Epilepsy is the most prevalent neurological disease and is characterized by recurrent seizures. Epilepsy affects about 50 million people worldwide. Ineffectiveness of the drugs, along with their serious side effects make any safe and effective herbal medicine an attractive possibility.
EPILEPSY AND OXIDATIVE STRESS

- Oxidative stress is both a consequence and contributor of epileptic seizures.
- Therefore diets, environmental factors, and therapies which reduce oxidative stress in the body, and particularly the brain, may help control seizures.

ION CHANNELS AND EPILEPSY

- Voltage-gated and ligand-gated ion channels on neurons control the delicate balance between neuronal excitation and resting states in the brain.
- Changes in expression of voltage-gated ion channels, especially sodium and calcium channels, and GABA and glutamate ligand-gated channels appear to play roles in the occurrence of epilepsy.
- Many herbs are known to act via all of these mechanisms.

ALLERGIES, DIETS, AND STRESS

- Though not 100% curative, removal of all food and environmental allergens may reduce oxidative stress in entire body, including the brain.
- Gluten sensitivity may trigger seizures and gluten avoidance should be considered for epileptic patients.


VACCINES AND SEIZURES

- There are several published studies reporting an increased risk of seizures following vaccination.
- Some researchers suggest that a “cytokine storm” situation where elevated cytokine/chemokine responses to the vaccine activated NF-κB raising febrile reactivity.
VACCINES AND SEIZURES

- An MMRV vaccine released in Germany in 2009 found the main risk period to be the first 5-12 days post immunization.


- Australia epidemiology officials reported a significant increase in febrile seizures in children under 5, with the CSL trivalent influenza vaccine.


VACCINES AND SEIZURES

- Other studies have found small but statistically significant increase in the risk of febrile seizures following some forms of the MMRV vaccine.

VACCINES AND SEIZURES

- In 2010, use of seasonal trivalent influenza vaccine was suspended for children <5 years of age.


VACCINES AND SEIZURES

- One cohort study examining 323,247 US children from the Vaccine Safety Datalink born from 2004 to 2008, was analyzed looking for an association between the timing of childhood vaccination and the first occurrence of seizure.

- The study reported that infants displayed no association of 1st onset seizure to the timing of vaccinations,

- But in the 2nd year of life, there WAS an increased incidence of 1st onset of seizures following MMR vaccination.

VACCINES AND SEIZURES

- To determine if underlying physiologic or immunologic factors contributed to vaccine-triggered febrile seizures, Kaiser Permanente of Southern California reviewed children aged 6 months to 3 years over an 8 year period having been diagnosed with a 1st onset febrile seizure.

- Of the 3348 incidents of Febrile Seizures 11% were Vaccine Associated and 89% were not.

- Other variables that appeared to increase the risk of FS include low gestational age, winter month vaccination, and children with 1 minute Apgar score of less than 3.


DRAVET SYNDROME EPILEPSY

- Dravet Syndrome is an epileptic encephalopathy caused by SCN1A-mutations associated with seizure onset after vaccination in infants.

- Although Dravet syndrome is a rare genetic epilepsy syndrome, one study found that 2.5% of post-vaccination seizures occurred in children with this disorder.

- Knowledge on the specific characteristics of vaccination-related seizures in this syndrome might promote early diagnosis and indirectly, public faith in vaccination safety.

CARNITINE AND EPILEPSY

- Carnitine deficiency is relatively common in epilepsy, especially in those with concomitant intellectual disability, children with low body weight, and those on long term antiepileptic drugs.

- One study found that 17% of children with epilepsy displayed carnitine deficiency.

- Because supplementation with carnitine will do no harm, carnitine might be implemented for all pediatric epileptics.


KETOGENIC DIET FOR EPILEPSY

- The ketogenic diet (KD) is a high-fat, low-carbohydrate diet that induces a metabolic response similar to fasting.

