Is There Any Scientific Basis of Hawan to be used in Epilepsy-Prevention/Cure?

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Epilepsy is a neuropsychiatric disorder associated with religiosity and spirituality. Nasal drug delivery systems are the best for diseases related to brain. In older times RishiMuni, ancient scholars and physicians used to recommend Hawan for mental peace and well being. Gayatri Mantra also tells that sughandhim (aroma, fragrance) puushtivardhanam (gives rise to good health). Om triambkum yajamahe, sughandhim puushtivardhanam, urvarukmavandhanaat, mrityumokshyamamritaat! Hawan is a scientific experiment in which special herbs (Hawan Samagri) are offered in the fire of medicinal woods ignited in a specially designed fire pit called agnikuñda. Hawan seems to be designed by the ancient scholars to fight with the diseases of the brain. Our metadata analysis demonstrates that the components of Hawan are having a number of volatile oils that are specifically useful for epilepsy through one or the other mechanism of action. Due to high temperature of fire the vapors of these oils enter into the central nervous system through nasal route. The routine of performing Hawan might keep the threshold value of the therapeutic components in the body and help in preventing epilepsy. In the present manuscript authors have tried to highlight and integrate the modern and ancient concepts for treatment and prevention of epilepsy. (2015;5:33-45)

Key words: Epilepsy, Hawan, Traditional therapies, Volatile oil

Introduction

Epilepsy is a neuropsychiatric disorder with high prevalence among children and young adults. In India, about 10 million people suffer from epilepsy with a prevalence of about 1.9% in rural areas and 0.6% in urban locales. The greater prevalence of epilepsy in rural areas is a testament to impact of stigma that surrounds this illness on levels of treatment that Indians receive. About 95% of people in India who suffer from epilepsy are never treated for it and almost half of sufferers do not have access to anti epileptic drugs.¹,² It is the most expensive chronic neurological brain disorder in Europe.³,⁴ According to the World Health Organization and the World Bank, the costs of epilepsy constitute 0.5% of all diseases.⁵

In ancient as well as present times, epilepsy has been associated with religiosity⁶ and spirituality. People with epilepsy of comparable severity may differ widely in quality of life (QOL). A study considered the possible role of spirituality and it has been reported that spirituality could contribute to QOL in epilepsy.⁷ In another study, the complementary and alternative approaches have been successfully demonstrated in epilepsy management.⁸

In ancient times this disease was considered as a sacred disease and a number of superstitious measures used to be taken to prevent/cure it. Vajurveda advocates performing of Hawan every day, morning and evening to attain spiritual enlightenment, mental peace, purification of the mind and environment.⁹ From time immemorial, human beings have used smoke of medicinal plants for curing disorders. Smoke produced from natural substances has been used extensively in many cultures and famous ancient physicians have described and recommended such use. Under the Saraswati-Indus civilization 7500 BC,¹⁰ the great Rishis (saints) used to perform agnihotra-yagnas to purify the environment as described in Rigveda-the most ancient compilation of knowledge on earth by sublimating the Hawan samagri (mixture of wood with odoriferous and medicinal herbs) in the fire accompanied by the chanting of Vedic mantras described in Rigveda.¹¹ Smoke produced at high temperatures is considered as a simple way of administering a drug, which exhibits rapid pharmacological activity when inhaled. The sublimated vital elements and herbal medicines inhaled in Yagya first reach the...
Na\(^+\) and outflow of K\(^+\) through these channels that contribute to epilepsy through Hawan. The present manuscript is intended to highlight the scientific evidences that support possible prevention/cure of epilepsy. The present manuscript is designed to highlight the modern and ancient concepts for treatment and prevention of epilepsy.

