Original Article

Anti-Parkinson's Potential Of Acorus Calamus Linn: A Review

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Abstract

Acorus calamus Linn is a species of perennial, semi aquatic, aromatic herb with creeping rhizomes; it belongs to the family Acoraceae. In Ayurveda Acorus calamus Linn is also known as VACHA and publically known as Bacha or sweet flag. It is a highly valued herb as it acts as a rejuvenator for brain and nervous system. It is a main medhya drug, which has the property of improving the memory power and intellect. Acorus calamus (AC) has been used as traditional Indian and Chinese prescriptions for its beneficial effects on cognitive and memory enhancement, anti-aging and anticholinergic activity. Scientific-asarone possessed to have antidepressant, anticonvulsant, anti-inflammatory, analgesic, antipyretic, antispasmodic, cytoprotective, immunomodulatory, antidiarrheal, antimicrobial, β and αstudies reported AC and its active constituents anthelmintic, insecticidal, and hypolipidemic effects. This review presents a pragmatic description that deals with chemical constituents and neuropharmacological properties of Acorus calamus for easy and better understanding of the outstanding medicinal potential of this very special plant.

Keywords: Neuropharmacology; Anti-depressant; Anti-convulsant; Nervous system; Traditional medicine.

INTRODUCTION

The most familiar disease after Alzheimer's disease (AD) is Parkinson's disease (PD) which comes second under neurodegenerative disorder, with an overall prevalence of 300 per 100,000 that raises from 41in the 40–49 years' age range to 1903 in people older than age of 80 years. PD has been traditionally considered as a pure movement disorder secondary to focal degeneration of dopaminergic neurons in the substantia nigra, but, in recent years, the clinical phenotype has been better illuminated, showing that PD is a multisystem neurodegenerative disorder with motor and nonmotor features. Among motor symptoms and signs, the cardinal ones (bradykinesia, rest tremor, and rigidity) are mainly ascribed to the loss of dopaminergic neurons, but those involving posture, balance, and gait are largely secondary to degeneration of non-dopaminergic pathways and significantly contribute to impairment and disability in advanced PD patients. The peripheral and central nervous system consists of numerous neurotransmitter deficiencies that include autonomic (orthostatic hypotension, genital and urinary disturbances and constipation) features and psychiatric (apathy, hallucinations, depression and delusions), pain, olfactory dysfunction, sleep disorders, cognitive impairment (involvement of executive functions, memory, and visuospatial functions up to dementia) all collectively adverse the quality of life (QoL) and patient's disability.

THE FUNCTIONAL ANATOMY AND PATHOPHYSIOLOGY OF THE BASAL GANGLIA AND THE ROLE OF THE CEREBELLUM

The basal ganglia (BG) include the striatum, which comprises the caudate nucleus, putamen and nucleus accumbens, the globus pallidus that is divided into an external segment (GPe) and an internal segment (GPi), the substantia nigra that can be divided into a pars compacta (SNc) and a pars reticulata (SNr), and the subthalamic nucleus (STN). The main input region of the BG is the striatum, which receives afferents from many regions of the cerebral cortex, including motor and premotor, cingulate, and prefrontal cortices, and the intralaminar nuclei of the thalamus. The major output regions of the BG are the GPi and the SNr, which project to the thalamus modulating activity of cortical regions and to the brainstem. The input and output regions are connected via either the direct or the indirect pathways, both of which arise from the matrix medium spiny neurons of the striatum (Figure 1), while the striosomes medium spiny neurons control dopaminergic projections from the SNc.

