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REVIEW ARTICLE

Clinical Trials and Ethnomedicinal Uses of *Acorus calamus* – A Review

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ABSTRACT

Acorus calamus (Araceae) is a perennial herb, distributed across many countries and continents is a unique medicinal plant used in treating many ailments. It contains several aromatic oils in the rhizome of which asarone, eugenol are primary active principles known to have multiple uses in aroma therapy, curing human ailments especially disorders related to nervous system and also in plant protection. Reviews on the herb used in the treatment of diabetes, obesity, anxiety, hypertension, memory impairment, sedation, insomnia, hypnotic, increasing antibodies, cardio vascular diseases, anti-inflammatory, anti-convulsant, antioxidant and antidepressant are presented with clinical observations. The ethnomedicinal uses of A calamus in Asian continent consisting India, Sri Lanka, Nepal, China, Russia are reported. In other continents such as Europe, Africa the herb is used as traditional medicine and the uses are listed. **Key words:** Acorus calamus, clinical trials, ethnomedicinal uses,

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INTRODUCTION

Acorus calamus is popularly known as sweet flag, sway or muskrat root. In addition, it is also known as beewort, bitter pepper root, calamus root, flag root, gladdon, myrtle flag, myrtle grass, myrtle root, myrtle sedge, pine root, sea sedge, sweet cane, sweet cinnamon, sweet grass, sweet myrtle, sweet root, sweet rush, and sweet sedge, sweet cane and sweet grass [1]. It is referred by different names in different languages. Bach, Safed Bach, Ghorbach (Hindi); Okhidak (Manipuri); Vekhand (Marathi); Vashambu, Pullai valathi (Tamil); Vaembu, Vashampa (Malayalam); Baje, Vacha, Athi Baje, Kavana, Dagade, naaru beru (Kannada); Bach, Ghora bach (Bengali); Bach (Aassamese); Hnim Rimtui (Mizo); Vacha, Vachaa Bacha, Bhadra (Sanskrit); Bhojo (Nepali) [2]. A calamus is found in as many as 42 countries ranging in altitude as high as 1800 m to 900 m above sea level. The herb is known to be originated from India.

Plant description

Acorus belongs to the family Acoraceae (Araceae) and its technical name is *Acorus calamus* L. It is an herbaceous perennial plant growing to a height of nearly 2 m and its leaves are erect yellowish brown, radical, with pink sheathing at their bases, sword-shaped, flat and narrow, tapering into a long acute point, and have parallel veins. The leaves have smooth edges which can be wavy or crimped. The solid triangular flower stem rise from the axils of the outer leaves. A semi-erect spadix emerges from one side of the flower stem. The spadix is solid, cylindrical, tapers at each end and is 5 to 10 cm length. A covering spathe, as is usual with Araceae is absent. The spadix is densely crowded with tiny greenish yellow flowers. Each flower contains six petals and stamens enclosed in a perianth with six divisions, surrounding a three celled, oblong ovary with a sessile stigma. The flowers are sweetly fragrant. The fruit is a berry filled with mucus, which when ripe falls into water and disperse by floating. In Asan countries it fruits sparingly and propagates itself mainly by growth of its rhizome, forming colonies [3].

Chemical composition

The leaves and rhizome contain a volatile oil which has characteristic odor and aroma. Apart from medicinal uses the oil is used in aroma therapy, foods, alcoholic beverages and bitters. It is widely used in

India, China, European countries and worldwide. The main constituents of oil are beta asarone (nearly 75%), methyl isoeugenol (nearly 40%) and alpha asarone, saponins, lectins, sesquiterpinoids, ligans and steroids. The chemical composition may vary according to plant type (diploid, triploid or tetraploid), geographical distribution. The dried powder is also used as insecticide [3]. Nearly 145 constituents have been isolated and identified, including phenylpropanoids, sterols, triterpene glycosides, sesquiterpenoids, triterpenoid saponins, alkaloids and monoterpenes from A calamus. Phenylpropanoids (chiefly, asarone and eugenol) and sesquiterpenoids are considered to be the principal effective compounds [4].