- KD was established as effective in treating medically refractory epilepsy since the 1920s.

- The bulk of the research has shown at least 50% efficacy in controlling some types of seizures.


Cochrane Database Syst Rev. 2012 Mar 14;3:CD001903. Ketogenic diet and other dietary treatments for epilepsy. Levy RG1, Cooper PN, Giri P.

KETOGENIC DIET AND EPILEPSY

- Fatty acids are the most important constituent of the KD, with the aim of approximately 90% of calories coming from fat, and continued for 24 months.

- Polyunsaturated Fatty Acids (PUFAs) have anticonvulsant properties and reduce the complications associated with the high-fat diet.

- PUFA-enriched diet therapy is likely to increase the efficacy of diet therapy and reduce complications of a high-fat diet in children with refractory epilepsy.

THE KETOGENIC DIET

THE DAILY DIET INCLUDES EATING:

- Avocados
- Fish
- Nuts
- Coconut milk
Some researchers report that many children with seizures prefer high fat foods, and this may be indicative of a higher success rate of a ketogenic diet.


The mechanism that improves seizure control involves oxidation of fatty acids yielding ketone bodies, which appear to modulate neurotransmitters and exert protective antioxidant effects on neurons, although the extent of the biochemistry is not yet understood.

KETOGENIC DIET RELATED DIETS

- A modification of the KD is the use of medium chain triglycerides (MCTs) as an alternative fat source, introduced in the 1970s.

- A modified Atkins diet is another alternative.

- A low glycaemic index diet is another alternative.

MCT DIET FOR EPILEPSY

- The medium-chain triglyceride diet (MCTD) attempts to improve the palatability of the KD by allowing more carbohydrates and protein yet preserving ketosis.

- Although initially found equally effective as the classic KD, use of the MCTD often causes frequent gastrointestinal side effects such as cramps, diarrhea, and vomiting, and may actually be less desirable in the long run.
MCT DIET AND EPILEPSY

- MCT Diet can still promote ketosis, even though the diet allows some proteins and carbs, because MCT oils are more ketogenic than long-chain triglycerides.


MCT DIET FOR EPILEPSY

- One study of 50 patients reported excellent seizure control for children with refractory epilepsy, minimal S/A and remains viable for those with large appetites, who tolerate more calories, or cannot follow the restrictions of the classic KD.

KD CLINICAL TRIAL

- A multicenter study involving 315 epileptic children was conducted in Scandanavia and reported the KD to be effective and well tolerated, even for patients with therapy-resistant epilepsy.
- Long-term efficacy of KD was comparable or even better than Anti-Epileptic Drugs.
- The possible SA of kidney stones was reported to be mitigated by the addition of potassium citrate supplements.
- The data indicated that response was most predicted by seizure-frequency, but not by age, seizure-type or etiology.


KETOGENIC DIET FOR DRAVET SYNDROME

- There is strong evidence for the use of the ketogenic diet in Dravet syndrome.
- A study of 32 children with genetically confirmed DS were analyzed as to age at treatment initiation, treatment lag, seizure frequency, different seizure types, especially prolonged seizures and status epilepticus.
- The Ketogenic diet was proven an effective treatment and should be considered as an early treatment option in infants with DS.

FATTY ACIDS AND EPILEPSY

- *Nigella sativa* oil has been used for thousands of years for culinary and medical purposes.

- *Nigella* seed oil has anticonvulsant and antioxidant activities reported to have anti-epileptic effects.

- *Nigella* oil decreases oxidative injury in kindled mice suggesting neuroprotective ability via inhibition of reactive oxygen species.


NIGELLA FOR EPILEPSY
Grape Seeds – Vitis vinifera

- Grape seed extract has neuroprotective activities due to its antioxidant properties.
- Animal models of epilepsy suggest neuroprotection via inhibition of Nitric Oxide pathways.


