Study Guide

GENERALIZED ANXIETY

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Etiology:

The amygdala is the part of the brain responsible for perception and assessments of threats. It receives almost immediate but raw input from the sensory thalamus and some more input from the sensory cortex. If an external stimulus perceived as a threat, the amygdala triggers an action potential, which then communicates to areas of the brain that activate the sympathetic nervous system- commonly referred to as our "fight-and-flight" response.

Long-term potentiation of trauma or chronic stress is theorized to occur because frequent stimulation of a neuron increases receptivity to sensory inputs or enhances presynaptic release of neurotransmitters.[1] This is known as upregulation and one consequence of upregulation is that it takes increasingly smaller amounts of a stimulus to initiate an action potential.[2] This lowered threshold results in hyperreactivity and overstimulation of the nervous system.

Cholecystokinin (CCK) an excitatory neuropeptide that bonds with CCK receptors located in the basolateral amygdala contributing to this process. Intravenous cholecystokinin-tetrapeptide (CCK-4) administration provokes panic anxiety in people, accompanied by adrenocorticotropic hormone (ACTH) and cortisol release.[3] CCK-A receptors appear to be involved in modulating sensitization.[4] It's use is being investigates as a weight loss aid, which I think is a poor choice given the possible effects.

There appears to be a genetic vulnerability to the effects of upregulation, but researchers have not come to any sort of consensus on the cause. Some studies indicate GAD sufferers have reduced numbers of GABA receptors or have deficient levels of GABA.

Recall that Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter and is known to counterbalance the action of the excitatory neurotransmitter glutamate. The brain circuits in the amygdala are thought to be comprised of inhibitory networks of GABAergic interneurons making this neurotransmitter primarily responsible for modulating anxiety.[5]

HPA Involvement - Upregulation of corticotrophin-releasing hormone expression by the paraventricular nucleus of the hypothalamus stimulates the pituitary to release more adrenocorticotropic hormone, which in turn travels to the adrenal

Discussion Protocol

Mary is a 35 yo who has been previously diagnosed with mild-moderate anxiety but is not currently taking medication. Her allostatic load is significant and you gather from her intake she is one of our "fried and dried" types and you discuss diet and moderate exercise and hydration.

She is complaining of difficulty sleeping due to rumination and restless legs.

She also complains of general muscle tension in her neck and "heart flutters" which get worse when she lays down at night.

Why might you suggest the following regimen?

Herbal Intervention

Hawthorn HEtOH (tincture)
2 mL (40 drops) b.i.d.

California Poppy HEtOH (tincture) 1 mL (10 drops) b.i.d.

and

Passionflower HEtOH
3 mL (60 drops) at bedtime

or

Kava HEtOH (tincture)
2 mL (40 drops) at bedtime

Nutritional Intervention

Magnesium Lactate 100 mg t.i.d

Vitamin B6 750 mg

glands and triggers the release of cortisol, adrenalin and noradrenalin effecting all noradrenergic systems in the body.[6]

Enteric Nervous System- As we discussed in the physiology lesson, early in fetal development the neural crest differentiates into the central nervous system and the mass of neural tissue in the gastrointestinal tract known as the enteric nervous system. The enteric nervous system has its own reflexes and sensory capabilities which it communicates to the brain through via the tenth cranial nerve (the vagus nerve).[7] Vagal communication regulates heart rate variability (HRV) and triggers the parasympathetic nervous system. 90 percent of vagal communication flows from the gastrointestinal tract toward the brain.[8] Intestinal microbiota regulates the production of neurotransmitters that influence mood and behavior via the enteric nervous system.[9]

Research has shown that anxiety disorders are associated with reduced heart rate variability and reduced parasympathetic tone which is a phrase used to indicate the basal level of activity of the parasympathetic system.[10] There is a growing body of research that supports to the idea that poor gastrointestinal health or dysbiosis contribute to this by impairing vagal function and communication.[11]

Pathology:

Prolonged hyperreactivity and over stimulation of the nervous system may lead to dysregulation of various systems in the body including increased sympathetic tone which means that individuals basal level of sympathetic activity is elevated. Anxiety mimics chronic stress in this regard, but sufferers are more likely to experience fear or reactions that seem out-of-proportion to their present situation.[12]

Imbalances in neurotransmitter (GABA, serotonin, and dopamine) function in the brain leads to overactivity of the hypothalamic-pituitary adrenal axis (HPA-axis) which stimulates the adrenal gland to release cortisol, DHEA, adrenaline and noradrenaline in response to triggers."[13]