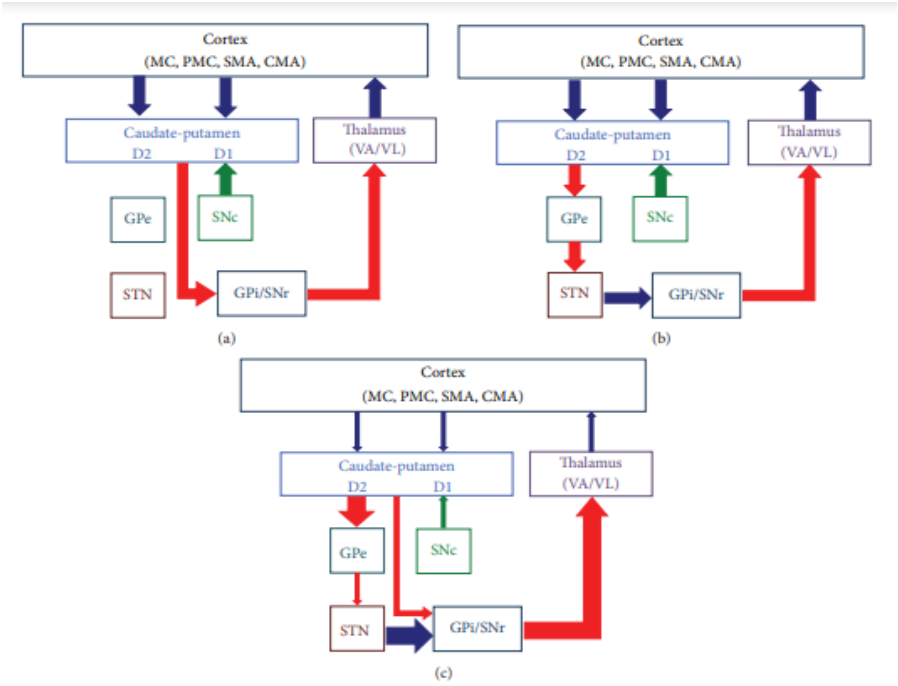

Figure 1: Simplified view of the functional anatomy of the basal ganglia

THE NEUROPATHOLOGY OF PARKINSON'S DISEASE

The classical pathologic substrate for PD is the accumulation of neuronal inclusions composed of α-synuclein and called Lewy bodies and neurites and neuronal loss (Raja Sankar *et al.*, 2009). Neuronal loss is most marked in the SNc, but Lewy bodies in PD extend well beyond this region. Based on the distribution of α-synuclein pathology, a staging scheme for PD has been proposed

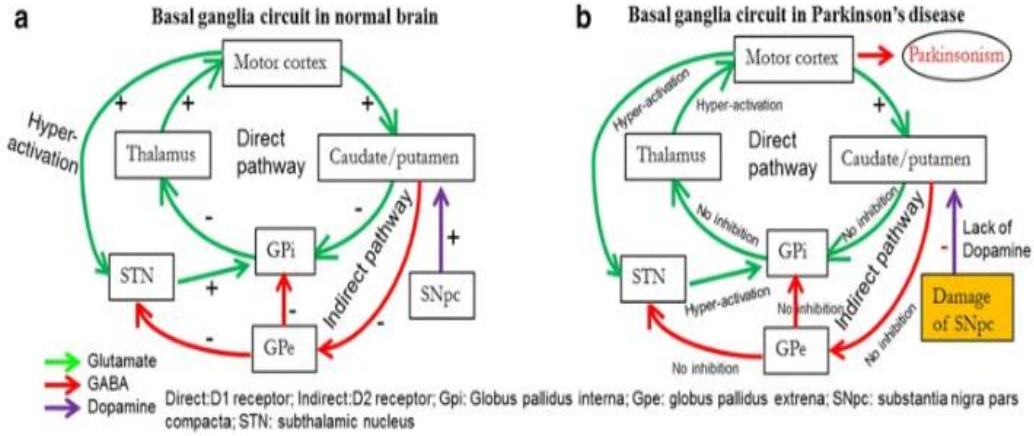

Figure 2: (a) Neuronal circuit in basal ganglia in normal brain (b) Degeneration of substantia nigra pars compacta (SNpc) impairs cortico-striatal circuit in PD brain

Symptoms Of Parkinson's Disease

Primary motor symptoms

- Resting Tremor
- Rigidity
- Slow movement (bradykinesia).
- Balance and coordination problems.

