A REVIEW ON THE EFFECT OF *ACORUS CALAMUS* IN DIFFERENT CANCERS

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ABSTRACT: Since, ancient time medicinal plants have been using to treat various human ailments. Cancer is group of diseases with similar characteristics. Cancer can occur in all living cells in the body and different cancer types have different natural history. Epidemiological studies have shown that 70- 90% of all cancers are environmental. Lifestyle-related factors are the most important and preventable among the environmental exposures. The modern systems of medicine have certain limitations and serious consequences which can alter the normal physiological process. Herbal medicines are known for their safety and efficacy in treating diseases effectively without producing any untoward effects. The present review provides the medicinal importance of Acorus Calamusas anticarcinogenic agent. The source for the present review was taken from literature survey carried through the findings from suitable keywords in databases, PubMed, Google Scholar and Web of Science and Scopus, etc. This review provides the detailed information on Acorus Calamusand phytochemical compounds as anti-cancer agents.
Key words: Anti-cancer activity, Acorus Calamus, Phytochemical compounds, botanical description.

I. INTRODUCTION

In normal situations, the cells grow and divide as the body needs them. This process is disturbed when a new cell from the body does not require and old cells don't die when they should. These extra cell lumps together form a growth or tumour. Cancer is characterized by a rapid and uncontrolled formation of abnormal cells, which may mass together to form a growth or tumour, or proliferate throughout the body, initiating abnormal growth at other sites. If the process is not arrested, it may progress until it causes the death of the organism [1]. Apoptosis or programmed cell death is a highly organized physiological process to eliminate damaged or abnormal cells. It also plays a major role in embryogenesis where apparently normal cells undergo apoptosis. It is involved in maintaining homeostasis in multicellular organisms**.** According to current estimates, a pharmaceutical firm invests $1 billion in the development of a medicine. The targeted medicines and "magic bullets" of today are highly pricey. According to estimates, the majority of people worldwide cannot afford these sophisticated medicines [2]. Safety is a key subject of concern in addition to expensive expense. Finding a medication that is reliable, inexpensive, and efficientproblem facing contemporary medicine. Ayurveda is a conventional medical practice that dates back around 6,000 years to India.Ayurveda is the Science of Life; Ayu means "Life" and Veda means "knowledge or science" in Sanskrit. It is intended to furtherrather than treating a sickness, emphasize lifespan and excellent health. There are three main types of physical characteristics (or "prakriti")centered on the three "doshas" of Vata, Pitta, and Kapha. A sickness develops from any imbalance in these doshas. ToThe Ayurveda suggests a personalized therapy based on a person's "prakriti" in order to restore the equilibrium. Doshas couldimpacted by the diet and kind of life a person follows. In Sanskrit, the word "vaayu" is where the word "vata" originates.denotes air. Inadequate air intake (vaayu) and an unbalanced metabolism (the two other potential causes of oxidative stress)the pitta and the kapha tridoshas). Since oxygen ions make up reactive oxygen species (ROS) produced by the organism,hydroxyl radicals, peroxides, etc. To completely quench them, one would need a mix of diverse antioxidant kinds.Although plant polyphenols are a strong source of antioxidants, their capacity to smother many types ofROS, suggests that a mixture of phytochemicals may be required to treat the illness [3]. *Acorus calamus* (*A. Calamus*) which is also known as *sweet flag* (*Araceae family*) is a beneficial and medicinal plant that has been used in herbal therapies and human health care preparations in the Asia for a long time [4]. The origin of *A. calamus* is thought to be India, through now it is also found in other parts of the world including Asia Minor, Sri Lanka, Burma, Japan, China, southern Russia, Europe, and northern USA. This plant is a perennial plant and was spread outside its native area in Asia [5]. *A.calamus* possesses a long history of use for healing purposes in India and China [6]. In India, *A.calamus* have been applied to treat gastric problems, stomach cramps, and cancer [7], as well as to inhibit the side effects caused by hallucinogens [6]. *A.calamus* is known as an

important plant in Ayurvedic medicine in that it is viewed as a "rejuvenator" for the nervous system and as a therapeutic agent for digestive disorders. *A.calamus* has been referred to as a "wonder drug" in popular European books on medicinal herbs and frequently exploited as a nervine in folk medicine which results from its tranquilizing effects of cis-isoasarone. *A. calamus* extract has been used in traditional Chinese prescription due to its beneficial effects on memory and learning performance; also, anti-aging effect in senescence has been reported for this plant [8]. Various extracts of *A. calamus* have anti-diabetes, anti-proliferative, immunosuppressive, hypolipidemic and anti-carcinogenic effects and the rhizomes and leaves were found to possess anti-carcinogenic activity in human lymphocytes [9].The present review provides the medicinal importance of *Acorus Calamus* as anticarcinogenic agent.