**Biochemical/molecular view of epilepsy**

Epileptic seizures caused by imbalance between excitatory and inhibitory processes in the brain are due to abnormalities in the membrane properties of neurons, changes in the ionic micro environment surrounding the neuron, decreased inhibition of neurotransmission (by gamma-amino butyric acid, GABA) or enhanced excitatory neurotransmission by the acidic amino acid glutamate. All ionotropic glutamate receptors are permeable to Na\(^+\) and K\(^+\) and it is the influx of Na\(^+\) and outflow of K\(^+\) through these channels that contribute to membrane depolarization and generation of the action potential. The n-methyl d-aspartate (NMDA) receptors also has a Ca\(^{++}\) channel that is blocked by Mg\(^{++}\) ions in the resting state, but under conditions of local membrane depolarization, Mg\(^{++}\) is displaced and channel becomes permeable to Ca\(^{++}\) ions. Influx of Ca\(^{++}\) tends to further depolarize the cell, and is also thought to contribute to Ca\(^{++}\) mediated neuronal injury under conditions of excessive neuronal activation (e.g. status epilepticus) potentially leading to cell death, a process termed excitotoxicity. Neuronal firing may lead to a number of neurochemical changes and cascades of events at the cellular and molecular level like mitochondrial dysfunction, increased ROS and nitric oxide (NO) which precedes neuronal degeneration and death with possible subsequent epileptogenesis. Experimental data indicate involvement of NO in pathophysiology of epileptic seizures by decreasing synaptosomal GABA up-take and reduced availability of GABA at the synapses leading to an increase of neuronal firing. Mitochondria are emerging as key participants in cell death because their association with an over-growing list of apoptosis-related problems. Peroxidation of neuronal membranes modifies their electrophysiological properties and leads to abnormal bioelectric discharges of neurons. Among diseases involving dysfunction in the mitochondrial structures, epilepsy is prominent. Mitochondria have important vital functions such as energy production, cellular harm control, neurotransmitter synthesis and free radical production however, it is still not clear which of these functions is affected in epileptic seizures. It is interesting to note that oxygen stress and mitochondrial dysfunction may both cause and be caused by epileptic attacks. Now a day work is focused on the possible interaction between oxidative stress resulting in disturbance of physiological signaling roles of calcium and free radicals in neurons, mitochondrial dysfunction, cell damage and epilepsy. Role of oxygen stress has been well demonstrated and discussed in experimental animal model of epileptic seizures.

**Mechanism of action of present drug module for epilepsy**

The objective of the therapeutic management of seizures with medication is to control the seizures with minimal adverse side effects. Although the actions of each AED have unique characteristics and some drugs may act by multiple mechanisms, the anti-seizure actions of these drugs can be grouped into four broad categories like, modulation of voltage-dependent sodium, calcium or potassium channels; increase in GABA-ergic inhibition via actions on GABAA receptors; or on GABA synthesis, reuptake, or degradation, decreased synaptic excitation via actions on ionotropic glutamate receptors; or modulation of neurotransmitter release via presynaptic mechanisms. The drugs presently available for epilepsy are having renowned side effects like tolerance, dependence, and long term defects like psychosis, osteoporosis etc.

**What is Hawan**

Hawan is a Sanskrit word which refers to any ritual that involves making offerings into a consecrated fire. It was done by ‘Rishis’ in early period and is an important religious practice in Hinduism where they are part of most Sanskar ceremonies. They are also prevalent in current-day Buddhism and Jainism. A consecrated fire is the central element of every Hawan ritual however the procedure and items offered to the fire vary by occasions/ceremony or by the benefit expected from the ritual. A Hawan (homam, yagya or agnihotra) is a scientific experiment in which special herbal/plant medicinal preparations (Hawan Samagri) are offered in the fire of medicinal woods ig-
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the diseases of the brain. The components of Hawan are having a number of volatile oils that volatilize due to high temperature of fire. The vapors of these oils enter into the central nervous system through nasal route. The routine of performing Hawan might keep the threshold value of the therapeutic components in the body and help in preventing epilepsy (Fig. 1). The scientific studies conducted on various components of Hawan clearly demonstrates that Hawan was designed for multifaceted action to clean the environment as well as to cleanse the body of the toxins responsible for causing diseases related to brain. Hawan fumes are not only used for the disinfection of air but also it can be environmentally oppressed for the physical, mental, intellectual and spiritual development based on nano-technology of Hawan.