Excess cortisol seems to be the primary underlying causes of many of the somatic symptoms that present with anxiety. When the body is bombarded with consistently high levels of cortisol , it can disrupt endocrine function resulting in health complaints such as insomnia, abdominal weight gain, hypertension, hair loss, and muscle mass loss.[14]

Presentation:

There are several subtypes of anxiety disorders including: general anxiety disorder (GAD), panic disorder, various phobias, social anxiety disorder (SAD), post-traumatic stress disorder(PTSD), obsessive-compulsive disorder (OCD), and separation anxiety disorder.

For the most part this handout focuses on GAD as characterized by excessive and persistent worrying that is hard to control, apprehensiveness and irritability and somatic symptoms such as increased fatigue and muscular tension.[15] Physical symptoms (generally attributed to elevated levels of cortisol/adrenalin in the body) may include pounding heart or palpitations, muscle tension and spasms, gastrointestinal upset, headaches, and insomnia.

Healthcare providers makes the diagnoses based on the following criteria. They should have observed three of the following six complaints lasting for longer than six months and should have determined that outside stressors are not in proportion with these feelings. What this means is that someone living in a war zone or an unsafe location should not be diagnosed with anxiety for having a normal reaction to a stressful situation. Complaints include:

Fatigue
Irritability
Lack of concentration
Muscle tension – tension headaches are a secondary indication.
Restlessness, a general feeling of unease, or vague persistent agitation
Sleep disturbances

Anxiety attacks, which are sometimes referred to as panic attacks, are episodes of intense panic or fear, which occur suddenly. Presentation varies but may include "shortness of breath or smothering sensations; palpitations, pounding heart, or accelerated heart rate; chest pain or discomfort; choking; and fear of going crazy or losing control."[16] Ask a lot of questions of clients reporting anxiety attacks. Medical professionals are often quick to jump to this diagnosis without looking for root causes such as myocarditis. Chest pain and palpitations often result in fearfulness, regardless of the cause.

Long Term Health Impacts

Harvard medical researchers have identified connections between anxiety disorders and several chronic physical illnesses, including cardiovascular disease, chronic respiratory diseases, and gastrointestinal disease.

Medical Approach to Treatment

Your client's healthcare provider may have recommended cognitive behavioral therapy, applied relaxation or medications such as SSRIs (selective serotonin reuptake inhibitors) (serotonin-norepinephrine reuptake inhibitors), benzodiazepines such as Lorazepam. Benzodiazepines prevent deep sleep resulting in general fatigue during the day.

Practitioner Notes and Goals

First determine if the use of phytotherapy is being considered as an adjunct or primary intervention. Most of my clients come to me because they have a diagnosis and want to learn about alternatives to modern pharmaceuticals but many of the following suggestions work with either approach. Remember that it is outside of your scope-of-practice to diagnose anxiety. Be sure to refer undiagnosed clients to a mental health provider if you have any concerns. The goals of case management include:

- Introducing client to foods and beverages which support healthy nervous system function using what you have learned from our nutrition module and the targeted information provided below.

- Teaching clients about various botanical intervention which will help to support nervous system function-particularly in activating the parasympathetic cascade.
- Introducing clients to a variety of mind-body practices in the hopes of finding one that "clicks" with them. Nature is great and we plant people love to tell people to get out there but sound healing can be a nice choice for those people who just aren't outdoorsy. Remember its about meeting the client where they are.
- Assess the quality of client's support network and help develop an emergency self-care plan.
- Connect your client with the appropriate mental healthcare providers. I have an ongoing relationship with a couple of counselors in my town who I know are supportive of integrative practice and will work with my clients in a positive manner.

Nutrition

Think about the foods we talked about when feeding someone who is grieving or recovering from trauma, like my *Brotchán dobrónach*. Stress hormones (catecholamines) like adrenaline and noradrenalin are decreased by carbohydrate consumption. Anxiety is somewhat akin to living in a constant state of sympathetic excess so a supportive diet should still emphasize easily digestible foods but I tend to back off on the sugary foods. We don't want that to become an everyday crutch due to their glycemic load.

