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Medicinally Important Phytoconstituents of Sweet Flag (Acorus Calamus): A Critical Overview

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KEYWORDS
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ABSTRACT:

Now a day there has been a notable increase in interest in medicinal plants. The cause of this is growing knowledge of the limitations of synthetic chemotherapeutic drugs. Natural products and herbal remedies are currently highly sought after worldwide. Ayurveda serve as a "goldmine" for novel medicinal products to treat various chronic diseases. This review article provides the detailed description of Acorus calamus (Vacha) one of most important medicinal plant. Acorus calamus (Sweet flag) used in the treatment of various illnesses such as epilepsy, memory loss, dysentery, chronic diarrhea, intermittent fever etc. A broad range of chemical constituents isolated from the rhizomes and leaves part includes A-asarone, b-asarone, c-asarone, calamene, calamenenol, calameone, a-pinene, b-pinene etc. From a long ago Acorus calamus has been used for various purposes and many of its uses has to be scientifically not proven. The present review attempt to explore its traditional uses and pharmacological bioactive compounds present in it.

INTRODUCTION

As of right now, pharmaceutical companies are estimated to invest $1 billion to develop a new medicine. The targeted treatments and miracle cures of today are highly costly. The ancient Indian therapeutic system known as Ayurveda dates back almost 6,000 years. The word Ayur means "life," while the word Veda means "knowledge or science." Together, these two words translate to "the Science of Life." Instead of treating an illness, its goal is to encourage lifespan and excellent health[29].

Acorus calamus Linn. (Acoraceae), Vacha in Sanskrit, is a fragrant, mid-term, perennial herb used in Chinese and Ayurvedic medicine, Indian traditional medicine. The rhizomes of the plant are brown in hue, twisted, cylindrical, curled, and have short nods. Radiant green in color, the leaves have a sword-like form with rounded edges and a thicker center[22]. In the temperate and subtropical zones of the Northern and Southern Hemispheres, including India, Kazakhstan, China, and Japan, the genus *Acorus* L. is widely dispersed. *Acorus*, sometimes known as "Chang Pu" in Chinese, was originally mentioned as a first-rate variety in Shennong's Material Medicine source. It was used to cure epilepsy, palpitations, stomach pain, bruises, amnesia, and other conditions[32].

Vacha, a primary Medhya medication that enhances intelligence and memory, holds a unique position in Ayurveda medicine. It is widely employed in therapies because of its significant pharmacological qualities, which include those of Deepana (appetizer), Pachana (Digestive), Vamaka (Emetic), Medhya (Brain tonic), Kanthya (Good for throat), Sanjnasthapana (Restores lost consciousness), Vedanasthapana (Anodyne), etc.[24].

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The Indian Ayurvedic medical system employed the mysterious root as a general sedative and to cure a wide range of ailments, including bronchitis, fever, and asthma. Dioscorides said that using a funnel to inhale the smoke of a medicine may heal a cough. The rhizome contains potent anticonvulsant qualities in addition to a lovely, aromatic fragrance. Flavonoids, essential oils, and saponins are some of the components in the rhizome of *Acorus calamus*. Records state that the essential oil extracted from *Acorus calamus* has the ability to chemically sterilize, prevent insects from feeding, and repel insects[7].

Taxonomical Classification[23]

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

Vernacular Names

Arabic: Vaj, Vash, OudulVaj; Sanskrit: Bhadra, Bhutanashini, Vacha; Hindi: Bach, Ghorbach, Safedbach; Kashmir: Vachi, Vaigandar; English: Sweet flag, Calamus, Myrtle grass; Gujarati: Gandhilovaj, Godavaj; Persian: Agar, Agartuki; Kannada: Baje, Vasa; Tamil: Vasambu, Pullai-valathi; Urdu: Bach, Vaj; Nepali: Bojho; Ayurvedic: Vacha; Unani: Vaj Turki, Bacch; Italy: Plant of Venus[7].

