REVIEW ARTICLE

Studying the pharmacological basis of an antiepileptic ayurvedic formulation - Sarasvata churna

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Abstract

Epilepsy or Apasmara is a common chronic neurological disorder affecting millions worldwide. Abnormal neuronal discharge occurs during seizures. A person with epilepsy is loaded with a variety of synthetic anticonvulsants, which has associated toxicities and degenerative effects on some essential biochemicals and brain antioxidant enzymes on prolonged use. Ketogenic and Atkins diet are sometimes prescribed by neurologists as adjuvant with modern antiepileptics, but their limited use and associated side effects have led to focus on some alternatives. *Nidanparivarjan, Shodhan chikitsa, Bahiparimarjan, Rasayana chikitsa, Sattvavajaya* and *Avasthika chikitsa* are basic approaches for treatment of disorders or ailments in Ayurveda. *Rasayana chikitsa* is preferred for the long-term management of epilepsy, which involves the use of *Medhya Rasayana* which is a collection of herbs in minute quantities such as *Mandukaparni, Yashtimadhu, Guduchi, Tinospora, Ashwagandha, Shankhpushpi, Vacha,* and *Brahmi*. Sarasvata churna is an ayurvedic formulation and as mentioned by *Bhavaprakasha* and Ayurvedic Formulary of India and is a compound ayurvedic formulation containing *Saussurea lappa*, *Withania somnifera*, *Rock salt*, *Carum roxburghianum*, *Cuminum cyminum, Carum carvi*, *Piper longum*, *Piper nigrum*, *Zingiber officinale*, *Cissampelos pareira*, *Convolvulus pluricaulis*, *Acorus calamus*, and *Bacopa monnieri*. Besides possessing tremendous curing potential, Sarasvata churna is not being prescribed by neurologists for the treatment of epilepsy due to lack of animal and clinical safety data. In this study, the individual component drugs of Sarasvata churna are intensively investigated on pharmacological basis for their respective role in overcoming epilepsy so as to understand the actual mechanisms behind the potential of this thousand years old remedy for epilepsy.

Key words: Apasmara, Ayurvedic, *Bhavaprakasha*, epilepsy, *Rasayana chikitsa*, *Medhya Rasayna*, Sarasvata churna

INTRODUCTION

Epilepsy or Apasmara is known to humanity since the time of Acharya Charaka. Epilepsy is a common chronic neurological disorder affecting more than 2% population worldwide. Epilepsy is a complex disorder of brain electrical activity that results in recurrent convulsions.[1,2] Seizures occur due to abnormal neuronal discharge. Oxidative stress is one of the major role players in seizure genesis. The levels of various enzymatic or non-enzymatic antioxidants such as reduced glutathione (GSH), glutathione peroxidase (GPx), glutathione reductase, glutathione-S-transferase, superoxide dismutase (SOD), and catalase are disturbed during seizures.[3] A person with epilepsy is normally loaded with a variety of synthetic anticonvulsants. Conventional treatment approach primarily consists of anticonvulsant medications such as hydantoins and barbiturates. Although these drugs often control or reduce the frequency of convulsions in majority, some patients show little or no improvement. Synthetic anticonvulsants are associated with hepatotoxicity, aplastic anemia, and deleterious effects on

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some essential biochemicals such as vitamin D,[4] carnitine,[5] vitamin K,[6] and folic acid[7] on prolonged use. Some neurologists prescribe a ketogenic and Atkins diet as adjuvant along with synthetic anticonvulsants. These diets are supposed to suppress the onset of seizures but have nothing to do with post-seizure neuronal repair and toxicities associated with anticonvulsants. In addition, the use of these combinations is limited to severe drug-resistant epilepsies along with associated complications such as constipation, low bone density, weight loss, menstrual irregularities, nutritional deficiencies, and increase in triglyceride levels and cholesterol/high-density lipoprotein ratios.[8,9]