Instead consider the way healers traditionally presented the flavor "sweet" in the forms of whole grains, root vegetables and dried fruits. These types of foods were thought to tonify and balance energy in the body. *Āyurvedic* practioners might recommend marrow stocks and nourishing fatty meats as part of a *vatā* reducing diet, but the focus here is still more on vegetables/grains than meat. Meat is prepared by slow-cooking and adding lots of warming spices to improve digestion.[17] Meat broths and stewed meats are both excellent sources of many of the amino acids mentioned below and more easily digested than a medium-rare steak. For those who don't eat meat, there is clinical support of coconut milk acting as anxiolytic agent which probably has a lot do with its high content of amino acids especially cystine and phenylalanine.[18]

This is one of those times that I have to give a nod to traditional wisdom. On occasion I have a client whose individual constitution is not well suited to carbohydrates but overall I have found it to be effective. We still prepare these foods according to the season and the constitution of the person using herbs and spices to balance them energetically.

Macronutrient Focus- A few RCT's have confirmed that carbohydrates, in healthy forms of whole grains , root vegetables and dried fruits may help stressed clients by improving depressive mood states and lowering cortisol response.[19] I especially like oats. There is clinical research that polyphenols in oats inhibit the expression of pro-inflammatory cytokines and that tocotrienols also have neuroprotective properties,[20] which supports their use in traditional foods made for those recovering from nervous exhaustion as I mentioned in the unit on domestic medicine.

- Whole grains, legumes, root vegetables, and fruits with high fiber are sources of carbohydrates that have a lower glycemic index. For those avoiding wheat, focus on gluten-

free recipes like brown rice congee made with mung beans or an oat porridge if the individual can tolerate hordenine. For those avoiding grains, this can be accomplished by adding nutrient dense root vegetables such as beets, sweet potatoes, rutabaga, winter squash, pumpkin. carrots, Yukon gold red potatoes.

Micronutrient Focus - B-Complex vitamins and the minerals magnesium, calcium, potassium, and zinc are necessary for electrical impulses to move along the nerves properly. Magnesium has some clinical support in addressing anxiety especially when combined with B6. Most successful RCTs utilized magnesium lactate. Inositol (B8) is an intracellular messenger that has shown to have "positive effects on patients with panic disorder" and had performed comparably to Luvox (SSRI) in trials.[21]

- ✖ Inositol should not be used as a supplemental intervention in conjunction with SSRIs.

Antioxidants- Proper brain function creates a high demand for molecular oxygen which means that oxidative stress in the body can rob the brain of the form of oxygen it requires. This is one of the ways that systemic inflammation likely contributes to depression. Phenolic compounds in foods such as resveratrol from grapes, catechins from green tea, curcumin from turmeric and various flavonoids from berries. address oxidative stress by scavenging for free radicals AND modulating the inflammatory response by acting on various signaling pathways. Refer to the lesson on phenols for a complete explanation of this.

- Smoothies made in a way that leaves the fiber in the beverage can also be a quick way of getting berries and greens into the diet but be wary of the old juicing machines that remove the fiber from the fruit. Fiber is important for regulating blood sugar and promoting intestinal health.

Amino Acids: Several of the amino acids which cross the blood brain barrier and important because the brain needs them to build neurotransmitters which makes them vital in the diet, however large doses of these amino acids can create or exacerbate neurotransmitter imbalances because they compete for the same transport systems. That's why I am not a fan of supplementing with them, but clients frequently do so I will run through them briefly.

Aromatic Neurotransmitters

L-tryptophan is the precursor to serotonin and melatonin which is a metabolite of tryptophan synthesized by the pineal gland. It is covered in depth in the module on sleep architecture. Large doses of tryptophan (or its metabolite 5-HTP) may reduce dopamine levels.

- One way to boost tryptophan circulation in the brain without supplementation is to temporarily raise the ratio carbohydrates to protein in your diet by boosting high carbohydrate foods with a low glycemic index. (I know.) This lowers the plasma levels of competitive amino acids raising circulating tryptophan which is then used for the synthesis of serotonin.[22]

- α-Lactalbumin is milk protein that contains a relatively large amount of tryptophan (Remember when I mentioned my people giving their children warm milk at bedtime sprinkled with a bit of nutmeg?)

Phenylalanine is the precursor to L-tyrosine which is the amino acid your body uses to make dopamine. Large doses of tyrosine can lower serotonin levels or reduce sulfur amino acid levels.

- Making sure you have proper amounts of iron and folate in your diet elevates levels of tyrosine hydroxylase which is the enzyme the brain uses to produces dopamine.

