e-ISSN: 2320-4230, p-ISSN: 2961-6085

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 12, Issue 03; 2024, 59-68

A Review on Pharmacological Properties of Acorus Calamus

Vibhor Sharma[1] & Jitendra Malviya[2]

[1] Research scholar, Sunrise University, Alwar Rajasthan.

[2] Research supervisor, Sunrise University, Alwar Rajasthan.

Received: 22-03-2024 / Revised: 24-04-2024 / Accepted: 27-05-2024

Corresponding author: Vibhor Sharma

Conflict of interest: No conflict of interest.

Abstract:

Ayurveda has the potential to be a valuable source of new anti-inflammatory substances for the treatment of chronic illnesses. This study aims to offer a comprehensive overview of a significant ayurvedic plant and its therapeutic use in diverse ailments. It is used in treating conditions such as bronchitis, nerve disorders, colic, chest discomfort, diarrhoea, flatulence, indigestion, rheumatism, cough, fever, depression, tumours, skin diseases, works as a cryoprotective agent, inflammation, and other neurological disorders. It has antimicrobial, anticancer, and maybe antidiabetic properties. Several active phytoconstituents have been identified and described from the leaves and rhizomes, which contain significant essential oils. The rhizome component of the plant has significant medicinal properties. The plant has two main bioactive chemicals, α-asarone and β-asarone, which are the primary constituents. The usage of α- and β-asarone is limited due to the genotoxicity and mutagenicity seen in several investigations at higher concentrations. The understanding of the active chemical components of Ayurvedic plants and the specific inflammatory pathways they suppress is still unclear.

***Keywords*:** Acorus, Diseases, Protection

INTRODUCTION

A pharmaceutical corporation typically invests around one billion dollars in the development of a medicine, according to current estimates. Current Magic bullets/targeted medicines are prohibitively costly. A majority of the global population is unable to afford these advanced medications, according to estimates. In addition to the significant expense, safety is a prominent cause for worry. Modern medicine has the issue of identifying a medication that is both safe, inexpensive, and effective. Ayurveda is an ancient therapeutic method that started in India some 6,000 years ago. The term "Ayu" refers to "Life" and "Veda" refers to "knowledge or science". Therefore, Ayurveda may be understood as the Science of Life. Its purpose is to foster optimal health and extend lifespan, rather than providing a remedy for a specific ailment. Three major bodily constitutions or features, known as "prakriti," have been classified based on three "doshas": Vata, Pitta, and Kapha. Any disruption in this dosha leads to the development of a disease. In order to

regain equilibrium, Ayurveda suggests a personalised treatment that takes into account each individual's "prakriti". One's doshas may be affected by the food consumed and the lifestyle followed. The name "vata" originates from the Sanskrit word "vaayu," which translates to air. Oxidative stress may result from inadequate inhalation of air (vaayu) and metabolic imbalance, specifically involving the two other tridoshas, pitta and kapha. Given that reactive oxygen species (ROS) produced inside the body consist of oxygen ions, peroxides, hydroxyl radicals, and other components, it is necessary to use a mixture of several kinds of antioxidants in order to completely neutralise them. Although plant polyphenolics are a beneficial source of antioxidants, they vary in their capacity to neutralise various types of reactive oxygen species (ROS). Thus, it may be necessary to use a mixture of phytochemicals in order to treat the condition.

Classification of *Acorus calamus*

Kingdom: Plantae

Sub-kingdom: Tracheobionta (Vascular plants)Superdivision: Spermatophyta

Division: Magnoliophyta (Flowering plants)Subclass: Arecidae

Order: Arales Family: Acoraceae Genus: Acorus L,

Spp: *griffithii* Schott,. *belangeii* Schott,. *cassia* Bertol

The Sanskrit name for Acorus calamus is Vacha, which is also known as Sweet flag in English. The plants include flavonoids, saponins, tannins, glycosides, volatile oils, mucilage, and other polyphenolic chemicals. The medicinal qualities are located in the rhizome of the plant. The primary constituents present in the leaves and rhizomes of Acorus calamus include α-pinene, Camphene, β-pinene, and bornyl acetate (Khwairakpam et al., 2018).

