

APPLIED EVIDENCE

New research findings that are changing clinical practice

Herbs for mental illness: Effectiveness and interaction with conventional medicines

Some herbs do work as claimed; all have the potential for downside activity as well

Practice recommendations

- Many of your patients may be self-treating with herbal preparations. Ask candidly about this possibility, and become familiar with the increasing evidence on efficacy and safety of alternative treatments
- A large meta-analysis and a Cochrane Review both suggest St. John's Wort (**A**) is as effective as conventional antidepressants and more effective than placebo for mild to moderate depression. With patients taking St. John's Wort and a conventional antidepressant, remain alert for a potentiating effect, "serotonin syndrome." Use with caution if the patient must also receive anticoagulants, oral contraceptives, or antiviral agents.
- The efficacy and safety of ginseng (**B**, in terms of psychological well-being) and evening primrose (**C**) for depression are not well established.
- Kava-kava (**A**, for short-term treatment for anxiety treatment) has well-known anxiolytic properties, but its potential adverse effects, particularly liver toxicity, dramatically reduce its usefulness. Valerian, though commonly used for anxiety (**C**, for insomnia and anxiety), is not well supported by good data.

- Ginkgo has shown promise in improving cognitive function in dementia, and its side effects are few and uncommon (**A**, for cognitive function in dementia). Monitor carefully if there is concomitant anticoagulant therapy.

Based on epidemiologic estimates, it may be that 20% to 30% of your patient population is using alternative/complementary medicines.¹ Twenty percent of adults who take prescription medicine also rely on herbal products,² and patients who use herbal products the most are those with chronic conditions.³

Included in this group are persons with mental health problems, who, compared with the general population, report a much greater use of alternative treatments, including herbal and homeopathic remedies.⁴ These remedies, when used to treat psychiatric symptoms, may produce changes in mood, thinking, or behavior, and they may interact with a number of conventional medications.³

Largely uncharted territory. With the exception of St. John's Wort for depression and ginkgo for dementia, minimal evidence is currently available to recommend the use of herbal medicines as the primary treatment for mental illness.

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TABLE 1

Safety of common herbal products

HERB	INTERACTIONS WITH DRUGS	ADVERSE EFFECTS
St. John's Wort	Anticoagulants, oral contraceptives, antiviral agents, digoxin, SSRIs Potential for other interactions due to induction of hepatic enzymes	Photodermatitis, delayed hypersensitivity, gastrointestinal tract upset, dizziness, dry mouth, sedation, restlessness, constipation Mania and hypomania
Evening primrose	Phenothiazines, nonsteroidal anti-inflammatory drugs, corticosteroids, beta-blockers, anticoagulants	Nausea, softening of the stool, headache Worsening of epilepsy symptoms
Ephedra	Anesthetic agents, MAO inhibitors, antihypertensives, antidepressants	Hypertension, palpitations, tachycardia, stroke, seizures, death Psychosis, affective disturbances
Ginseng	MAO inhibitors, stimulants, haloperidol, warfarin	Insomnia, hypertension, diarrhea, restlessness, anxiety, euphoria Mania
Kava-kava	Benzodiazepines, alcohol, barbiturates	Dizziness, mild gastrointestinal disturbance, yellow discoloration of skin, hair, and nails Hepatitis Kava dermatopathy
Valerian	Barbiturates, anesthetics, CNS depressants	Headaches, excitability, uneasiness, gastrointestinal effects, dizziness, cardiac disturbances
Ginkgo	Anticoagulants	Headaches, gastrointestinal tract upset, nausea, vomiting, skin allergy
Yohimbine	Sibutramine, heart/blood pressure medications, lithium, morphine, alcohol	Headaches, sweating, agitation, hypertension, restlessness Psychotic symptoms, mania, seizures

FAST TRACK

St. John's Wort was superior to placebo and comparable with conventional antidepressants

Although some herbs have been found to be effective at specific doses for specific conditions, there is no evidence to show their superiority to conventional drug treatments, nor has their safety been established for use during pregnancy and lactation.⁸

Helping patients navigate. Nevertheless, our patients are increasingly turning to alternative therapies, and it is therefore critical that we clinicians avail ourselves of current knowledge and that

investigators pursue intensive clinical research to establish safety (TABLE 1) and efficacy. Additionally, greater understanding of the biochemical and pharmacological effects of these herbs may uncover novel treatments or yield fresh insights into basic disease mechanisms.⁹

The herbal remedies discussed in this article are those commonly used for psychiatric conditions. Their effectiveness and potential for adverse side effects and interactions are assessed.

