

Botanical Strategies for Migraines and Depression



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Introduction

Migraine headaches and depression, most commonly found in women, affect the lives of many. These conditions are often difficult to treat due to the wide range of causes and treatment plans available. Botanical medicines can be effective in treating these conditions due to the chemistry involved in depression and migraines. By examining scientific evidence, the central nervous system, mechanisms of action, and the historical and anecdotal uses of these plants, their effectiveness in treating migraines and depression will be demonstrated. The following herbal medicines will be discussed in this paper:

- Feverfew (*Tanacetum parthenium*)
- Ginger (*Zingiber off.*)
- Butterbur (*Petasites hybridus*)
- St. John's wort (*Hypericum perforatum*)
- Ginkgo (*Ginkgo biloba*)
- Lemon balm (*Melissa off.*)
- Black cohosh (*Actaea racemosa*)
- Red clover (*Trifolium pretense*)
- Rhodiola (*Rhodiola rosea*)

Migraines

Migraine headaches begin in the nervous system and are a neurological condition. They begin when the sensitive nervous system of a migraine sufferer is faced with an environment that can reduce her migraine threshold. Risk and trigger factors include hormonal changes, alcohol consumption, skipping meals, sleep deprivation, medications and other stressors. The neurochemical balance of the nervous system changes, which can cause prodromal symptoms. If that state progresses, the migraine threshold is crossed, activating the migraine “generator” in the brainstem. A wave-like effect occurs across the cerebral cortex, activating neurons, as well as the trigeminal nerve branches and the vascular structures the nerve supplies.

As the branches of the trigeminal nerve are activated, neuropeptides are released from the nerve, producing inflammation of the small arteries in the meninges, which then stimulate platelet aggregation. This stimulates serotonin release, and potentiates the migraine process. The nerve impulses are then transmitted back to the brainstem. As this process continues, brainstem reflexes are activated that produce the migraine-related symptoms, including nausea, vomiting and photophobia.

Types of migraines

Migraine headache sufferers are most commonly women. In women, about 40% of migraines are non-menstrual migraines, while the other 60% are menstrual migraines. Menstrual migraines can be menstrual-related or pure-menstrual migraines. The pure-menstrual migraines happen right before, with, during or right after the menses. Menstrual-related migraines can happen either earlier in the PMS phase or at ovulation. There are other common hormonally-related migraines in women, including those during pregnancy and those that are postpartum. Perimenopausal migraines are also caused by a hormonal shift, leading to an exacerbation of migraines during this time period, whether a pre-existing migraine sufferer or not.

Migraines during pregnancy

Migraines can actually occur for the first time during pregnancy. About 65% of the time, if there are pre-existing migraines, they improve during pregnancy. Women with pre-existing true menstrual migraines typically are the ones that improve. Less commonly, if a patient has pre-existing migraines, pregnancy can make those pre-existing migraines worse, especially during the first trimester. In women with pre-existing migraines that have an aura, their headaches are actually likely to worsen during pregnancy. In either case, the headaches during pregnancy tend to improve over the course of the pregnancy. Even if the first trimester period is riddled with migraines, they will become less frequent, less intense and not last as long over the course of the pregnancy. They may completely remit all together.

In those women who continue to have migraines at the end of their first trimester, they will probably continue to suffer migraines throughout their pregnancy and postpartum. At this point, herbs that are safe to use during pregnancy can be considered.

Botanical adaptogens

Multiple factors occur during the onset of a migraine. Hormonal shifts, especially the change in estrogen, are a trigger of the serotonin, vascular stability, and platelet aggregation issues in the brain. Feverfew, ginger and butterbur target these multiple mechanisms.

*Feverfew (*Tanacetum parthenium*)*

Feverfew is the most popular herb for migraine prevention. A member of the daisy family, feverfew is rich in sesquiterpene lactones. The most predominant of those is parthenolide. Feverfew inhibits platelet aggregation and histamine release, some of the mechanisms involved in migraines. It has also been shown to inhibit the release of serotonin from platelets, leading to an improvement in blood vessel tone and decrease of the smooth muscle response to endogenous vasoactive substances, like prostaglandins, norepinephrine, acetyl choline and bradykinin. Feverfew also inhibits prostaglandin synthesis and the release of arachidonic acid.