Scientific evidences for effect of Hawan on epilepsy

The purpose of Hawan is to enhance the energy of the human body and make it healthy and progressive. The therapeutic value of Hawan is based on the ingredients used (Table 1). One of the main ingredients used is cow “Ghee” or “Clarified Butter” which has enormous beneficial properties. This ghee when burnt like oil will produce natural fumes that heal the respiratory system and clear any blood clots and bacterium affecting the nasal, lungs and veins. In the bible, the Book of Samuels, Chapter 2, “the burning of sins, using the sticks and clarified butter” infers that ghee was frequently used for fire rituals in biblical times. Essential oil constituents that penetrate the nasal passages, skin or lungs have direct actions on the autonomic nervous system that can be grouped as relaxing or stimulating in terms of basic responses such as heart rate, blood pressure and respiration, in addition to localized dermal and bronchial effects. The direct neuro-pharmacological properties of an essential oil, aroma of the oil may exert a pleasant response via the olfactory system in turn, altering the hypothalamic control of hormones and neurotransmitters. The medium chain fatty acids in pure Ghee get converted into ketones and supply the epilepsy patient brain with the energy it needs to survive and if given on a continual basis will support processes in the brain that are involved in healing and repair.
Table 1. Therapeutic mechanism of action and active constituents of different components of Hawaiian Samagri on epilepsy

| S. No | Name/botanical name | Active component | Mechanism of action |
|-------|----------------------|------------------|---------------------|
| 1.    | Saffron *Crocus sativus* | Crocetin, picrocrocin, safranal, isophorone, 2,2,6-trimethyl-1,4-cyclohexanediol, 4-ketoisophorone, 2-hydroxy-4,4,6-trimethyl-2,5-cyclohexadien-1-one as well as 2,6,6-trimethyl-1,4-cyclohexadiene-1-carboxaldehyde | Increase in seizure threshold. Increase GABA-ergic neurotransmission. Improve tonic clonic seizures. |
| 2.    | Jatamansi *Nardostachys jatamansi* | Valeranone, Calerene, patchoul, α-gurjunene, aristolone, β-maaliene, spathulenol | Increase in seizure threshold, Inhibit the electroshock convulsions. Increase GABA, 5-HT, 5-HIAA. |
| 3.    | Coconut *Cocos nucifera* | Monounsaturated fatty acids, Saponins | Inhibit PTZ induced convulsions. Increase GABA level, serotonin level. |
| 4.    | Sesame seeds *Sesamum indicum* | 1-(5-methyl-2-furanyl)-1-propanone, 3-formylthiophene, 2-propyl-4-methylthiazole, 2-ethyl-4-methyl-1H-pyrrole, 2-ethyl-6-methylpyrazine, 2-ethyl-5-methylpyrazine, 2,6-diethylpyrazine, 2-ethyl-2,5-dimethylpyrazine, 1-(2-pyridyl) ethanone, and 1-(1-methyl-1H-pyrrol-2-yl) ethanone | Decrease ROS, MDA in epileptics. |
| 5.    | Clove *Eugenia caryophyllus* | Eugenol, acetyl eugenol, β-caryophyllene, vanillin, crategid acid, tannins, galloctannic acid, methyl salycylate, flavonoids eugenin, kaempferol, rhamnetil, eugenitin and triterpenoids like oleanolic acid. | Increase onset of convulsions. Reduce duration of convulsions. Delay onset on seizures. Increase GABAergic and glycinergic activity. |
| 6.    | Nutmeg *Myristica fragrans* | Myristicin and macelignan | Inhibit seizures. Reduce severity of seizures. |
| 7.    | Nagkesar *Mesua ferra* | Sesquiterpene, diterpenes, triterpenes, carboxylic acids and saturated hydrocarbons | Reduce HLTE. Inhibit MES induced convulsions. Increase the onset time of seizures. Decrease duration of seizure. |
| 8.    | Tagar *Valeriana wallichii* | Valerian, valipotriates and GABA sesquiterpene, diterpenes, triterpenes, carboxylic acids and saturated hydrocarbons | Sedative action. Decrease HLTE. Anticonvulsant activity. |
| 9.    | Agar *Aquilana malaccensis* | Sesquiterpenes, benzylacetone, guaiene, anisylacetone and chrome derivatives | Sedative action. |
| 10.   | Nagarmotha *Cyperus rotundus* | Cyperone, selinene, cyperene, cyperotundone, patchulenone, sugeonol, kobusone and isokobusone, pinene (monoterpene) derivatives of sesquiterpenes such as cyperol, isocyperol and cyperone. | Anticonvulsant action. |
| 11.   | Ber *Zaphus jujuba* | Flavonoids, sapoins, tannins, vitamin A, vitamin B, sugars, mucilage, calcium. Anticonvulsant action. | |
| 12.   | Phoolmakhane *Nelumbo nucifera* | N-nornuciferine, O-nornuciferine, nuciferine, and roemerine, protein, amino acids, unsaturated fatty acids, minerals, starch, and tannins. | Decrease tonic extensor convulsions. |
| 13.   | Mango *Mangifera indica* | PGG, polyphenolics, flavonoids, triterpenoids, mangiferin, catechin, isomangiferin, mangiferin, alanine, glycine, y-aminobutyric acid, Kinic acid, shikimic acid, Increase GABA levels. and the tetracyclic triterpenoids cycloart-24-en-3β, 26dial, 3-ketodammar-24 Anticonvulsant action. | Increase PTZ and MES induced convulsions. |