Medicinal properties

The herb has been utilized for centuries in various traditional health systems like Avurveda, Unani, Siddha, and Chinese medicine to address a wide range of health issues including bronchitis, chest pain, nervous disorders, diarrhea, digestive problems, flatulence, gas, indigestion, rheumatism, sedative, appetite loss, colic, cramps, cough, fever, inflammation, depression, tumors, hemorrhoids, skin diseases, numbness, general debility, and vascular disorders. Additionally, the herb is recognized for its insecticidal, larvicidal, antibacterial, mutagenic, cytotoxic, hepatoprotective, anticonvulsant, neuroleptic, smooth relaxant, and smooth muscle stimulant properties. [5, 6]. A calamus is known to possess several properties which are useful to mankind. The herb is extensively used in traditional health practices. In rural parts of many countries such as India, Tibet, China, Burma, Pakistan, Nepal, Russia and Indo Malayan countries the herb is a household herb. The herb is known to possess antidiabetic, anti-obesity, antioxidant, anti-inflammatory and immunomodulatory properties as confirmed by clinical and preclinical reports. Also, it is reported to alleviate the metabolic and neurological disorders, such as anticonvulsant, antidepressant, antihypertensive, anti-inflammatory, immunomodulatory, neuroprotective, cardioprotective, and anti-obesity effects. Metabolic disorders are characterized by hypertension, hyperglycaemia, abdominal obesity, and hyperlipidaemia, which may worsen the neurological disease risk. Improper diet (high calorie intake), lifestyle (e.g., smoking, chronic alcohol consumption, sedentary habits), affect the liver and can further lead to fatty liver disease. In this review article we present the latest results available from the published literature.

Antidiabetic

Diabetes has assumed a status of general disorder amongst public. India accounts to nearly 17% of the total number of diabetes patients in the world, thus often India is referred to as "diabetes capital of the world." As per the estimates nearly 80 million people are suffering from diabetes in India and the numbers may rise to 135 million by 2045 [7]. At global level 425 million people are suffering from diabetes [8]. There are over 1200 plants in local health traditions identified to treat diabetes but only 30 percent of them are investigated pharmacologically and chemically [9]. Over a period, the antidiabetic plants have been shortlisted to be just over hundred plants that are usefully made use in therapy. The plants used in alleviating diabetes can be single plant or in combination with other plants. However the efficacy of herb depends on the active principle in the herb, the synergistic effects of other herbs to treat the disorder. Comparative evaluation of several India herbs has been done and found that A calamus is possessing antidiabetic property [10]. Several clinical studies have been conducted to consider that A calamus is a promising herb to treat Type 2 diabetes mellitus [11, 12].

Antiobesity

According to the fifth round of survey conducted between 2019 and 2021 by National Family Health Survey (NFHS), in India, about 6.4 percent of women and 4.0 percent men, aged between 15 - 49 are found to be obese. Similarly, around 17.6 percent of women and 18.9 percent men are considered overweight in the same age group but not obese [13]. Obesity is a great health concern since it leads to failure of many vital organs in the body. Thus, obesity is considered a dreadful silent killer amongst many ailments. According to a study, about 650 million people were obese in 2016, and nearly 23.6 million are expected to die from cardiovascular diseases by the year 2030[14]. Some of the complexities such as hypertension, hyperglycaemia, abdominal obesity, and hyper-lipidaemia can be characterised as metabolic disorders. These disorders also contribute greatly to human ill health. They may cause serious concern and risk to human life. Sedentary life style, intake of high calories, alcoholic addiction, smoking addiction etc also contributes to risking of human life [15]. A calamus is a promising herb to treat obesity complexities in humans. Studies conducted in beta asarone treated rats recorded wight loss and also inhibited metabolic transformations [16]. In *in vitro* investigations the aqueous extract has demonstrated lipid lowering activity through inhibition of pancreatic lipase percentage [17]. A calamus powder administered on 24 patients of both sexes with hyperlipidemia resulted in significant reduction in skinfold depth, fatigue, and excessive hunger [18]. A combination of drugs namely A. Calamus, Cyperus rotundus, Cedrus deodara, ginger, Aconitum Heterophyllum, T. chebula when administered on 30 obese patients of both sexes aged 14–50 years, a significant improvement in extreme sleep, body heaviness, fatigue, and excessive hunger was reported [19]. In clinical trials 20 obese patients of both sexes were treated with *Acorus calamus* rhizome powder, for studying the antiobesity property of the herb. Significant results and improvement in extreme sleep, body heaviness, fatigue, and excessive hunger are reported by the authors [20].