HISTAMINE ANTAGONISTS AND EPILEPSY

- H(3) antagonists increase the release of brain histamine, acetylcholine, noradrenaline, and dopamine, neurotransmitters that are known to modulate cognitive processes.
- The ability to release brain histamine supports attention and vigilance, but histamine also modulates other cognitive domains such as short-term and long-term memory.
- Histamine may also play a role in Epilepsy.
HISTAMINE ANTAGONISTS AND EPILEPSY

- Temporal Lobe Epilepsy pathogenesis is multifaceted
- Histamine activity in the CNS is one possible trigger.
- H3 receptor antagonists are therapeutic in some cases

Kainic acid is an excitotoxin that provokes neuronal inflammation and death, and is used to trigger seizures in animal research models of seizure.

Pretreatment with H3 antagonists can protect against Kainic-acid induced seizures.

Both migraine and epilepsy may be preceded by an olfactory aura.

Zh Nevrol Psikhiatr Im S S Korsakova. 2014;114(4 Vypusk 2 Epilepsy):82-88. Migraine and epilepsy: an attempt to analyze disorders in Pontius Pilate in the romance "Master and Margarita" by M. Bulgakov, Damulin IV1.

Seizures triggered by light or smell are referred to as “Reflex Epilepsy”.

Although poorly understood and presumed rare, seizures are known to be triggered by smell or olfactory stimulation.

Injecting kainic acid into an olfactory bulb in rats initiates seizures which are first propagated to the amygdala and the hippocampus unilaterally, and then propagated to the unilateral sensori-motor cortex.

**OLFACTORY SEIZURES AND INVOLVE LIMBIC STRUCTURES**

**AND OBSERVED CLINICALLY AS 3 DISTINCT STAGES**

- **Stage 1** - staring
- **Stage 2** - masticatory movements
- **Stage 3** - rearing and falling (in rats)


**OLFACTORY REFLEXES AND SEIZURES**

- **Artemesia** is mentioned in folkloric herbals as possibly triggering seizures.

- **Lavendula** is mentioned as an aroma that can possible abort or abolish a seizure at its onset.
Animal studies have investigated common essential oils for their effects on motor and behavioral activity, initiation of tonic-clonic seizures, seizure latency and severity, and percentage of survival.


- *Rosmarinus officinalis*, *Ocimum basilicum*, *Mentha spicata*, *Mentha pulegium*, *Lavandula angustifolia*, *Mentha piperita*, *Origanum dictamus*, and *Origanum vulgare* essential oils were inhaled 60 minutes prior to intraperitoneal injection of a lethal dose of PTZ.

- Mentha was the most effective with all mice surviving
GARDENIA AROMA AND SEIZURES

- Gardenia are beloved aromatic flowers and have been used in the Middle East to treat epilepsy and mania.
- Gardenia lucida aromatic oleo gum resin is the source of essential oil shown to significantly potentiate the barbitone induced hypnosis and offered significant protection against the intensity and frequency of convulsions and mortality rate in both the convulsant models.

- A significant decrease in locomotion, motor impairment and loss of gripping reflex was also observed.
- The essential oil of the oleo gum resin of Gardenia lucida is a CNS depressant and anticonvulsant with central muscle relaxant properties.

DENNETIA AROMA AND SEIZURES

- Essential oils from *Dennetia tripetala*, an Annonaceae family plant have been shown to have anticonvulsant effects.


VETIVERIA AND SEIZURES

- *Vetiveria zizanioides* is an aromatic grass commonly known as Vetiver, used in Ayurvedic medicine for seizures.
- Anticonvulsant activity has been demonstrated in mice.

LAVENDULA AND SEIZURES

- Repeated application of *Lavandula officinalis* has been recommended for a long time in Iranian traditional medicine for epilepsy and dementia.
- *Lavandula officinalis* extract shows anti-epileptogenic properties greater than those of valproate.
- *Lavandula officinalis* suppresses brain nitric oxide elevations in kindled mice more so than valproate.
- *Lavandula officinalis* also decreases brain MDA levels.