1.1. Botanical description of *Acorus Calamus*[10].

The botanical description of *Acorus Calamus was represented in Table 1.1*

Table 1.1.* Botanical description *Acorus Calamus

Kingdom	**Plantae**
Sub-kingdom	***Tracheobionata (Vascular plants)***
Super division	Spermatophyta
Division	Magnoliophyta (Flowering plants)
Subclass	Arecidae
Order	Arecidae
Family	*Acoraceae*
Genus	Acorus L

1.2. Vernacular names: Vernacular Name Arabic: Vaj, Vash, Oudul Vaj; Sanskrit: Bhadra, Bhutanashini, Vacha; Hindi: Bach, Ghorbach, Safed bach; Gujarati: Gandhilovaj, Godavaj; Kashmir: Vachi, Vaigandar; Persian: Agar, Agarturki, Kannada: Baje, Vasa; English: Sweet flag, Calamus, Myrtle grass; Urdu: Bach, Vaj; Tamil: Vashambu, pullai-valathi; Nepali: Bojho; Ayurvedic: Vacha; Unani: Vaj turki, Bacch; Italy: Plant of Venus [11].

1.3. Different biological actions of *Acorus Calamus*

The various biological actions of *Acorus Calamus* were illustrated in Figure 1.1.

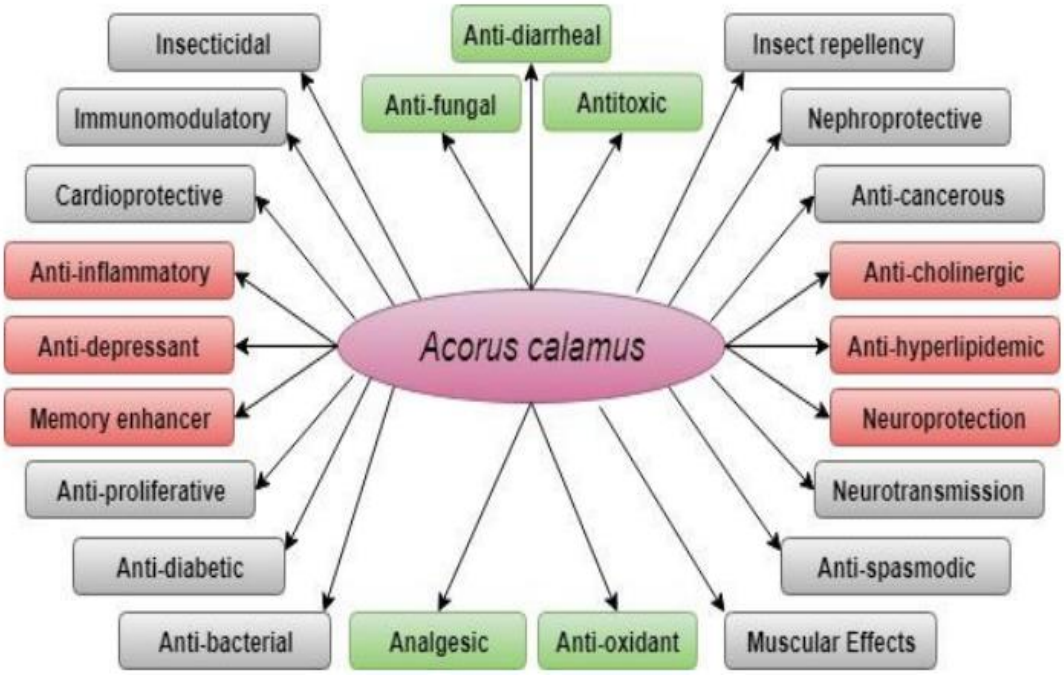

Fig.1. Various biological actions of Acorus Calamus[26]