Distribution and Botanical Description

Particularly from India and China, it is a widely used traditional, highly endangered, medicinal, and aromatic plant species. The vast majority of its growth occurs in the marshy expanses of the Kashmir Valley, especially in the Hokhersar and Shalbug marshes (Ganderbal), Manasbal Lake, Anchar Lake, Srinagar, and other marshy areas. From Kashmir in the northeast to the Himalayas, where it reaches elevations of 1500–2200 m, A. calamus is found throughout a wide range of India[3]. *Acorus calamus* Linn. is a herbaceous perennial with long, continuously branched, smooth, pinkish, or pale green cylindrical rhizome that measures approximately 3/4 inch in diameter. Its leaf scars are brown, white, and spongy. It has very thin roots. It has few, sporadically alternating leaves[21].

Medicinal Value of *Acorus calamus*

The Ayurvedic belief is that the rhizomes have reddish-brown tonic, stimulant, nauseant, emmenagogue, expectorant, aphrodisiac, diuretic, cathartic, spasmolytic, parasitical, and flatus-relieving properties that aid in the treatment of illnesses such as schizophrenia, epilepsy, memory loss, dysentery, chronic diarrhea, intermittent fever, bronchial catarrh, tympanitis, otitis media, colic, asthma, cough, and tumors of the glands and abdomen[15]. According to Patthanaik et al., (2013), they are also used to treat rheumatism, eczema, and renal and liver problems[16]. These substances have a variety of pharmacological activities, according to modern pharmacology, and they can be used to treat conditions involving the nervous system, heart, and digestive system, such as indigestion, depression, anxiety, hyperglycemia, and hyperlipidemia, as well as conditions like Alzheimer's disease, gastric colic, and stress[32].

Due to their clinically demonstrated benefits, such as their anti-inflammatory, analgesic, antipyretic, immunomodulatory, and adaptogenic properties, people are becoming more interested in herbs and herbal medications. Furthermore, usage of synthetic drugs has increased the risk of bad drug reactions, prompting people to look to nature for safer solutions [25].

Table 1. Ayurvedic terms indicating properties of *Acorus calamus*[20]

Ayurvedic term	Use/properties
Vantikrut	Induces vomiting in Vamana therapy (a therapy where the patient is made to vomit)
Vanhikrut	Used as appetizer in dyspepsia
Vibandhhara or Adhanahara	Carminative
Shulaghni	Antispasmodic (relieves abdominal pain)
Shakrut vishodhini	Removes stool from body
Mathrushodihni	Act as a diuretic
Bhodhaneeya	Arousing consciousness

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Karshini	Reduces body weight
Rokshoghni	Checks or destroys the organisms
Bhutaharet/Jantuharet	Antimicrobial or antihelminthic properties
Anilhara or Vatanasaka	Anti-inflammatory, analgesic, pain reducing
Vednasthapaka	Analgesic, anti-inflammatory, arthritis
Lekhana	Lipid lowering
Swaralu	Improving speech or voice
Smarani	Memory promoter
Shleshmaghni	Pacifies kapha
Vijaya	Victory over diseases
Mangalya	Helps to keep Healthy

PHYTOCHEMISTRY OF *ACORUS CALAMUS*

There have been reports of a broad range of chemical components from the rhizomes of *Acorus calamus*. The oil of *Acorus calamus* rhizomes has been examined by many workers for their chemical constituents including A-asarone, b-asarone, c-asarone, calamene, calamenenol, calameone, a-pinene, b-pinene, camphene, p-cymene, azulene, eugenol methyl ether, dipentene, methyleugenol, eugenyl acetate, eugenol, isoeugenol, methyl isoeugenol, calamol, asaronaldehyde, terpinolene, 1,8-cineole, camphor, a-caryophyllene, and hydrocarbons. Additionally, the oil includes fatty acids including butyric acid ester heptylic acid and its ester palmitic acid[14]. By using GC-MS, several volatile oil constituents were detected and measured: acorenone (13.4%), iso-acorone (11.6%), (Z)-sesquilavandulol (11.0%), and 7.7% of dehydroxy isocalamendiol. Additional ingredients include coumarine (0.048%), saponin (1.748%), acofuran, a sesquiterpenoid (0.1-0.5%), and coumarine (0.048%). In addition to this, the plant also contains starch, tannins, acorenone, calamenone, shyobunone, lucenin, acoradin, calamusenone, methyleugenol, calamenol, α-pinene, acorine, and acoretine[30]. The degree of polyploidy of the different *Acorus* cytotypes, subvarieties, and/or species affects the amount of asarone in the essential oil of *Acorus* spp. beta-Asarone (90–96%) is widely distributed in tetraploid forms. It is reported that around 80% of *Acorus calamus* var. angustata ENGER (tetraploid) is beta-asarone. Additional components identified from this plant include alkaloids, flavanoids, gums, lectins, mucilage, phenols, quinine, saponins, sugars, tannins, and triterpenes. There are reports of a variety of sugars, including fructose (79.1%), glucose (20.7%), and maltose (0.2%). The roots include the tricyclic sesquiterpene calamenone as well as the sesquiterpenes calamendiol and isocalamendiol. Terpenoids such as calamine, calamenol, calamenone, eugenol, camphene, pinene, and asaronaldehyde are also present in the volatile oil. Calamus oil contains a sesquiterpenoid called acorafuran[20]. *Acorus* (20.81%) contains methyl eugenol ether, a phenylpropanoid component of comparatively good quality[32].