Anxiety

Anxiety is considered as a type of mental health condition that makes it difficult to get through the day. The symptoms include feelings of nervousness, panic and fear as well as sweating and a rapid heartbeat. Thus anxiety is certainly a disorder which warrants medication [21]. A calamus has been found to effectively treat anxiety related problems and several publications are in the public domain. 70% hydroalcoholic extract of *A. calamus* was found effective to treat anxiety which is a present-day mania on many youths especially in unemployed youth. 33 patients of both sexes (20 male and 13 female) with anxiety disorder were treated with the drug and found that there was a significant reduction of anxiety and stress-related disorder [22].

Hypertension

Hypertension, commonly referred as high blood pressure is a common ailment but can be serious if not treated appropriately at right time. If the pressure on blood vessels of a person is high ie., 140/190 or higher, then, that person is suffering from hypertension [23]. Rhizomes of A calamus is known to possess antihypertensive effect as per the results obtained from the clinical data using rats. The herb was tried on its own and as well in combination with *Gymnema sylvestre*. Results have showed that the antihypertensive effect was better in combination with *G sylvestre* than A calamus alone [24]. A combination of *A. calamus, C. pluricaulis, Bacopa monnieri, T. cordifolia, C. fistula, A. indica, S. lappa, Tribulus terrestris* (Shankhapushpyadi Ghana Vati) administered on 20 hypertensive patients of both sexes, recorded significant relief in raised systolic blood pressure, diastolic blood pressure [25].

Memory impairment

With aging, loss of memory is also a serious concern of health and often referred as dementia. The symptoms of memory impairment are many folded. A person keeps asking the same question repeatedly. Forgetting the common words while speaking and trying hard to recollect. It could be mixing up of words which may be totally unconnected. Taking long time to complete familiar tasks. Or it could be misplacing items in a totally unconnected place. These are few symptoms of dementia of a person. The magnitude of the problem can vary person to person or with time it could assume a severe proportion even forgetting a family member also [26]. Several trials have been conducted using A calamus in combination with other drugs to evaluate the efficacy of A calamus in treating dementia in humans. A combination of A. *calamus, Tinospora cordifolia, Achyranthes aspera, Embelia ribes, Convolvulus pluricaulis, T. chebula, S. lappa, Asparagus racemosus*, cow ghee, and sugar (Guduchyadi Medhya Rasayana) was tried on 138 patients of both sexes aged 55–75 years with senile memory impairment. The results were highly encouraging to record significant improvement in terms of recall memory, cognitive impairment, amnesia, concentration ability, depression, and stress [27].

Sedative effect

Sedation, also known as "monitored anesthesia care". Sedation is a condition where the patient is made to feel drowsy and relaxed. Depending on the requirement of a patient different levels of sedation are administered [28]. The dried aqueous extract exhibited anti-hyperthermic and sedative effect without producing any respiratory depression. This clinical trial was conducted on 40 healthy volunteers, of both sexes aged between 18–50 years with a pre-medicant for anesthesia [29].

Insomnia

Insomnia is a disorder of sleeplessness. There could arise a problem in falling asleep or staying asleep with insomnia30. This leads to many connected disorders related to nervous problems, hence treating insomnia is as important as any other ailment. A combination of drugs of *A. calamus, Valeriana wallichii, N. jatamansi* was tested against insomnia and other related disorders. Accordingly, a trial was conducted consisting of 24 insomnia patients of both sexes aged 18–75 years. Results showed a significant effect of drug on patients suggesting significant improvement in sleep duration, in the initiating time of sleep, and in quality of sleep [31].

Tranquilizer and hypnotic

Hypnotics are medications used to induce, extend, or improve the quality of sleep, and to reduce wakefulness during sleep. The most commonly used hypnotics include benzodiazepine receptor agonists (BzRAs), antidepressants, antipsychotics, antihistamines, and melatonin (or melatonin receptor agonists) [32]. Hypnotics are used for the treatment of insomnia which is characterized by difficulties with falling asleep or maintaining sleep. Many drugs are used as hypnotics such as benzodiazepines and Z-drugs. There is also a possibility of using plant-based drugs and they have also been found useful to be

used as hypnotic drugs. A drug Brahmyadiyoga which is a combination of *A. calamus, Centella asiatica, Rauvolfia serpentina, Saussurea lappa, Nardostachys jatamans*i, was found to serve as brain tonic, tranquillizer, hypnotic, and sedative. The clinical trials were conducted on 10 schizophrenia patients33 of both sexes aged 18–40 years.