Secondary motor symptoms

- Difficulties in swallowing and chewing.
- Muscle cramps and dystonia
- Sexual dysfunction.
- Changes of speech and voice

Primary non-motor symptoms

- Depression

- Dementia and or cognitive dysfunction
- Problems in sleep (insomnia)

Secondary non-motor symptoms

- Gesture and emotional changes
- Urinary problems and constipation
- Sweating and skin problems
- Blood pressure
- Pain

Diagnosis

Presently, the diagnosis of Parkinson's is primarily based on the common symptoms outlined above. There is no X-ray or blood test that can confirm the disease. However, non-invasive diagnostic imaging, such as positron emission tomography (PET) can support a doctor's diagnosis. Conventional methods for diagnosis include:

- The presence of two of the three primary symptoms
- The absence of other neurological signs upon examination
- No history of other possible causes of parkinsonism, such as the use of tranquilizer medications, head trauma or stroke
- Responsiveness to Parkinson's medications, such as levodopa

Medical treatment

The majority of Parkinson's patients are treated with medications to relieve the symptoms of the disease. These medications work by stimulating the remaining cells in the substantia nigra to produce more dopamine (levodopa medications) or by inhibiting some of the acetylcholine that is produced (anticholinergic medications), therefore restoring the balance between the chemicals in the brain. It is very important to work closely with the doctor to devise an individualized treatment plan. Side effects vary greatly by class of medication and patient.

Levodopa

Developed more than 30 years ago, levodopa is often regarded as the gold standard of Parkinson's therapy. Levodopa works by crossing the blood-brain barrier, the elaborate meshwork of fine blood vessels and cells that filter blood reaching the brain, where it is converted into dopamine. Since blood enzymes (called AADCs) break down most of the levodopa before it reaches the brain, levodopa is now combined with an enzyme inhibitor called carbidopa. The addition of carbidopa prevents levodopa from being metabolized in the gastroinstenal tract, liver and other tissues, allowing more of it to reach the brain. Therefore, a smaller dose of levodopa is needed to treat symptoms. This advance also helps reduce the severe nausea and vomiting often experienced as a side effect of levodopa. For most patients, levodopa reduces the symptoms of slowness, stiffness and tremor. It is especially effective for patients that have a loss of spontaneous movement and muscle rigidity. This medication, however, does not stop or slow the progression of the disease. Levodopa is available as a standard (or immediate) release formula or a long-acting or "controlled-release" formula. Controlled release may provide a longer duration of action by increasing the time it takes for the gastrointestinal tract to absorb the medication. Side effects may include nausea, vomiting, dry mouth and dizziness. Dyskinesias (abnormal movements) may occur as the dose is increased. In some patients, levodopa may cause confusion, hallucinations or psychosis.

Dopamine agonists

Bromocriptine, pergolide, pramipexole and ropinirole are medications that mimic the role of chemical messengers in the brain, causing the neurons to react as they would to dopamine. They can be prescribed alone or with levodopa and may be used in the early stages of the disease or administered to lengthen the duration of effectiveness of levodopa. These medications generally have more side effects than levodopa, so that is taken into consideration before doctors prescribe dopamine agonists to patients. Side effects may include drowsiness, nausea, vomiting, dry mouth, dizziness and feeling faint upon standing. While these symptoms are common when starting a dopamine agonist, they usually resolve over several days. In some patients, dopamine agonists may cause confusion, hallucinations or psychosis.

COMT inhibitors

Entacapone and tolcapone are medications that are used to treat fluctuations in response to levodopa. COMT is an enzyme that metabolizes levodopa in the bloodstream. By blocking COMT, more levodopa can penetrate the brain and, in doing so, increase the effectiveness of treatment. Tolcapone is indicated only for patients whose symptoms are not adequately controlled by other medications, because of potentially serious toxic effects on the liver. Patients taking tolcapone must have their blood drawn periodically to monitor liver function. Side effects may include diarrhea and dyskinesias.