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CANNABIDIOL AND SEIZURES

- Cannabidiol is the major nonpsychotropic compound of *Cannabis sativa*.
- Growing evidence suggests Cannabidiol to have anticonvulsant properties with a good safety profile.
- Cannabidiol is a possible therapy for treatment-resistant epilepsy.

CANNABINOID PATHWAYS AND SEIZURES

- One mouse study dosed a cannabis-derived drug rich in cannabidivarin and containing cannabidiol.
- Anticonvulsant effects were demonstrated on in various types of induced seizures.

Cannabidivarin-rich cannabis extracts are anticonvulsant in mouse and rat via a CB1 receptor-independent mechanism. Hill TD1, Cascio MG, Romano B, et al

CANNABINOID PATHWAYS AND SEIZURES

- There are anecdotal case reports of cannabinols and other marijuana-based medicines reducing seizures dramatically.
- One published study reports a pediatric case where seizures were reduced from 50 per day down to 2-3 per month, and the patient was weaned from anti-epileptic drugs.

### MATERIA MEDICA

Many Herbs Historically Recommended for Seizures, have now been found to act as GABA agonists (amongst other mechanisms).

- **Scutellaria lateriflora** (Skullcap)
- **Valerian officinalis** (Valeriana)
- **Hypericum perforatum** (St Johnswort)
- **Withania somniferum** (Ashwagandha)

### MATERIA MEDICA

Other herbs may act as neuroprotectants, anti-oxidants, and anti-inflammatories and reducing hyperexcitability.

- **Withania somniferum** (Ashwagandha)
- **Panax ginseng** (Ginseng)
- **Centella asiatica** (Gotu Kola)
- **Ganoderna lucidum** (Reishi)
- **Trichosanthes**
MATERIA MEDICA

- Herbs may alter the ratios between excitatory and inhibitory neurotransmitters, reduce hyperexcitability, reduce inflammatory processes, and other mechanisms simultaneously.

TRICOSANTHES TRICUSPIDATA

- *Tricosanthes tricuspidata* mediates oxidative stress and may reduce epileptic seizures.
- One animal investigation suggested that oxidative stress and lipid peroxidation goes up at the time of a seizure and that *Trichosanthes tricuspidata* attenuates oxidative stress as evident by decreased lipid oxidative damage and nitrite-nitrate content and restored the level of enzymatic antioxidant defenses in hippocampus.

TRICOSANTHES TRICUSPIDATA

- Involvement of free radicals during epilepsy is further confirmed by histopathological analysis which showed the loss of neuronal cells in hippocampus CA1 and CA3 pyramidal region. Our findings strongly support the hypothesis that TTME has anticonvulsant activity accompanied with the strong antioxidant potential plays a crucial role in reducing the oxidative stress produced by seizure.

ZINGIBER OFFICINALE

- *Zingiber officinale* or ginger, is a well-known antioxidant herb with reported neuroprotective effects.
- Ginger was investigated in an animal model of seizure disorders and was shown to have an anticonvulsant effect and increased the seizure threshold.
- The proposed anticonvulsant effects include interactions with inhibitory and excitatory system, antioxidant mechanisms, and calcium channel inhibition.

GANODERMA LUCIDUM

- The Reishi mushroom, *Ganoderma lucidum*, also referred to as Lingzhi in China, has long been used as an energy and vitality tonic and immune modulator.

- *Ganoderma lucidum* may protect hippocampal neurons by promoting neurotrophin-4 expression and inhibiting N-Cadherin expression.


PANAX GINSENG

- *Panax ginseng*, a well-known immune and endocrine modulating herb and has also been shown to help protect from hippocampal damage in cases of status epilepticus.

- Oligosaccharide fractions have displayed anticonvulsant and neuroprotective actions.

