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Review Article

CURRENT STATUS ON BIOLOGICAL ACTIVITIES OF *ACORUS CALAMUS* - A REVIEW

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ABSTRACT

The review emphasis on the current status of the researches in *Acorus calamus* highlighting their number of useful biological activities. The *Acorus calamus* most extensively investigated phytochemically and pharmacologically. Number of bioactive constituents was identified and characterized from the leaves and rhizomes and their essential oils. Major chemical constituents identified are alpha and beta asarones which is responsible for therapeutic and medicinal properties of *Acorus* species. Several, recently published reports have revealed many newer useful bioactivities of leaves and rhizome extracts, essential oils and isolated chemical constituents such as anti-inflammatory, immunosuppressive, anti-adipogenic, antimicrobial, fungicidal, insulin sensitizing/antidiabetic, neuroprotective, wound healing, mitogenic, insecticidal, anthelmintic, allelopathic, antiepileptic, antispasmodic activities and inhibitor of acetylcholinesterase. This article highlights the various biological activities studied in *A. calamus.*

Keywords: *Acorus calamus*, Beta asarone, Alpha asarone, Calamus oil, Sweet flag.

INTRODUCTION

The genus *Acorus* consists of 40 species. Few species such as *A. calamus* (Linn.), *A. christophii, A. tatarinowii* (Schott.) and *A. gramineus* (Solandin Ait.) Were studied for their medicinal properties. It is a perennial, semi-aquatic and smelly plant, found in both temperate and sub temperate zones. It can grow up to 6 feet tall with branched aromatic rhizome, cylindrical up to 2.5 cm thick, purplish-brown to light brown externally and white internally. The leaves of *A. calamus* have a single prominent mid vein and on both sides slightly raised secondary veins and many fine tertiary veins (Fig1). Flowers are light brown and densely packed in sessile cylindric spadix. Fruits are oblong, turbinate berries with a pyramidal top. Seeds are few and pendant from the apex of the cells [1]. *A. calamus* exhibits polyploidy. It includes four cytotypes, diploid (2n = 24), triploid (2n = 36), tetraploid (4n = 48) and hexaploid (6n = 72). The plants reproduce sexually by seed and asexually by rhizome (Fig 2). *A. calamus* has been investigated most extensively among others and reported as a good source of valuable phyto-constituents with useful bioactivities. *A. calamus* is widely used in the traditional system of medicine for gastrointestinal disorders such as colic pain, diarrhea, dysentery, and the radix in the therapy of diabetes in traditional folk medicine of America and Indonesia [2]. It is reportedly useful in improving digestion, clearing speech and curing infantile fever, coughs, bronchitis and asthma. The roots of *A. calamus* are used in tonic, antiseptics and insecticidal preparations [3]. The rhizome is also used as abortifacient, carminative, diaphoretic, febrifuge, stimulant and vermifuge. In the past, several research articles have reported on the chemical compositions and bioactivities of different parts of *A. calamus* [4, 5]. The rhizomes, roots and essential oil extracted from rhizomes of *A. calamus* are reported to possess several important biological activities including antimicrobial [6], allelopathic [7], anticellular and immunosuppressive [8]. *A. calamus* essential oil also possesses antigonadal activity in insects [9]. Aromatic oils obtained by alcoholic extraction of the rhizome are used in the pharmaceutical and oenological industries [10]. These studies revealed the presence of α- and β-asarones as the major component in different plant parts. In addition to asarones, rhizomes and roots possess caryophyllene, isoasarone, methyl isoeugenol and safrol in lesser amounts.