PTZ, pentylenetetrazole induced; GABA, gamma-aminobutyric acid; ROS, reactive oxygen species; MDA, malondialdehyde; MES, maximal electroshock seizure; HLTE, hind limb tonic extension

Another important ingredient in Hawaiian is “Camphor” from the plant *Cinnamomum camphora*. When the camphor is burnt in the fire ritual, the body’s breathing system is cleared quickly and the person will experience a “high” or elevated feeling during the ceremony.43
The use of CO₂ as a cerebral stimulant to assist the patients suffering from lack of ventilation is common in medical world. Its use to control and cure many mental disorders is also known to medical science. Small amounts of CO₂ inhaled by the persons performing Yagna acts as a stimulant and more and more aromatic fumes are inhaled which help in curing mental disorders.44

*Crocus sativus* L. contains important constituents like crocetin, picrocrocin, safranal, which are main component for characteristic aroma. Safranal is the aglycon of picrocrocin and are responsible for many pharmacological actions.45 Saffron increased the seizure threshold, the ability of saffron in to elevate seizure threshold and block pentylenetetrazole-induced (PTZ) convulsions can be attributed to its modulatory effect on GABA neurotransmission. The probable mechanism of anti epileptic activity has been shown to be by increasing the GABAergic neurotransmission. They showed that acute administration of saffron showed protection against PTZ induced convulsions. The animals showed only mild clonic convulsions followed by recovery. This may be because of their interaction with GABA benzodiazepine receptor complex. Another study also showed that pretreatment with saffron offered a significant protection both during the development of PTZ-induced kindling and also once kindling was established. It may be due to blockade of GABAergic mechanism by both acute and chronic treatment of saffron.46,47 In another study, ethanolic and aqueous extracts decreased the duration of tonic seizures.48,49 Among the constituents of saffron extract crocin is mainly responsible for the above pharmacological activities. In traditional medicine, the stigmas of this plant have been used as an anticonvulsant remedy.50 The aqueous and ethanolic extracts of *C. sativus* have shown anticonvulsant activity in PTZ and maximal electroshock seizure (MES)-induced seizures. Agents affecting the PTZ test can inhibit absence seizures. The extracts have also been shown to improve tonic clonic seizures.49 The mechanism (s) of anticonvulsant activity of the extracts is not clear. Saffron has been reported to have some behavioral effects on the central nervous system. In one study an alcoholic extract of decreased the motor activity and prolonged the sleeping time induced by hexobarbital.51 Another component of saffron, crocin did not show any effect in pentylenetetrazole-induced convulsions in mice.52

Jatamansi is a reputed Ayurvedic herb and used in various multiple formulations. Jatamansi has been used in the treatment of many disease and has several activities including anticonvulsant activity, anti-parkinson’s activity, tranquilizing activity, hepatoprotective, neuroprotective etc.53 Rao et al.54 have studied ethanol extract of the roots of *N. jatamansi* DC for its anticonvulsant activity and neurotoxicity, alone and in combination with phenytoin in rats. The results demonstrated a significant increase in the seizure threshold by root extract against MES model as indicated by a decrease in the extension/flexion ratio. Valeranone prolonged barbiturate anesthesia, impaired rotorod performance, inhibited electroshock convulsions, and potentiated the hypothermic effects.55 Limited results from behavioral tests revealed that an extract from *N. jatamansi* exhibited significant antidepressant activity.56 In another study the effect of acute and subchronic administration of alcoholic extract of the roots of *N. jatamansi* DC on nor epinephrine (NE), dopamine (DA), serotonin (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), GABA, and taurine on male albino Wistar rats was conducted. The acute oral administration of the extract did not change the level of NE and DA but resulted in a significant increase in the level of 5-HT and 5-HIAA. A significant increase in the level of GABA and taurine was observed in the drug-treated groups when compared to the controls. A 15-day treatment resulted in a significant increase in the levels of NE, DA, 5-HT, 5-HIAA, and GABA.57