Dosing

A common dose of feverfew is 125 mg of a dried feverfew that is standardized to 0.2% parthenolide content.

Research

In a questionnaire-type survey study completed in 1983, roughly 70% of the migraine sufferers who ate one to four feverfew leaves daily over a prolonged period of time claimed that the herb actually decreased the frequency and/or intensity of their attacks.¹

In another small study, 17 migraine patients were given either feverfew at 15 mg a day or placebo. Eight patients who remained on the prophylactic feverfew experienced continued relief of the migraines over a six-month period. The nine receiving placebo had an almost three-fold increase in their migraines. Although this is a small sample size, without any clear method of randomization, it is part of a body of information and rationale used in prescribing this plant for migraines.²

A late 1980s, double-blind, 4 month crossover study looked at 72 patients who were randomly given either one capsule of a dried feverfew leaf or placebo. They then switched to the other group for an additional 4 months. For the 59 patients who finished the study, it was observed that the feverfew treatment was associated with a reduction in the average number of acute migraines and the severity of attacks. It also decreased the degree of vomiting.³

Ginger (Zingiber off.)

Research

Recent studies have found that the active ingredients, gingerols and shogaols, are actually capable of inhibiting platelet aggregation, one of the mechanisms that cause migraines.

It is believed that gingerols can inhibit prostaglandin synthetase and leukotriene biosynthesis. By inhibiting these inflammatory neurotransmitters, similar to feverfew, ginger can have a role in migraine prevention. Although there are no published studies on ginger for this use, there are some case reports. A 42-year-old woman with a long history of migraines discontinued all medications for 2–3 months and began taking just simple dried ginger, about 500 to 600 mg of dried ginger, at the onset of her visual auras. That dose was repeated every 4 hours for 4 days. She began to notice improvement within a half-hour of taking the ginger. When she added ginger to her daily diet, just as a culinary herb, the migraines decreased in frequency and severity.

¹ Johnson, MIMS Magazine, 1983

² Johnson E, et al. BMJ 1985(291): 569

³ Murphy et al. Lancet 1988

Dosing

A dose of 500 mg four times a day, or 100–200 mg four times daily if the standardization contains 20% gingerol and shogaol, can be used for pain relief, as an acute dosing. In acute cases, 200 mg every 2 hours up to 6 times daily might also be used. Although there is no good evidence for this, that daily dose can be reduced for prophylactic purposes to 500 mg a day. For acute smooth muscle spasms, such as dysmenorrhea, a dosage of 250–500 mg 4 times a day can be taken.

Butterbur (Petasites hybridus)

Butterbur is an important herb in migraines. In a double-blind, placebo-controlled trial, 33 patients were given a butterbur product at 50 mg twice a day, while 27 received placebo for 12 weeks. These patients were frequent headache sufferers. When reviewing the results over the course of the study, compared to the baseline status, butterbur reduced the frequency of attacks by 46% after just 4 weeks. Butterbur also reduced the frequency of the attacks by 60% after 8 weeks, and then dropped down to about 50% after 12 weeks. When compared to placebo, butterbur significantly reduced the frequency of the migraine attacks and some accompanying symptoms, as well as the number of days per month with a migraine. The duration and the intensity of the pain were also diminished, although they were not statistically significantly different than placebo.⁴

Treatment plan for migraines

As part of the treatment plan, looking for other lifestyle or dietary triggers, such as alcohol, caffeine, or the time spent at a computer screen, should be considered. Additionally, there are therapeutic foods for migraine sufferers, such as ginger. Whatever the treatment plan, it should include these three herbs: feverfew, ginger and butterbur. Adding 50 mg twice a day of butterbur extract, 1 capsule four times a day of feverfew, or 1 capsule four times a day of ginger to the treatment plan should be considered. Certain other interventions including riboflavin, magnesium, and 5-HTP may also be helpful. Low magnesium levels may be associated with headaches, cerebral blood vessel stability might be related to riboflavin, and the 5-HTP may be related to serotonin issues. If necessary, Advil, Tylenol or Imitrex should be included in the treatment plan.