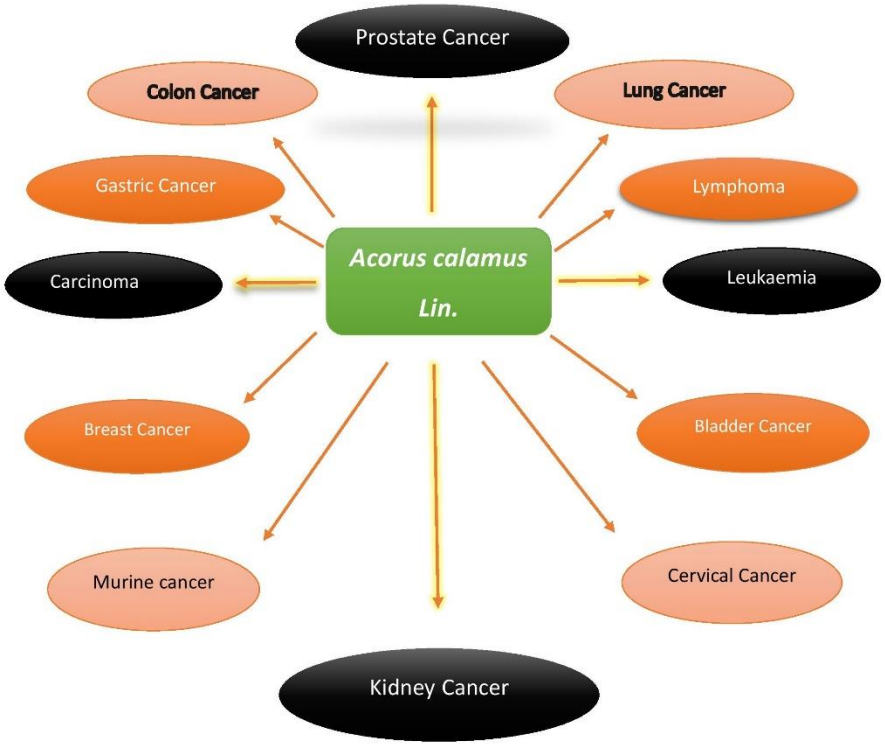

Fig.2. Reported studies of Acorus Calamus in Different Cancers.

1.4. Phytochemical constituents

Photochemical studies have reported the presence of glycosides, flavonoids, saponins, tannins, polyphenolic compounds, mucilage, volatile oil and bitter principle. The plant has been reported for the presence of glucoside, alkaloid and essential oil containing calamen, clamenol, calameon, asarone and sesquiterpenes. It also contains a bitter glycoside named acorine along with eugenol, pinene and camphene. The plant has been extensively investigated and a number of chemical constituents from the rhizomes, leave and roots of the plant have previously reported which includes β- asarone, α- asarone, elemicine, cisisoelemicine, cis and trans isoeugenol and their methyl ethers, camphene, P-cymene, α-selinene, bgurjunene, β-cadinene, camphor, terpinen-4-ol, aterpineol and a calacorene, acorone, acrenone, acoragermacrone, 2-deca -4,7 dienol, shyobunones, linalool and preisocalamendiol are also present. Acoradin, galangin, 2, 4, 5-trimethoxy benzaldehyde, 2, 5 dimethoxy benzoquinones, calamendiol, spathulenol and sitosterol have been isolated from Acorus calamus. Alcoholic extracts of the triploid A. calamus were characterized by a higher percentage of β-asarone (11%), which was the main compound, followed by higher percentage [12]. The few phytoconstituents present in this plant were depicted in **Figure 1.1 and 1.2.**

II. METHODOLOGY

Published articles in connection with anticancer activity of *Acorus Calamus*retrieved from PubMed, Science Direct, Taylor and Francis, BMC, ACS, Google scholar, Web of Science, Scopus and other literature database. Some articles were found by tracking citations from publications. The research key words used were anti-canceractivity. In this review briefly discussed the recent scientific findings regarding the anticancer activities of *Acorus Calamus*plants and indicatedtheareas where further study is required. The literature collections were restricted to publications in English language.

2.1 . Anticancer activity of *Acorus Calamus*

S.G Funde et al., **(2015)** represented the anticancer activity of the extracts was investigated using MTT assay on human colon cancer cell line HT-29. A mitochondrial enzyme in living cells, succinate-dehydrogenase, cleaves the tetrazolium ring, converting the MTT to an insoluble purple formazan. Therefore, the amount of formazan produced is directly proportional to the number of viable cells.Methanol, ethanol, propanol, extracts significantly inhibited cancer cell growth (HT-29 cell lines) compared to acetone, acetonitrile and ethyl acetate extracts. At a concentration of 15 µg/mL, the percentage of anticancer activity of ethanol, propanol, acetonitrile and methanol

extracts (66.56, 63.50, 62.14, 61.32%), was found significantly higher than acetone and ethyl acetate extracts(46.12 and 49.89%). The negative activities of Water extract to HT-29 cell lines which did not inhibit cancer cell growth, but apparently increased the growth rate of cancer cells. However, more confirmative studies will be essential in the future [13].

