



EPILEPSY

BOTANICAL AND NATURAL INTERVENTIONS

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EPILEPSY

- ▶ 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.

Adv Exp Med Biol. 2014;813:211-29. *Are alterations in transmitter receptor and ion channel expression responsible for epilepsies?* Powell KL1, Lukasiuk K, O'Brien TJ, et al.

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.

Int J Neurosci. 2014 Dec 18. *Cryptogenic focal epilepsy and "hidden" celiac disease in adulthood: a causal or accidental link?* Casciato S1, Morano A, Albin M, et al.

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- κ B 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.**

Vaccine. 2014 Feb 3;32(6):645-50. *Risk of febrile convulsions after MMRV vaccination in comparison to MMR or MMR+V vaccination.* Schink T1, Holstiege J2, Kowalzik F3, et al.

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

Vaccine. 2014 Jun 24;32(30):3861-8. *Evaluation of the bioactivity of influenza vaccine strains in vitro suggests that the introduction of new strains in the 2010 Southern Hemisphere trivalent influenza vaccine is associated with adverse events.* Rockman S1, Dyson A2, Koernig S2, et al.

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.**

CMAJ. 2014 Aug 5;186(11):824-9. *Risk of febrile seizures after first dose of measles-mumps-rubella-varicella vaccine: a population-based cohort study.* MacDonald SE1, Dover DC2, Simmonds KA2, Svenson LW2.

VACCINES AND SEIZURES

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

Vaccine. 2014 Apr 17;32(19):2204-8. *General practice encounters following seasonal influenza vaccination as a proxy measure of early-onset adverse events.* Dey A1, Gidding HF2, Menzies R3, McIntyre P4.

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.**

Pediatrics. 2014 Jun;133(6):e1492-9. *Timely versus delayed early childhood vaccination and seizures.* Hambidge SJ1, Newcomer SR2, Narwaney KJ2, et al

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.

Vaccine. 2014 May 7;32(22):2574-81. *Exploring the risk factors for vaccine-associated and non-vaccine associated febrile seizures in a large pediatric cohort.* Tartof SY1, Tseng HF2, Liu AL3, et al.

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.

PLoS One. 2013 Jun 6;8(6):e65758. *Prevalence of SCN1A-related dravet syndrome among children reported with seizures following vaccination: a population-based ten-year cohort study.* Verbeek NE1, van der Maas NA, Jansen FE, et al.

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.

Brain Dev. 2014 Dec 26. pii: S0387-7604(14)00289-7. *Carnitine deficiency: Risk factors and incidence in children with epilepsy.* Fukuda M1, Kawabe M2, Takehara M2 et al

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.

J Hum Nutr Diet. 2010 Apr;23(2):113-9. *Efficacy of dietary treatments for epilepsy.* Neal EG1, Cross JH.

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

Epilepsy Res. 2014 Dec;108(10):1912-6. *Ketogenic diet in pediatric patients with refractory focal status epilepticus.* Caraballo RH1, Flesler S2, Armeno M3, et al.

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

KETOGENIC DIET AND EPILEPSY

- **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.**

Seizure. 2014 Nov 8. pii: S1059-1311(14)00300-8. *Exploring the relationship between preferences for high fat foods and efficacy of the ketogenic and modified Atkins diets among children with seizure disorders.* Amari A1, Turner Z2, Rubenstein JE2, Miller JR3, Kossoff EH2.

KETOGENIC DIET AND EPILEPSY

- **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.**

Clinics (Sao Paulo). 2014 Dec;69(10):699-705. *Neurobiochemical mechanisms of a ketogenic diet in refractory epilepsy.* Lima PA1, Sampaio LP2, Damasceno NR3

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.**

Biomed J. 2013 Jan-Feb;36(1):9-15. *Medium-chain triglyceride ketogenic diet, an effective treatment for drug-resistant epilepsy and a comparison with other ketogenic diets.* Liu YM1, Wang HS.

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.**

Epilepsia. 2008 Nov;49 Suppl 8:33-6. *Medium-chain triglyceride (MCT) ketogenic therapy.* Liu YM1.

KD CLINICAL TRIAL

- ▶ A multicenter study involving 315 epileptic children was conducted in Scandinavia 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.

Eur J Paediatr Neurol. 2015 Jan;19(1):29-36. *Effectiveness of the ketogenic diet used to treat resistant childhood epilepsy in Scandinavia.* Hallböök T1, Sjölander A2, Åmark P3, et al.

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.

Epilepsy Res. 2015 Jan;109:81-9. *Efficacy and tolerability of the ketogenic diet in Dravet syndrome - Comparison with various standard antiepileptic drug regimen.* Dressler A1, Trimmel-Schwahöfer P1, Reithofer E1, et al.

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.**

Epileptic Disord. 2013 Sep;15(3):295-301. *The clinical outcome of adjuvant therapy with black seed oil on intractable paediatric seizures: a pilot study.* Shawki M1, El Wakeel L, Shatla R, et al.