Phenylpropanoid

Phenylpropanoids are a class of naturally occurring chemicals having a wide range of biological action. The traditional Chinese herb *Acorus calamus* var. angustatus produced a total of 22 known and 3 undescribed phenylpropanoids. Besser, whereby α-asaronol, β-asaronol, 1,2,4-trimethoxy-5-(3-methoxypropyl) benzene, and 3-(2,4,5-trimethoxyphenyl)propan-1-ol demonstrated potential protective properties against oxidative stress in neurons[1]. The n-BuOH percentage of rhizome extracts from *Acorus tatarinowii* allowed for the identification of four known lignan analogues, a known asarone-derived lignin, and eight unique and seven previously reported asarone-derived phenylpropanoids[8]. Perret et al. (1995) reported that the hexane extract of the Chinese medicinal herb *Acorus grarnineus* contained the phenylpropanoids α and β-asarone (Figure 1 (a & b)[17]. The essential oil and hexane extract showed strong antibacterial action against *Propionibacterium* acne[12].

From the *Acorus calamus*, the phenylpropanoid substances (Z)-Asarone, (E)-Asarone, and Estragole (Figure 1 (d)) were isolated[11]. According to Lee et al. (2004), β-asarone had a minor impact on the growth of *Bacillus subtilis*, *Erwinia carotovora* subsp. carotovora, *Ralstonia solanacearum*, and *Xanthomonas campestris* pv. Vesicatoria[13]. The results of extracting oil from *Acorus calamus* showed the presence of α-Asarone, elemicine (Figure 1 (e), cisisoelemicine (Figure), and methyl ethers of of cis and trans isoeugenol[26]. Most of the phenylpropanoids were extracted using steam distillation. Several phenylpropanoids were extracted

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and isolated using chloroform extract, such as isoeugenol methyl ether (Figure 1 (f)), γ asarone (1, 2, 4-trimethoxy-5 (2-propenyl) benzene (Figure 1 (g), In Figure 1 (h), cis-asarone (cis-1,2,4- trimethoxy-5(2-propenyl) benzene is revealed. 1,2,4-trimethoxy-5(2-propenyl) benzene (trans-asarone) Figure 1 (i) shows asarylaldehyde (2,4,5- trimethoxy benzaldehyde) (Figure 1 (k) coupled with ascoramone (1,2,4-trimethoxy-5 (2-propanoyl) benzene (or) 1(2,4,5-trimethoxyphenyl)-propan-2-one). In addition, phenyl indene derivatives were identified by their structures and isolated.

3, 2, 3-dihydro-4,5,7-trimethoxy-3-(2,4,5-trimethoxy phenyl) indene, Z-3-(2,4, 5-trimethoxy phenyl)-2-propenal, and -1-ethyl-2-methyl (Figure 1 (m)[4]. Wang and colleagues (2014) reported the pharmacokinetic analysis of elemicin, cismethyl isoeugenol, β-asarone, and α-asarone following oral administration of the essential oil of the rhizomes part of *Acorus tatarinowii* Schott.[28]. Yu et al. (2016) reported the discovery of asarotonide, a new phenylpropanoid with a rare natural acetonide group, from the rhizomes of *Acorus gramineus* (Figure 1(n), was discovered from the rhizomes of *Acorus gramineus* and possesses a rare natural acetonide group[31].

