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# Ayurveda and botanical drugs for epilepsy: Current evidence and future prospects

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#### ABSTRACT

The understanding of epilepsy has progressed since its earliest impression as a disease associated with paranormal and superstitious beliefs. Landmark advances have been made in deciphering the pathophysiological substrates involved in the disease process, and treatment advances have contributed significantly to ameliorating the seizures. However, disease-modifying agents are yet to be discovered. Ayurveda is a system of medicine that stresses a holistic approach to disease, and treatment is focused on disease modification and symptom management. Herbs form the core of Ayurveda medicine; though many of them have been studied for their anticonvulsant activity, very few actually mention the reference of these herbs in Ayurveda literature. Other therapeutic interventions used in Ayurveda are relatively unexplored, and future research will need to focus on this. The current manuscript briefly discusses the understanding of epilepsy as per Ayurveda and reviews herbs that have been studied for their anticonvulsant activity mentioned in Ayurveda literature.

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#### 1. Introduction

Epilepsy is a chronic neurological disease that, although occurring intermittently, can have lasting changes in the neural circuitry. The disease has a strong propensity for comorbidities including psychiatric and cognitive impairments [1]. Antiepileptic drugs, though effective in symptomatically controlling seizures, do not prevent or reverse the pathological process that underlies epilepsy. Though antiepileptic drugs are generally well tolerated, there still is a need to search for new drugs with fewer side effects and better efficacy [2]. World over. it has been observed that, in cases of chronic conditions, there is a growing tendency to seek other systems of health care. This health-seeking behavior may be complementary or alternative to the existing medical system being used. There are many complementary systems including acupuncture, botanicals, and music therapy, and such systems are being used for epilepsy care. Ayurveda is one amongst a small group of such diverse health-care systems with an inherent holistic theoretical framework of health and disease. Many of the Ayurveda treatments have the potential of not only relieving symptoms but also modifying the pathophysiology of the disease.

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Ayurveda is a functional science and attributes diverse bodily function to three dynamic principles similar to humors (dosha) known as vata (responsible for movement), pitta (responsible for transformation), and *kapha* (responsible for anabolic activities) [3,4]. Physiology is identified by the harmony in the functioning of these dynamic principles, and pathology is identified by the discordance in their functions affecting the structural elements (*dhatu*) and the elimination of wastes (mala) [5]. Few aspects of epilepsy as per Ayurveda have been detailed in earlier publications [6,7]. The disease epilepsy is similar to a condition detailed as Apasmara in the earliest Avurveda literature sometime around 800BCE-400CE including Charaka Samhita, Sushruta Samhita, and Ashtanga Hridaya [3,5,8]. The diagnosis of Apasmara is based on astute observation of the symptomatology, and the main presenting feature of the disease is, as the name defines, 'loss of consciousness'. Apasmara is due to an aberration of not only the physical bioentities vata, pitta, and kapha dosha but also that of the psychological (manasika) attributes satva (serenity), rajas (passion), and tamas (ignorance). It manifests physical symptoms like alarming movements (bibhatsa cheshta, referring to the involuntary movements during the seizures) and psychological symptoms like perversion of memory and cognition (smriti-buddhi samplava) and temporary loss of consciousness (tamah pravesha). A distinct prodromal (purvarupa) stage of the disease has been elaborated with symptoms of hallucinations - auditory and visual (ashabda shravana and asanti rupa darshana), loss of appetite (anannabhilasha), sweating (sweda), weakness (dourbalya), body ache (angamarda), etc. Apasmara is subclassified based on the predominance







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of the biological entities *vata*, *pitta*, and *kapha*; the intensity and duration of the ictus and the associated symptoms are variable based on this predominance [3].