■ Depression

St. John's wort

St. John's Wort (*Hypericum perforatum L.*) is a popular herbal treatment readily used by the public in various forms, such as tablets and teas. Efficacy of hypericum—one of the hypothesized active ingredients in St. John's Wort—in the treatment of depression was reported in the texts of the ancient Greek physicians Hippocrates, Pliny, and Galen, and it continued to be cited throughout the Classical, Renaissance, and Victorian eras. Its contemporary usage as an antidepressant has been supported by more rigorous evidence than any other herbal remedy.⁹

Efficacy. Evidence of efficacy in mild to moderate depression has been reported in a meta-analysis of 23 randomized trials with a total of 1757 outpatients, in which extracts of St. John's Wort alone (20 of 23 trials) or in combination with other herbs (3 of 23) were tested against placebo (15 trials) or antidepressant drugs (8 trials).¹⁰ St. John's Wort was reported to be clearly superior to placebo and comparable with conventional drug treatment, with lower side-effect and dropout rates. Similarly, a recent Cochrane Review of 27 trials and 2291 patients concluded that St. John's Wort was more effective than placebo in treating mild to moderately severe depression; however, there was inadequate evidence to determine whether the herb was as effective as traditional antidepressants.¹¹

The superiority of hypericum to placebo has been called into question, however, by a large-scale, multicenter, double-blind case report tabulation. The study, conducted with 200 patients across 11 academic medical centers in the United States, found no evidence that St. John's Wort was more efficacious than placebo.¹² Another such trial also concluded that St. John's Wort was not an effective treatment for major depression. In addition, the herb was found to be no different than sertraline, which was also indistinguishable from the placebo, further confusing the issue.¹³ Strength of recommendation (SOR) is level A for the evidence in support of St. John's

Deficiencies to overcome

Because many alternative options do not require the approval of the US Food and Drug Administration (FDA), products sold in health food stores can be purchased without a prescription or the provision of any clinical advice or professional review. The quality of many herbal preparations is thus unpredictable, with the content varying not only from brand to brand but also from batch to batch.⁵

A working knowledge of the pharmacologic data and clinical literature is necessary to properly counsel, diagnose, and treat patients who may be using herbal products. However, 1 study reported that only 5% of British doctors claimed more than a poor knowledge of herbal medicine,⁶ and another survey revealed that most psychiatrists who do not recommend herbal products avoid doing so because they feel uncomfortable with their current knowledge of alternative therapies.⁷ Alarming, the latter study reported that among psychiatrists who do not recommend herbal treatments, the safety of such treatments is not an issue in their decision-making process.

Wort as an antidepressant.

Mechanisms of action. The mechanisms for the antidepressant effects of St. John's Wort are not fully understood, although monoamine oxidase (MAO) inhibition, inhibition of serotonin receptor expression, serotonin reuptake inhibition, and reduction of cytokine expression have all been suggested as means of its activity.⁹

Herb-drug interactions. Evidence suggests St. John's Wort contains both inhibitory and inducing constituents for the cytochrome P-450 (CYP) system, resulting in both inhibition and induction on the CYP system.¹⁴ Consequently, it's difficult to predict which drugs St. John's Wort will interact with in a significant way.¹⁵ Best estimates of its activity suggest it has minimal short-term activity; when used for a longer period, it will inhibit the CytP450-3A4, 2C19, and 2D6 systems (**TABLE 2**). Therefore, St. John's Wort may alter the blood levels of such medications as anticoagulants,¹⁶ oral contraceptives,¹⁸ and antiviral agents,¹⁹ possibly resulting in serious consequences.^{16,17} Exercise caution when initiating treatment for patients already taking St. John's Wort.