Nutmeg (*Myristica fragrans*, *MF*) possesses anticonvulsant activity against PTZ, MES and lithium-pilocarpine induced seizures and lower doses were more effective in inhibiting seizures. The *MF* was without any significant effect on picrotoxin-induced convulsions and motor coordination but potentiated haloperidol induced catalepsy significantly. *MF* indicated signs of both CNS depression as well as stimulation. In various animal models of seizures used in study, the anticonvulsant activity of *MF* decreased with increasing doses. In status epilepticus, the animals receiving *MF* in a dose of 10 mg/kg reduced the severity of seizures at much earlier time. These observations support the biphasic effect of *MF* on the central nervous system. *MF* was without any effect on the duration of pentobarbitone-induced sleep. Though the MES test predicts activity against generalized tonic-clonic and cortical focal seizures and the PTZ test against absence seizures, the underlying neuronal abnormality is poorly understood. Diminution of brain GABA level has been reported after subconvulsive dose of PTZ.58 Picrotoxin, the antagonist of GABA at the postsynaptic receptors, induced seizures in all the animals and its effect was not antagonized even at the dose of 100 mg/kg suggesting that GABA may not be involved in the anticonvulsant activity of *MF*.59,60

Nagkeshwar (*Mesua ferrea*) is also a component of *Hawan samagri*. The ethanolic extract of *M. ferrea* flowers have been reported to reduce the duration of Hind limb tonic extension in a dose dependent manner against MES model and inhibited MES-induced convulsions.
Data also showed that *M. ferrea* flowers significantly increased the onset time and decreased the duration of seizures by electroconvulsive shock.\(^6\) Agarwood smoke functions as an endocrine disruptor and Agar wood have sedative property.\(^6\) Tagar wood *Valeriana wallichii* is an important component of Hawan reported to contain valepotriates and valerinic acids (with putative pharmacological activities). Root hydroethanolic extract have shown a dose dependant reduction of hind limb tonic extensor phase indicating potential antiepileptic effect on grand mal type of epilepsy in man. The extract didn’t show any adverse effects on motor coordination.\(^6\) Wood extract used for its sedative action and anticonvulsant activity\(^6\) have CNS depressant action and also have anti-convulsant effect.\(^6\)

Clove is also an important part of Hawan Samagri. Clove essential oil (CEO) has been shown to significantly increase the onset of convulsion and reduce its duration in dose dependent manner compared to the control for strychnine and picrotoxin-induced convulsion. The study indicates anticonvulsant, anxiolytic and hypnotic activity of CEO. The anticonvulsant activity of a novel compound is not measured only by its ability to prevent convulsions but also to delay the onset of seizures or to reduce death rate.\(^6\) These observations also suggest that the CEO has considerable glycnergic and GABA-ergic potentiating mechanisms. Glycine and GABA are amino acids, which act as inhibitory neurotransmitters in the central nervous system and their inhibition has been implicated in convulsions. Strychnine, a potent spinal cord convulsant, blocks glycine receptors selectively to induce excitatory response in the central nervous system. Picrotoxin, on the other hand, blocks GABAA receptors to induce generalized seizures.\(^6\) The anticonvulsant action of the CEO was probably due to inhibition of the effects of strychnine and picrotoxin at glycine and GABAA receptor sites respectively. CEO has also been shown to act against neurotoxic death usually caused by chemical convulsants.\(^6\)