Selegiline

This medication slows down the activity of the enzyme monoamine oxidase B (MAO-B), the enzyme that metabolizes dopamine in the brain, delaying the breakdown of naturally occurring dopamine and dopamine formed from levodopa. When taken in conjunction with levodopa, selegiline may enhance and prolong the effectiveness of levodopa. Side

effects may include heartburn, nausea, dry mouth and dizziness. Confusion, nightmares, hallucinations and headache occur less often and should be reported to the doctor.

PLANT PROFILE

Plant name

Acorus calamus Linn

Figure 3: Acorus calamus Linn

Scientific classification

Kingdom: Plantae
Clade : Tracheophytes
Clade : angiosperms
Clade : monocots
Order : Acorales
Family : Acoraceae
Genus : *Acorus*
Species : *A. calamus*

Botanical description

It is known by a variety of names, including cinnamon sedge, flag root, gladdon, myrtle flag, myrtle grass, myrtle sedge, sweet cane, sweet myrtle, sweet root, sweet rush and sweet sedge. *A. calamus* is probably indigenous to India and now found across Europe, Southern Russia, Northern Asia Minor, China, Japan, Burma, Sri Lanka, and Northern US *A. calamus* was valued as a stimulant, bitter herb for the appetite and as an aid to the digestion. In North America, the decoction was used for fevers, stomach cramps and colic; the rhizome was chewed for toothache and powdered rhizome was inhaled for congestion. In Ayurvedic medicine Calamus is an important herb, and is valued as a "rejuvenator" for the brain and nervous system, and as a remedy for digestive disorders. It is known by a variety of names, including cinnamon sedge, flag root, gladdon, myrtle flag, myrtle grass, myrtle sedge, sweet cane, sweet myrtle, sweet root, sweet rush and sweet sedge. *A. calamus* is probably indigenous to India and now found across Europe, Southern Russia, Northern Asia Minor, China, Japan, Burma, Sri Lanka, and Northern US*A. calamus* was valued as a stimulant, bitter herb for the appetite and as an aid to the digestion.

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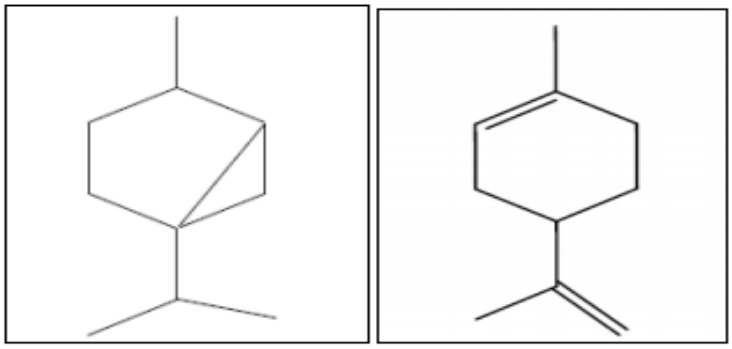
Acorus calamus (Acoraceae), also known as Vacha in Sanskrit, is a mid-term, perennial, fragrant herb which is practiced in the Ayurvedic (Indian traditional) and the Chinese system of medicine. The plant's rhizomes are brown in color, twisted, cylindrical, curved, and shortly nodded. The leaves are radiant green, with a sword-like structure, which is thicker in the middle and has curvy margins. Several reports ascertained a wide range of biological activities involving its myriad of active phytoconstituents. In this sense, the intent of this review is to assemble and summarize the geographical distribution, ethnopharmacology, phytochemistry, mechanism of action of A. calamus along with preclinical and clinical claims that are relevant to manage neurological and metabolic disorders. To the best of our knowledge, so far, none of the published reviews has described all the characteristics of this medicinal plant (Vineet Sharma *et al.*, 2020).