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Learn which herbs can inhibit or induce the cytochrome P-450 system

TABLE 2

Effects of common herbs on cytochrome P-450 enzymes

	CYTOCHROME P-450		
	CYP450-3A4	CYP450-2C19	CYP450-2D6
St. John's Wort	++++ inhibition (short-term?) Long-term induction in intestinal wall ⁹⁹	+++ inhibition	++ inhibition
Kava-kava ¹⁰⁰	++ inhibition	++ inhibition	++ inhibition
Valerian	+ inhibition	+ inhibition	0
Fish oil, omega-3 fatty acids	+++ inhibition	++++ inhibition	+ inhibition

Key: ++++ = very potent; ++ = potent (detectable); + = mildly potent; 0 = does not inhibit

Note: Caution should be undertaken when developing tables such as these, as the data came from a variety of in vivo and in vitro animal and human studies using simplified models (eg, cDNA-expressed CYP enzymes) of which there are significant interspecies variations in the activity of these systems. As well, in the presence of some pathological inflammatory states such as during an infection, the enzyme activity of the CYP can be modulated through cytokines and other mediators of inflammation.¹⁰¹

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Reports of ginseng's effectiveness for depression conflict dramatically

The potential of St. John's Wort to interact with standard prescribed antidepressants, possibly to produce a "serotonin syndrome," is also a concern. Gordon²⁰ reported a case in which a woman taking St. John's Wort became groggy, weak, and lethargic shortly after taking a single 20-mg dose of paroxetine. This patient had tolerated St. John's Wort and paroxetine separately, suggesting a drug-herb interaction.³ St. John's Wort has also been implicated in reducing blood levels of digoxin when the two are taken together,²¹ and 1 study documented that 8% of psychiatrists treating patients who had used St. John's Wort reported drug interactions between the herb and another agent.²²

Adverse effects. In general, fewer adverse effects are seen with hypericum than with conventional antidepressants but they may include photodermatitis, delayed hypersensitivity, gastrointestinal tract upset, dizziness, dry mouth, sedation, restlessness, and constipation. Use of St. John's Wort is contraindicated during pregnancy and lactation, for patients who experience intense exposure to strong sunlight, and for patients with a pheochromocytoma.²³

There are several anecdotal reports of mania or hypomania associated with the herb. For example, O'Breasail and Argouarch²⁴ reported 2 cases of persons with no history of bipolar disorder who developed hypomanic episodes after taking St. John's Wort. Likewise, Moses and Mallinger²⁵ reported 3 cases of possible mania induction associated with the herb.

Ginseng

This herb is derived from the root of *Panax ginseng* and has been used as a cure-all in Eastern folk medicine for thousands of years.²⁶ Today, both Chinese ginseng (*P ginseng* CA Meyer) and North American ginseng (*P quinquefolius* L) are associated with the treatment of mood and anxiety disorders and are used to reduce stress and fatigue and to improve endurance.

Efficacy. A systematic review of 16 double-blind randomized controlled trials found that ginseng did not improve cognitive function or psychomotor and physical performance.²⁷ Another review reported conflicting results from several studies.²⁸ For example, 1 double-blind randomized controlled trial of postmenopausal women who received either a placebo or ginseng

for 16 weeks revealed the superiority of ginseng on measures of psychological well-being.²⁹ Another double-blind randomized controlled trial, however, failed to find an effect of ginseng on positive affect, negative affect, or total mood disturbance in 83 healthy adults who took the herb for 8 weeks.³⁰ Thus, at best, SOR=B for the evidence in support of ginseng, but only at best in relation to psychological well-being.

Mechanisms of action. The key active components of *Panax ginseng* are ginsenosides, a group of steroidal saponins that target a multitude of tissues to produce pharmacologic responses. The overall pharmacology of ginseng is complex due to the ability of ginsenosides to initiate multiple actions in the same tissue. Attele and colleagues³¹ provide an in-depth review of these mechanisms.

Herb-drug interactions. Ginseng may potentiate the effect of MAO inhibitors,³² stimulants (including caffeine), and haloperidol.³³ In addition, a case study suggests a probable interaction with warfarin.³⁴

Adverse effects. Reported side effects include insomnia, hypertension, diarrhea, restlessness, anxiety, and euphoria.³⁵ There is at least 1 report of ginseng-induced mania, which occurred within 4 to 10 days of a patient's interrupting a lithium and amitriptyline treatment.²⁶

Evening primrose

Evening primrose (*Oenothera biennis* L) is a plant native to North America. The oil pressed from its seed is marketed as a nutritional supplement, and it has been used to treat many disorders, including premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD), both which are marked by affective disturbances.^{36,37}