Nagaramtha (*Cyperus rotundus*) is an important herb in the Ayurveda.\(^6\) Cyperotundone and α-cyperone compounds have been reported from essential oil of C. rotundus rhizomes. The effect of *Cyperus esculentus* and *Cyperus rotundus* essential oils has been reported as anticonvulsant (MES produced convulsion). The results showed dose dependent activity in the maximal electroshock (MES) induced convulsion in comparison to Diclofenac sodium.\(^7\) Nagarmotha is also known to have Iso curcumenol used as sedative.\(^7\) Nelumbo nucifera have reduced the tonic extensor convulsion induced by MES.\(^7\) The wood of *Ziziphus jujuba* is used in Hawan and the hydro-alcoholic extract of *Z. jujuba* demonstrate the anticonvulsant effect as well as amelioration of cognitive impairment induced by seizures in rats.\(^7\)

The ethanol extract of *Cocos nucifera* was tested for possible pharmacological effects on experimental animals. Pretreatment with extract caused significant protection against PTZ induced convulsions. The behavioral studies on mice indicate CNS depressant activity of the ethanol extract of *C. nucifera* EECN potentiated significantly the duration of pentobarbital, diazepam and meprobamate induced sleep in mice, suggesting probable tranquilizing action as well as CNS depressant action.\(^7\) It was found to increase the brain serotonin and GABA level in mice (unpublished data). Therefore, profound analgesic and anticonvulsant activities produced by extracts may be related to the increased brain serotonin and GABA level in mice.\(^7\)

The mechanism whereby extract depressed awareness, touch and pain responses, righting reflex, pinna reflex, corneal reflex, and grip strength may also be due to synapse block of the efferent pathway or by overall CNS depressant action.\(^7\) The exact chemical components responsible for such CNS depressant activity of extract are not known. Preliminary phytochemical studies revealed that it contains saponin which might be responsible for anticonvulsant properties of extract.\(^7\) The extracts also enhanced sleeping time, analgesic, and anti-convulsant activities and reduced different behavioral reflexes. In a study 1,2,3,4,6-penta-O-galloyl-β-d-glucopyranose (PGG) isolated from methanolic leaf extracts of *Mangifera indica* showed significant and dose-dependent inhibition of *Mangifera indica* showed significant and dose-dependent inhibition of PTZ and MES-induced convulsions. Furthermore, PGG administration showed significant decrease in the locomotor activity as an indication of its CNS-depressant property; also, PGG has significantly increased the GABA levels in the cerebellum and whole brain other than the cerebellum. In conclusion, PGG isolated from *M. indica* showed potent anticonvulsant activity, and possible mechanism may be due to enhanced GABA levels in the brain.\(^7\)

The pathogenesis of epilepsy has been strongly affected free radicals and authors have tried to hypothesize antioxidant action (Table 2) of each component of Hawan Samagri. Components of Hawanlike Guggal, Saffron, Almond, Jatamansi and Coconut scavenge free radicals and hence might be helpful to stop the pathogenesis of the disease. *Sesamum indicum*, Sesamin is a well-known antioxidant from sesame seeds and it scavesnge free radicals and significantly decreased ROC.\(^8\)

Nitric Oxide is an important neurotransmitter and also related to synaptic plasticity, neuronal excitability regulation, and epileptic activity.\(^8\) NMDA glutamate receptors activate calcium release via NMDA receptor that consequently activates calcium calmodulin pathway to increase neuronal nitric oxide synthase protein expression.
Table 2. Components of Hawan Samagri along with probable multiple mechanism of action