Using estrogen in women that have true menstrual migraines or menstrual-related migraines can reduce migraines. The once-a-week Estradiol patch provides more stability than an oral or a cream delivery. Depending on when the migraines occur, the patch may be used one week before the onset of the period, or may be started at mid-menses. This can be an important part of the overall treatment plan in women who have menstrual-related migraines.

A sample plan to reduce the frequency, intensity, and duration for a premenstrual migraine might include a PMS herbal product and/or the estrogen patch. If the headache is 2 days

⁴ Mauskip A, et al. Headache 2000; May: 420

premenstrual, then the Estradiol 0.025 patch should be used on day 21, if the patient has a 27 or 28-day cycle. In this sample, the focus would be on feverfew and ginger capsules, at a dosage of 500 to 600 mg once a day, every day. In considering supplements, 600 mg of magnesium, 400 mg of riboflavin and 200–600 mg 5HTP may be added daily. Finally, food sensitivities and other triggers should be determined and avoided. Therapeutic foods, such as berries, leafy greens, brightly colored fruits and vegetables, and eggs, should also be added to the treatment plan.

When treating perimenopausal migraines, one might add a type of hormonal intervention, usually estrogen. An Estradiol patch 0.0375–0.05 on days 14 and 21 may be a good option. In the treatment plan, food sensitivities and other triggers should be determined and avoided. When considering botanical medicines, the treatment plan might include 50 mg of butterbur twice a day, 1 capsule of feverfew four times a day and/or 1 capsule of ginger four times a day. Supplements can also be added to the treatment plan. They may include 600 mg of magnesium daily, 400 mg of riboflavin daily and 200–600mg of 5HTP daily. Black cohosh should be avoided in women experiencing perimenopausal migraines, because one of its side effects can be headaches.

Depression

Depression has a large variety of causes and symptoms. Treatment varies depending on the severity of the depression and the presenting symptoms. One important factor in the treatment of depression is to determine alcohol usage, because alcohol is a depressant. Secondly, investigate any sleep issues, which can dramatically impact depression. Through due diligence, these details should emerge in a good, methodical medical history.

Causes of depression

Depression has a variety of causes, including: food allergies, heavy metals, nutritional issues, medications, recreational drugs, alcohol, nicotine, sleep problems, stress, trauma or medical conditions. These medical conditions may include a new serious diagnosis, life–altering or threatening illness, infections, chronic pain, PMS, postpartum, perimenopause or early menopause, hypothyroid, insomnia or sleep apnea.

In terms of supplements for depression, there are a variety of choices, including L–Tryptophan, 5–HTP, phenylalanine, tyrosine, S–adenosyl–methionine (SAME), B12, B6, folic acid, magnesium and fish oils. Evidence shows that the following botanical medicines can treat at least mild to moderate depression:

- St. John’s wort
- Ginkgo
- Lemon balm
- Black cohosh
- Red clover
- Rhodiola

St. John's wort (Hypericum perforatum)

The primary use of St. John's wort is for the treatment of depression, particularly mild to moderate depression in adults and teens. It should not be ruled out completely in the treatment of major depression, but a judgment call needs to be made about when and if someone needs a prescription medication. St. John's wort may also be used in the treatment of seasonal affective disorder, viral infections and insomnia. St. John's wort demonstrates four types of mechanisms of action, including inhibition of MAO, modulation of IL-6, inhibition of serotonin uptakes and agonist action of sigma receptors.^{5, 6, 7}



Research

The use of St. John's wort declined recently, probably due to a study where St. John's wort was compared to one of the SSRIs. The media reported that St. John's wort did not work but failed to mention that the prescription drug did not work either. Investigative medical journalism from Harvard researchers has shown that prescription antidepressants do not really work statistically differently than placebo for mild to moderate depression.