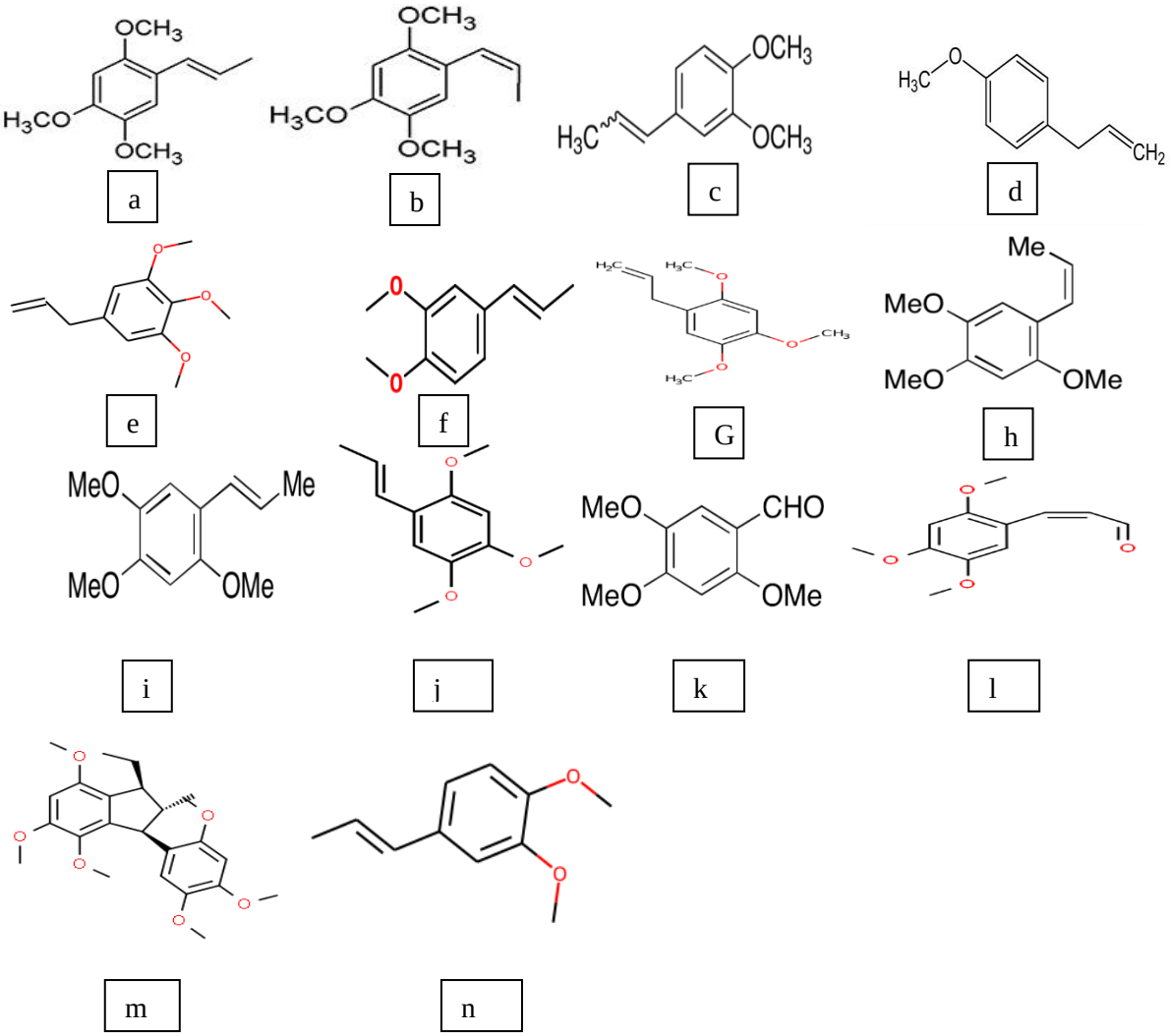

Figure 1: Figure showing the structures of various phenylpropanoid compounds isolated from *Acorus calamus*