Increasing immunoglobulin levels

Immunoglobulins are called antibodies. Antibodies are proteins that the immune system makes to fight germs, such as viruses and bacteria. When the body is exposed to germs, the body makes unique antibodies that are specifically designed to destroy only those germs34. There are good number of plant drugs which can aid and support the body to increase antibodies. Bala – a combination of *A. calamus, Emblica officinalis, E. ribes, T. cordifolia, Piper longum, Glycyrrhiza glabra, C. rotundus, A. heterophyllum* was found to significantly improve in immunoglobulin levels after 6 months35 in 24 neonates of both sexes, weighing 2.5–3 kg body weight.

Mental balance

Mental balance can be defined as the healthy psychological state of someone with good judgment. The psychological state of someone who is functioning at a satisfactory level of emotional and behavioural adjustment can be considered as a healthy person [36]. Several trials have been conducted to assess few drugs which are known to support mental balance. A drug having a combination of *A. calamus, T. cordifolia, Hedychium spicatum, C. pluricaulis, E. ribes, ginger, A. aspera, T. chebula,* and cow ghee known as Vachadi Ghrita was administered on 90 healthy individuals of both sexes aged 40–50 years for assessment of cognition. The clinical trial results demonstrated that there was a significant change in the mental balance score, holding of like and different pairs, late-immediate memory, and also improved digestion [37].

Ischemic heart disease

Technically ischemic means that an organ (e.g., the heart) is not getting enough blood and oxygen. Ischemic heart disease, also called coronary heart disease (CHD) or coronary artery disease, is the term given to heart problems caused by narrowed heart (coronary) arteries that supply blood to the heart muscle38. Coronary heart disease (CHD) is the most common type of heart disease, in USA killing approximately 382,820 people annually. Every year about 805,000 Americans have a heart attack [39]. According to WHO reports, cardiovascular diseases (CVDs) are the leading cause of death globally, taking an estimated 17.9 million lives each year [40]. The number of deaths due to heart attacks in India has remained consistently over 25,000 in the last four years41 and heart attacks account to 28 percent of deaths in India. *Acorus calamus* rhizome powder administered on 45 ischemic heart disease patients, was found to have an Improvement of chest pain, dyspnoea on effort, reduction of the body mass index, improved ECG: reduced serum cholesterol, reduced serum LDL, and increased serum HDL [42].

Anti-Inflammatory and Immunomodulatory Effect

Commonly associated diseases with chronic inflammation are multiple and few of them are cardiovascular disease, diabetes, malignancy, auto-immune disease, chronic hepatic and renal diseases. Any agent which fights against these inflammatory diseases is called as anti-inflammatory. Clinical trials conducted with A calamus have proven anti-inflammatory and immunomodulatory. Methanolic extract of the rhizome prevented the VCAP-1 an intercellular expression on the surface of mouse myeloid leukaemia and murine endothelial cells [43]. Butanolic fraction inhibited phospholipase C (PLC) pathway in platelets presumably acting on protein kinase [44].

Anticonvulsant Effect

Anticonvulsant drugs are those which prevent convulsions by controlling abnormal electrical activity in the brain. Anticonvulsants are used to treat epilepsy and other seizure disorders [45]. The methanol extract showed anticonvulsant effects [46] through gamma-aminobutyric acid (GABA) pathway in the central nervous system. The raw and processed rhizome exhibited notable anticonvulsant activity by minimizing the span of the tonic extensor period in rats, whereas the processed rhizome showed better therapeutic activity than the raw [47].