Biological activities of *acorus calamus*

Antimicrobial activity

β-asarone an important chemical constituent of *A. calamus* has also been reported to possess antibacterial activity. The α- and β-asarones identified as the major constituents have often been attributed to antibacterial properties of the *A. calamus* whole plant, roots, rhizomes and essential oil [6]. Phongpaichit *et al*. evaluated antimicrobial activity from purified fraction of β-asarone obtained from column chromatographic preparation of the crude methanol extract of *A. calamus* rhizomes on various microorganisms including bacteria, yeasts and filamentous fungi. It exhibited high activity against filamentous fungi: *Trichophyton rubrum, Microsporum gypseum* and *Penicillium marneffei* with IC50 values of 0.2, 0.2 and 0.4 mg/ml, respectively. However, it showed moderate activity against yeasts: *Candida albicans, Cryptococcus neoformans* and *Saccharomyces cerevisiae* (MIC 0.1-1 mg/ml) and low activity against bacteria (MIC 5-10 mg/ml). Scanning electron microscopic observation revealed that hyphae and conidia treated with this fraction were shrunken and collapsed, which might be due to cell fluid leakage [11]. Similarly, crude dichloromethane extract [12], and ethanol extract of *A. calamus* rhizomes have also been demonstrated to possess antifungal activity [13]. The ethanol extract of *A. calamus* inhibited clinical isolates of *C. albicans.* Ghosh et al. described that the antifungal activity of acorus is because of haem peroxidase which is synthesized and accumulated in the plant during pathogenesis [14]. The haem peroxidase later was isolated and purified from the leaf epidermal cells and lumen tissues of xylem. Several previously published reports have documented a number of plant species synthesizing and accumulating similar type of proteins as a part of their chemical defense system to protect themselves from the attack of pathogens. Their synthesis however is triggered only during pathogenesis. The haem peroxidase of *A. calamus* is a class III peroxidase and significantly inhibits growth of phytopathogens such as *Macrophomina phaseolina*, *Fusarium moniliforme* and *Trichosporium vesiculosum*. The anitifungal activity of *A. gramineus* rhizome derived material is also reported against phytopathogenic fungi apart from human pathogenic microorganisms [15]. The α-asarone and asaronaldehyde present in the rhizome derived material have fungicidal properties against *Botrytis cineria*, *Erysiphe graminis*, *Phytophthora infestans*, *Puccinia recondita*, *Pyricularia grisea* and *Rhizoctonia solani*.

The *in vitro* antibacterial activity of essential oil obtained by hydrodistillation from dried rhizome of sweet flag has been reported [16]. Extracted oil was tested against strains of phytophathogenic bacteria like *Xanthomonas vesicatoria* 67, *Erwinia caratovora subsp., Pseudomona sp* and *Bacillus sp strain* 1044. But no inhibitory activities were observed. De *et al.* Has reported antimicrobial activities of *A. calamus* and described lack of convincing antibacterial activity. Different concentrations of petroleum ether extract of the rhizome were tested for antibacterial activity and the

maximum activity was observed at 2000 mg which is the highest concentration tested beyond which the inhibition zone did not increase [17]. Among the four types of bacteria tested, high inhibition zone was observed on *P. aeruginosa* (1.62 cm) followed by *S. aureus* (1.62 cm). *E. coli* and *B. subtilis* show smaller zone of inhibition (1.34 and 1.04 cm, respectively). MIC test shows that the minimum inhibition concentration is 0.25 mg/ml for *P. aeruginosa*, *S. aureus*, *B. subtilis*, and 0.5 mg/ml for *E. coli* [18]. Antimicrobial activity of *A. calamus* rhizome and leaf extracts prepared using different solvents (petroleum ether, chloroform, hexane and ethyl acetate) was evaluated. Extracts obtained with ethyl acetate among others were found to be highly effective. Rhizomes and leaf ethyl acetate extracts exhibited pronounced antifungal activity. In addition, authentic alpha and beta asarone were also tested for their antimicrobial potential. Both alpha and beta asarone exhibited very strong antimicrobial activities against the fungi and yeasts than those of rhizome and leaf extracts. The study clearly suggested that *A. calamus* rhizomes and leaves possess active principle namely alpha and beta asarones which is believed to be responsible for their antimicrobial activities [19].