- *Panax*, at the least, can do no harm and might be initiated for such patients while all options are being explored.

**WITHANIA SOMNIFERA**

- *Withania somnifera*, Ashwagandha, of the Solanaceae Family has been historically used for stress symptoms, insomnia, and epilepsy.
- The Withanolides, are credited with many medicinal effects.
- *Withania* has been found to compare favorably to phenytoin in controlling seizures.
- *Withania* is considered safe and to have neuroprotective properties as well.


**Salvia miltiorrhiza**

- *Salvia miltiorrhiza*, Danshen or Chinese Red Sage is used in TCM to treat neurological, cardiovascular, and cerebrovascular disorders and is included in traditional formulations for seizures.
- Tanshinone IIA is a prescription drug in China to address cerebral ischemia
- Tanshinone IIA has demonstrated anticonvulsant properties in animal studies modifying seizural thresholds.

**FICUS SUR FORSSK**

- *Ficus* species are important medicines worldwide.
- An African species, *Ficus sur* Forssk is reported to have anticonvulsant activity with GABAergic, glycinergic, serotonergic and glutaminergic system interactions.


**CRINUM GLAUCUM**

- *Crinum glaucum*, an Amaryllidaceae family plant whose bulb is used in folk medicine to treat cough, asthma and convulsions.
- An animal model of epilepsy revealed likely GABAnergic, nitrergic and glutaminergic systems to exert its effects.

PASSIFLORA INCARNATA

- **Passiflora incarnata** has been used historically for epilepsy, insomnia, neurosis and neuralgia, stress, muscle tension and anxiety, but quality clinical trials are lacking.


HYPERICUM PERFORATUM

- **Hypericum perforatum** has been researched for anxiety and depression.

- **Hypericum scabrum** is a lesser known species reported to have anticonvulsant effects via GABAnergic effects.

- Nitric oxide radical scavenging is another possible mechanism involved in the anti-epileptic effects.

**ACORUS TATARINOWII**

- Acorus tatarinowii, contains Alpha (α)-asarone a TCM for treating epilepsy, cough, bronchitis, and asthma.
- α-asarone affects GABAA receptors as well as voltage-gated Na(+) channels inhibiting the spontaneous firing of output neurons treating cough and raising the seizural threshold.

*Front Pharmacol*. 2014 Mar 11;5:40. Identification of both GABAA receptors and voltage-activated Na(+) channels as molecular targets of anticonvulsant α-asarone. Wang ZJ1, Levinson SR2, Sun L1, Heinbockel T1

**VISCUM AND PHORADENDRON**

- Mistletoes of the Loranthaceae and Viscaceae are hemiparasitic plants and important medicinal herbs presently processed into parental and other forms of anticancer medicine.
- Folkloric applications are broad and include epilepsy.
HYOSCYAMUS NIGER

- **Hyoscyamus niger** is nightshade with toxic and hallucinogenic potential but long used as a CNS medicinal herb as well. Long central nervous system have been known for many years.
- Animal studies show anticonvulsant activity against picrotoxin-induced seizures in mice.
- The exact mechanism(s) by which the plant exerts its anticonvulsant activity is not determined yet.


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LAVENDULA

- Animal studies have shown Lavender to protect from chemically-induced seizures.

GLYCYRRHIZA GLABRA

- Glycyrrhiza, Licorice has reported anti-convulsant activity via antioxidant neuroprotection.
- Licorice attenuates lipid peroxidation due to increase in antioxidant enzymes.
- Licorice protect the brain from ROS induced neuronal damage in animal models of seizure.

*Indian J Pharmacol*. 2013 Jan-Feb;45(1):40-3. Anti-convulsant action and amelioration of oxidative stress by Glycyrrhiza glabra root extract in pentylenetetrazole-induced seizure in albino rats. Chowdury B1, Bhattamisra SK, Das MC.

HAPPY TRAILS!!