Treatment of Apasmara is multipronged and includes pharmacologic and nonpharmacologic measures. The exact combination of medication is arrived at after a thorough examination of the subject based on disease factors and host factors. The paroxysmal nature of the disease was recognized, and diverse treatments during an ictus and at other times were advocated. These include therapies like oleation (snehana) and sudation (svedana), cleansing (shodhana) therapies such as emesis (vamana) and purgation (virechana), colonic administration of medicaments (basti), and nasal administration of medicines (nasya) in varied forms. These are complemented with suitable internal medications prepared in different pharmaceutical forms that include freshly prepared juices of herbs (svarasa), pastes (kalka), lipid-based formulations (sneha – oil- or ghee-based preparations), decoctives (kashaya), powders (churna), fermented preparations (asava-arishta), and pills (vati), etc. [3,5,8,9]. Some of the herbal formulations used are Aswagandharishtam [9], Saraswatarishtam [10], Kalyanaka churna, Saraswata churna [11], Brahmi ghrita, Dadhika ghrita, Kalyanaka ghrita, Maha kalvanaka ghrita, Kushmanda ghrita, Panchagavya ghrita, Maha Panchagavya ghrita, Siddarthaka ghrita, Tiktaka ghrita [5], and Mahayogaraja guggulu [10]. Herbomineral/mineral formulations widely prescribed for Apasmara are Manasamitravatakam, Mritasanjeevani gutika [12], Apasmarahara rasa, Apasmarari rasayana [13], Bhootabhairava rasa, Smritisagara rasa, [14], Chaturbhuja rasa [15], Chaturmukha rasa, Chintamani chaturmukha rasa, Tapyadi lauha, Vatakulantaka rasa, Yogendra rasa [9]. As the pathogenesis of Apasmara is attributed to a discordance of the psychological entities too, nonpharmacologic interventions like psychotherapy also form an integral part of treatment. This is referred to as Satvavajaya chikitsa and involves behavioral therapies for the psyche. It aims at harmonizing the functioning of the different components of the psyche including intellect (*dhi*), fortitude (*dhriti*), and memory (*smriti*) of the patient [3,16].

#### 2. Current evidence for Ayurveda botanicals in epilepsy

A cursory literature review was performed using the electronic database PubMed, with the keywords Ayurveda, seizures, epilepsy, anticonvulsant, extracts, and herbs, up to February 2015. The herbs/extracts/ formulations that have been studied for antiepileptic activity in animal/human studies were identified. It was interesting to note that close to 60 different herbs that have been mentioned in Ayurveda literature have been studied for antiepileptic activity. While some of these studies related to the use of the herb in Ayurveda, many did not seem to acknowledge the same. The studies conducted have also been on herbs that may not have been indicated for the specific condition of epilepsy in Ayurveda but, nevertheless, have shown potent antiepileptic activity. The majority of the studies were in animal models, some were ethnobotanical survey studies, and very few were clinical studies in human population. It was also observed that some of the human studies were performed in settings outside India, based on their history of traditional use of the same herb as told in Ayurveda literature. Complementary and alternative medicine use, including Ayurveda, is widely prevalent not only in India but also in the Western countries. The available evidence for Ayurveda botanicals is categorized and described under (1) studies of single herbs/extracts, (2) studies of polyherbal formulations, and (3) clinical studies in human population.

#### 2.1. Studies of single herbs/extracts

Some of the main herbs used in Ayurveda for treating *Apasmara* are discussed in detail. Other herbs that may not have been indicated for *Apasmara* per se in Ayurveda literature but have been studied for their effect in epilepsy have been summarized in Table 1.

#### Table 1

Herbs tested for anticonvulsant activity, described in Ayurveda literature.