Acidic Neurotransmitters

L-Glutamine is synthesized in the body by skeletal muscle and other tissues.
It is a common precursor for both glutamate and GABA production in the CNS. Phosphate-activated glutaminase catalyzes a reaction that removes one functional group of this amino acid to form glutamate a primary excitatory neurotransmitter in the brain.

Glutamate decarboxylase catalyzes a reaction which results in glutamate giving up a carboxyl module to become GABA. This is supposed to be our body's natural way of ridding itself of excess glutamate. GABA is metabolized through a reaction catalyzed by GABA-transaminase.

Because dietary glutamate is an acid (you may also see it called glutamic acid) it does not traverse the BBB well or have much effect on amino acid levels in the brain with exception of perhaps large amounts of concentrated food additives like MSG. Most free L-glutamic acid in brain is derived from local synthesis from L-glutamine.[23]

It is rarely deficient in the CNS, although persistently high levels of cortisol may lower the body's store of glutamine. It is also known to protect the lining of the gastrointestinal tract and is far more useful as a supplement for that reason. (see more in the GI module)

- ✖ Individuals with reduced liver function may not metabolize large amounts of supplemental glutamine properly and it is contraindicated in people with serious renal dysfunction. When someone tells me they are highly reactive to MSG or glutamates I always encourage them to go in for a blood work up that assesses the function of these organs.

N-Acetyl-cysteine is a sulfur amino acid that raises Glutathione (GSH) levels.[24], but again it is a competitive amino acid and excessive doses can lower dopamine and serotonin levels. Food sources include onions, garlic, leeks, chives, shallots, pork, chicken, eggs, milk, and cottage cheese

L-theanine improves production of dopamine and serotonin and appears to play a role in the formation of GABA, perhaps by binding with GABA receptors as it is structurally similar.

- Think back to the " black or green tea?" discussion that this is amino acid present in tea (*Camellia sinensis)* and probably why we put black tea in Grandma's Whiskey Revival.

Choline is the precursor to acetylcholine (ACh) which is important to the activation of the parasympathetic nervous system. Sources of choline are covered in the nutrition module. Some preparations are being investigated because they seem to inhibit the acetylcholinesterase (AChE) which is the enzyme responsible for hydrolyzing and breaking down ACh in the system. Their therapeutic goal is to improve the function of the nervous system and cognition and memory processes as a consequence.

Mind-Body Therapies

There are many mind-body therapies we have discussed previously which can be used effectively as adjuncts to conventional medical treatment or phytotherapy. Consistent practice of one of the

following may help to gradually shift the way the mind perceives and reacts to external stimuli. Journaling as a form of processing thoughts may help to curb rumination. Imagery/sensory awareness exercises are especially useful in acute situations such as an anxiety attack. Performing repetitive visual-spatial tasks such as knitting, crocheting, counting prayer beads or even rubbing a worry stone may reduce symptoms of exposure to traumatic stress[25] but also help by keeping the mind distracted from things like nail biting. Other useful modalities include:

Art therapy in the form of music, dance, or other creative artistic expression
Meditation or mindfulness exercises that incorporate deep, diaphragmatic breathing
Relaxation methods involving regular repetition of words: *Pranava* mantra, *Dhikir,* Rosary, Benson's relaxation response.
Forest bathing
Sound healing therapies

Exercise

About ten years ago researchers discovered what they called the intensity threshold effect. Summed up quickly exercising around 40 percent of your capacity lowers cortisol while higher intensity training does the opposite.[26] Anxiety sufferers do well participating in mindful movement disciplines such as yoga, tai chi, or qigong. Swimming or walking may even be better than jogging and running- especially in those who are suffering from physical symptoms associated with elevated cortisol. In some cases hydrotherapy in the form of medicated baths may be a better starting place.

Phytotherapy

Traditionally nervous tension was viewed as a sign of heat and addressed with "nervines" that were considered to have cooling properties. Today we have a more refined understanding of why some botanical interventions impact the nervous system, but those old energetic observations still hold true. For example, many "cooling" anxiolytic herbs contain constituents called cyanhydric glucosides which increase parasympathetic tone.[27] If you can increase this basal level of parasympathetic activity in your body, it helps your nervous system to shift down more quickly from fight-and-flight, so it calms an excitatory state. When you think about new substances in that framework it is easy to view GABA or acetylcholine as "cooling" substances. Note one herb I avoid with anxiety is *Valeriana officinalis* (Valerian). Despite it modern use valerian is a cerebral stimulant and has a stimulating effect on some people. It's better when combined with hops, but the problem remains that much of the time if an anxiety sufferer experiences this reaction the first time they try a formula, you have lost their confidence for good.