Initial studies indicated that St. John's wort extract's antidepressant action may be based on its ability to inhibit monoaminoxidase. Upon closer inspection, it was thought that this mechanism of action was probably not sufficient to explain the clinical effects that were being seen and studied with St. John's wort. Additional mechanisms are likely and have been investigated with a variety of findings. For example, it has been reported that St. John's wort extract has demonstrated a 50% serotonin reuptake inhibition when used with a 0.3% hypericin content extract.

A 2006 Cochrane Review included a total of 37 trials, restricted to patients with major depression. The combined response rate ratio for the St. John's wort extracts compared with placebo from six larger trials was 1.15. From six smaller trials, it was a more robust 2.06. In the trials with patients suffering from mild to moderate depression, the response rate ratio

⁵ Linde et al 1996, Scharder et al 1998, Schrader 2000; Woelk 2000; Uebnelhack et al 2004; Kapser et al 2006

⁶ Martinez, et al.1994

⁷ Schulz. 1994

from six larger trials was 1.71, and from five smaller trials it was 6.13. Compared with the SSRIs used in these studies, the response rates were similar with St. John's wort. The Cochrane Review also demonstrated that patients given the hypericum dropped out of the trials much less frequently from adverse effects compared to dropout rates from the antidepressants, especially the older antidepressants. The overall conclusion from the Cochrane Review is that while the research is inconsistent, there is good evidence about the effectiveness of St. John's wort for mild to moderate depression. The use of St. John's wort for major depression is more unclear.

St. John's wort has also been studied for its use in treating premenstrual depression. A small, prospective, uncontrolled observational study about 12 years ago evaluated the use of St. John's wort for PMDD. The study used a dose of a 300 mg 0.3% hypericin tablet once a day, which is a third of the full dose of 3 times a day. In this study, the overall PMS scores between baseline and the end of the trial showed a 51% decrease in symptom scoring, meaning improvement. In particular, the mood scale had a 57% improvement, demonstrating the effectiveness of St. John's wort in treating premenstrual depression.⁸

In another study, St. John's wort was used along with chaste tree, a very strong herb for PMS, in perimenopausal women. The combination product of 5,400 mg of St. John's wort (standardized to contain 990 mcg hypericins, 9 mg hyperforin and 18 mg flavonoid glycosides), and 1,000 mg of chaste tree, was used in treating PMS-like symptoms in women who were perimenopausal. The active treatment group, the St. John's wort/chaste tree group, was statistically superior to placebo for reduction of total PMS-like symptoms, as well as a subgroup of those who had PMS depression and PMS food cravings.⁹

St. John's wort has also been evaluated in menopausal women. In a non-placebo-controlled study conducted in women who had menopause symptoms, researchers found that a total of 900 mg significantly improved psychological and psychosomatic symptoms, as well as a feeling of sexual well-being throughout the group. This likely has to do with the fact that as mood improves, patients feel better about themselves. This, in turn, can improve libido.¹⁰

Safety

The most prominent reports recommend if a patient is taking an SSRI, they should not take St. John's wort.¹¹ There have been some cases of serotonin syndrome reported in the literature that may have been caused by concomitant use. In this day and age, many patients are on not one, but two SSRIs.¹² In my opinion, if a patient is on one SSRI and St. John's wort, it is not going to be any more impactful on serotonin than a second SSRI.¹³ However, if they are on two SSRIs, St. John's wort should not be added.

⁸ Stevinson, Ernst. BJ Ob/Gyn 2000

⁹ J Alternative and Comp Medicine 2009; 15(9): 1045-1048

¹⁰ Grube B, et al. Adv Ther 1999; 16:177

¹¹ Clin Psychiatr News 1998: 26: 28

¹² Am Family Phys 1998; 57: 950

¹³ Pharmacother 2000; 20: 568-574

St. John's wort can be added if the patient is in the process of tapering down on their antidepressant. If a patient is doing well on an SSRI, but wants to discontinue it, St. John's wort can be added for about a month before tapering the prescription SSRI. Although there are questions about St. John's wort with anesthesia, there is no in vivo effect of St. John's wort that would be of concern.¹⁴