Anthelmintic activity

The synergistic anthelmintic activity of *A. calamus* and *Vitex negundo* was studied by Merekar *et al.* The study showed that the ethanolic extract of *A. calamus* rhizomes and root part of *V. negundo* exhibited dose dependent anthelmintic activity against earthworms. Also the synergistic anthelmintic activity of *A. calamus* and *V. negundo* is significantly more than the individual activity of both the plants. The results concluded that the combination of *A. calamus* with *V. negundo* is more potent than individual drug for its anthelmintic action, which will be beneficial to reduce dose and any possible toxicity of the herbal drugs and will be more suitable for formulation of suitable dosage form [20]. An experiment to test the anthelmintic activity was carried out in our laboratory. The study was done to evaluate the anthelmintic activity of rhizome extract of *A. calamus* and to compare the activity with commercial beta and alpha asarone in earthworms. Different concentrations of beta and alpha asarone (1-5 mg/mL) and rhizome extract (2-10 mg/mL) were studied. The evaluation parameters involved the determination of time of paralysis and time of death of the worms. The results were dose dependent and higher activity was observed in beta asarone at 5 mg/mL concentration compared to alpha asarone and rhizome extract [21].

Fig. 1: *A. calamus* whole plant

Fig. 2: *A. calamus* rhizome

Antioxidant properties of *A. calamus*

In the past few years, there has been much attention on the antioxidant properties of medicinal plants to minimize the harmful effects of free radicals. Several reports on protective effect of *A. calamus* on free radical scavenging have been published. A recent study has revealed antioxidant activities of methanolic extract of *A. calamus* leaves and rhizomes [22]. *A. calamus* was also found to be useful in scavenging excess production of oxygen free radicals due to continuous exposure to loud noise which pose a serious health problem [23]. Hazra *et al.* have demonstrated inhibitory role of *A. calamus* in ferric chloride-induced epileptogenesis in rat. *A. calamus* also possesses the ability of preventing the development of FeCl(III)-induced epileptogenesis by modulating antioxidant enzymes which in turn exhibit the potentiality of *A. calamus* to be developed as an effective anti-epileptic drug [24]. *A. calamus* has protective roles against radiation induced DNA and membrane damage in murine cells and human peripheral blood leukocytes [25]. The degree of lipid peroxidation caused is used as criteria to study membrane damage due to radiation exposure. Thiobarbituric acid reacting substances (TBARS) are often implicated in measurement of lipid peroxidation. *In vitro* DNA damage is measured by assessing the radiation induced relaxation of supercoiled plasmid DNA (pBR322). Alkaline single cell gel electrophoresis or comet assay are used to monitor any damage to cellular DNA induced by γ-radiation [26]. The capability of scavenging free radicals by *A. calamus* extracts has been suggested for its radioprotective effects. In another study, the steam volatile fraction of the roots and rhizomes of *A. calamus* were used to prolong the sleeping time of mice along with pentobarbital, hexobarbital and ethanol. It also helps to reduce the 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 [27].

Anti-inflammatory activity

Hyeri *et al.* reported the anti-inflammatory activity of *A. calamus* leaf extract with given emphasis to the mechanism of action on human keratinocyte HaCaT cells. The HaCaT cells were treated with chemicals like polyinosinic, polycytidylic acid and peptidoglycan to induce the inflammatory reactions. RT-PCR, ELISA assay, immunoblotting and immunofluorescence staining were used for the assessment of anti-inflammatory activity of the extract. HaCaT cells induced the pro-inflammatory cytokines like interleukin-8 (IL-8) and/or interleukin-6 (IL-6) expressions after treatment with polyinosinic, polycytidylic acid or peptidoglycan. However, leaf extract inhibited the expression of IL-8 and IL-6 RNA and protein levels and attenuated the activation of NF-kB (Nuclear Factor-KappaB) and IRF3 (Interferon regulatory factor 3) after polyinosinic and polycytidylic acid treatment. Extract also inhibited expression of IL-8 and activation of NF-kB following peptidoglycan induction. From the result it is concluded that *A. calamus* leaf extract inhibits the production of pro-inflammatory cytokines through multiple mechanisms [28].