Sl	Botanical name	Sanskrit name	Reference
1	Albizia lebbeck (L.) Benth.	Shirisha	[17,18]
2	Aloe vera (L.) Burm.f.	Kumari	[19]
3	Anacyclus pyrethrum (L.) Link, D.C.	Akarakarabha	[20.21]
4	Anethum graveolens L.	Shatapushpa	[22,23]
5	Anisomeles malabarica (L.) R.Br.	Gojihva	[24]
6	Anthocephalus cadamba Mig.	Kadamba	[25]
7	Antiaris toxicaria Lesch.	Valkala	[26]
8	Argyreia speciosa (L.f.) Sweet	Vriddhadaruka	[27.28]
9	Asparagus racemosus Willd.	Shatavari	[29]
10	Bixa orellana L.	Raktabeeia	[30]
11	Boerhavia diffusa L.	Punarnava	[31]
12	Brassica nigra (L.) Andrz.	Raiakshavaka	1321
13	Bryophyllum pinnatum (Lam.) Oken.	Pashanabheda	1331
14	Butea monosperma (Lam.) Taub.	Palasha	[18,34]
15	Caesalpinia sappan L.	Kuchandana	[35]
16	Calotropis gigantea (L.) W.T.Aiton	Arka	[36]
17	Calotropis procera W.T.Aiton	Arka	[37]
18	Capparis decidua Edgew.	Kareera	[38]
19	Carum copticum Benth. & Hook.f.	Yavani	[39]
20	Cedrus deodara (Roxb. ex D.Don.) G.Don	Devadaru	[40]
21	Cicer arietinum L.	Chanaka	[41]
22	Cissus auadrangularis L.	Asthishrinkala	[42]
23	Croton tiglium L.	Iavapala	[43,44]
24	Cyperus rotundus L.	Musta	[45]
25	Delphinium denudatum Wall.	Nirvisha	[46-51]
26	Emblica officinalis Gaertn.	Amalaki	[52.53]
27	Ficus carica L.	Phalgu	[54]
28	Ficus religiosa L.	Ashwattha	[55.56]
29	Glycyrrhiza glabra L.	Yashtimadhu	[57-61]
30	Hibiscus rosa-sinensis L.	Iapakusuma	[18]
31	Hyoscyamus niger L.	Parasika yavani	[62]
32	Indigofera tinctoria L.	Neelini	[63]
33	Marsilea quadrifolia L.	Sunishanna	[64,65]
34	Mimosa pudica L.	Lajjalu	[66]
35	Moringa oleifera Lam.	Shigru	[67,68]
36	Myristica fragrans Houtt.	Jatiphala	[69,70]
37	Nardostachys jatamansi DC.	Jatamamsi	[71]
38	Nigella sativa L.	Kalajaji	[72–78]
39	Ocimum sanctum L.	Tulasi	[79,80]
40	Ocimum gratissimum L.	Vishnupriya	[81,82]
41	Orchis latifolia L.	Shalabhamishri	[83]
42	Passiflora incarnata L.	Krishnakamala	[84-87]
43	Portulaca oleracea L.	Brihatlona	[88]
44	Pinus roxburghii Sarg.	Sarala	[89]
45	Punica granatum L.	Dadima	[90]
46	Ricinus communis L.	Eranda	[29,91]
47	Rubia cordifolia L.	Manjishta	[92]
48	Sesbania grandiflora Poir.	Agasti	[93]
49	Smilax china L.	Madhusnuhi	[94]
50	Solanum nigrum L.	Kakamachi	[95,96]
51	Trichosanthes tricuspidata Lour.	Kakanasa	[97]
52	Vetiveria zizanioides Nash.	Usheera	[98]
53	Vitex negundo L	Nirgundi	[99]
54	Zingiber officinale Roscoe.	Ardraka	[100,101]
55	Ziziphus jujuba Lam.	Badara	[102]

#### 2.1.1. Acorus calamus L. (Vacha)

Vacha has been described as a rasayana (rejuvenation) drug in Ayurveda. It is administered by various routes including oral and nasal and indicated for use in varied pharmaceutical forms. The earliest study was on *A. calamus*, wherein the effects of acorus oil and its isolated active principles, asarone and  $\beta$ -asarone were assessed on convulsions [103,104]. While acorus oil and asarone had protective effects on convulsions induced by electroshocks or leptazol,  $\beta$ -asarone seemed to facilitate them. Four decades later, a study showed that pretreatment with *A. calamus* modulated antioxidant enzymes, thereby preventing the development of FeCl(3)-induced epileptogenesis [105]. A more detailed observation by Bhat et al. demonstrated that purifying *A. calamus* in the classical method as has been described in Ayurveda, i.e. by successively boiling *A. calamus* in *Gomutra* (*cow's urine*), *Mundi kwatha* 

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