Efficacy. A systematic review³⁸ of the efficacy of evening primrose oil in the treatment of PMS revealed few clinical trials of adequate methodology. The authors found only 2 well-controlled studies, both which failed to show beneficial effects for

Methods used for this review

Literature searches were conducted using Medline, PsycInfo, and the Cochrane Library electronic databases, and by consulting bibliographies of pertinent publications. We focused primarily on meta-analyses and large-scale case report tabulations at an evidence level of **1b**. Additionally, articles selected included those that discussed the use of herbal treatments for mental illness, as well as those that addressed drug-herb interactions between herbal and traditional psychiatric drug treatments.

the herb. Thus, at best, SOR=C for the evidence in support of evening primrose.

Mechanisms of action. Gamma linolenic acid, a precursor of prostaglandin E and several other active substances, is the main constituent responsible for the therapeutic effects of evening primrose.³⁷

Herb-drug interactions. This herb has the potential to interact with phenothiazines, nonsteroidal anti-inflammatory drugs, corticosteroids, beta-blockers, and anticoagulants.⁹

Adverse effects. Although it is generally safe, evening primrose oil has occasionally exacerbated the symptoms of epilepsy.³⁹ Other adverse effects are nausea, softening of the stool, and headache.³⁷

Ephedra

Ephedra (*Ephedra sinica*) is an evergreen shrub native to Asia used in traditional Chinese medicine for thousands of years. In recent decades, ma-huang, the extract derived from this herb, has been a common ingredient in many natural supplements that promote increased energy, mood enhancement, and weight loss.^{40,41} In early 2004, the FDA banned the sale of dietary products containing ephedra due to concerns over its adverse effects.⁴²

Efficacy. Research on ephedra's efficacy is largely focused on its role in weight loss, and there is little evidence that evaluates it as a mood enhancer. A comprehensive meta-analysis⁴³ assessed 20 controlled trials with a treatment duration of at least 8 weeks and concluded that ephedra, when administered alone or with caffeine,

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Support for evening primrose is primarily anecdotal

promotes modest short-term weight loss (0.9 kg/month more than placebo). However, not all of the included studies were randomized or double-blind, and no data were available on long-term effects. A smaller systematic review⁴⁴ of 5 double-blind studies also found the combination of ephedra and caffeine stimulated weight loss, but it was unclear whether 2 of the trials were randomized. Thus, SOR=A for the evidence in support of weight loss in the short term. There is no evidence in support of it as a mood-enhancing treatment.

Mechanisms of action. The primary constituents of ephedra are ephedrine-type alkaloids. As a sympathomimetic agonist at both α - and β -adrenergic receptors, ephedrine enhances cardiac rate and contractility, peripheral vasoconstriction, bronchodilation, and central nervous system stimulation.⁴¹

Herb-drug interactions. Ephedra should not be used with anesthetic agents,⁴⁵ MAO inhibitors,^{46,47} antihypertensives, or antidepressants.⁴¹

Adverse effects. The relative risk of adverse reactions to ephedra is more than 100 times greater than that of all other herbs.⁴⁰ As noted by Jacobs and Hirsch,⁴⁸ between 1993 and 1997 the FDA had received 34 notices of death and reports of approximately 800 medical and psychiatric complications all directly linked to ephedra. A more recent review⁴⁹ indicated that hypertension, palpitations, tachycardia, stroke, seizures, and death are related to ephedra use. The herb has also been noted to induce symptoms of psychosis and affective disturbances.^{50,51}

■ Anxiety Kava-kava

Kava-kava is derived from the dried rhizome of the oceanic kava plant (*Piper methysticum*), and it has been cultivated for thousands of years throughout the South Pacific, where it is consumed as a psychotropic drink for recreational and medicinal purposes.⁵² Kava has been shown to alleviate anxiety symptoms,⁵³

and it has euphoric and muscle relaxant properties, although its effect on arousal and alertness appears to be minimal.⁹ It is commonly used in Europe and North America for its anxiolytic effects.