Antimalarial analogues from β-asarone

The antimalarial structure activity relationship of a series of methoxylated chalcones (A-CH=CH-CO-B) against *Plasmodium falciparum* (3D7 strain) using fluorescence-based SYBR Green assay has been reported by Kumar *et al.* The study has revealed that electron releasing methoxy groups on ring A and electron withdrawing groups on ring B increases antimalarial potency where as the positional interchange of these groups causes a decrease. In particular, 2, 4, 5-trimethoxy substitution pattern at ring A provided potent analogues which were easily derived from abundantly available natural β-asarone rich *A. calamus* oil [29].

Immunosuppressive activity

In the past and recent time plants and their, products have been extensively investigated for possible immunomodulatory and anticellular properties. Modulation of immune response to alleviate disease has been of interest since long. Mehrotra *et al.* have

evaluated the anticellular and immunomodulatory properties of ethanolic extract of *A. calamus* rhizome. The ethanolic extract inhibited proliferation of mitogen (phytohaemagglutinin; PHA) and antigen (purified protein derivative; PPD) stimulated human peripheral blood mononuclear cells (PBMCs) [30]. In another study, a pectic polysaccharide with D-galacturonic acid as major content was isolated from the rhizomes of *A. calamus*. Structural analysis of pectic polysaccharide with NMR spectroscopy predicted that it contains the regions of a linear 1, 4-α-D-galactopyranosyluronan which represents a major component of the macromolecule and considerable amount of galacturonic acid residues was not methoxylated. This pectic polysaccharide from *A. calamus* in low concentrations was able to stimulate *In vitro* IL-12 and nitric oxide production by murine macrophages. It also induced TNF-α secretion by human peripheral blood mononuclear cells, reduced arginase activity but did not affect IL-10 secretion by murine macrophages or human peripheral blood mononuclear cells. In addition, the polysaccharide promoted *in vivo* Th1 immune response in mice which were immunized with sheep red blood cells (DTH and quantity of plaque-forming cells) and down regulated serum level of IgG1 and IgE during Th2-dependent immune response induced by ovalbumin. The polysaccaride increased Th1-induced edema and suppressed Th2-induced paw swelling in adoptive systems. Thus, the pectic polysaccharide from *A. calamus* represents a promising immunomodulating agent that stimulates M1-polarized macrophages and promotes Th1-oriented adaptive immune response. The polysaccharide can be used for the treatment of infectious**,** oncological diseases or for IgE-mediated disorders [31].

Antidiarrhoeal activity

Diarrhoea is a national problem especially among children and contributes too much morbidity and mortality. Many medicinal plants that are conveniently available in India have been reported to be effective against diarrhoea and dysentery, as they are used by local people as traditional folklore medicine. Manonmani *et al.* have shown that prior treatment with some plant extracts had a protective effect on the intestinal tract [32]. Gricilda and Thomas evaluated the aqueous and methanolic extract of *A. calamus* for antidiarroheal activity against castor oil induced diarrhea in male Swiss *albino* mice along with other three plants namely *Pongamia glabra*, *Aegle marmelos* and *Strychnos nux-omica* that have not been studied so far. Methanol extracts of the plants significantly reduced the total weight of wet feces in a dose dependent manner. *A. calamus* is a common drug given for the relief of abdominal complaints in children [33]. This study also proved that among the four plant extracts, though all had significant antidiarrhoeal effect, methanol extracts are more effective than aqueous extracts. *Strychnos nux-omica* could not be used due to toxicity. *A. calamus* produced an antidiarrhoeal effect which was dose dependent. The essential oil, aqueous and alcoholic extract of *A. calamus* also relaxed the tone of isolated intestine of guineapigs [34].