Antioxidant effect

Antioxidants are man-made or natural substances that may prevent or delay some types of cell damage. Antioxidants scavenge free radicals from the body cells and prevent or reduce the damage caused by oxidation [48]. The protective effect of antioxidants continues to be studied around the world. Antioxidants are found in many foods including fruits and vegetables. Studies conducted to assess A calamus for its antioxidant property found significant effects. The in vitro antioxidant activity of acetone, acetonitrile, alcoholic, and aqueous extracts of *A. calamus* rhizomes exhibited free radical scavenging activity. Strong antioxidant effect was noticed in the acetone extract, followed by acetonitrile and methanol, while in the aqueous extract, recorded poor antioxidant activity [49]. The aqueous extract exhibited superior antioxidant effects in metal ion chelation, lipid peroxidation, and DPPH assays [50,51]. Ethanol and hydro-alcoholic extracts of *A. calamus* roots and rhizomes were studied for antioxidant potential against DPPH compared with butylated hydroxyanisole (BHA) and silymarin. Ethanol and hydro-alcoholic extracts showed free radical scavenging activity of 59.13 ± 18.95 and 56.71 ± 19.54, respectively [52,53,54]. The essential oil isolated from *A. calamus* showed strong antioxidant efficacy against the β -carotene/linoleic acid bleaching test and DPPH free radicals [55]. The methanol extract of the *A. calamus* rhizome was evaluated against the free radical scavenging activity, and found to be IC50 value at 704 µg/mL. The IC50 of the essential oil was 1.68 µg/mL, which showed virtuous free radical scavenging activity in the DPPH test [56].

Antidepressant

Antidepressants are a type of medicine used to treat clinical depression. They are used to treat a number of disorders such as anxiety, post-traumatic stress disorder etc [57]. Few reports comprising of A calamus suggesting positive effects of antidepressant are presented. Interaction of the methanolic A. calamus rhizome extract with the adrenergic, dopaminergic, serotonergic, and GABAergic system was found responsible for the expression of antidepressant activity [58]. In another study, the methanolic A. calamus leaf extract showed significant activity through a reduction in the immobility period in the tuberculin skin test and forward surgical teams [59]. Through interaction with the adrenergic and dopaminergic system, the hydro-alcoholic extract was normalized to the over-activity of the hypothalamic pituitary adrenal axis [60]. Sobers capsules (a herbo-mineral formulation containing A. calamus) were evaluated by tail suspension and forced swimming tests in mice. At the oral dose of 50 mg/kg for 14 days, capsules exhibited insignificant impact on locomotor activity, and caused antidepressant effects in experimental animals [61]. Tensarin (the traditional medicine of Nepal containing A. calamus) was evaluated for the anxiolytic effect in mice using the open field test (OFT), activity monitoring along with the passive avoidance test. At all three dose levels (50, 100, 200 mg/kg), Tensarin produced an anxiolytic effect in a dose-dependent way by an improvement in rearing, number of passages, and duration of the period employed by mice [62].

Ethnomedicinal uses

In rural India the herb is used to treat many ailments and few of the results are reported herewith. The paste obtained from rhizome of A calamus is used against eczema in many countries along with the leaves of *Azadirachta indica* and paste of Curcuma aromatica rhizomes [63]. The paste obtained for the rhizomes of A. calamus and Curcuma aromatica and seeds of Argemone Mexicana is applied to treat many types of skin diseases63. The paste of rhizome of *A calamus* is used in treating cough, stuttering, ulcer, fever, dermatitis, scab and sores [64]. The rhizome paste is given with cow milk to treat gastric disorders [65]. Rhizome paste of A. calamus along with fruits of Myristica fragrance and Calunarejan spinosa is given in mother's milk to children to treat cold, cough and fever [66]. Infusion of dried rhizomes (collected and stored in the autumn season) is consumed to serve as carminative, flavoring, tonic and also to treat head lice infestation [67,68]. The paste of A Calamus rhizome is given with honey to cure Epilepsy, dysentery, mental illnesses, diarrhoea, kidney and liver disorders [69]. Rhizomes are used to treat wounds, fever and body pains [70,71]. In some parts of the country fresh ground rhizomes is mixed with hot water and given for 3 days to treat dysentery [72]. Dried powder of A Calamus rhizomes is used as stimulant [73]. The rhizome paste of A calamus is used to treat external injuries [74], stomach ache, wherein the ash of the A calamus rhizomes is applied as dermal application [75]. Similarly, the root paste with coconut husk juice as external application serves as otitis76, and fresh leaves as option [77]. The rhizome is used in treating several neurological disorders, gastrointestinal problems, respiratory ailments, to increase menstrual flow, as analgesic, contraceptive, herpangina [78,79,80].