Use of St. John's wort should be avoided in bipolar patients just as SSRIs are avoided in bipolar patients who have mania as part of their expression.¹⁵ The kind of depression a patient has is important to consider. St. John's wort may be used with patients with unipolar depression, but not bipolar depression.¹⁶

Potential drug interactions

There is a theory that St. John's wort drug interactions are probably due to the cytochrome P450 enzyme system and particularly its ability to induce CYP3A4.¹⁷ This seems to be the consensus theory, however, there is a study that actually contradicts those findings.¹⁸ When it comes to using St. John's wort with other medications, absolute avoidance may not be required, but caution should be taken. There are case reports and/or pharmacological studies that have indicated that St. John's wort may reduce serum levels of many different drugs: Indinavir,¹⁹ Cyclosporine,²⁰ Tacrolimus,²¹ Theophylline,²² Digoxin, Warfarin, birth control pills,²³ Irinotecan²⁴ and Gleevec.

Oral Contraceptive Pills

There have been three published studies on the concurrent use of St. John's wort and birth control pills. The first one included women who were on a 35 mcg estrogen birth control pill for 3 months. During the second and third cycle, they were also given 300 mg three times a day of St. John's wort. Researchers then tested the blood levels of hormones and evaluated bleeding. There was a significant increase in the clearance of norethindrone and a significant reduction in the half-life of the ethinyl estradiol in the pill.²⁵ There were no changes in FSH, LH, or progesterone, and there were no pregnancies. But 2 of the 12 women experienced breakthrough bleeding in the control group versus 7 of the 12 in the St. John's wort plus the birth control pill group. This implies that there is the potential that they might have ovulated, causing the breakthrough bleeding. When a woman has abnormal bleeding with her birth

¹⁴ Annals Pharmacother 1999; 33: 502

¹⁵ Biol Psychiatry 1999;46: 1707-8

¹⁶ J Clin Psychopharmacol 2000; 20: 115-117

¹⁷ Clin Pharmacol Ther 2000; 67: 451-457

¹⁸ Pharmacol Letters 2000; 66: 133-139

¹⁹ Lancet 2000; 355: 547-548

²⁰ Lancet 2000; 355: 547-48, Lancet 2000; 1912, Hepatology 2000; 33: 853-55, Ann Pharmacother 2000; 34: 1013-1016

²¹ Nephrol Dial Transplant 2003; 18: 819-822

²² Ann Pharmacother 1999; 33:502

²³ Eur J Clin Pharmacol 1999; 55: A22, Clin Pharmacol Ther 1999; 66:338-45, Lancet 1999; 354: 2104-16, J Clin Pharmacol 2003; 56: 683-690

²⁴ J Natl Cancer Inst 2002; 94: 1247-1249

²⁵ Clin Pharmacol Ther 2003; 74: 525-535

control pill, she might be less compliant with the pill or make some change, which then increases her risk of getting pregnant.

In a second study, women were given a 20 mcg pill and a different progestin, alone, and then with St. John's wort added. Participants were given 300 mg of St. John's wort twice a day for 1 month and 3 times a day the next month. Again, no significant change in any hormones that were measured, but more women had inter-cyclic bleeding during their cycles.²⁶

The third, most recent study actually showed there was no breakthrough bleeding. The rationale here might be that it was actually a lower dose of St. John's wort. It was 250 mg twice a day, in a liquid, not a capsule. It contained 0.2% hypericin, not 0.3%, which means lesser amounts of St. John's wort. No differences in the half-life or the pharmacokinetics of the estrogen or progestin and no breakthrough bleeding were noted, demonstrating that a lower dose may be effective.²⁷

Dosage and toxicity

The overwhelming majority of the studies on depression have used St. John's wort extract, standardized to the 0.3% hypericin, but in recent years they were standardized to hyperforin as well. Both marker compounds are used for standardization. The most common dose is 300 mg 3 times a day.