Anticancer activity

Rhizomes of the two species *A. calamus* and *A. gramineus* has been reported to possess novel lectins purified by affinity chromatography on mannose linked epoxy-activated Sepharose 6B [35]. The molecular weight of lectins was determined by gel filtration chromatography and identified as 56 kDa for *A. calamus* and 55 kDa for *A. gramineus*. In SDS–PAGE, both lectins migrated with a subunit molecular mass of 13.6 kDa and 13.5 kDa respectively under reducing and non-reducing conditions thus indicating the absence of disulphide linkages. *Acorus* lectins readily agglutinated rabbit, rat and guinea pig erythrocytes. Both the lectins had the ability to react with RBCs from sheep, goat and human ABO blood groups after neuraminidase treatment.

The lectins were inhibited by mannose/glucose and their derivatives. Methyl-α-D-mannopyranoside could inhibit lectin activity at a concentration of 3.12 mM while free mannose was inhibitory at 6.25 mM. These lectins showed potent mitogenic activity towards mouse splenocytes and human lymphocytes. Both lectins significantly inhibited the growth of J774, a murine macrophage cancer cell-line and to lesser extent WEHI-279, a B-cell lymphoma. Extract from both species inhibited the growth of J774 to 67% and 40% and they inhibited the growth of WEHI-279 to 24% and 30% respectively.

Insecticidal activity

The α- and β-asarone isolated from the essential oil of *A. calamus* rhizomes are potent growth inhibitors and anti-feedants to the variegated cutworm. β-asarone added to artificial diet significantly inhibited growth and feeding of first-, third and fourth-instar larvae, while α-asarone exhibited an anti-feedant effect alone. Gross dietary utilization (ECI- efficiency of conversion of ingested food) was decreased when the diet was supplemented with β-asarone or when this compound was topically applied to fourth- instar larvae. Inhibition of growth occurred even at the lower dose (5 µg/larva) primarily as a result of decreased efficiency of conversion of digested food (ECD), even though the approximate digestibility (AD) of the food was unchanged [36]. In another study 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 bioactive constituents of *A. gramineus* rhizomes were characterized as phenylpropenes, α- and β-asarones by spectroscopic analyses. The potencies of these compounds varied according to insect species, compound and dose. In a test with female adults of *Nilaparvata lugens*, β-asarone caused 100, 83 and 40% mortality at 1000, 500 and 250 ppm respectively, whereas 67% mortality was achieved at 1000 ppm of α-asarone. Against 3 rd instar larvae of *Plutella xylostella*, β-asarone gave 83 and 50% mortality at 1000 and 500 ppm, respectively, whereas α-asarone at 1,000 ppm showed 30% mortality. Against female adults of *Myzus persicae* and 3rd instar larvae of *Spodoptera litura*, α- and β-asarones both were ineffective at 2000 ppm. The *A. gramineus* rhizome derived constituents merit further study as potential insectcontrol agents or as lead compounds against *N. lugens* and *P. xylostella* [37].