Here arises the need to look for some alternative treatment approach for the long-term management of epilepsy with least toxicities, side effects, and increased patient compliance. Ayurveda, a science of life, is being practiced in the Indian sub-continents since thousands of years. Ayurveda prescribes *Medhya Rasayana* therapy for epilepsy and other brain disorders. *Nidanparivarjan, Shodhan chikitsa, Bahiparimarjan, Rasayana chikitsa, Sattvavajaya and Avasthika chikitsa* are basic approaches for treatment of disorders or ailments in Ayurveda. *Rasayana chikitsa* is preferred for the long-term management of epilepsy which involves the use of *Medhya Rasayana* which is a collection of herbs such as *Mandukaparni*, *Yashtimadhu*, *Guduchi*, *Tinospora*, *Ashwagandha*, *Shankhpushpi*, *Vacha,* and *Brahmi*. The ayurvedic literature *Sharangdhar Samhita* has also highlighted the concept of polyherbalism to achieve greater therapeutic efficacy. The active phytochemical constituents of individual plants are insufficient to achieve the desirable therapeutic effects. When multiple herbs are combined in a particular ratio, it will give a better therapeutic effect and reduce the toxicity.[10]

There are a number of standard and non-standard ayurvedic polyherbal formulations such as *Brahmi Ghrita*, Epic-Q, Mentet, Formepi-4, *Asthamangal Ghrita*, *Panchgavya Ghrita*, and Sarasvata churna claim to help in the management of epilepsy.[11-19] Sarasvata churna, as mentioned by *Bhavaprakasha* and Ayurvedic Formulary of India, is a compound preparation containing the dried roots of Kushta (*Saussurea lappa*), dried roots of *Ashwagandha* (*Withania somnifera*), powdered *Lavana* (*Rock salt*), dried fruits of *Ajamoda* (*Carum roxburghianum*), dried fruit of *Jeeraka* (*Cuminum cyminum*), dried fruit of *Krishna Jeeraka* (*Carum carvi*), dried fruit of *Pippali* (*Piper longum*), dried fruit of *Maricha* (*Piper nigrum*), dried rhizomes of *Shunti* (*Zingiber officinale*), dried whole plant of *Patha* (*Cissampelos pareira*), dried whole plant of *Shankapushpi* (*Convolvulus pluricaulis*), dried rhizomes of *Vacha* (*Acorus calamus*). All above ingredients are triturated with fresh juice of *Brahmi* (*Bacopa monnieri*).

Modern pharmacological studies proved that individual component drugs in Sarasvata churna possess excellent immunomodulatory, adaptogenic, antioxidant, nootropic, and antiepileptic activity whereas some other ingredients are found to increase bioavailability and maintain metabolism and digestion. Combined effects of ingredients of Sarasvata churna are considered best not only to prevent the onset of seizures but also to help in restoring the levels of various enzymes, thereby reducing the effects of oxidative stress on the neurons preventing recurrence of seizure and promoting the neuronal repair by various mechanisms. The pharmacological study observations for various component drugs of Sarasvata churna are as follows.

Ashwagandha (*W. somnifera* Dunal)[20-23]

Withania root extracts alone and in combination with gamma amino butyric acid (GABA) abolished the extensor phase in subcutaneous pentylenetetrazole (scPTZ) model. Aqueous extracts have shown increased threshold in scPTZ model and are responsible for GABAergic-mediated anticonvulsant activity. Withanolide A and Withanosides IV and VI predominantly induced axons and dendrites outgrowths in cell lines, suggesting its role in neuroregeneration. Ashwagandha posses neuroprotective, neuroregenerative and GABAergic modulatory potential.

Patha (*C. pareira*)[24-28]

Alkaloidal and hydroalcoholic fractions of roots were found to act by increasing the activity of antioxidant enzymes catalase (CAT), SOD, GPx and decreasing the activity of acetylcholinesterases (AChE), thereby decreasing the free radicals and increasing the cholinergic functions ultimately resulting in decrease in neurodegeneration and memory impairment in hippocampus. Hydroalcoholic extract also possesses nootropic and hepatoprotective effect.