Vernacular names (Fritz *et al.*, 2008)

- English Calamus, Sweet flag
- Bengali Bach
- Gujarat Vekhand
- Ayurvedic Vacha
- Unani Bacch
- Hindi Bajai Gora bach, Vasa bach
- Marathi Vekhand
- Tamil Vasambu
- Telugu Vadaja, Vasa
- Kannada Baje
- Malayalam Vayambu
- Sanskrit Bhutanashini, Ugra Gandha, Jatila
- Italy Plant of Venus

PHYTOCONSTITUENTS OF VACHA

- **Monoterpenes:** A number of monoterpenes have been reported in the plant. Some of the monoterpenes reported are as α and β-pinenes, myrcene, Para-cymene, α-terpinen, β-phellandrene, gammaterpinene, Terpinolene, Thujane and Limonene. They were isolated by steam distillation from volatile oil. (Raja *et al.*, 2009)



(A) (B)

Figure 4: (A) thujane and (B) Limonene

- **Xanthone glycosides:** A new xanthone glycoside was isolated from the rhizome part. It was designated as 4, 5, 8-trimethylxanthine-2-O-β-D'Glucopyranosyl (1-2)-O-β-D-galactopyranoside. (Raja *et al.*, 2009).

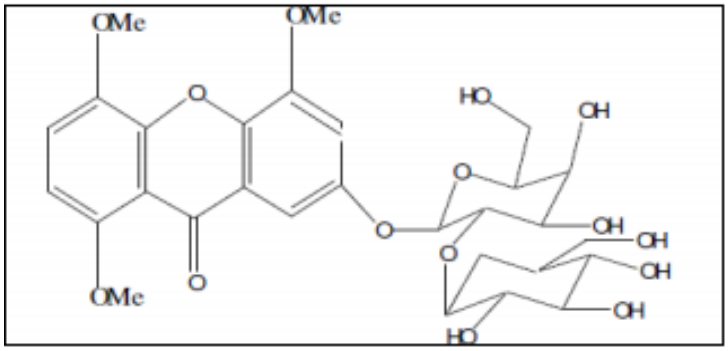


Figure 5: 4, 5, 8-trimethoxyxanthone-2-O-β-D-glucopyranosyl (1-2)-O-β-D'Galactopyranoside

- **Lignans:** A lignan was isolated from the rhizome part of the plant and it was designated as acoradin. It was evaluated using benzene from chloroform extract of the *Acorus calamus.* (Raja *et al.*, 2009).

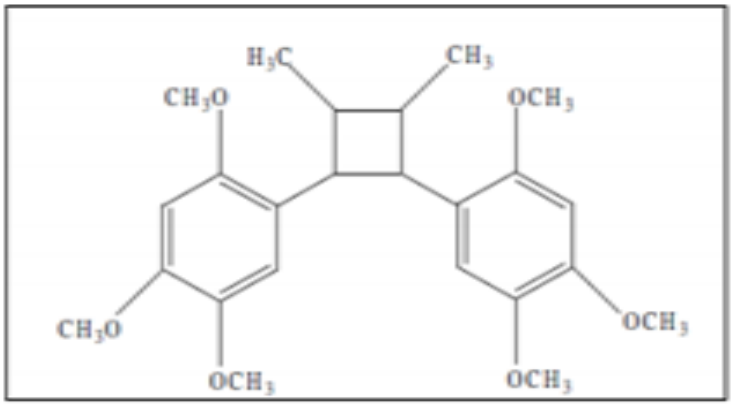


Figure 6: Acoradin

- **Steroids:** A β-Sitosterol is isolated from the plant *Acorus calamus*. (Hui-Lan Yeh and Wm. H. Adolph (1938).