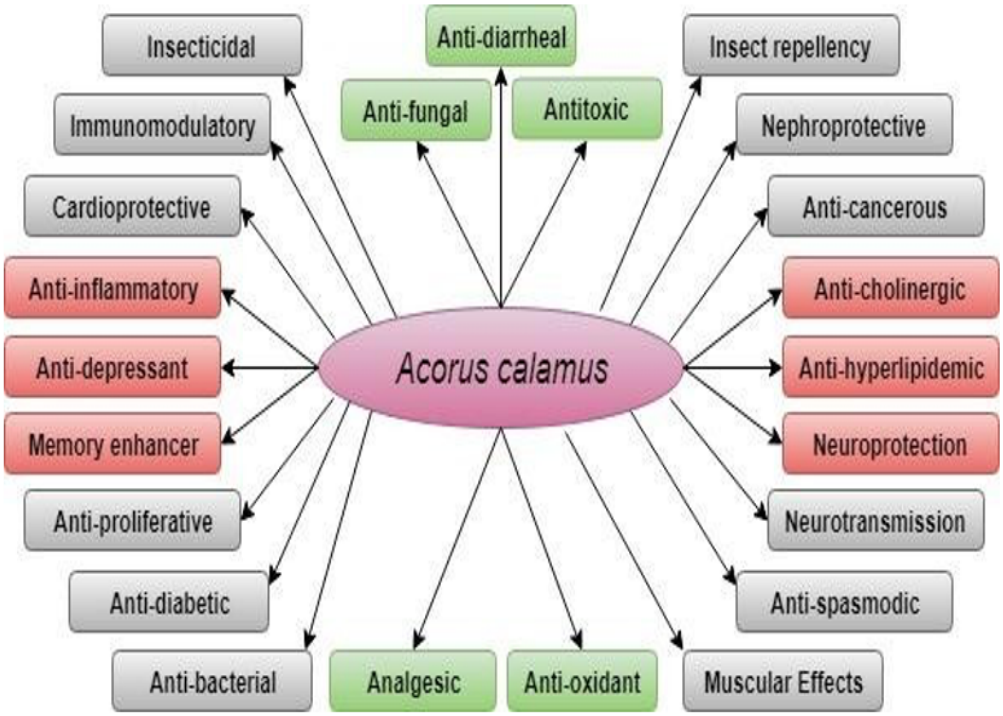

Fig 1: Uses of *Acorus calamus*

Table 1: Acorus calamus

S.No	Uses	Function
1	**Nephrology**	Acorus calamus extracts enhance the activity of kidney enzymes superoxide dismutase, glutathione peroxidase, and catalase, while reducing the amount of mono-dialdehyde content in cases of acetaminophen toxicity. The study by Singh, Pharm, Sharma, and Malviya (2011) demonstrated the preventive effect of a substance in preventing tissue necrosis and kidney damage generated by acetaminophen in experimental rats.
2	**Neurology**	
	Cholinergic Neurotransmission	The extract of Acorus calamus has a significant inhibitory effect of 53.7+/-5.5% on the acetylcholinesterase enzyme. This inhibitory effect is more powerful compared to other substances, with an inhibitory concentration (IC) of 10.67+/-0.81µg/mL. This increased potency may be attributed to the presence of β-asarone, which has an IC of 3.33+/-0.02µM (Feng, Yu, Qin, Gao, & Yao, 2015)
	GABAergic Neurotransmission	Petroleum ether extract of *Acorus calamus* rhizome showed promise through GABA receptors signalling through α β γ subtype (Sabitha Rani, Satyakala, Sandya Devi, & Suryanarayana Murty, 2003). It enhanced the signalling through the GABA receptor to 277+/- 9.7% of control at 100µg/mL. It is mostly due to presence of β-asarone (EC of 171.5+/- 34.6µM to reach 1200+/-163% of control) and (+)-dioxosarcoguaiacol (Zaugg et al., 2011).
	Neuroprotection	Acrylamide-induced neurotoxicity is reduced in rats when given a dose of 25mg/kg of a 50% ethanolic extract of the rhizome over 10 days alongside acrylamide as assessed by limb paralysis; the increase in dopamine receptor content and the reduction in glutathoine are normalized (Shukla et al., 2002).
3	**Analgesia**	The alcoholic component of the rhizome extract may inhibit 15.16% and 54.51% of the acetic acid-induced writhing response at doses of 250mg/kg and 500mg/kg, respectively. The oral intake of the rhizome extract at a dosage of 100-200mg/kg for a period of 14 days, in combination with vincristine, has the ability to effectively decrease neuropathic pain. This reduction in pain has been evaluated using Von Frey hair tests and the sciatic functional index, and the potency of this effect is similar to that of pregabalin at a dosage of 10mg/kg (Khan & Islam, 2012; "full-text," n.d.). This extract, administered at the same dosage as mentioned before, has shown effectiveness in both a model of neuropathic pain involving tibial and sural nerve transection, and a model of sciatic pain involving chronic constriction damage (Forouzanfar & Hosseinzadeh, 2018; Muthuraman & Singh, 2012).