Gayathri MN et al., (2017) Acorus calamus is a plant used in traditional medicine. The Acorus calamus most extensively investigated phytochemically and pharmacologically. Cancer is characterized by a rapid and uncontrolled formation of abnormal cells. Apoptosis or programmed cell death is a highly organised physiological process to eliminate damaged or abnormal cells. Extractives of different parts of Acorus calamus and calamus oil are widely used now in pharmaceuticals, traditional systems of medicines for a number of ailments Acorus calamus decreased cell viability in malignant cells in a concentration dependent manner [14].

Merekar et al.,(2021)β-asarone an important chemical constituent of *A. calamus* has also been reported to possess antibacterial activity. The synergistic anthelmintic activity of *A. calamus* and *Vitex negundo* was studied by the induction of apoptosis leads to an activation of caspases. These enzymes are cysteine proteases that are produced by the cell as inactive pro- enzymes. After activation the pro–caspase is hydrolysed to its active form, caspase. Caspases belong to a family of proteases which are responsible for the cell death induction. The activation of the caspase induces the cell fragmentation and thus the development of "apoptoticbodies [15].

Raj Kumar et al., (2009) The present work evaluated the cytotoxicity of methanolic and aqueous extracts of rhizome of Acorus calamus Linn. which is a well-known medicinal plant used in traditional treatment. Both extracts were found to be cytotoxic as determined by Allium cepa root tip assay and XTT assay in MDA-MB-435S and Hep3B cell lines. Results of the study indicate that the plant possesses antitumor properties and may serve as a potential source for investigation and development of anticancer drugs. In this study, both extracts of A. calamus rhizome showed cytotoxicity. The results indicate that these plant products might act against development of cancer. There was a significant concentration and time dependent decrease ($p<0.05$).The study concludes that rhizome of Acorus calamus might be considered as a potential source of metabolites which could be developed as precursors for anti-cancer drugs. Isolation and purification of these active compounds are in prospect [16].

Gaidhani S.N et al., (2009) The hydro-alcoholic extractrhizome of Acorus calamus, was evaluated for their antiproliferative activity on fourteen cancer cell lines. These plant extracts were tested by sulforhodamine-B (SRB) assay for its anti-proliferative activity and extractwas found active against prostate cancer cell line (DU145) [17].

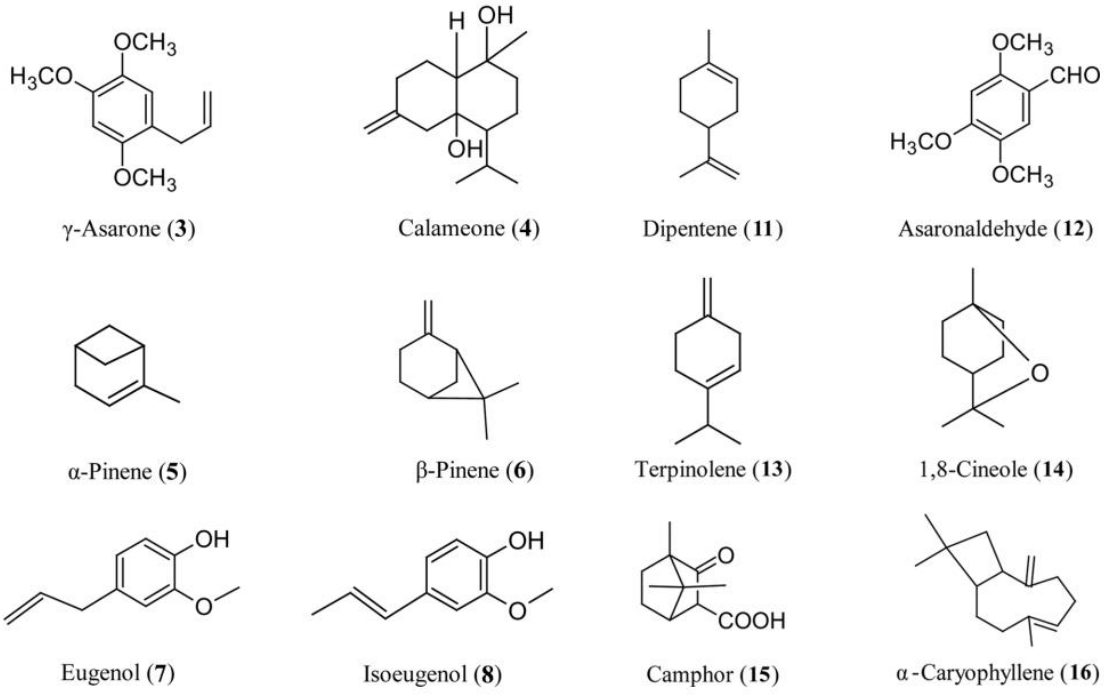

Fig.3. Phytoconstituents of Acorus calamus L

Pulok Kumar Mukherjee et al., (2007)AC is a mild co-carcinogen and may interfere with normal pregnancy inter-reactions. The effects of b-asarone on chromosomes were studied in human lymphocyte cultures. A very strong effect on the induction of structural chromosome aberrations was found after metabolic activation and cellular damage occurred. The results demonstrate clearly the genotoxic potency of b-asarone and suggested that

