -terpineol and α -

calacorene, acorone, acenone, acoragermacrone, 2-deca-4,7-dienol, shyobunones, linalool and preisocalamendiol are also present. Acoradin, galangin, 2, 4, 5-trimethoxybenzaldehyde, 2,5-dimethoxybenzoquinone, calamendiol, spathulenol and sitosterol have been isolated from *Acorus calamus*.⁹ 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%), E- β -ocimene (3.28%), camphor (1.54%), calarene (1.42%), α -selinene (5.02%) and β -cadinol (2.00%), when compared to the diploid *A. calamus*. The latter had higher percentages of isoshyobunone (8.62%), β -sesquiphellandrene (3.28%), preisocalamendiol (22.81%) and acorone (26.33%).¹⁰

8. PHARMACOLOGICAL ACTIVITY OF ACORUS CALAMUS

8.1. Antiinflammatory: ACL inhibited the expression of IL-8 and IL-6 RNA and protein levels, and attenuated the activation of NF- κ B and IRF3 after polyI:C treatment. ACL also inhibited expression of IL-8 and activation of NF- κ B following PGN induction. These results suggest that ACL inhibits the production of pro-inflammatory cytokines through multiple mechanisms and may be a novel and effective anti-inflammatory agent for the treatment of skin diseases. 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. 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.¹¹

8.2. Hypolipidemic: 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.¹²

8.3. Antiepileptic: Treatment with *Acorus calamus* (200 mg/kg b.w., p.o. for 14 days) and also diazepam (DZ, 20 mg/kg b.w., i.p.) decreased the WDS behavior, spike wave discharges with single isolated positive waves, and a significant decrease in activity of superoxide dismutase and level of lipid peroxidation was observed in cerebral cortex with respect to those observed in FeCl₃ induced epileptic group. Data presented in this study clearly show that *Acorus calamus* possesses the ability for preventing the development of FeCl₃ induced epileptogenesis by modulating antioxidant enzymes, which in turn exhibit the potentiality of *Acorus calamus* to be developed as an effective anti-epileptic drug.¹³

8.4. Licidal: *Acorus calamus* L. is well known for insecticidal and pesticidal activity. Dried rhizomes of *A. calamus* were subjected to exhaustive sequential

extraction with four solvents n-hexane, chloroform, methanol and distilled water respectively. All four fractions were studied for *in vitro* licide activity using Goat-lice *Damalinea caprae* (Trichodectidae) as experimental organism. Only n-hexane and chloroform fractions showed licide activity. significant decrease in mean time required to kill the lice was observed at concentration 1% w/w and 10 % w/w when compared to 1 % w/w lindane solution.¹⁴

8.5. Anticholinestrase: *In vitro* acetylcholinesterase (AChE) inhibitory potential of the hydroalcoholic extract and of the essential oil from *Acorus calamus* (AC) rhizomes and that of its major constituents were evaluated based on the Ellman's method. GC/MS analysis of the oil revealed that the major constituents were beta-asarone (79.54%) and alpha-asarone (8.47%). The IC₅₀ values were obtained for the hydroalcoholic extract, the essential oil, beta-asarone and alpha-asarone and were 182.31+/-16.78 microg/mL, 10.67+/-0.81 microg/mL, 3.33+/-0.02 microM and 46.38+/-2.69 microM, respectively. Physostigmine was used as standard inhibitor with an IC₅₀ value of 0.28+/-0.015 microM. The experimental observations revealed that the AC essential oil and its constituents have significant AChE inhibitory potential. beta-Asarone, the major phytoconstituent present in the essential oil, showed the maximum inhibitory potential.¹⁵

8.6. Antiadipogenic: The cytotoxic effect of calamus oil on 3T3-L1 cells was

studied using the MTT assay. Calamus oil concentrations of up to 125 lg/ml did not significantly influence cell viability. During the differentiation of 3T3-L1 cells into adipocytes, cells were treated with various concentrations of calamus oil every three days for nine days, and the amounts of intracellular oil droplets were determined by triglyceride assay. intracellular triglyceride content was significantly reduced by treatment with calamus oil, and this effect was concentration-dependent. The level of lipid accumulation at the highest concentration (125 lg/ml) was 35% of that of the MDI-treated positive control cells.¹⁶

8.7. Airway disorders

8.7.1. Bronchodilator: 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 a non-parallel shift at higher concentrations (0.01mg/mL), with reduction of maximum response, similar to rolipram.