Kustha (*S. lappa*)[29-35]

Ethanolic, methanolic, and chloroform extracts of roots exhibited strong antioxidant potential in *in vitro* 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging and aluminum nitrate models due to the presence of phenolic and flavonoids content. *Brahmi Ghrita's* petroleum ether and ethanolic extracts exhibited antiepileptic activity through GABAergic mechanism in scPTZ, maximal electroshock (MES), and picrotoxin-induced seizure models by increasing latency to convulsions and reducing mortality. Chlorogenic acid present in the drug has shown strong antioxidant potential in *in vitro* DPPH, nitric oxide, superoxide radicals scavenging along with its ability to inhibit lipid peroxidation and GSH oxidation.

Shweta Jiraka (*C. cyminum*)[36-44]

Crude methanolic extract and essential oil of fruits possess strong antioxidant potential in DPPH,

2,2'-azinobis-(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS), ferric reducing antioxidant power (FRAP), and other models due to phenolic composition of volatile oil. Antiepileptic action by neuronal membrane mediated cellular changes. Essential oil found to possess antiepileptic activity in scPTZ and MES models.

Krishna Jiraka (*C. carvi*)[45-50]

Aqueous extract and essential oil found to have anticonvulsant potential against scPTZ model. Epoxycarvone, a constituent of essential oil, also found to possess anticonvulsant potential against scPTZ and MES models. Phenolic extracts was found to possess strong antioxidant activity against DPPH free radicals and superoxide anion radicals. The reducing ability of the extract was found to be better than butylated hydroxytoluene (BHT) and comparable to butylated hydroxyanisole.

Maricha (*P. nigrum*) and *Pippali* (*P. longum*)[51-59]

Methanolic extract of *P. nigrum* fruits was found to be very effective against MES and scPTZ models. Piperine, the principal compound, decreased mortality in the MES-induced seizure model, delayed the onset of tonic–clonic convulsions in the strychnine, picrotoxin, and scPTZ tests, and reduced associated mortality. Piperine enhanced the bioavailability of phenytoin significantly, possibly by increasing the absorption. Aqueous and alcoholic extracts of *P. longum* were found effective against scPTZ and MES models, respectively. Piperine also shown protection against pilocarpine-induced convulsions and proved that neuroprotective activity of piperine may be attributed to its P-glycoprotein inhibition, cycloxegenase-2 inhibition, Ca++ channel blocking, and cytochrome (CYP3A4) enzyme inhibition activities and involvement of GABAergic system in convulsion control.

Shunti (*Z. officinale*)[60-65]

Hydroalcoholic extract of rhizomes have prolonged the onset time period of myoclonic, prevented generalized clonic, and increased the threshold for the forelimb tonic extension seizures in scPTZ model and also shown to prevent lamotrigine-induced hepatotoxicity. Significant decrease in the duration of tonic hind limb extension was observed after ethanolic extract administration in MES model. The presence of vitamins, 6-gingerol, and other polyphenolic compounds in aqueous extract has shown good antioxidant potential in DPPH free radical scavenging model.

Radhuni (*C. roxburghinum*)[66-72]

C. roxburghianum seed extract possesses blood pressure lowering, vasorelaxant and cardiac modulatory potential, occurred possibly through Ca++ antagonism, nitric oxide modulatory and phosphodiesterase inhibition mechanisms. Oil from seeds reported to contain up to 80% D-carvone which possess strong antioxidant potential against *in vitro* DPPH, ABTS, and FRAP tests.

Brahmi (*B. monneira*)[73-82]