The best demonstration of the excellent safety record of St. John's wort is a large-scale German study, which included over 3,000 patients. The frequency and intensity of depression symptoms were reduced by about 50%. The frequency of undesired side effects was small and statistically insignificant: gastrointestinal upset in less than 1%, allergic reactions in less than 1%, fatigue in 0.4%, and some restlessness in 0.26%.

Ginkgo (Ginkgo biloba)

The active components of ginkgo leaves are the ginkgo flavone glycosides or the ginkgo heterosides. These are flavanoid molecules with sugars attached and they are unique to ginkgo. There are several terpene molecules that are unique to ginkgo, called the ginkgolides and bilobalide, as well as some organic acids.

²⁶ Br J Clin Pharmacol 2003;56:683-690

²⁷ Eur J Clin Pharmacol 2009; 65: 287-294



The following pharmacological effects have been observed, studied and recorded with ginkgo: stabilization of the cell membranes, inhibition of lipid peroxidation of cellular membranes, activation of the cellular membrane sodium pump, enhancement of the use of oxygen and glucose, enhancement of circulation in the hippocampus and striatum, an increase in nerve transmission rate, improvement in the synthesis and turnover of brain neurotransmitters, normalization of acetylcholine receptors in the hippocampus, inhibition of beta-amyloid, vasodilation (a direct stimulation of the release of endothelium-derived relaxing factor and prostacyclin), inhibition of platelet aggregation, adhesion and degranulation, and inhibition of platelet-activating factor.

PMS

Ginkgo can be considered when treating PMS. In a study of 165 women ages 18-45 with long term PMS, mood was improved by using 80 mg of the ginkgo biloba standardized extract twice a day starting mid cycle.²⁸ In a study comprised of 80 people, 40 mg of standardized Ginkgo extract or a placebo was given three times a day from day sixteen of the cycle to day five of the next cycle. Self-administered questionnaires were given to the participants whose diagnosis of PMS had been established according to conventionally accepted criteria. A significant decrease in the overall severity of symptoms (physical and psychological) was noted in both the Ginkgo group and in the placebo group. The average decrease in the Ginkgo group was 23.68%, as compared to the placebo group, which showed a decrease of 8.74%.²⁹

Safety

A well-tolerated and safe botanical, side effects of Ginkgo are uncommon. In 44 double-blind studies involving 9,772 patients taking ginkgo, the number of side effects reported has been extremely small. The most common is gastrointestinal discomfort (only 21 cases out of almost 9,772 patients), seven headaches, and six cases of dizziness.³⁰

²⁸ Rev. Fr. Gynecol Obstet 88:447-57, 1993

²⁹ Rev. Fr. Gynecol Obstet 1993; 88: 447-457

³⁰ Perfusion 2005; 18

Ginkgo can decrease blood pressure, an obvious potential therapeutic benefit, which can be counterproductive in people who already have low blood pressure. There have also been several case reports that have documented bleeding associated with ginkgo use, both as a monotherapy and in combination with other agents that predisposed to bleeding. There was one case report of a subarachnoid hemorrhage in a 61-year-old man taking a reasonable dose, 120 to 160 mg a day, for longer than 6 months.

A case of spontaneous intracerebral hemorrhage was reported in a 56-year-old man who self-medicated with ginkgo and another in a 70-year-old man who was also taking aspirin. Intracerebral hemorrhage occurred in a case where a 78-year-old woman was using Ginkgo along with warfarin. There are, though, other studies, such as a 2 week study of 32 healthy volunteers that did not reveal any alteration of platelet function or coagulation parameters

Cautions and interactions

Although Ginkgo is usually well-tolerated in most healthy adults, caution is warranted. Side effects include dermatologic allergic hypersensitivity, dizziness, restlessness, seizure exacerbations, decrease in blood pressure, mild gastrointestinal discomfort and in one documented case, bleeding. If a patient were on aspirin or warfarin, a different treatment option should be considered. The more elderly the patient, the more caution should be exercised. Due to the potential effect on platelet aggregation, ginkgo should be stopped 2 weeks before surgery. There have been other studies that have analyzed the pharmacokinetics and in all the case reports, there is an unlikely risk of bleeding.³¹ A review of 44 clinical trials was unable to find a single case of bleeding. Because the data is confusing, it comes down to your personal clinical judgment on when to exercise caution in regard to the potential for bleeding associated with ginkgo usage.