Sesquiterpenoid

Terpenoids, sometimes called isoprenoids, are a diverse group of compounds found in nature that are composed of five carbon isoprene units. Terpenes, sometimes referred to as terpenoids, are classified into various groups: hemiterpenes (C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), sesterterpenes

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(C25), triterpenes (C30), and tetraterpenes/carotenoids (C40). The largest class of terpenoids, sesquiterpenoids, are found in a wide range of natural environments. Two of the earliest sesquiterpenoids to be isolated from nature were β-cardinene from oil of cade (juniper tar) and β-caryophyllene from clove oil. Sesquiterpenoids, or C15 molecules, are produced when three isoprene units condense. From the ethanol extract of *Acorus calamus* rhizomes, calamusins L–Q, six new sesquiterpenoids, and fourteen previously identified ones were isolated.

Every new molecule was evaluated for its neuroprotective properties against PC12 cell injury generated by OGD, serum withdrawal, and rotenone. A recently discovered sesquiterpene cadinane with a propan Two new sesquiterpenes were identified from the ethanol extract of the *Acorus calamus* L. rhizome: (2R,6R,7S,9S...)named (1R,4R,6S,10R), -1(10),4-cadinadiene2,9-diol, and -2-ylidene1 hydroxy-7(11)-cadinen-5,8-dione (a & b) in Figure 2 [28]. Balam et al. reported finding á-Ursolic acid, isocalamendiol, and acorenone in the plant extract of *Acorus calamus* (Figure 2 (c, d, & e)). The plant extracts' rhizomes yielded the sesquiterpenes Epishyobunone, 2, 6-diepishyobunone, and Shyobunone (Figure 2 (f)). Aristolene, kessane, and b-Gurjunene (Figure-2 (g, h, i)) are among the sesquiterpenoids present in the essential oil composition of *Acorus calamus* roots from the Indian state of Uttarakhand's foothills[27]. α selinene, bgurjunene, and β cadinene, calacorene, acoragermacrone, calamendiol, spathulenol, and cadinol (Figure-2 (j, k, l & m)), isoshyobunone, beta-sesquiphellandrene, preiso calamendiol, 1β, 7α(H) cadinane 4α, 6α, 10α triol, 1α, 5 β guaiane 10α O ethyl 4β, 6 β diol, and 6β,7β(H) cadinane 1α,4α, 10α triol[30]. 3.-Carene, 1,4-Cineole, Limonene, 1,3,8-p-Menthatriene, Eucalyptol, Isobornyl acetate, Valencene, Aromadendrene, and Germacrene D (Figure-2 (n & o) have been isolated from the plant extract of *Acorus calamus*[11].