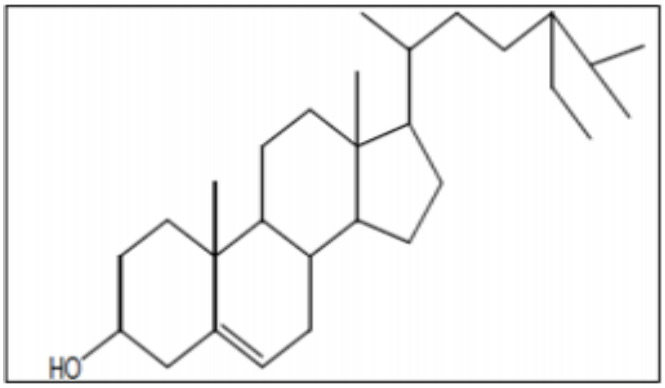


Figure 7: β-Sitosterol

- **Flavones:** 5, 7-dihydroxyflavone (Galangin) isolated from the plant *Acorus calamus* (Stahl and Keller 1981).

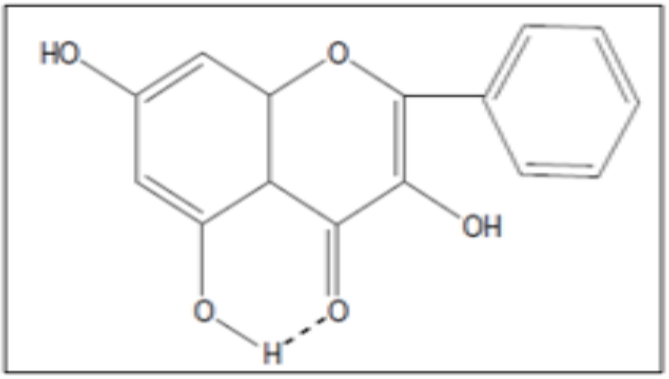


Figure 8: 5, 7-dihydroxyflavone

Medicinal usages of vacha

The rhizomes of sweet bag (*Acorus calamus*) are used for numerous medicinal purposes. The herb is used both internally as well as externally. In rheumatism, rheumatic fever and indiamed joints, the paste applied externally alleviates the pain and swelling. Internally sweet flag is valuable in a vast range of diseases. It is effective for digestive ailments such as flatulence, loss of appetite, abdominal dull pain and worms. The powder of sweet □ag given with lukewarm salt-water, induces vomiting and relieves phlegm, while easing coughs and asthma. In epilepsy, the powders of sweet bag, Brahmi and jatamamsi work well, when given with honey. The popular Ayurvedic formulation Sarasvata Choorna, which contains sweet bag, is commonly used to treat epilepsy, hysteria and as a brain tonic. Granule Asabi (Unani preparation) is an excellent nervine tonic which improves memory, reception as well as the speech. As it stimulates the uterine contractions, so it is used to augment the labour pains. It is also salutary in dysmenorrhoeal (Nadkarni KM 2005).

Helps in brain rejuvenation

Vacha has been described for rejuvenating the brain and calming the nervous system, which brings down the excitement level and soothe worries. Besides it also helps people who suffer from epilepsy. For treating anxiety and epileptic attacks, 4g of vacha powder along with honey can be taken safely once a day. Also, make sure to follow a healthy diet routine by avoiding packed and junked foods which ultimately prevents conditions like constipation

Helpful in curing respiratory disorders

Vacha is useful especially in treating throat disorders such as sore throat, hoarseness, strep throat, asthma, and the symptoms associated with them. It is also useful for colds and sinus infections. The roots are cut into small betel nut pieces and are kept under the tongue of the patient. It will immediately help to lessen the severity of the attack.

Helps in voice clarity

Vacha is an effective remedy - take 1-2g of vacha powder with honey and apply it on the tongue. It will enhance the speech capabilities, pitch and quality of voice. It is immensely helpful for singers, executives and other professionals who need to speak often.

Helps in managing hernia

Hernia happens when an organ slips into the adjacent weeker tissues from its original place; can be in the lower abdomen or under the naval or down in the testicles. A patient experiences pain and swelling in this condition. Hernia can be managed by applying mixture of vacha powder and neem seed meal (leftover after the neem oil is extracted, also known as 'khali' in hindi) on the affected site with pressure and tie that area with a cotton cloth. It will strengthen the weaker tissues and muscles by regenerating them. Vacha will be helpful not only during the initial stages of hernia, but will also avoid its recurrence.