Neuropharmacology. 2005 Sep;49(4):456-64. *Antiepileptogenic and antioxidant effects of *Nigella sativa* oil against pentylenetetrazol-induced kindling in mice.* Ilhan A1, Gurel A, Armutcu F, Kamisli S, Iraz M.

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.

Acta Physiol Hung. 2013 Jun;100(2):224-36.
The involvement of iNOS activity in the anticonvulsant effect of grape seed extract on the penicillin-induced epileptiform activity in rats. Per S1, Tasdemir A, Yildirim M, et al.



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

HISTAMINE ANTAGONISTS AND EPILEPSY

- ▶ 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.

Brain Res. 2014 Sep 18;1581:129-40. *Histamine H3 receptor antagonism by ABT-239 attenuates kainic acid induced excitotoxicity in mice.* Bhowmik M1, Saini N1, Vohora D2.

OLFACTORY REFLEXES AND 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.*

OLFACTORY REFLEXES AND SEIZURES

- ▶ 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.

Clin EEG Neurosci. 2014 Jul 9. *Reflex Epilepsy Triggered by Smell. Ilik F1, Pazarli AC2*

OLFACTORY/LIMBIC SEIZURES

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)

Brain Res. 1995 Sep 25;693(1-2):207-16. *Limbic seizures originating in the olfactory bulb: an electro-behavioral and glucose metabolism study.* Araki T1, Kato M, Kobayashi T

OLFACTORY REFLEXES AND SEIZURES

- *Artemesia* is mentioned in folkloric herbals as possibly triggering seizures.
- *Lavendula* is mentioned as an aroma that can possibly abort or abolish a seizure at its onset.



OLFACTORY REFLEXES AND SEIZURES

- ▶ **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.**

Epilepsy Res Treat. 2013;2013:532657. *Increased seizure latency and decreased severity of pentylenetetrazol-induced seizures in mice after essential oil administration.* Koutroumanidou E1, Kimbaris A, Kortsaris A, et al.

OLFACTORY REFLEXES AND SEIZURES

- ▶ ***Rosmarinus officinalis*, *Ocimum basilicum*, *Mentha spicata*, *Mentha pulegium*, *Lavandula angustifolia*, *Mentha piperita*, *Origanum dictamnus*, 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.



GARDENIA AROMA AND SEIZURES

- 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.

J Ethnopharmacol. 2013 Oct 7;149(3):621-5.
 Neuropharmacological screening of essential oil from oleo gum resin of *Gardenia lucida* Roxb.
 Shareef MZ1, Yellu NR, Achanta VN.



DENNETIA AROMA AND SEIZURES

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

Phytomedicine. 2013 Nov 15;20(14):1315-22.
Hypnotic, anticonvulsant and anxiolytic effects of 1-nitro-2-phenylethane isolated from the essential oil of *Dennettia tripetala* in mice. Oyemitan IA1, Elusiyan CA, Akanmu MA, Olugbade TA.

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.

Pharm Biol. 2013 Dec;51(12):1521-4.
Anticonvulsant activity of ethanol extracts of *Vetiveria zizanioides* roots in experimental mice. Gupta R1, Sharma KK, Afzal M, et al.



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.

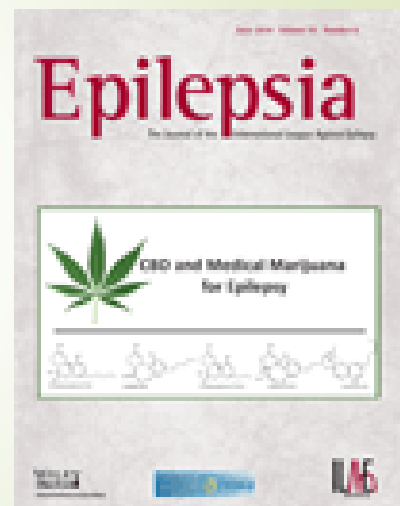
J Ethnopharmacol. 2013 Jun 21;148(1):152-7. Anti-epileptogenic and antioxidant effect of *Lavandula officinalis* aerial part extract against pentylenetetrazol-induced kindling in male mice. Rahmati B1, Khalili M, Roghani M, et al.



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.

Epilepsia. 2014 Jun;55(6):787-90. The case for assessing cannabidiol in epilepsy. Cilio MR1, Thiele EA, Devinsky O.



CANNABINOID PATHWAYS AND SEIZURES

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

Br J Pharmacol. 2013 Oct;170(3):679-92. Cannabidiol-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 cannabinoids 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.

Epilepsia 2014 Jun;55(6):783-6. The case for medical marijuana in epilepsy. Maa E, Figi P

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-inflammatory and reducing hyperexcitability.

- *Withania somniferum* (Ashwagandha)
- *Panax ginseng* (Ginseng)
- *Centella asiatica* (Gotu Kola)
- *Ganoderma 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 *Tricosanthes 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.

Neurochem Res. 2013 Aug;38(8):1715-25. *Tricosanthes tricuspidata* modulates oxidative toxicity in brain hippocampus against pilocarpine induced status epilepticus in mice. Smilin Bell Aseervatham G1, Sivasudha T, Suganya M, et al.

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.