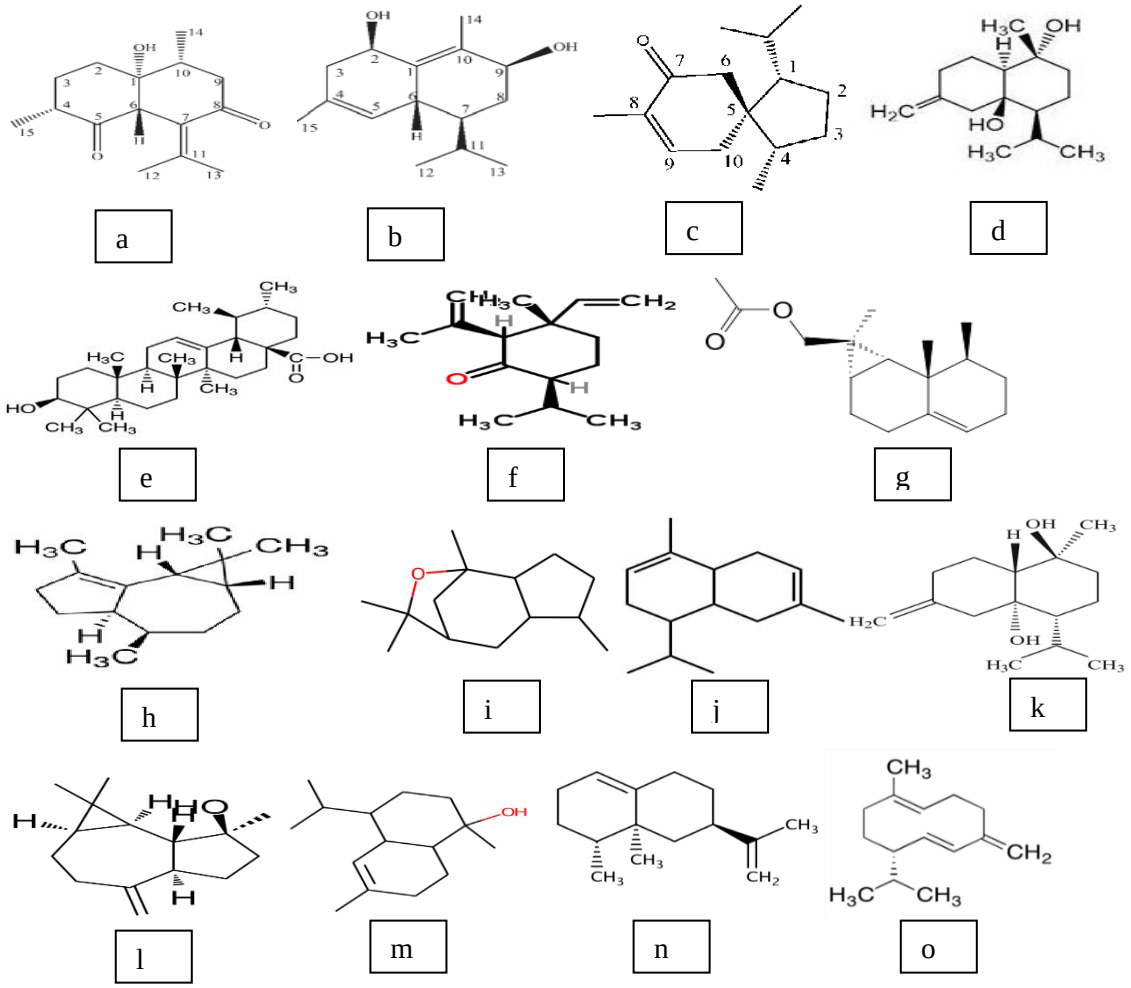

Figure 2: Figure showing the structures of various sesquiterpenoids compounds isolated from *Acorus calamus*

Monoterpenoids

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The oil extract of *Acorus calamus* was found to include monoterpenes like myrcene, para-cymene, α-terpinen, β-phellandrene, gammaterpinene, Thujane (Figure 3 a,b,c,d,e & f), and Limonene[4]. Calaren, camphor, acorone, p cymene, linalool, and camphene are among the recognized terpenoids found in *Acorus calamus* (Figure-3 g & h).