The effect of *A. calamus* rhizome oil was also studied on hemocytes of the tobacco armyworm, *Spodoptera litura*. The last instar larva was oral administrated with rhizome oil at the concentration of 500 and 1000 ppm and its effect on ultrastructure of hemocytes and hemogram was evaluated. The oil was administered in topical application at 250 mg dose to pupae to ascertain its effect on total and differential hemocyte counts. At both scanning (SEM) and transmission electron microscopic (TEM) levels, the major effect of oil treatment was observed on plasmatocytes (PLs) and granular hemocytes. The result obtained from SEM study revealed that the cytoplasmic projections of granular hemocytes were reduced, while the filopods of plasmatocytes remained unaffected. The vacuolization in the cytoplasm and degeneration of the organelles in both plasmatocytes and granular hemocytes was observed by TEM. However, no such deformities were observed in prohemocytes, spherulocytes and oenocytoids. A dose dependent decrease was observed in the larval body weight and hemolymph volume 24–72 h after treatment. In comparison to the controls, the maximum percentage growth inhibition was recorded to be 58.28 and 66.48, respectively, at 500 and 1000 ppm after 72 h of treatment. Similarly, the percentage reduction in hemolymph volume was 61.38 and 69.05 respectively, at 500 and 1000 ppm. Total hemocyte count in larvae evaluated from five recorded hemocyte types namely plasmatocytes, prohemocytes, oenocytoids, spherulocytes and granular hemocytes decreased only after 48–72 h of treatment. The maximum decrease in total hemocyte count was recorded to be 29.15 and 49.05% at 500 and 1000 ppm, respectively, after 72 h of treatment. There was continuous decline in total hemocyte count in pupae after 24–72 h treatment. Differential hemocyte count study revealed that both the concentrations of oil in 6th instar larvae of *S. litura* caused a decrease in prohemocytes, plasmatocytes, spherulocytes and increase in oenocytoids and granular hemocytes after 24–72 h of treatment. Since *A. calamus* oil treatment causes the injury to both plasmatocytes and granular hemocytes and also affects the hemogram, it can be inferred that cellular defence reactions of *S. litura* are impaired [38].

Anti-adipogenic activity

Several research groups have focused on anti-adipogenic activity of *Acorus* spp. The first report published on anti-adipogenic potential was the hypolipidemic activity of *A. calamus* in rats. It is the

saponins that are present in the ethanol extract of *A. calamus* which was found to possess hypolipidemic activity. Even water extract of *A. calamus,* if used in high concentration, has been reported to show the hypolipidemic activity [39]. Another study found that ethanol extract devoid of β-asarone enhances differentiation in mouse adipocytes in a way similar to rosiglitazone [40]. Adepocyte differentiation is measured as a function of triglyceroids and protein expression of the glucose transporter in adepocytes. Thus, properties of *A. calamus* have increased their prospects to be used in the treatment of type 2 diabetes. Very interestingly, recent study has reported inhibitory effect of β-asarone, a component of essential oil of *A. calamus* on inhibition of adipogenesis in 3T3-L1 cells. The mechanism of action of inhibitory action of β-asarone suggests that β-asarone suppresses the expression of adipogenic transcription factors. Earlier study by Lee *et al.* have reported that asarone from *A. calamus* has the potential to inhibit adipogenesis and stimulates lipolysis in 3T3-L1 adipocytes. Asarone reduces intracellular triglyceride levels and stimulate the phosphorylation of hormone sensitive lipase which triggers lipolysis in adipocytes [41].

Antidiabetic activities

The radix of *A. calamus* is widely used in the therapy of diabetes in traditional folk medicine of America and Indonesia. Si *et al*. reported the insulin releasing and alpha-glucosidase inhibitory activity of *A. calamus* extract *In vitro* using HTT-T15 cell line and *in vivo* in fasted and glucose/amylum challenged normal mice. *A. calamus* improves postprandial hyperglycemia and cardiovascular complications [42]. The hypoglycemic effects of *A. calamus* extract could be via mechanisms of insulin releasing and alpha-glucosidase inhibition. Wu *et al*. have studied the insulin sensitizing activity of ethyl acetate fraction of *A. calamus in vitro* and *in vivo.* Owing to the ability of insulin sensitizing, ACE has the potential to be useful for the treatment of diabetes and cardiovascular complications without body weight gain [43]. An antidiabetic study reported that oral administration of methanolic extract of *A. calamus* showed a significant restoration of the levels of blood glucose in streptozotocin induced diabetic rats. After 21 days of extract treatment to the streptozotocin induced diabetic rats the biological parameters like blood glucose, LDL and HDL cholesterol, glucose 6 phosphatase, fructose 1,6 bis phosphatase, levels and hepatic marker enzymes were decreased whereas plasma insulin, tissue glycogen and glucose 6 phosphate dehydrogenase levels were increased significantly when compared with diabetic control. Their study concludes the antihyperglycemic activity of *A. calamus* in streptozotocin induced diabetic rats [44].