Cholinergic Herbs- Some anxiolytics have constituents which are direct parasympathetic mimetics in that they mimic the action of acetylcholine (ACh) directly stimulating cholinergic receptors (nicotinic and muscarinic] which in turn stimulates the parasympathetic nervous system. Indirect acting parasympathomimetic nervines may have constituents that promote the release of ACh or are acetylcholinesterase inhibitors. When this enzyme is inhibited its slows the breakdown of ACh. Lobeline, a constituent in *Lobelia inflata*, and the nicotine in *Nicotinia tabacum* are both nicotinic receptor agonists which have shown to have anxiolytic-like effects.[28] Hydroethanolic extracts of wormwood, lemon balm, and angelica also act as mild nicotinic receptor agonists.[29]

Oxytocic Herbs - The oxytocin produced by our body and released through the posterior pituitary in response to pleasing touch or social interaction, has an anxiolytic effect and reduces cortisol response to stress.[30] It also induces analgesia in people suffering low back pain and other types of persistent pain.[31]

Certain anxiolytics mimic oxytocin in the body in its capacity to stimulate the release of prostaglandin hormones and consequently may improve parasympathetic tone. The allocryptopinein *Eschscholzia californica* (California poppy) is a known oxytocic which is why the herb is contraindicated in pregnancy [32]as is the alkaloid stachydrine in L*eonurus cardiaca* (motherwort).[33]

Adaptogens - Recall that adaptogens are agents which that promote a healthy response to stress by normalizing HPA activity.[34] While we have already talked about these, five stand out when considering anxiety.

1. *Avena sativa* (oats) - Triterpene compounds present in extracts made from immature oats harvested from higher aerial parts of oat plants "exert 'adaptogenic' effects within human hormonal systems, as a consequence of their structural similarity to oestradiol and glucocorticoid hormones."[35]
2. *Withania somnifera* (ashwagandha) - The withanolides in *Withania* may mimic GABA in the body.[36]
3. *Centella asiatica* (Gotu kola) stimulates an enzyme that degrades glutamate and inhibits cholecystokinin production by binding to cholecystokinin receptors in the body. In one DBRCT, Gotu kola was shown to significantly reduce startle response in participants given an acute dose of 12 grams.[37]
4. *Ganoderma lucidum* (reishi) is something I have added to the list recently after reading some admittedly dicey preclinical research about its actions as an anxiolytic which led me to research making a more convincing case for its use in modulating chronic oxidative stress and particularly protecting against neurodegeneration. [38]
5. *Rhodiola rosea* has been theorized to restore impaired cortisol sensitivity but of all of these I use it least often because it is too stimulating and drying for many people.

Herbal Support for Comorbid Depression and Anxiety

Some nervines that that strongly suppress nervous system activity may be contraindicated in depressed individuals. This is important because anxiety and depression often present at the same time. A lay rule of thumb I was taught is that herbs that make a person sleepy should be avoided in depressed individuals except at perhaps at bedtime.

Addressing depression is the subject of another handout however there are some botanical preparations that are recommended for both conditions. *Hypericum perforatum*, (St. John's wort) has been involved in many trials in the treatment of depression and has been found to be as there was an interesting DBRCT which paired it with kava. Other herbs such as *Crocus sativus* (saffron) *have* shown promising results in human trials.[39] The adaptogens *Withania somnifera*, *Ocimum sanctum*, and *Rhodiola rosea*, may be specifically useful for those who also suffer from depression.

Herbal Support for Anxiety Attacks

For cases of acute anxiety, panic attacks, or immediate support after trauma, the following herbs prepared as hydro-ethanolic extracts (tinctures), given in acute dosages may more strongly suppress nervous system activity: *Lobelia inflata* (lobelia) *Humulus lupulus* (hops), and *Piper methysticum* (kava). Many herbal practitioners recommend the anemone species for panic disorders, but I have been unable to find much research support for that and I have had mixed results with the herb clinically. I personally use a combination of the extracts of wormwood, lemon balm, and green angelica seeds, I mentioned above. I feel like the seeds have a faster acting and more dispersive effect.