only Acorus with low content of b-asarone should be used (Abel, 1987). a-Asarone was mutagenic to Salmonella typhimurium in a concentration-dependent fashion. a-Asarone–induced mutagenicity required a premutagenic mixture containing liver S-9 fraction and NADPH. The mutagenicity of asarone was comparable with that induced by aflatoxin [18].

Coca HB et al., (2018) Vascular endothelial growth factor-A (VEGF-A), thought to be the single most important angiogenic factor in prostate cancer. Poly-(ADP-ribose) polymerase (PARP) involved in apoptotic process and cleavage of PARP serves as a marker of cells undergoing apoptosis. Acorus calamus have long been considered to have anti-carcinogenic and medicinal properties especially in Asia. We examined whether ethanolic extract of *A. calamus* root affects the survival of prostate cancer LNCaP cells and induces apoptosis and angiogenesis of these cells in vitro. Cells were incubated during 24 and 48 hours with various doses of extract. Extract with these concentrations reduced the number of LNCaP living cells up to 44 % as compared to the control at dose and time dependent manner at 24 and 48 hours. Significantly alterations were observed at cleaved PARP, VEGF-A protein and gene expression amounts after 24 and 48 hours. The present study reveals the possibility that ethanolic extract of A. calamus root possesses a dose and time dependent anticancer, apoptotic and anti-angiogenic property [19].

III. DISCUSSION

Sweet flag is the common name of *Acorus calamus L*. belongs to the family *Araceae*. This perennial herb, which is indigenous to central Asia, India, and the Himalayan region, is found commonly on the banks of streams and in damp marshy places. It is commonly known as Bach in India [20]. It has been used in Indian medicine for ages. In addition, it has been used in traditional medicine of other countries such as China, Nepal and Pakistan. New pharmacological studies have almost confirmed the traditional uses of sweet flag as an antispasmodic, anthelminthic, anti-epileptic, antidepressant, anti-inflammatory, and antibacterial agent. In addition, there is a correlation between some traditional uses of sweet flag and those of new studies. For example, modern phytochemical and pharmacological studies have been revealed that α- and β-asarone is one of the major components of sweet flag possessing strong anti-bacterial, antifungal, anthelminthic, neuroprotective, antiepileptic activity [21].Currently, mosquito larvicidal activity of sweet flag is investigated by the author and his colleagues.Major chemical constituents identified in sweet flag are α- and β-asarones along with other constituents, other constituents such as caryophyllene, isoasarone, methyl isoeugenol, and safrol are also responsible for medicinal activity but most of the biological actions of sweet flag have been attributed to presence of α- and β-asarones. In a recent finding beta-asarone was shown to possess ameliorative potential in cognitive impairment thereby suppressing the neuronal apoptosis. Moreover, alpha-asarone is also noted reduce the excitatory action by stimulation of glutamate uptake and inhibition of excitatory neurotransmitter transporter mediated current [22]. Some chemical constituents of sweet flag β-asarone in particular, have been demonstrated to possess toxic effects like prolonged vomiting, hallucinogen, carcinogenic, and genotoxic action in dose dependent manner. Thus, low level of β-asarone could only be acceptable for therapeutic use, and the level of β-asarone can be minimized by decoction process. Although, a significant data advocatethe therapeutic potential of the sweet flag in various ailments there is only little conclusive evidence regarding its acute and sub-acute toxicity [23,24 and 25].

IV. CONCLUSION

This review helps to understand the effect of the anticancer activity of the *Acorus Calamus*. The accessibility of treating cancer diseases with herbal medicine or plant-derived compounds and not a necessity of laborious pharmaceutical synthesis seems the approach is highly attractive. As per the presented data, many literature studies offered the anticancerimportance of crude and/or solvent extracts of the various plants' parts. Though the anticancer property was proved in these investigations, further attention and extensive study are required in exploring the phytochemical and pharmacological profile of the active principles. It will be helpful to pharmacologists, scientists, and health professionals to develop new safer pharmaceutical products with thrombolytic properties.

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