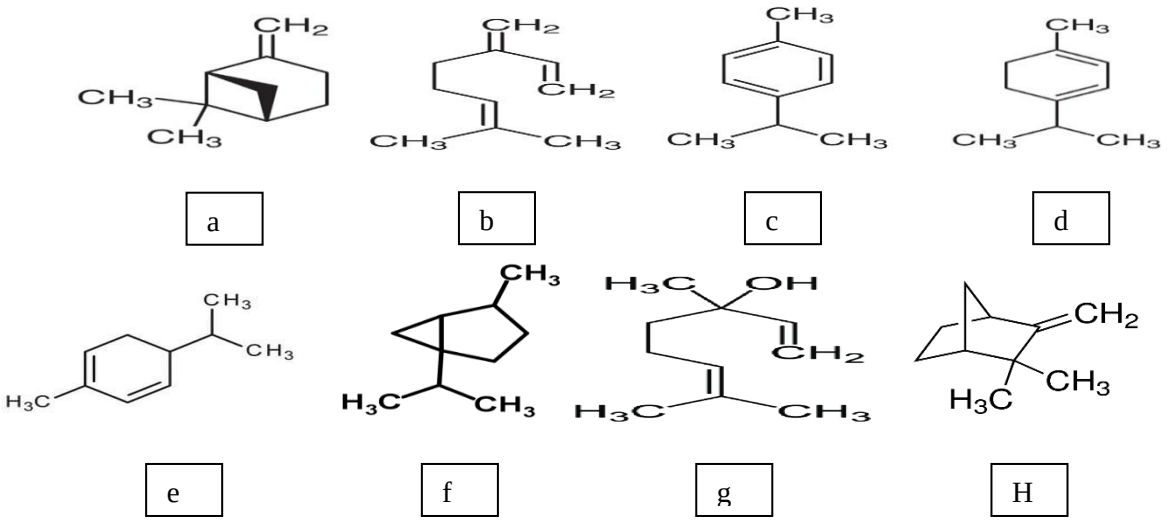

Figure 3: Figure showing the structures of various monoterpenoids compounds isolated from *Acorus calamus*

Flavone

Khawariakamp et al. (2018) reported that the plant sections of *Acorus calamus* contained the primary flavonoids Genistin, Sakuranin, and Retusin (Fig. 4 (a, b, c)[11]. The plant *Acorus calamus* yielded 5, 7-dihydroxyflavonol (Galangin) (Fig. 4 d)[4]. Balakumbahar et al., 2020 reported that flavones like apigenin and 4',7-dimethyl ether were present in the *Acorus calamus* extract (Fig. 4 (e & f)[2].

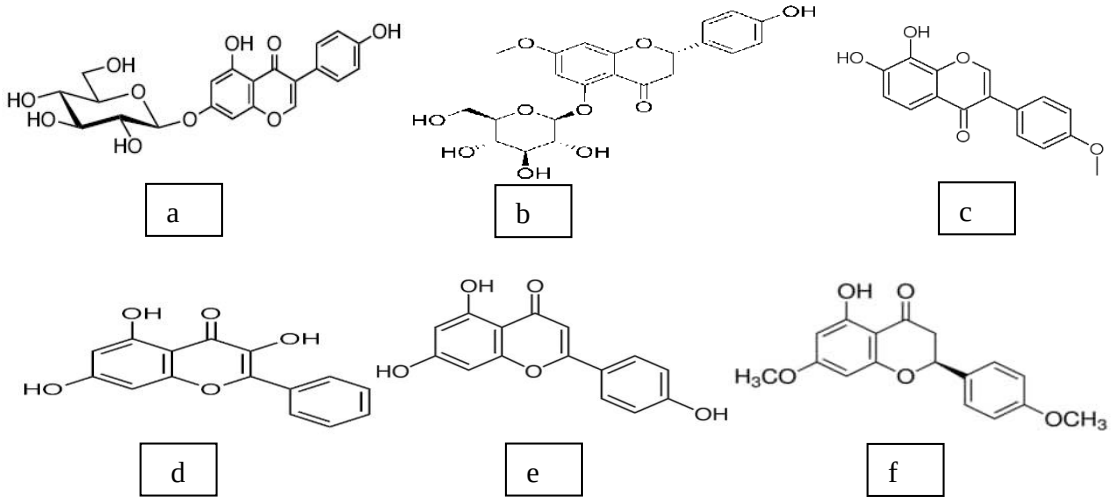

Figure 4: Figure showing the structures of various flavone compounds isolated from *Acorus calamus*

Xanthone glycosides

Chemical investigation of the rhizome of *Acorus calamus* has yielded a novel xanthone glycoside called 4, 5, 8-trimethoxyxanthone-2-O-β-D-glucopyranosyl (1 2)(Fig. 2.10(a)) -O-β-D-galactopyranoside[18]. Another unique xanthone glycoside that was obtained from the rhizome of *Acorus calamus* is 8-dihydroxy-3, 7-dimethoxyxanthone-4-O-α-L-rhamnosyl (1→2)-O-β -D-glucopyranoside (Fig 5 (b)[5].