4	**Depression**	50-100mg/kg of methanolic extract of Acorus calamus when injected to experimental rats for seven days showed dose-dependent anti-depressant activity with a potency comparable to 5mg/kg imipramine (Chellian, Pandy, & Mohamed, 2018; Pawar, Anup, Shrikrishna, & Shivakumar, 2011).
5	**Memory and Learning**	β-asarone's oral ingestion at a dose of 12.5-50mg/kg for 28 days is able to preserve cognition in rats with a potency as compared to 0.33mg/kg donepezil hydrochloride. Donepezil hydrochloride is associated with a reduction in hippocampal apoptosis rates (Geng et al.,2010; Zhou, Nie, & Liu, 2016).
6	**Cardiovascular Health**	
	Cardiac Tissue	An aqueous methanolic extract of rhizomes causes depressant effects on cardiac issue invitro ie 55%-60% reduction in heart rate and ventricular contractile force. Its EC value range lies in 110-130 µg/mL (A. J. Shah & Gilani, 2012).. 100-200mg/kg of the rhizome extract for 30 days alongside isoproterenol induces cardiotoxicity in animal models (ZHANG et al., 2005). It also found to be better in reducing cardiotoxicity with potency as compared to 9mg/kg amlodipine as standard drug (B. K. Singh, Pillai, Kohli, & Haque, 2011).
	Blood Flow	An aqueous-methanolic extract of the rhizome causes relaxation at an EC value of 2.5mg/mL in a manner similar to methacholine. It was alsoable to reduce precontraction induced by a high potassium concentration with an EC of 230µg/mL (Patel, Vaghasiya, Thakor, & Jariwala,2012).
	Blood Pressure	In hypertensive experimental rats, 250mg/kg of ethyl acetate extract causes attenuation in increased systolic and diastolic blood pressure. There was also attenuation in plasma renin and oxidative biomarkers (MDA and glutathione) in the kidneys (Patel et al., 2012).
7	**Anticancer effects**	The β-asarone, has carcinogenic effects. It has shown anticarcinogenic activation of α-asarone on the human carcinoma cells as documented in some experimental reports (Das, Swamy, Koti, & Gadad, 2019b).
8	**Antihyperlipidemic effects**	It was reported that there were decrease in the concentrations of cholesterol and triglycerides and increase in the concentrations of HDL of rats who were given alcoholic or aqueous extract for 30 days at a certain dosage while takinh atherogenic diet. These effects also occurred in rats which consumed saponins from the isolates of alcoholic extract (RS Parab, 2003)..
9	**Antibacterial effects**	The rhizome showed antibacterial action (in terms of zone of inhibition of bacterial growth) in vitro against methicillin-resistant *Staphylococcus aureus* (MRSA) and strains of gram- negative bacteria (like *Escherichia coli*, *Shigella dysenteriae*, *S. sonnei* etc.) which produces β-lactamase. These antibacterial actions were