Alcoholic extracts exhibited strong antioxidant potential against ferric sulfate, cumene hydroperoxide, and DPPH free radical scavenging tests in a dose-dependent manner. In a comparison of 1-deprnyl (antiaging, nootropic drug) and *B. monnieri*, it was found to enhance antioxidant/detoxification enzyme activity in the spleen, brain, heart, thymus, and mesenteric lymph nodes thereby showing neuroprotection. Bacoside A and Bacopaside I (biomarker) treatment also improved antioxidant enzyme activities including SOD, CAT, GPx and markedly inhibited the increase in malondialdehyde (a free radical marker) content of the brain. *B. monnieri* showed excellent neuroprotection against pilocarpine-induced epilepsy. *Brahmi Ghrita* and Saraswatarishta were found to possess excellent antioxidant and neuroprotective activity against MES-induced epilepsy model. Increased acetylcholine (ACh) and decreased anticholinesterase activity were observed with different extracts of bacopa when screened for antiepileptic activity in scPTZ model. *B. monnieri* and Bacoside-A treatment reverses epilepsy associated changes to near control suggesting that decreased GABA receptors in the cerebral cortex have an important role in epileptic occurrence. Deep analysis of various *in vivo* and *in vitro* studies has shown that *B. monnieri* acts via the following mechanisms–antioxidant neuroprotection (via redox and enzyme induction), AChE inhibition and/or choline acetyltransferase activation, β-amyloid reduction, increased cerebral blood flow, and neurotransmitter modulation (ACh, 5-hydroxytryptamine, dopamine).

Bach (*A. calamus* Linn.)[83-87]

Benzene extract of rhizomes was found to possess excellent antioxidant activity both *in vivo* and *in vitro* in various models such as DPPH, FRAP, superoxide anion, and hydroxyl ion scavenging models. β-asarone (biomarker) and methanolic extracts of *A. calamus* exhibited promising protection against MES, isoniazid, and pilocarpine-induced epilepsy. Ethanolic extract was found to be effective in generalized tonic–clonic convulsions but not in petit mal epilepsy in scPTZ and MES models.

Shankhpushpi (*C. pluricaulis* Choisy.)[88-97]

Aqueous extract of *C. pluricaulis* has shown potent anticonvulsant activity in strychnine pentylenetetrazole-induced epilepsy models and afforded neuroprotection against scopolamine-induced neurotoxicity by increasing

AChE activity within the cortex and hippocampus. Reduced activities or contents of glutathione reductase, SOD, and reduced GSH within the cortex and hippocampus induced by scopolamine were elevated by the extract. Methanolic extract found to possess antioxidant activity comparable with ascorbic acid and shown anticonvulsant activity by reducing mean recovery time from convulsions in MES model. Aqueous extract from *C. pluricaulis* has shown significant neuroprotection against Aluminum chloride induced neurotoxicity in rat cerebral cortex by maintaining antioxidant enzymes levels and increasing activity of AChE. Pretreatment with scopoletin (isolated from chloroform and ethyl acetate fractions of *C. pluricaulis*) significantly attenuated the loss in body weight, improved the locomotor activity, grip strength, and gait abnormalities. It also has altered the increased malondialdehyde and nitrite levels, restored SOD, and reduced GSH enzyme activity in the striatum and cortex in 3-nitropropionic acid-treated groups. The free radical scavenging activity of methanolic extract of *C. pluricaulis* and the standard (BHT) was found to be highest at 100 ug/ml which was 52.56% and 93.48%, respectively. The concentration of *C. pluricaulis* needed for 50% inhibition was found to be 90.56 µg/ml whereas 29.02 µg/ml needed for BHT showing its antioxidant potential. Ethanolic extract of petals has shown anti-anxiety potential in plus maize model, whereas methanolic extract has shown significant protection against tonic convulsion induced by transcorneal electroshock, which was also comparable with that of the standard drug phenytoin.

CONCLUSION

Sarasvata churna is a potential ayurvedic formulation for management of epilepsy and other brain-related disorders, but lack of therapeutic and clinical safety data limits its use to the ayurvedic practitioners only. The pharmacological findings from individual component drugs of Sarasvata churna shows that it possesses immense antiepileptic potential which is further potentiated by antioxidant, immunomodulatory, and nootropic activities of the component drugs. The formulation needs to be explored as a whole on the basis of both *in vivo* and *in vitro* modern pharmacological experimentations along with its proper standardization so as to evolve a time-tested, effective, and clinically safe formulation with supportive clinical data. The formulation can be beneficial in long-term management of epilepsy if formulated with proper care with standards.

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