In Pakistan, the whole plant is used against diarrhoea as oral source. Also, it is used as colic [81]. In Nepal the infusion of roots is administered against blood pressure [82]. Similarly, the juice prepared from the rhizomes is used against cough, headache, snake bite, sore throat and pain, dysentery [83]. The rhizome is also against neurological and respiratory complications [84]. Whole plant of A calamus is used in Malaysia against Rheumatism, diarrhoea, dyspepsia, and hair loss [84]. In Tibet the herb is used against many ailments. The dried rhizome of A calamus is given with *Saussurea lappa, Ferula foetida, Terminalia chebula, Cuminum cyminum, Inula racemose* and *Zingiber officinale* for treating fever and gastrointestinal complications [85]. The rhizomes are used against cancer treatment86. In China, The Chinese traditional health system is highly popular and herbs are used in their health systems. Accordingly A calamus rhizome is used in treating gastrointestinal, respiratory, neuroprotective, analgesic, contraceptive and cancer complications [87,88,89]. The rhizome of A calamus squeezed with stem of *Coccinia cordifolia* in water is given to patients to treat against Antipyretic and ear-related disease. The rhizome of A calamus with vinegar, Alpinia galanga, Zingiber purpureum is administered to detoxify the body. External

application of rhizome paste is used in herbal baths as analgesic90. The rhizome paste is used against haemorrage91. Further, the rhizome is also used as approdisiac by administering through oral [92] and as an hallucinating agent by mixing with Indian hemp and *Podophyllum pleianthum* [93]. The rhizome is used as dermal care agent to obtain fair skin by using leaves of A calamus with Artemisia vulgaris [94]. In Indonesia, the rhizomes are used through oral means to treat gastrointestinal ailments [95] and rhizomes blended with chalk and magnesium oxide96. In England, the rhizomes are used to treat gastrointestinal problems and as well antibacterial and analgesic agent. Rhizomes are also used against dysentery, and chronic catarrh along with Gentiana campestris [97]. Rhizomes are also used against malaria [98]. In Europe the rhizome of A calamus is widely used against obesity, gastrointestinal problems, respiratory complication [99,100]. In Republic of South Africa the rhizome is used as tooth powder, tonic and aphrodisiac. Gastrointestinal problems are also treated using the rhizome101. In Germany rhizome is used to increase menstrual flow and as well for gastrointestinal complications [102,103. In Java, the rhizome is used to increase lactation [104]. In Lithuania, the rhizome is used to treat chest pain and diarrhoea97. In Lithuania, Rhizomes and leaves are taken with sugar for treating chest pain and diarrhoea97. To get relief from pain, gout and rheumatism, the leaf decoction is applied externally to get relief105. In New Guinea the rhizome is used orally to treat miscarriage106. In Philippines the decoction of Acorus rhizome is used orally to treat gastrointestinal disorders and as well rheumatism in elderly people101. In Russia traditional health healers use rhizome as oral syrup to treat typhoid, syphilis, baldness, fever and cholera [107]. In Thailand rhizomes are used to treat fever and as well as blood purifier[108]. In Turkey the herb is used both internally to treat cough, tuberculosis and externally to treat wounds [109]. The rhizome is also used to treat gastrointestinal disorders [110] in Turkey. In Arab countries also the herb is used in gastrointestinal complications and as well to treat tuberculosis [111,112]. The rhizome decoction is taken internally. In Brazil the decoction of rhizome is consumed internally to treat parasitic worms in the stomach [113]. In Argentina the rhizome is consumed internally to cure dysmenorrhea [114]. In USA the rhizome is used to treat many ailments such as gastrointestinal disorders, respiratory disorder and as well as abortifacient, stimulant, tonic [115]. In Korea the rhizome is used by traditional health healers to enhance life span and as well to improve memory [116]. In Sri Lanka the rhizomes are administered to treat worm infestation and cough along with milk in the form of paste [117].

CONCLUSION

The perennial herb *Acorus calamus* is pharmacy by itself since it can cure many ailments. The herb is used in many countries and continents for its unique medicinal properties which are detailed in the paper. The references which are spread out have been put in a place for clear understanding of the herb and for better usage and furtherance of more trials tp prospect the herb.

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