P**rotective effect**

Free radicals and other reactive species are considered to be an important causative factor in the development of neurodegenerative diseases. The roots and rhizomes of *A. calamus* have been used in the ancient systems of medicine for the treatment of various neurological disorders. Cho *et al.* have evaluated neuroprotective actions and action mechanisms of the isolated asarone as well as α- and the β-asarones obtained commercially [45]. Asarones mainly serve as NMDA receptor-channel blocker [3H] MK-801 and inhibits the specific bindings in a concentration-dependent fashion. However, the α-asarone is a more potent inhibitor of [3H] MK-801 bindings which is consistent with its more potent neuroprotective action than the β-asarone or the isolated asarone. Their study concludes that the asarone exhibits neuroprotective action against the NMDA- or Glu-induced excitotoxicity through the blockade of NMDA receptor function. Shukla *et al*. have reported the neuroprotective potential of ethanol: water (1:1) extract of rhizomes of *A. calamus* in middle cerebral artery occlusion (MCAO)-induced ischaemia in rats [46]. With application of *A. calamus* rhizome extract, a significant improvement in neurobehavioural performance such as Rota-Rod performance and grid walking as compared to the MCAO group was noted. Thus *A. calamus* rhizome extract displayed neuroprotective effects in the rat model of ischaemia.

Neuroprotective activities

Prasad *et al*. have undertaken a study to investigate the protective effects of *A. calamus* on nickel chloride (NiCl2)-induced renal oxidative stress, toxicity and cell proliferation response in male Wistar rats. Nickel is a major environmental pollutant known for its clastogenic, toxic and carcinogenic potential. The study has demonstrated the role of oxidative stress and its relation to renal disfunctioning suggesting a protective effect of *A. calamus* on NiCl2-induced nephrotoxicity in a rat experimental model [47]. Rhizomes also have protective roles against acrylamide induced neurotoxicity in rats [48].

The search for new drugs from plants for the treatment of Alzheimer's disease has been documented in several recently published reports. In this perspective, *A. calamus* owing to its medicinal properties has been evaluated for its anti-Alzheimer's potential. The first report of anti-Alzheimer's potential of the β-asarone from *A. tatarinowii* has been published [49]. The β-asarone has capability of suppressing neuronal apoptosis in the beta-amyloid hippocampus injection rats. The mechanism elucidated indicates that β-asarone attenuate Abeta (1-42 amino acid peptide)-induced neuronal apoptosis in hippocampus by reversal down-regulation of Bcl-2, Bcl-w, caspase-3 activation and c-Jun N-terminal kinase (JNK) phosphorylation.

O**ther useful bioactivities**

Scientific literature shows tremendous bioactive potential of *A. calamus*. The pharmacological and ecological significance of *A. calamus* whole plant and its major chemical constituents such as α- and β-asarone as well as essential oil is rapidly increasing owing to their unlimited bioactive potential. In recent years several research groups have undertaken studies to evaluate plant's wide spectrum bioactive potential as wound healing, mitogenic, insecticidal, anthelmintic, allelopathic, antiepileptic, antispasmodic and inhibitor of acetylcholinesterase. All these studies encourage newer possible therapeutic applications of *A. calamus* extract in concerned diseases. Jain *et al*. has suggested wound-healing activity of ethanolic extracts of *A. calamus* leaves. Treatment of ethanolic extract has been found to be promising for healing of wound induced by an excision- and incision-based wound model in both male and female rats [50].