Efficacy. A Cochrane review⁵⁴ of 6 double-blind randomized controlled trials that used a common outcome measure (Hamilton Anxiety Scale) concluded that kava is significantly superior to placebo as a short-term treatment for anxiety. The authors note, however, that further investigation is required to determine long-term efficacy and safety. Another meta-analysis⁵⁵ of 7 double-blind randomized controlled trials also suggests that, relative to a placebo, kava is an efficacious treatment for anxiety. Thus, SOR=A for the evidence in support of short-term efficacy in kava in anxiety. However, long-term data in terms of safety and efficacy has not been shown.

Mechanisms of action. Kavapyrones are the major constituents of this herb and are responsible for its pharmacologic activity. The mechanisms of their anxiolytic effect are still unclear. One line of research suggests that kavapyrones might mediate sedative effects by influencing gamma-aminobutyric acid (GABA)(A) receptor binding,⁵⁶⁻⁵⁸ whereas another theory posits that kavapyrones are a reversible inhibitor of human platelet MAO-B.⁵² Others have suggested the inhibition of voltage-gated ion channels as a potential mechanism of action.^{59,60}

Herb-drug interactions. This herb has the potential to interact with benzodiazepines,⁶¹ and the combination with central nervous system depressants like ethanol and barbiturates can produce synergistic effects.^{56,62}

Adverse effects. Liver damage has been reported in patients who use kava.⁶³⁻⁶⁵ A recent study⁶⁶ analyzed 29 cases of purported liver dysfunction in addition to 7 cases that have already been published; the authors concluded that kava ingestion was the direct cause of liver injury in 3 cases, a probable cause in 21 cases, and a possible cause in 12 cases. The most frequent liver injury was necrosis. Other adverse effects

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The risk of serious side effects with kava far outweighs its mild anxiolytic effect

of this herb include dizziness, mild gastrointestinal disturbance, and a temporary yellow discoloration of skin, hair, and nails.⁶⁷ In addition, long-term administration of kava at higher doses may cause scaling of the skin on the extremities, also known as *kava dermatopathy*.⁶⁸

Valerian

Valerian (*Valerian officinalis*) is a root extract, with purported healing properties that can be traced to ancient Greece and Rome. Today, valerian root preparations are used for their sedative, anxiolytic, and antidepressant properties. The herb, a GABA agonist,⁹ is commonly used in the treatment of sleeplessness and the management of anxiety associated with muscle tension.¹⁰

Efficacy. A recent systematic review of randomized clinical trials (including reports in all languages) assessed the efficacy of valerian in patients with insomnia.⁶⁹ Nine randomized, double-blind, placebo-controlled trials satisfied the inclusion criteria; however, even in these studies questionable methods in randomization, blinding, compliance, withdrawal, confounding variables, diagnostic criteria, and statistical analysis rendered contradictory results, and the authors concluded that evidence for valerian in the treatment of insomnia is inconclusive.

Data to confirm valerian's effectiveness as an anxiolytic are also minimal. One randomized placebo-controlled pilot study examined the effects of valerian on generalized anxiety disorder; 36 patients were treated with placebo, diazepam, or valerian extract for 4 weeks.⁷⁰ The authors found a significant reduction in the psychic factors of anxiety with diazepam and valerian. However, the study was limited by the small number of patients in each group, relatively low dosages of the active agents, and a short duration of treatment. Similar studies⁷¹ suffer from the same shortcomings, and thus further research is necessary to assess the effect of valerian on anxiety. Thus, SOR=C for the evidence in support of valerian as a somnolent and as

a anxiolytic, and further research is necessary to assess the effect of valerian in insomnia and anxiety

Mechanisms of action. Valerian's constituents include sesquiterpenes of the volatile oil (including valeric acid), iridoids (valepotriates), alkaloids, furanofuran lignans, and free amino acids such as GABA, tyrosine, arginine, and glutamine.⁷² The precise mechanisms of action are still unclear, though it has been suggested that all of the active constituents act synergistically to produce a clinical response. Research has also demonstrated modulation of GABA neurotransmission and receptor function (see Houghton⁷³ for a comprehensive review of valerian's pharmacology).