Rat bites

Vacha is very useful in the treatment of rat bites. Take 4g of vacha powder along with rice water (simply obtained by soaking rice in water for 1 hour) for 7 days. It will help to subside all the symptoms due to the rate bite and the hazardous viruses present in the saliva of rats will also get eradicated.

Obesity

Vacha is extensively used in the treatment of obesity. Take 2.5-5g of vacha powder with lukewarm water in the morning and evening to reduce your weight.

Joint swelling

Mix vacha powder in flaxseed oil. Apply it gently on the affected joints and it would be helpful in reducing the joint pain and swelling for the people suffering from arthritis.

Ear infections

Grind the roots of the plant and add water to it. Use it as an eardrop and put 1-2 drops of it with a cotton bud so that the drops stay for some time. The pain and the infection in my ear get relieved.

Natural mosquito repellent

Vacha can be planted in your gardens to ward off the mosquitoes. The sticks of sweet flag can also be burnt in the house. The smoke emitted will keep mosquitoes and even snakes far from home.

Pharmacological Effects

Anti HIV activity

40 traditional Asian medicinal plants were screened against HIV-1 reverse transcriptase. The results showed that the crude extracts from plants Cinnamomum loureiroi (stem bark), Quercus infectoria (fruit), Plumbago indica L. (root), and *Acorus calamus* (rhizomes) showed strong HIV1 reverse transcriptase inhibition effects. The efficiency of anti-HIV-1RT activity was reported as 50% inhibitory concentrations (IC50). This showed that the hexane crude extracts from *Acorus calamus* L. and *A. heterophyllus* Lam. contained potent activity against HIV-1 RT Silprasit K *et al*., 2011.

Cytotoxic effect

Rajkumar *et al*., used methanolic and aqueous extract of *Acorus calamus* plant and further studied cytotoxic effect. From whole study they concluded that it might be act against the cytotoxicity in time and concentration dependent manner Rajkumar V *et al*., 2009.

Immunosuppressive activity

Mehrotra *et al*., evaluated anti cellular and immunosuppressive potential of methanolic extract of *Acorus calamus*. The methanolic extract of *Acorus calamus* rhizome showed anti proliferative and immunosuppressive properties. This

extract causes the tumor necrosis through which inhibits the proliferation of mitogen, antigen stimulated peripheral blood mononuclear cells in humans, nitric oxide and interleukins 2 Mehrotra S *et al*., 2003.

Antifungal activity

Methanolic extract of 40 higher plants representing 23 families were tested for antifungal activity against some phytopathogenic fungi. The two most active plants showing potent antifungal activity were *Acorus calamus* and Piper betel. The rhizome extract of A. calamus exhibited highest antifungal activity inhibiting the mycelial growth completely (100%) against all the 6 test pathogens. P. betel exhibited more than 50% inhibition against most of the test fungi. The mmethanolic extract of several higher plants could be used as alternative source of antifungal agents for protection of plants or crops against fungal infection Begum J *et al*., 2007

Antibacterial activity

The aqueous and mmethanolic extracts of *Acorus calamus* was evaluated for antibacterial activity against clinically important bacteria viz. Bacillus subtilis (MTCC 441), Staphylococcus aureus (MTCC 96), Escherichia coli (MTCC 443), Proteus mirabilis (MTCC 1429), Pseudomonas aeruginosa (MTCC 424). The in-vitro antibacterial activity was performed by agar well diffusion method. The mmethanolic extracts of A. calamus was active against all the investigated bacterial strains while aqueous extract was totally inactive against the studied gram negative bacterial strains (*E. coli, P. mirabilis and P. aeruginosa*) and showed moderate antibacterial activity against gram positive bacteria B. subtilis and Stap. aureus at high concentration (200ml).

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