Phenylpropenes (*Z*)- and (*E*)-asarones found in *A. gramineus* rhizome has been reported to show insecticidal activities against stored product pests like *Sitophilus oryzae, Callosobruchus chinensis* and *Lasioderma serricorne* [51]. Two research groups have reported allelopathic effect of *A. tatarinowii* and *A. calamus* plants on algae and water-bloom forming algal species. The root system of *A. tatarinowii* was reported to excrete some chemical substances which arrest the algal growth. These substances tend to destroy some chlorophyll-A molecules and seem to act as inhibitor of photosynthesis in algae. However, effects of root derived substances on algae are concentration dependent and more interestingly at their low concentration they promote algal growth and inhibit the growth at a concentration near a definite threshold value [52]. Hu *et al.* report described the allelopathic effects of *A. calamus* water extracts on the growth of two water bloom-forming algal species, *Microcystis aeruginosa* and *Chlorella pyrenoidosa* [53].

Shah and Gilani provides pharmacologic basis to the medicinal use of *A. calamus* in cardiovascular disorders. Blood pressure-lowering and vascular modulator effects of *A. calamus* extract are mediated through multiple pathways [54]. *A. tatarinowii* has been reported to show 'Kaiqiao' effect in rats have beneficial effects on ultrastructure and permeability of blood-brain barrier [55]. Besides the Kaiqiao effect, *A. tatarinowii* has been reported to possess antiepileptic effect. The rhizome extract and volatile oil of *A. tatarinowii* display anticonvulsive effects in pentylenetetrazol (PTZ) kindling models. In addition, both extracts prevents convulsion-related GABAergic neuron damage in the brain in the prolonged PTZ kindling model.

A study conducted by Mukherjee *et al.* has revealed the acetyl cholinesterase (AChE) inhibitory potential of *A. calamus* essential oil and its constituent, β-asarone [56]. Antispasmodic effect of *A. calamus* has also been reported [57]. It has been suggested that the plant extracts contains chemical constituents which are responsible for calcium channel blockade and result in spasmolytic activity. Although *A. calamus* has widespread use in the traditional system of medicine for gastrointestinal disorders such as colic pain and

diarrhoea, this study has validated its traditional use in gastrointestinal disorders with strong mechanistic base. The spasmolytic effects of crude extracts, ethyl acetate and n-hexane fractions were studied in the isolated rabbit jejunum preparation. However, n-hexane fraction has potent spsamolytic effects. In recent times usefulness of *A. calamus* extract has been tested to develop environment friendly control measures. The study of Ghosh *et al* has highlighted the efficacy of *A. calamus* extract against cattle tick *Rhipicephalus microplus.* They tested large number of extracts prepared with ethanol, hydroethanol and hot water aganst the cattle tick. More importantly, these extract are safe and did not show any reaction in animals treated even with 50% of the concentration[58].

CONCLUSION

In the present article we have discussed the chemical composition and bioactivities of comparatively less studied plants belong to Acoraceae. Several recently published reports have highlighted tremendous bioactive potential of *Acorus* sps plants and their products particularly alpha and beta-asarones. The genus *Acorus* comprises 40 species however only few species such as *Acorus calamus* (Linn.), *Acorus christophii, Acorus tatarinowii* (Schott.) and *Acorus gramineus* (Solandin Ait.) have been sufficiently investigated for their chemical composition and bioactivities. Pharmacological and medicinal significance of the Acoraceae is constantly increasing due to many promising bioactivities such as, anti-inflammatory/ immunosuppressive, anti-adipogenic, antimicrobial, fungicidal, insulin sensitizing/antidiabetic, neuroprotective activities. Most strikingly, beta-asarone from *A. Tatarinowii* has anti-Alzheimer's potential. Besides *Acorus* spp possess many other promising biological activities. However, recent studies supports the different pharmacological activities of *Acorus* species it remains incomplete unless significant clinical trials are conducted. Therefore these are high time for investigations of chemical composition and bioactivities of the other members of the Acoraceae and also look deeper into the mechanism of action of bioactive constituents. More importantly, a lot of clinical trial experiments should be conducted in future to harness maximum benefit of bioactive potential of *Acorus* species.

CONFLICT OF INTERESTS

Declared None

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