Herb-drug interactions. Valerian has the potential to prolong thio-, pental-, and pentobarbital-induced sleep and should, therefore, not be combined with barbiturates.^{74,75} It may also potentiate the sedative effects of anesthetics and other central nervous system depressants.⁴⁵

Adverse effects. Adverse effects with this product are rare, but when they occur they may include headaches, excitability, uneasiness, gastrointestinal effects, dizziness, and cardiac disturbances.⁷⁶⁻⁷⁸

■ Dementia Ginkgo

Ginkgo extracts are derived from one of the oldest known tree species (*Ginkgo biloba* L). They have been used in traditional Chinese medicine for 5000 years for a variety of purposes and are believed to be helpful in the treatment of memory impairment caused by dementia.⁷⁹ The herb is also used to treat stress, fatigue, chronic cerebrovascular insufficiency, and cerebral trauma, and to improve endurance.⁹

Efficacy. Evidence for ginkgo's efficacy is encouraging, but more rigorous research is needed. Kleijnen and Knipschild⁸⁰ reviewed 40 controlled trials on the use of ginkgo to treat "chronic cerebral insufficiency." Only 8 of the studies were deemed to be of good quality, although all but

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Data confirming valerian's effects as a somnolent and anxiolytic are minimal

TABLE 3

Recommendations for clinicians

Ask your patients if they are using natural health products or seeing a natural health practitioner. Recognize that they may be covertly self-medicating with herbal or alternative treatments. Better-studied alternative treatments should be substituted.

Create an environment where patients are not reluctant to disclose the use of natural health care.

If the patient is seeing a naturopathic doctor, obtain contact information so that the specifics of the therapy can be requested.

Communicate directly with the naturopathic clinician about changes in treatment choices that are taking place in the ongoing care of the patient. This may often include sending consultation letters and other information to all individuals involved in the treatment of the patient.

Acquire good reference materials on natural health products. Suggestions: *Natural Alternatives to Prozac* by Michael T. Murray, ND, and *The Textbook of Natural Medicine* by Joseph Pizzorno, ND and Michael T. Murray, ND.

Never underestimate the potential risk of possible chemical inter-actions between medications.

Make contact with a community naturopathic doctor who can answer questions about specific natural health products.

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Ginkgo was superior to placebo in delaying the course of dementia

1 found clinically significant improvement in symptoms including memory loss, concentration difficulties, fatigue, anxiety, and depressed mood.

Another meta-analysis⁷⁹ identified more than 50 articles on the effect of ginkgo on the cognitive function in Alzheimer patients, but only 4 studies were found to be properly blinded and placebo-controlled with well-characterized subjects. The authors concluded that ginkgo appears to have a modest effect on cognitive function in Alzheimer's but note that further research is necessary.

A systematic review by Ernst and colleagues⁸¹ concluded that ginkgo was superior to a placebo in delaying the clinical course of dementia. The authors reported on 9 placebo controlled, double-blind randomized trials including 1497 patients in their analysis.

Ginkgo has also been used to treat impotence, including antidepressant-induced sexual dysfunction. In 1 trial, 60 patients with proven arterial erectile dys-

function who had not previously responded to papaverine showed improvement with a daily dose of 60 mg of ginkgo over 12 to 18 months.⁹ However, further research must be undertaken in this domain, in part because this trial was not blinded, with both doctors and patients aware of who was receiving the ginkgo treatment.

Thus, SOR=A for the evidence in support of ginkgo as a cognitive enhancer in mild to moderate dementia, and B for the evidence in support of ginkgo as a treatment for erectile dysfunction.

Mechanisms of action. Ginkgo leaves contain several bioactive compounds, including flavonoids, terpenoids (ginkgolide, bilbobide), and organic acids. Although the mechanisms of action are only partially understood, the main effects appear to be related to its antioxidant properties, which require the synergistic action of the principal constituents.⁸² These compounds act as free radical scavengers.⁸³ Other pharmacologic actions involve anti-hypoxic and antiplatelet effects.⁸⁴

Herb-drug interactions. Researchers have suggested that ginkgo may potentiate other anticoagulants or increase bleeding over time,^{85,86} which can be attributed to ginkgolide B, a potent inhibitor of platelet-activating factor needed for inducing arachidonate-independent platelet aggregation.⁸⁷ Caution should be exercised when ginkgo is taken in conjunction with anticoagulant treatment (including aspirin) or when there is a risk of bleeding (eg, peptic ulcer disease and subdural hematoma).^{9,86}

Adverse effects. Side effects from ginkgo appear to be relatively uncommon; however, they may include headaches, gastrointestinal tract upset, nausea, vomiting, and a skin allergy to the ginkgo fruit.^{17,88}