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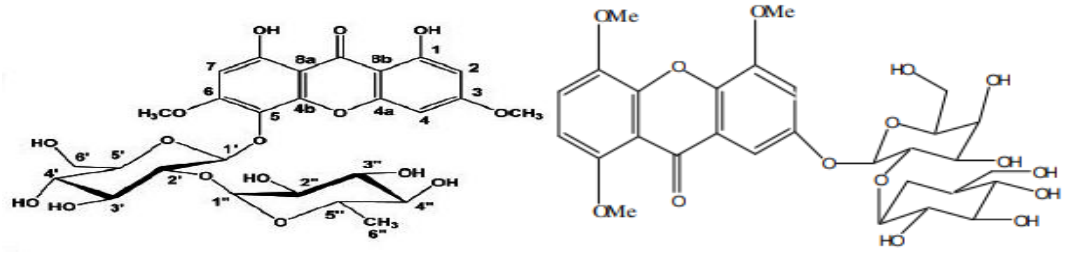

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Figure 5: Figure showing the structures of various xanthone glycosides compounds isolated from *Acorus calamus*

Lignans

Acoradin, a lignan identified from the plant's rhizome, was extracted (Fig 6 (a) Benzene from an *Acorus calamus* chloroform extract was used to elute it[4].

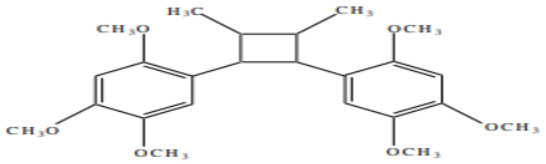

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Figure 6: Figure showing the structures of various lignans isolated from *Acorus calamus*

Steroids

Galangin and β-sitosterol were separated from the petrolbenzene (1:1) eluate and have a flaky texture. Based on its physical and spectral characteristics, it was determined to be β-sitosterol (Figure 7 (a)[19].

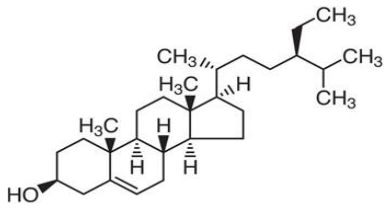

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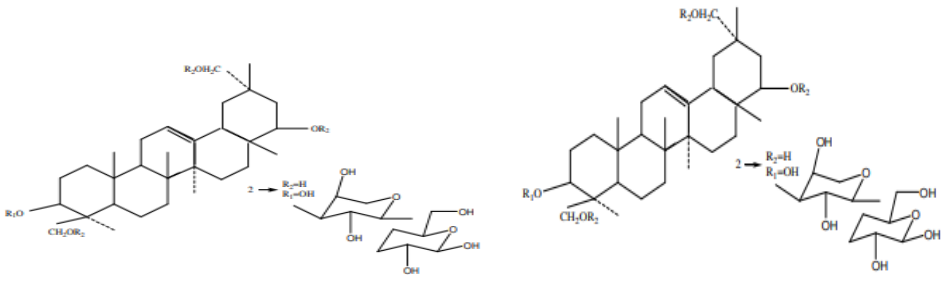
Figure 7: Figure showing the structures of various steroids compounds isolated from *Acorus calamus*

Triterpenoid saponins

The following characteristics apply to the two newly discovered triterpenoid saponins: One can find 1) 1β, 2α, 3β, 19α-tetrahydroxyurs-12en-28-oicacid-28-O {-β-D-glucopyranosyl (1-2)} β- D-galactopyranoside (Fig 8). 2) 3-β, 22α, 24-29-tetrahydroxyolean-12-en-3-O-{-β-D-arabinosyl (1-3)}-β-D-arabinopyranoside (Figure 8 a & b).



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CONCLUSION

Herbal medicines are in significant demand in both developed and developing nations due to their wide range of biological activity, greater safety compared to synthetic pharmaceuticals, and lower cost. Many people utilize *Acorus calamus* as a herbal remedy. Asarone, sesquiterpenoids, caumarine, and saponin are all said to be present in this herb. It has hypolipidemic, neuroprotective, anticonvulsant, and antioxidant qualities. *Acorus calamus* also demonstrates antibacterial, immunomodulatory, and anticellular action, as well as protection against nephrotoxicity. *Acorus calamus* is a complete gift from nature, so it is necessary to fully utilize its potential in the fields of pharmaceutical and medical sciences for innovative and profitable applications. This review concludes that *Acorus calamus* is an amazing herb that has been used since the Ancient and Vedic periods to treat a variety of ailments. Therefore, it has been demonstrated by the many examined literatures that *Acorus calamus* can be successfully explored for a variety of marketable formulations.

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