Summary

I have listed several anxiolytic herbs on the chart below. For a complete list refer to the module on nervines. Most of the anxiolytics on the list achieve their goal by modulating GABA in some way- often interacting with $GABA_A$ receptors. But basically, anxiety is best addressed stimulating production of GABA or making sure the GABA we do produce sticks around longer and works more effectively. While I mention some constituents specifically, it is worth noting that many of these herbs have several phytochemical constituents working together synergistically. Sometimes when they test the individual chemicals, they do not have the whole plant effect on receptors!

In all cases remember to keep in mind a client's individual constitution when formulating. Also refer back to the discussion on acute, therapeutic, and maintenance dosing and remember that while beverage teas are great for nutrition and maintenance, you are unlikely to see any sort of quantifiable clinical results from drinking chamomile or lemon balm tea daily.

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Herb	Active Constituent	Notes	Dosage
Piper methysticum (kava)[1]	kavalactones kavain and dihydrokavain	$GABA_A$ receptor positive modulators, ligand binding at all subtypes.[1]	Acute 600 mg q.d.[2] Capsules – 60- 120 mg kavalactones b.i.d 2-4 capsules Tincture 5 mL q.d.
Avena sativa (oats)	Triterpene compounds present in immature oats	Direct modulation of nuclear glucocorticoid and oestrogen receptor functioning.[2]	Tincture 1–4mL t.i.d.
Matricaria recutita L. (German chamomile)	luteolin, bisabolol, apigenin, eugenol	Luteolin modulates the activity of the endocannabinoid system through inhibition of FAAH enzyme. Bisabol is possible benzodiazepine (BZD)receptor ligand. Apigenin is a (BZD) receptor ligand.[3]	Capsules – 500 mg- b.i.d[3] Tincture- 2 - 4ml b.i.d
Humulus lupulus (hops)	humulene, myrcenol, and xanthohumol	Myrcenol $GABA_A$ receptor response potentiation[4] Glutamic acid decarboxylase inhibition.	Acute 5 mL q.d. Tincture 2-4 mL t.i.d.
Crataegus oxyacantha (hawthorn)	Quercetin and kaempferol	$GABA_A$ receptor agonists.[5]	Tincture 5–10 mL t.i.d.
*Eschscholzia californic*a (Californian poppy)	Protopine, allocryptopine, S- reticuline (found in fractionated N-Methyllaurotetanine)	Stimulates the binding of $GABA_A$ receptor agonists.[6] Possibly bio transformed to alkaloid that binds at μ-opioid receptors.[7]	Tincture 1–3 mL t.i.d.
Salvia officinalis (sage)		AChE-inhibiting[8]	Capsules 150- 300 mg b.i.d. 2-3 mL b.i.d
Scutellaria lateriflora (skullcap)	Scutelaterin A, baicalein, baicalin, chrysin, and wogonin	Baicalein weak BZD receptor ligand selective partial GABAA receptor antagonism while wogonin has exhibited anxiolytic properties through some interaction with BZD receptors in the GABA system[9]	Tincture 2-4 mL t.i.d..
Melissa officinalis (lemon balm)	Triterpenoids: rosmarinic acid, oleanolic acid, ursolic acid	Elevation of GABA levels via inhibition of GABA-transaminase probably due to rosmarinic acid.[10]	Tincture 2-4 mL t.i.d.
Passiflora incarnata (passionflower)	Flavonoids: chrysin, b-carboline Alkaloids,	$GABA_A$ BDZ positive allosteric modulation. $GABA_A$ and $GABA_B$ receptor subtype affinities.	Acute - 500mg or 5 mL q.d. Tincture 2 mL b.i.d.
Myristica fragrans (nutmeg)	terpene hydrocarbons terpene derivatives (linalool, geraniol, terpineol) and phenylpropanes (myristicine, elemicine, safrol)	Modulates the activity of the endocannabinoid system through inhibition of the enzymes.[11] Increase the levels of monoamine neurotransmitters serotonin (5-HT), norepinephrine, and dopamine.[12]	I use nutmeg as a corrigent in anxiety formulas. It is warming, stimulates digestion and contributes to the overall effect.

[1] This botanical may drowsiness and is best used at bedtime in conjunction with other nervines during waking hours.

[2] 600 Mg Herb Pharm Kava Capsules = 180 mg kavalactones

[3] Freeze dried and standardized to 1.2% apigenin.

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