Sexual dysfunction
Yohimbine

Yohimbine is an alkaloid derived from the cortex of the Central African tree *Corianthe yohimbe*.⁸⁹ The bark of the tree

TABLE 4

Internet resources about herbal products⁰

The Natural Pharmacist (\$) www.tnp.com
Evidence-based content developed and reviewed by physicians and pharmacologists; sections on herbs and supplements, health conditions, and drug interactions; information referenced

Natural Medicines Comprehensive Database (\$) www.naturaldatabase.com
Well-referenced, comprehensive database

Complementary and Alternative Therapies (Bandolier) www.jr2.ox.ac.uk/bandolier/booth/booths/altmed.html Evidence-based content; abstracts of systematic reviews, meta-analyses, or other studies about herbal therapies

National Center for Complementary and Alternative Medicine
www.nlm.nih.gov/nccam/camonpubmed.html
Access to PubMed's CAM database

HerbMed www.herbmed.org
Access to scientific evidence about the use of herbs for health

\$ = paid subscription required; all websites accessed April 5, 2005.
Table adapted from Gardener.¹⁰²

was used traditionally to enhance virility. Today, yohimbine is still reputed as an aphrodisiac and used as a remedy for erectile problems.⁹⁰

Efficacy. Overall, the efficacy of yohimbine in the treatment of erectile dysfunction appears promising, although, as with studies of other herbal products, clinical trials often suffer from methodological flaws. Carey and Johnson⁹¹ conducted 4 independent meta-analyses to examine the effects of yohimbine alone or in combination with other drugs in controlled and uncontrolled trials. The authors found positive results for yohimbine across all 4 analyses, but they note that the highest-quality data were derived from controlled clinical trials when yohimbine was administered on its own. In their analysis, this included 242 patients across 4 studies. Another systematic review yielded similar results: a meta-analysis of 7 randomized, placebo-controlled trials including 419 patients demonstrated that yohimbine is superior to placebo⁸⁹ as a treatment for erectile dysfunction. Thus, SOR=A for the evidence in support of yohimbine as a treatment for erectile dysfunction.

Mechanisms of action. Yohimbine is an

alpha₂-adrenergic antagonist. Its blocking activity increases the release of noradrenaline and the firing rate of noradrenergic neurons in the central nervous system.⁹²

Herb-drug interactions. Yohimbine should not be taken with sibutramine, a serotonin and norepinephrine reuptake inhibitor. The concomitant use of the 2 products could unmask the peripheral effect of sibutramine and produce negative cardiovascular effects.⁹³ Potential interactions also exist with heart or blood pressure medications,⁹⁴ lithium,⁹⁵ morphine,⁹⁶ and alcohol.⁹⁷

Adverse effects. Adverse effects are not common with yohimbine; however, they may include headaches, sweating, agitation, hypertension, and restlessness.⁹⁸ Yohimbine has also been reported to contribute to psychotic symptoms, mania, and seizures, though such occurrences are not well documented.⁹

■ Growing need for the 2 worlds to merge

One of the most frequent scenarios encountered by the naturopath is the patient who is taking a psychotropic medication and wants to explore natural

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Yohimbine is superior to placebo as a treatment for erectile dysfunction

solutions to reduce the drug's unpleasant side effects or to enhance general well being. Sharing information is the key to a healthy treatment regimen for such individuals (TABLES 3 AND 4). The patient should inform both the physician and naturopath about health care decisions, the naturopath must encourage the patient to be candid with the physician about proposed treatments, and the physician can be helpful by communicating to the naturopath the extent of the patient's disorder.

Professionally, one must consider before asking a patient to discontinue one agent or the other whether the alternative treatment might be improving the patient's condition or reducing negative side effects caused by the psychotropic medication. On one hand, withdrawing the drug can destabilize the patient's condition, which may not be rapidly amenable to a botanical or nutritional treatment. Alternatively, to supplement an antidepressant, benzodiazepine, or antipsychotic regimen by adding an herbal preparation could lead to unpredictable interactions and unpleasant or even dangerous symptoms. For many cases of mild depression or mild anxiety disorder, natural therapies can be sufficient treatment. However, for more complicated cases, where little is known about the consequences of using alternative treatments, involvement by a clinician with more specialized training is recommended.

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