		related to the presence of flavonoids and phenolic compounds in the rhizome (Imam, Riaz, Azhar, Sofi, & Hussain, 2013).
10	**Anticholinesterase effects**	*In vitro* inhibition of acetylcholinesterase was found with methanolic root extract experimentation, it is due to the preence of *calamus's* essential oil. The IC_{50} for acetylcholinesterase inhibition was measurable for extract, as well as for the aqueous fraction of a partition of the rhizome in water and dichloromethylene (Mathew & Subramanian, 2014).
11	**Antidiabetic potential**	In a study it was screened that herbal extracts acts as activators of peroxisome proliferator- activated receptors as concentration dependent effect (shown in alcoholic extract of *calamus*) (Rau, Wurglics, Dingermann, Abdel-Tawab, & Schubert-Zsilavecz, 2006).
12	**Anti-diarrhoeal**	There was increase in the time of onset of diarrhea and decrease in total number of feaces and number of wet feaces in comparision to the total weight of wet feaces prior consumption of
		the rhizome extract (MD Kapadia, 2012).
13	**Antifungal effects**	In plants, β-asarone, as an isolate of *Acorus gramineus*, completely inhibited mycelial growth of some pathogenic fungi whereas in others, slight suppression was found (Lee, Lee, Yun, & Hwang, 2004). Calamus's leaves contain a class III haem peroxidase which, in the host's defense against pathogenic fungi, may inhibit hyphal growth of invasive pathogens in plants (Ghosh, 2006).
14	**Anti-inflammatory effects**	The alcoholic extract showed moderate anti-proteolytic activity with the trypsin's induction of hydrolysis of bovine serum albumin (BSA). It has also exhibited the inhibition of β- glucoronidase (Gacche & Dhole, 2006).
15	**Antioxidant effects**	The rhizome extract contains high quantities of vitamin C and overall polyphenolic substances. The presence of α-asarone, an active antioxidant molecule, in it may contribute to its ability to enhance the capacity and function of antioxidants in the brain, as shown by Rawat et al. (2016). The histological study revealed that the cerebral cortical tissues of rats, which were administered a specific dosage of α-asarone daily by intraperitoneal injection, had normal characteristics. This was seen prior to subjecting the animals to four hours of daily noise exposure for a period of 30 days. In rats that were exclusively exposed to noise, there was a reduction in the size of neurones and abnormal changes in the structure of cortical layers in the cerebral cortex. The study conducted by Bains et al. (2005) discovered that the combination of extract and acrylamide led to a rise in the levels of glutathione and the activity of glutathione-S-transferase in the striate body. In contrast, when acrylamide was used alone, these levels fell.

16	**Anti-proliferative effects**	There was inhibition of growth of cells in cultures with calamus's lectins, (isolated from rhizomes extract) (Ganjewala & Srivastava, 2011). However, calamus's antiproliferative effects apparently are not specific to any cells, given that inhibition of proliferation occurred in various human and murine cell lines in cultures with an alcoholic extract of the rhizome (*Research journal of pharmaceutical, biological and chemical sciences RJPBCS.*, n.d.).
17	**Anti-spasmodic effects**	It occurred through the blockage of calcium ion channels, a particular action with fraction of n-hexane. This fraction may contain constituents that are able to block calcium ion channels so that antispasmodic action results (Gilani, Shah, Ahmad, & Shaheen, 2006).
18	**Antitoxic effects**	There was reduction in concentration of serum creatinine, low blood urea nitrogen and lesser activity of kidney ornithine decarboxylase. Renal oxidative stress diminished with prophylactic calamus. There was decrease in the content of glutathione, glutathione-S- transferase, glutathione reductase, lipid peroxidation and in generation of hydrogen peroxide (P. D. Shah et al., 2012).
19	**Immunomodulatory effects**	Suppression was seen in the growth of mononuclear cells from human peripheral blood when cultured with a mitogen (phytohemagglutinin [PHA]) or an antigen (purified protein derivative of tuberculin) and the alcoholic extract. The extract caused a decrease in the generation of interleukin-2 (IL-2) and tumour necrosis factor-α (TNF-α) in a culture of human T lymphocytes (mononuclear cells from peripheral blood). PHA was used to induce the synthesis of IL-2, whereas lipopolysaccharide (LPS) was utilised to stimulate the creation of TNF-α. The formation of nitric oxide in murine macrophage cell line was suppressed following incubation with a specific quantity of the extract, as shown by Ravichandiran and Vishal in 2015. Nevertheless, lectins, which were a component of a different extract derived from rhizomes, had a mitogenic effect on T cells (Das, Swamy, Koti, & Gadad, 2019a).
20	**Insect repellency**	The insecticidal ability of calamus oil extract has been shown against Rhyzopertha dominica, also known as the lesser grain borer. Calamus has larvicidal properties. The roots' alcoholic extract exhibited larvicidal activity against the housefly, fleshfly (Chrysomyia bezziana), and culex (Culex quinquefasciatus) when exposed to it (Meenakshisundaram, Harikrishnan, Rani, & Anna, 2014).
21	**Muscular effects**	Roots/rhizomes's alcoholic extract inhibited contractions in rectus muscle and the extract produced negative inotropic and chronotropic effects (Motley, 1994).