| S. No | Name/botanical name         | GABA/serotonin/5-HIAA | Antioxidant activity | Nitric oxide level | NMDA |
|-------|-----------------------------|----------------------|----------------------|--------------------|------|
| 1.    | Saffron (Crocus sativus)    | ×                    | ×                    | ×                  |      |
| 2.    | Jatamansi (Nardostachys jatamansi) | ×     | ×                    |                    |      |
| 3.    | Coconut (Cocos nucifera)    | ×                    | ×                    |                    |      |
| 4.    | Sesame seeds (Sesamum indicum) | ×    | ×                    |                    |      |
| 5.    | Clove (Eugenia caryophyllus) | ×                    | ×                    |                    |      |
| 6.    | Nutmeg (Myristica fragrans) | ×        | ×                    |                    |      |
| 7.    | Nagkesar (Mesua ferra)      | ×        | ×                    |                    |      |
| 8.    | Tagar (Valeriana wallichii) | ×        | ×                    |                    |      |
| 9.    | Agar (Aquilana malaccensis) | ×        | ×                    |                    |      |
| 10.   | Nagarmotha (Cyperus rotundus) | ×    | ×                    |                    |      |
| 11.   | Ber (Ziziphus jujube)       | ×        | ×                    |                    |      |
| 12.   | Phoolmakhane (Nelumbo nucifera) | ×    | ×                    |                    |      |
| 13.   | Mango (Mangifera indica)    | ×        | ×                    |                    |      |
| 14.   | Ghee                        | ×        | ×                    |                    |      |
| 15.   | Camphor laurel (Cinnamomum camphora) | ×    | ×                    |                    |      |
| 16.   | Guggal (Commiphora weightii) | ×    | ×                    |                    |      |
| 17.   | Almond (Prunus amygdalus)   | ×        | ×                    |                    |      |
| 18.   | Gular (Ficus racemosa)      | ×        | ×                    |                    |      |
| 19.   | Chirongi (Bauchanania lanzari) | ×    | ×                    |                    |      |
| 20.   | Kapurkachri (Hedychium spicatum) | ×    | ×                    |                    |      |
| 21.   | Red sandal (Pterocarpus santalinus) | × | ×                |                    |      |

NMDA, n-methyl d-aspartate

and NO increment in brain different area. The higher NO level is able to increase the induction of generalized epilepsy. NO is known as a molecule that can easily react with O2− radicals in the brain and reduce the oxidative stress induced damage via deleting free radicals.82 It has been reported in a study that Hawan causes a reduction in NO levels in the atmosphere.83 The reduction in level of NO may be helpful in reducing the epileptic seizures. Other components of Hawan samagri have also been reported to reduce NO levels through various mechanisms (Table 2). Methanol extracts of Nardostachys jatamansi have been shown to exert inhibitory effect on nitric oxide (NO) production. The NO level decreased from 100% to 5.8% and this decreased levels could prove to have antiepileptic effect. NJ extracts down regulated iNOS in a dose-dependent manner.84 In another study saffron extract has been related to a decrease in the NO concentration.85 Lotus seed extract have been shown to possess free radical scavenging properties.86 Results showed that all the extracts inhibit nitric oxide accumulation and thus could be helpful in antiepileptic action. Results of a study showed that clove oil and its major constituent, eugenol, were the most active inhibitors of the nitric oxide production.86 C. rotundus rhizomes ethanolic exhibits its scavenging effect in concentration dependent manner on superoxide anion radicals, hydroxyl radicals, nitric oxide radical, hydrogen peroxide and it had a property of metal chelating and reducing power. This antioxidant activity could be helpful in preventing epilepsy.89 The methanol and EtOAc fraction of C. wightii has been shown to inhibit the NO formation by down regulation of iNOS and COX-2 gene expression.90 Guggulipid prevented the production of NO and ROS generation91 in rat astrocytoma cell line. Nishaa et al.92 and K. Kamalakara et al.93 have reported nitric oxide scavenging activity of M. ferrea pet ether and methanol extract. The biflavone and tannin fraction form Ficus racemosa bark extract has shown inhibitory action on nitric oxide and hydroxyl radicals in in-vitro studies.94 Cyperus rotundus extract suppressed the production of NO and the inhibition of NO production by the extract was due to the suppression of iNOS protein, as well as iNOS mRNA expression, determined by Western and Northern blotting analyses, respectively.95 Also, other constituents of C. rotundus including sugeonol and cyperone, could yield a modulatory effect on glutaminergic system, especially lowering the opening of NMDA receptor channels,96 which could lead to anticonvulsant effects. Ziziphus jujube (SZS) has been
shown to have sedative, analgesic and antiseizure effects.\textsuperscript{97-100} NMDA-induced intracellular Ca\textsuperscript{2+} increase was almost completely abolished by SZS\textsuperscript{101} a qualitatively stronger effect than other herbs that only partially diminished the Ca\textsuperscript{2+} response. The subsequent ROS production and cell death was also reduced by SZS. Similar to RP, SZS also suppresses glutamate release and may suggest additional protection for excitotoxicity.\textsuperscript{101} Ethanol extract of Valeriana abolished cell death in NMDA-stimulated mouse cortical neurons.\textsuperscript{102} In the same study, kainate-induced cell death was marginally decreased only, suggesting the selective effect of extract on NMDA-R over other glutamate receptor subtypes.\textsuperscript{102} An inhibitory effect on glutamate binding of NMDA-R was only observed when isoborneol was present at a high concentration.\textsuperscript{103} It is therefore likely that the NMDA-R-selective cellular effects reported by Jacobo-Herrera et al. were attributed to a high concentration of isoborneol or other extract constituents yet to be identified in the ethanol extract.\textsuperscript{102} Moreover, the use of whole extract in targeting NMDA-R activity is cautioned due to the multi-faceted effect on all glutamate receptor subtypes, ionicotropic and metabotropic. Evidence of the inhibition of postsynaptically located NMDA and kainite receptors by a hydro-ethanolic Crocus sativus L extract have been reported, which is partly mediated by trans-cocetin. These mechanisms contribute to the neuroprotective effect of saffron.\textsuperscript{104} Saffron has turned out to be the antagonist of postsynaptic NMDA receptors.\textsuperscript{105} Several studies have demonstrated that oxygen free radicals formed by xanthine/xanthine oxidase (X/XO) may be involved in the NMDA-mediated neurotoxicity and inhibitory action of glutamate uptake in glial cells.\textsuperscript{106-108} The results of another study showed that eugenol attenuated NMDA induced acute neurotoxicity and inhibited NMDA-induced elevation in neuronal Ca\textsuperscript{2+} uptake. Furthermore eugenol prevented acute neuronal swelling and reduced neuronal death and significantly reduced oxidative neuronal injury induced by X/XO.\textsuperscript{109} Eugenol increased the degree of INa activation and reversibly suppressed non-activating I\textsubscript{Na}. In addition, at higher concentrations eugenol diminished L-type Ca\textsuperscript{2+} current and delayed rectifier K+ current. In pilocarpine-induced seizures in rats, a lower seizure severity and mortality was noted, though no shorter seizure latency effect was observed. The mechanism of action was deduced to be the synergistic blocking of I\textsubscript{Na} and non-activating I\textsubscript{Na} affecting neuronal spontaneous action potentials.\textsuperscript{110} Mangifera indica L. extract attenuates glutamate-induced neurotoxicity on neurons.\textsuperscript{111}