8.8. Cardiac suppression: In isolated guinea-pig atrial preparations, crude extracts, its fractions and papaverine inhibited force and rate of contractions at higher concentrations than the smooth muscle while verapamil was equipotent. These data 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 phosphodiesterase in n-hexane fraction and a novel combination of anticholinergic, rolipram-like phos-

phodiesterase4 inhibitor in ethyl acetate fraction and associated cardiac depressant effect, provide a pharmacological basis for traditional use of *Acorus calamus* in disorders of airways⁸

8.9. 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 gain¹⁷

8.10. Radio protective: The radioprotecting activity of *Acorus calamus* extract after whole body exposure of mice to lethal and sub-lethal doses of irradiation in terms of radiation induced mortality and damages to cellular DNA and tissue antioxidant levels were studied. *A. calamus* extract (250mg/kg body weight) was orally administered to mice 1h prior to whole body radiation exposure. The antioxidant levels in the tissue homogenates of brain, liver and kidney of the irradiated mice were determined and cellular DNA damage was monitored by comet assay. Effect of administration of the extract on survival

of the animals exposed to acute lethal dose of 10Gy whole body radiations was also monitored. Administration of the extract significantly increased the activities of major enzymes of the antioxidant defense system specially SOD, catalase and GP xand levels of GSH in 2,6 and 10 Gy irradiated mice and decreased the formation MDA. The extract also decreased DNA strand breaks. The survival rate was found to be increased up to 5%. These studies highlight the role of *A. calamus* extract as good source of natural radioprotection agent and its therapeutic implications for radiation-induced injuries¹⁸

8.11. Anticonvulsant & analgesic: MEAC administered orally at the doses of 100 and 200 mg/kg, exhibited protective effect against the pain models in mice. Also the methanolic extract of *Acorus calamus* roots significantly increased the latency period in seizures induced by PTZ in mice. These obtained results indicate the analgesic as well as anticonvulsant effect *Acorus calamus* roots. *Acorus calamus* has been used for a long time in traditional medicine as a remedy for pain, convulsion, inflammation, and ulcer. the analgesic effects of methanolic extract of *Acorus calamus* roots (MEAC) have been evaluated using acetic acid induced Writhing response and Rat caudal immersion method. Whereas the anticonvulsant effect were investigated by utilizing pentylene tetrazol induced convulsion methods.⁹

8.12. Neuromodulatory: Methanol (ACME) and acetone (ACAE) extract of *Acorus calamus* leaves against APM

induced stereotypy and haloperidol induced catalepsy. APM induced stereotypy behavior, which reached peak at 15 min period. ACME (20 and 50 mg/Kg oral) administration significantly reversed stereotypy induced by APM. But ACAE at doses used (5, 20 and 50 mg/Kg oral) could not alter the stereotypy induced by APM. Whereas ACME (50 mg/Kg) and ACAE (20, 50 mg/Kg) administration significantly potentiated the haloperidol induced catalepsy in mice.¹⁹

8.13. Antidiarrhoeal: *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 nux-vomica* 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.²⁰

8.14. Immunosuppressive & anticellular
Plant extracts of *acorus calamus* show anticellular and immunomodulatory properties of ethanolic extract of *Acorus calamus* rhizome. This extract inhibited proliferation of mitogen and antigen stimulated human peripheral blood mononuclear cells. In addition, *A. calamus* extract inhibited growth of several cell lines of mouse and human

origin. It also inhibited production of nitric oxide (NO), interleukin-2 (IL-2) and tumor necrosis factor- α (TNF- α). Intracytoplasmic interferon- γ (IFN- γ) 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.²¹

8.15. 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.²²

8.16. Antihepatotoxic & Antioxidant

Acorus calamus at two dose level 250mg/kg and 500mg/kg show hepatoprotective & antioxidant activities on acetaminophen. Induced hepatotoxicity in rat. ethanol extract of *A, C* confers hepatoprotective & antioxidant activities. activities of *acorus calamus* compare to standard drug silymarin³

CONCLUSION

Through this review it can be concluded that *Acorus calamus* is a wonderful herb through which different diseases have been cured from the Ancient and Vedic periods. 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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Figure (a)



Figure (c)



Figure (b)



Figure (d)