22	**Neurologic effects**	The herb's ability to modulate antioxidant capacity is responsible for its neural protective properties. This study demonstrated neuroprotective effects in rats that were orally administered a rhizome extract (consisting of a 1:1 ratio of alcohol and water) for five days before and three days after the experiment. After a 72-hour occlusion, the behavioural evaluation score was shown to have improved. The incidence of paralysis in rats reduced when they were treated with a combination of the extract and acrylamide, a chemical known to elicit paralysis of the hind limbs in rats. A study conducted on a group of cortical neurones found that Acorus gramineus, a kind of essential oil extracted from rhizomes, had neuroprotective properties by inhibiting the activation of NMDA receptors. The primary component of the essential oil, asarone, effectively prevented excitotoxicity caused by NMDA or glutamate, as shown by Saroya and Singh in 2018.

Conclusion

Acorus calamus is used as a crucial component in many cocktail formulations utilised for the treatment and control of headache, sleeplessness, remittent fevers, delirium, hysteria, migraine, bodyache, neurodegenerative disorders, and severe inflammatory pain. The extraction and/or decoction of fresh rhizome parts are often used to alleviate severe inflammatory and neuropathic pain related to muscle, joint, vascular, and nerve injuries.

References

1. Bains, J. S., Dhuna, V., Singh, J., Kamboj, S. S., Nijjar, K. K., & Agrewala, J. N. (2005). Novel lectins from rhizomes of two Acorus species with mitogenic activity and inhibitory potential towards murine cancer cell lines. *International Immunopharmacology*, *5*(9), 1470–1478. https://doi.org/10.1016/J.INTIMP.2005.04.004
2. Chellian, R., Pandy, V., & Mohamed, Z. (2018). Alpha-asarone attenuates depression-like behavior in nicotine-withdrawn mice: Evidence for the modulation of hippocampal pCREB levels during nicotine-withdrawal. European Journal of Pharmacology, 818, 10–16. https://doi.org/10.1016/j.ejphar.2017.10.025
3. Das, B. K., Swamy, A. V., Koti, B. C., & Gadad, P. C. (2019a). Experimental evidence for use of Acorus calamus (asarone) for cancer chemoprevention. Heliyon, 5(5), e01585. https://doi.org/10.1016/j.heliyon.2019.e01585
4. Das, B. K., Swamy, A. V., Koti, B. C., & Gadad, P. C. (2019b). Experimental evidence for use of Acorus calamus (asarone) for cancer chemoprevention. Heliyon, 5(5), e01585. https://doi.org/10.1016/J.HELIYON.2019.E01585
5. Feng, X.-L., Yu, Y., Qin, D.-P., Gao, H., & Yao, X.-S. (2015). Acorus Linnaeus: a review of traditional uses, phytochemistry and neuropharmacology. RSC Advances, 5(7), 5173–5182. https://doi.org/10.1039/C4RA12049C
6. Forouzanfar, F., & Hosseinzadeh, H. (2018). Medicinal herbs in the treatment of neuropathic pain: a review. Iranian Journal of Basic Medical Sciences, 21(4), 347–358.