Apart from the significant physical and medical applications like cleansing of the environment, curing bodily ailments and augmenting vitality and physical potentials, yagyopat is also found to be of immense use in treatment of psychosomatic disorders and psychological and psychiatric problems. The sublimated vital elements and herbal medicines inhaled in Yagya first reach the brain and then to the lungs and other parts, the gross as well as the subtle components of the body. Thus, it has a direct healing effect on brain diseases and complexities. The body absorbs the heat of its sacrificial fire and inhaled the vapors of sublimated herbs through the skin-pores and respiration. This elevated level of antioxidants upon reaching the brain and the nerves eliminates the major cause of mental tensions. The specific energy currents reduced by yagyagni and mantra shakti have significant remedial effect on the disorders and diseases ranging from headache, migraine, cold to mental dullness, intellectual deficiencies, depression, insomnia, intemperance, epilepsy, schizophrenia and varieties of manias.\textsuperscript{112}

Conclusions

From the metadata analysis it seems that Hawan has been designed by the ancient scholars to fight with a plethora of diseases related to brain. As explained in text, more than 70% of the components of Hawan samagri are having a number of volatile oils that volatilize due to high temperature of fire. Most of the components have been found to be having anticonvulsant activity through one or the other mechanism. The action of maximum number of herbs is benzodiazepines, Phenobarbital, valproate like action that enhances GABA-ergic inhibition. It is quite likely that the other volatile components those have not been explored for anticonvulsant action could add to further therapeutic antiepileptic action. The components of Hawan seem to have multiple action in preventing epilepsy through scavenging of free radicals, increase in level of antioxidants, decrease in level of nitric oxide and other underlying mechanisms. From the pharmacological potentials of the components it can be concluded that the routine of performing Hawan might keep the threshold value of the antiepileptic elements in the body and help in preventing epilepsy however concerted efforts are required to prove the hypothesis.

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