Dosing

The dosage of Ginkgo can be a standardized extract containing 24% Ginkgo flavone glycosides. The usual dose is 40 mg three times a day, but some studies used 80 mg three times a day, or even 120 mg twice a day. Ginkgo should be taken for at least 12 weeks to determine its effectiveness.

Lemon balm (Melissa off.)

Lemon balm has traditionally been used in treating depression and cognition issues. In one study, 20 healthy adults were given three doses of lemon balm at the following doses: 600 mg, 1000 mg and 1,600 mg per day, given seven days apart. Cognitive ability and mood improved in all 20 adults. The highest dose, 1,600 mg a day, produced the most dramatic

³¹ Perfusion 2005;18

improvements in mental performance and increased calmness.³² At the lower doses, some increased speed of memory and retention were seen.

Black cohosh (Actaea racemosa)

There has been extensive research on black cohosh, particularly as it relates to menopausal women. One of the possible mechanisms is the effect on serotonin and dopamine receptors. It may be due to a selective estrogen receptor modifier, but there may be centrally mediated activity as well.³³ A second mechanism may be centrally mediated with possible action at the level of serotonin or dopamine receptors.³⁴

Black cohosh/St. John's wort

St. John's wort and black cohosh together can be an effective combination in reducing overall menopause symptoms, as reflected in three different studies. The menopause symptoms are measured by the Cooperman Index, also known as the menopause rating scale. In a recent double-blind randomized placebo controlled study, the average menopause rating scale score decreased 50% in the treatment group and 19.6% in the placebo group. On the Hamilton Depression Rating Scale, the score showed a 41.8% reduction in symptoms in the black cohosh/St. John's wort group and only 12.7% in the placebo.³⁵

In another study, a black cohosh/St. John's wort combination worked better than black cohosh alone for mood symptoms, as demonstrated by the Cooperman Index. This controlled open-label observational study treated 6,141 women at 1,287 outpatient gynecological clinics in Germany. The dosage was a 20 mg tablet twice a day of Remifemin, and, in some of the cases, 3.75 mg iCR extract and 70 mg of St. John's wort (frin 245 to 350 mg) was added to the Remifemin. This combination was effective in all the menopause symptoms, which includes depression. Black cohosh used alone also improved mood symptoms.³⁶

In a third study of perimenopausal and postmenopausal Korean women, the mean Kupperman index scores at four and twelve weeks were significantly lower in the treatment group using a black cohosh/St. John's wort combination. The average decrease in the Kupperman Index was 20 points in the treatment group, and only 8.2 points in the placebo group. Vaginal dryness and low libido did not improve, but average hot flash scores were significantly lower in the black cohosh and St. John's wort group.³⁷

³² Neuropsychopharmacology; July 2003

³³ Harnischfeger and Duker 1985; 4: 316-319

³⁴ Burdette and Chen 2003; 51(19): 5661-5670

³⁵ Uebelhack et al. Obstet Gynecol 2006; 107: 247-255

³⁶ Briese et al. 2007; 57: 405-414

³⁷ Chung 2007; 48(2): 289-294

Dosing

The most common researched dose of black cohosh alone is 20 to 40 mg standardized extract twice a day. There are no overt contraindications, but it is typically avoided during pregnancy and lactation. Black cohosh should not be used in patients with liver disease due to some questions about it being a causal agent. Recent research suggests it is not a probable but a possible causal agent. Black cohosh should be avoided if the patient is taking hepatotoxic drugs. There is one study showing that black cohosh interfered with Cisplatin, but studies show that Tamoxifen has a better ability to inhibit ER-positive breast cancer cells in vitro when black cohosh is added to the mix.³⁸

Red clover (Trifolium pretense)