https://doi.org/10.22038/IJBMS.2018.24026.6021

7. Gacche, R. N., & Dhole, N. A. (2006). Antioxidant and Possible Anti-Inflammatory Potential of Selected Medicinal Plants Prescribed in the Indian Traditional System of Medicine. Pharmaceutical Biology, 44(5), 389–395. https://doi.org/10.1080/13880200600751691
8. Ganjewala, D., & Srivastava, A. K. (2011). An Update on Chemical Composition and Bioactivities of Acorus Species. Asian Journal of Plant Sciences, 10(3), 182–189. https://doi.org/10.3923/ajps.2011.182.189
9. Geng, Y., Li, C., Liu, J., Xing, G., Zhou, L., Dong, M., … Niu, Y. (2010). Beta-Asarone Improves Cognitive Function by Suppressing Neuronal Apoptosis in the Beta-Amyloid Hippocampus Injection Rats. Biological & Pharmaceutical Bulletin, 33(5), 836–843. https://doi.org/10.1248/bpb.33.836
10. Ghosh, M. (2006). Antifungal properties of haem peroxidase from Acorus calamus. Annals of Botany, 98(6), 1145–1153. https://doi.org/10.1093/aob/mcl205
11. Gilani, A. ul H., Shah, A. J., Ahmad, M., & Shaheen, F. (2006). Antispasmodic effect ofAcorus calamus Linn. is mediated through calcium channel blockade. Phytotherapy Research, 20(12), 1080–1084. https://doi.org/10.1002/ptr.2000
12. Imam, H., Riaz, Z., Azhar, M., Sofi, G., & Hussain, A. (2013). Sweet flag (Acorus calamus Linn.): An incredible medicinal herb. International Journal of Green Pharmacy, 7(4), 288. https://doi.org/10.4103/0973-8258.122053
13. Khan, M. A., & Islam, M. (2012). Analgesic and cytotoxic activity of Acorus calamus L., Kigelia pinnata L., Mangifera indica L. and Tabernaemontana divaricata L. Journal of Pharmacy and Bioallied Sciences, 4(2), 149. https://doi.org/10.4103/0975-7406.94820
14. Khwairakpam, A. D., Damayenti, Y. D., Deka, A., Monisha, J., Roy, N. K., Padmavathi, G., & Kunnumakkara, A. B. (2018). Acorus calamus: a bio-reserve of medicinal values. Journal of Basic and Clinical Physiology and Pharmacology, 29(2), 107–122. https://doi.org/10.1515/jbcpp- 2016-0132
15. Lee, J. Y., Lee, J. Y., Yun, B.-S., & Hwang, B. K. (2004). Antifungal Activity of β-Asarone from Rhizomes of Acorus gramineus. Journal of Agricultural and Food Chemistry, 52(4), 776–780. https://doi.org/10.1021/jf035204o
16. Mathew, M., & Subramanian, S. (2014). In vitro screening for anti-cholinesterase and antioxidant activity of methanolic extracts of ayurvedic medicinal plants used for cognitive disorders. PloS One, 9(1), e86804. https://doi.org/10.1371/journal.pone.0086804
17. MD Kapadia, A. K. (2012). ANTIDIARRHOEAL ACTIVITY OF LEAVES OF ACORUS CALAMUS | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH. https://doi.org/http://dx.doi.org/10.13040/IJPSR.0975-8232.3(10).3847-50
18. Meenakshisundaram, A., Harikrishnan, T. J., Rani, N., & Anna, T. (2014). Evaluation of Extract from Sweet Flag Rhizome for Biological Activity against House Fly. Cloud Publications International Journal of Advanced

Veterinary Science and Technology, 3(1), 140–144.
19. Retrieved from http://scientific.cloud-journals.com/index.php/IJAVST/article/view/Sci-201
20. Motley, T. J. (n.d.). The Ethnobotany of Sweet Flag, Acorus calamus (Araceae). Economic Botany. SpringerNew York Botanical Garden Press. https://doi.org/10.2307/4255666
21. Muthuraman, A., & Singh, N. (2012). Neuroprotective effect of saponin rich extract of Acorus calamus L. in rat model of chronic constriction injury (CCI) of sciatic nerve-induced neuropathic pain. Journal of Ethnopharmacology, 142(3), 723–731. https://doi.org/10.1016/J.JEP.2012.05.049
22. Patel, P., Vaghasiya, J., Thakor, A., & Jariwala, J. (2012). Antihypertensive effect of rhizome part of Acorus calamus on renal artery occlusion induced hypertension in rats. Asian Pacific Journal of Tropical Disease, 2, S6–S10. https://doi.org/10.1016/S2222-1808(12)60114-5
23. Pawar, V. S., Anup, A., Shrikrishna, B., & Shivakumar, H. (2011). Antidepressant–like effects of Acorus calamus in forced swimming and tail suspension test in mice. Asian Pacific Journal of Tropical Biomedicine, 1(1), S17–S19. https://doi.org/10.1016/S2221-1691(11)60114-7
24. Rau, O., Wurglics, M., Dingermann, T., Abdel-Tawab, M., & Schubert-Zsilavecz, M. (2006). Screening of herbal extracts for activation of the human peroxisome proliferator-activated receptor. Die Pharmazie, 61(11), 952–956. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17152989
25. Ravichandiran, V., & Vishal, P. (n.d.). IN VITRO EVALUATION FOR IMMUNOMODULATORY ACTIVITY OF ACORUS CALAMUS ON HUMAN NEUTROPHILS. Int. Res. J. Pharm, 2015(7). https://doi.org/10.7897/2230-8407.06792
26. Rawat, S., Jugran, A. K., Bahukhandi, A., Bahuguna, A., Bhatt, I. D., Rawal, R. S., & Dhar, U. (2016). Anti-oxidant and anti-microbial properties of some ethno-therapeutically important medicinal plants of Indian Himalayan Region. 3 Biotech, 6(2), 154. https://doi.org/10.1007/s13205-016-0470-2
27. Research journal of pharmaceutical, biological and chemical sciences RJPBCS. (n.d.). Retrieved from https://www.researchgate.net/publication/280009991_The_Sweetness_and_Bitterness_of_Sweet_Flag_Acorus_calamus_L_-_A_Review
28. RS Parab, S. M. (2003). Evaluation of hypolipidemic activity of Acorus calamus Linn. in rats | R.S. Parab. Indian Drugs, 40(1), 25–29.
29. Retrieved from https://www.researchgate.net/publication/289140064_Evaluation_of_hypolipidemic_activity_of_Acorus_calamus_Linn_in_rats [29]. Sabitha Rani, A., Satyakala, M., Sandya Devi, V., & Suryanarayana Murty, U. (2003). Evaluation of Antibacterial Activity from Rhizome
30. Extract of Acorus calamus Linn. Journal of Scientiti c & Industri al Research (Vol. 62). Retrieved from http://nopr.niscair.res.in/bitstream/123456789/26317/1/JSIR 62%286%29 623-625.pdf
31. Saroya, A. S., & Singh, J. (2018). Neuropharmacology of Acorus calamus L. In Pharmacotherapeutic Potential of Natural Products in Neurological Disorders (pp. 129–134). Singapore: Springer Singapore.