Epilepsy Res. 2014 Mar;108(3):411-9. Acute administration of ginger (*Zingiber officinale* rhizomes) extract on timed intravenous pentylenetetrazol infusion seizure model in mice. Hosseini A1, Mirazi N2



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.

Int J Med Mushrooms. 2013;15(6):555-68. Anticonvulsant and neuroprotective effects of oligosaccharides from Lingzhi or Reishi medicinal mushroom, *Ganoderma lucidum*. Tello I1, Campos-Pena V, Montiel E, et al.

PLoS One. 2013 Apr 24;8(4):e61687. Intervention effects of ganoderma lucidum spores on epileptiform discharge hippocampal neurons and expression of neurotrophin-4 and N-cadherin. Wang SQ1, Li XJ, Zhou S, et al.



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.

Epilepsy Res. 2014 Feb;108(2):223-31. Ginseng extract attenuates early MRI changes after status epilepticus and decreases subsequent reduction of hippocampal volume in the rat brain. Suleymanova E1, Gulyaev M2, Chepurnova N2.



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.

J Complement Integr Med. 2013 Oct 15;10. Chemical and pharmacological standardization of Ashwagandhadi lehyam: an ayurvedic formulation. Rasheed A, Satyanarayana KV, Gulabi PS, Rao MS.



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 seizure thresholds.

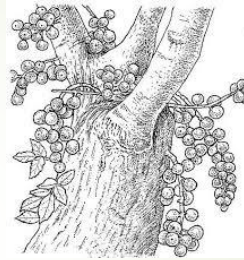
ACS Chem Neurosci. 2013 Nov 20;4(11):1479-87. Tanshinone IIA exhibits anticonvulsant activity in zebrafish and mouse seizure models. Buenafe OE1, Orellana-Paucar A, Maes J, et al.



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

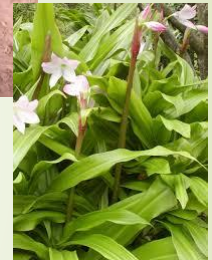
Pak J Biol Sci. 2013 Nov 1;16(21):1287-94. Mechanisms of anticonvulsant and sedative actions of the ethanolic stem-bark extract of *Ficus sur* Forssk (Moraceae) in rodents. Ishola IO1, Olayemi SO1, Yemitan OK2, Ekpemandudirí NK1.



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 GABAergic, nitrenergic and glutaminergic systems to exert its effects.

Pak J Biol Sci. 2013 Aug 1;16(15):701-10. Anticonvulsant, anxiolytic and hypnotic effects of aqueous bulb extract of *Crinum glaucum* A. chev (Amaryllidaceae): role of GABAergic and nitrenergic systems. Ishola IO1, Olayemi SO1, Idowu AR1.



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.

J Ethnopharmacol. 2013 Dec 12;150(3):791-804. *Passiflora incarnata* L.: ethnopharmacology, clinical application, safety and evaluation of clinical trials. Miroddi M1, Calapai G, Navarra M, Minciullo PL, Gangemi S.



HYPERICUM PERFORATUM

- *Hypericum perforatum* has been researched for anxiety and depression.
- *Hypericum scabrum* is a lesser known species reported to have anticonvulsant effects via GABAergic effects.
- Nitric oxide radical scavenging is another possible mechanism involved in the anti-epileptic effects.

Eur Rev Med Pharmacol Sci. 2013 Aug;17(16):2141-4. Anticonvulsant activity of *Hypericum scabrum* L.; possible mechanism involved. Ebrahimzadeh MA1, Nabavi SM, Nabavi SF, Ahangar N.



ACORUS TATARINOWII

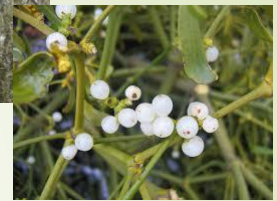
- *Acorus tatarinowii*, contains Alpha (α)-asarone a TCM for treating epilepsy, cough, bronchitis, and asthma.
- α -asarone affects GABAA receptors as well as voltage-gated Na(+) channels inhibiting the spontaneous firing of output neurons treating cough and raising the seizure threshold.

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. L on 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.

Pak J Pharm Sci. 2009 Jul;22(3):308-12. Effect of methanolic extract of *Hyoscyamus niger* L. on the seizure induced by picrotoxin in mice. Reza HM1, Mohammad H, Golnaz E, Gholamreza S



LAVENDULA

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

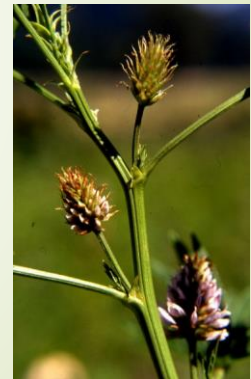
Pak J Biol Sci. 2011 Jun 1;14(11):634-40. Effect of hydroalcoholic extract of *Lavandula officinalis* on nicotine-induced convulsion in mice. Arzi A1, Ahamehe M, Sarahroodi S.



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. Chowdhury B1, Bhattamisra SK, Das MC.



HAPPY TRAILS!!