Red clover can be used with perimenopausal women for depression and anxiety. In a study, 109 perimenopausal or menopausal women were given 2 capsules daily of red clover extract totaling 80 mg of isoflavones, or a placebo for 3 months. After taking the red clover, women had significant change on both the Hospital Anxiety and Depression Scale (HADS) and the Zung's Self Rating Depression Scale (SDS). In the red clover group, there was a 75% reduction in anxiety and a 78.3% reduction in depression in the HADS scale, and an 80.6% reduction in the total SDS scale. After taking the placebo, the HADS and SDS scores were reduced only by an average of 21.7%.³⁹

Rhodiola (Rhodiola rosea)

Rhodiola has many diverse activities and actions: central nervous system, mood, cognition, cardiac impacts, neurological impacts, and immune modulating impacts. It is most commonly used for mild to moderate depression. It can also be used in treating fatigue, anxiety, moodiness, physical and medical performance, and stress.⁴⁰ Rhodiola contains a large number of active constituents: rosavin, rosin, rosarin, salidroside, rhodioloside, tyrosol, flavonoids (rodiolin and rodionin), phenolic antioxidants, including proanthocyanidins, quercetin, gallic acid, chlorogenic acid and kaempferol. Rhodiola preparations that are standardized to the rosavin marker compound and/or the tyrosol are most common. Tyrosol, in particular, can actually act to alleviate stress-induced depletion of brain catecholamines in the alarm phase of stress.

³⁸Blumenthal 2003; 15-22

³⁹ Maturitas 2010; 65: 258-261

⁴⁰ Winston and Maimes 2007



Depression

Rhodiola seems to impact serotonin and dopamine levels.⁴¹ In one study, rhodiola clearly caused improvement in overall depression and even insomnia, while the placebo group did not show any improvement. In this trial, three groups suffering with depression took a dosage of either 340 mg or 680 mg of standardized rhodiola per day for 6 weeks. The rhodiola group demonstrated improvement in overall depression, insomnia, emotional instability and somatization. Self-esteem showed no improvement. In the end, the trial concluded that the standardized extract showed anti-depressive potency in patients with mild to moderate depression when administered at these levels.⁴²

Dosing

Rhodiola dosage is usually given in 4–8 ml/d liquid extract, 200–600 mg dried root or 100 mg of extract standardized to 3% rosavins and 0.8–1% salidroside. An intake of 1,000 mg daily is considered to be a high dose. For mild to moderate depression, a dose of 170 mg to 340 mg per day for 6 weeks is most common.⁴³ To combat fatigue, a dosage of 200 mg 3 times per day is recommended. For insomnia, a 600 mg dose may be given.⁴⁴

Conclusion

Botanicals have been shown to be effective in the treatment of migraine headaches and depression. When treating migraines, feverfew, ginger and butterbur have been shown to be effective in reducing frequency, severity and duration. Side effects are minimal. There are many options for treating depression, including St. John's wort, Ginkgo, lemon balm, black cohosh, red clover and rhodiola. Typically used in treating mild to moderate depression, some botanicals may be used in combination with medications to treat major depression.

⁴¹ Kelly Alternative Medicine Review 2001; 6(3): 293-302

⁴² Darbinyan, Aslanyan et al. Nord J Psychiatry; 2007; 61(5): 343-348

⁴³ Daribinyan 2007; 61: 2343-2348

⁴⁴ Panossian and Wikman 2010; 3: 188-224

Contributor's biography

Dr. Hudson is a naturopathic physician. She graduated from the National College of Naturopathic Medicine in 1984 and has served the college in several capacities, including medical director, associate academic dean and academic dean. She is currently a clinical professor at NCNM, Southwest College of Naturopathic Medicine and Bastyr University. She has been in practice for more than 28 years and is the medical director of her clinic, A Woman's Time, in Portland, Oregon, and director of product research and education for Vitonica. Dr. Hudson was awarded the 1990 President's Award from the American Association of Naturopathic Physicians for her research in women's health, 1999 prestigious Naturopathic Physician of the Year Award, the 2003 NCNM Alumni Pioneer Award, and the 2009 Natural Products Association Pioneer Award. Dr. Hudson is a member of the Scientific Board of *Gaia Herbs Professional Solutions*.