https://doi.org/10.1007/978-981-13-0289-3_11

32. Shah, A. J., & Gilani, A. H. (2012). Aqueous-methanolic extract of sweet flag (Acorus calamus) possesses cardiac depressant and endothelial- derived hyperpolarizing factor-mediated coronary vasodilator effects. Journal of Natural Medicines, 66(1), 119–126. https://doi.org/10.1007/s11418-011-0561-7
33. Shah, P. D., Ghag, M., Deshmukh, P. B., Kulkarni, Y., Joshi, S. V., Vyas, B. A., & Shah, D. R. (2012). Toxicity study of ethanolic extract of Acorus calamus rhizome. International Journal of Green Pharmacy (IJGP), 6(1). https://doi.org/10.22377/IJGP.V6I1.234
34. Shukla, P. K., Khanna, V. K., Ali, M. M., Maurya, R. R., Handa, S. S., & Srimal, R. C. (2002). Protective effect of Acorus calamus against acrylamide induced neurotoxicity. Phytotherapy Research, 16(3), 256–260. https://doi.org/10.1002/ptr.854
35. Singh, B. K., Pillai, K. K., Kohli, K., & Haque, S. E. (2011). Isoproterenol-Induced Cardiomyopathy in Rats: Influence of Acorus calamus Linn.
36. Cardiovascular Toxicology, 11(3), 263–271. https://doi.org/10.1007/s12012-011-9121-3
37. Singh, R., Pharm, M., Sharma, K., & Malviya, R. (2011). Pharmacological Properties and Ayurvedic Value of Indian Buch Plant (Acorus calamus): A Short Review. Advances in Biological Research, 5(3), 145–154. Retrieved from https://pdfs.semanticscholar.org/1083/b32c25ce2afdd8ffbca3d72137b93eb23a89.pdf
38. Zaugg, J., Eickmeier, E., Ebrahimi, S. N., Baburin, I., Hering, S., & Hamburger, M. (2011). Positive GABA(A) receptor modulators from Acorus calamus and structural analysis of (+)-dioxosarcoguaiacol by 1D and 2D NMR and molecular modeling. Journal of Natural Products, 74(6), 1437–1443. https://doi.org/10.1021/np200181d
39. ZHANG, G., KIMURA, S., NISHIYAMA, A., SHOKOJI, T., RAHMAN, M., YAO, L., … ABE, Y. (2005). Cardiac oxidative stress in acute and chronic isoproterenol-infused rats. Cardiovascular Research, 65(1), 230–238. https://doi.org/10.1016/j.cardiores.2004.08.013
40. Zhou, Q., Nie, S., & Liu, Z. (2016). Effect of Donepezil Hydrochloride on Cognitive Function Med One Effect of Donepezil Hydrochloride on Cognitive Function Recovery of Rats With Alzheimer's Disease Effect of Donepezil Hydrochloride on Cognitive Function. https://doi.org/10.20900/mo.20160023