

Herbal supplements in older adults

Consider interactions and adverse events that may result from supplement use

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Ms. P is a 72-year-old widowed retired librarian who presents at your office seeking advice. Since her retirement last year, she has been complaining of a depressed mood. Ms. P has no past psychiatric history, but her mother suffered from recurrent bouts of moderately severe depression. An assessment of her symptoms shows that she is experiencing depressed mood, some anhedonia, decreased energy, and poor sleep. She has a history of atrial fibrillation, but otherwise is in good health. She takes coumadin 4 mg po qhs and a multivitamin daily. She tells you that she began taking St. John's Wort (*Hypericum perforatum*) from a nearby health food store after a friend had recommended it about one week ago. She is taking 300 mg tid and would like to know if it is "safe" for her to use. What should you advise?

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Disclosure: The authors have no real or apparent conflicts of interest with the information presented here.

Herbals history

Herbs and plants have been used to treat various medical and psychiatric conditions for many centuries, dating back to the early uses of belladonna as an aesthetic agent and lavender as an anesthetic. More recently, they have transmogrified into the realm of 'herbal supplements,' a designation causing many patients

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not to consider them serious medications. Currently, supplements are taken to treat psychiatric complaints, such as anxiety, dementia, depression, and insomnia. Supplements and herbs, however, do not require the same rigorous approval as do prescription medications. The Food and Drug Administration (FDA) only requires that supplement labels state, "These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease." Perhaps a more rigorous standardized evaluation of these supplements by the FDA is warranted.

Common belief holds that herbs

cannot harm you because they are not 'foreign,' like manufactured or chemical medications. This is a misplaced notion, for St. John's Wort is no more natural for one's body than is fluoxetine. Nearly 16% to 18% of adults in the United States regularly use herbal supplements.¹ Sales of herbal products in the United States doubled to \$16 billion between 1994 and 2000² and 23% of those >50 years use herbal products.³ There are about 15 million adults at risk of experiencing adverse interactions from prescription medication, herbs, and/or vitamin supplements, including nearly 3 million adults age 65 or older.^{4,5}

Given the misconception that herbal supplements have benign side effects, it is not surprising that one study found that almost two-thirds of patients do not tell their physicians that they are taking supplements.^{6,7} Therefore it is imperative to ask each patient to tell his health care provider every medication (prescribed and over-the-counter) as well as every vitamin and supplement that they are taking or have been taking recently. The physician should warn patients that such supplements may interfere with prescribed medications or that they may have side effects. As we shall review, it is important to consider the range of interactions and adverse events that can result from herbal supplements (Table 1). Wong et al⁷ provided an excellent review of herbal supplements, usage, and effects.

continued

Table 1 Commonly used supplements

Common uses	Side effects	Possible interactions	Possible mechanism
Ginkgo (Ginkgo biloba)			
Dementia, memory improvement, SSRI-related impotence	GI upset, headache	Anticoagulants, MAOI, digoxin, oral hypoglycemic	Improves vascular perfusion, antioxidant, MAOI A&B (questionable in human brain)
Kava (Piper methysticum)			
Anxiolytic, sedative, muscle relaxant, anti-convulsant	Rare skin rash, sedation, hepatotoxicity	Sedatives, levodopa	Through kavalactones with possible affinity for GABA receptors
St. John's Wort (Hypericum perforatum)			
Antidepressant	Photodermatitis, GI upset, dizziness, dry mouth, sedation	SSRI, MAOI, digoxin, oral contraceptives, loperamide, sedatives	Has affinity for GABA-A & B, 5-HT (1), central benzodiazepine receptor, MAO A & B
Valerian (Valeriana officinalis)			
Sedative	Rare		GABA-A receptor

SSRI = selective serotonin reuptake inhibitor; GI = gastrointestinal; MAOI = mono amino oxidase inhibitor; GABA = gamma aminobutyric acid
 Created for Geriatrics by J Hoblyn and JO Brooks III based on information from references 7 and 14.

Table 2 Commonly abused plants

Country	Route	Results	Side effects	Active ingredients
Khat				
Somalia, Yemen, East Africa, Middle East	Chewing the leaves, twigs, and shoots	Stimulant; methamphetamine-like rush	Anorexia, tachycardia, hypertension, chronic insomnia, irritability, violent behavior	Cathinone (most potent in leaves <48h old)
Betel nuts				
Arabia, India, Philippines, New Guinea	Chewing the nut with another plant leaf (like peppermint) and slaked lime to improve flavor	Mild euphoria, excitation	Blackened teeth over time, damage to oral and esophageal mucosa, cancer	Muscarine
Yohimbine				
Africa	Brewed in tea, taken orally	Increases acetylcholine activity and thus increases penile blood flow; euphoria and possibly hallucinations	Fatal in large doses	Unknown
Ephedra				
Deserts worldwide	Tea, pills, extracts	Stimulant	Death in overdose, cardiovascular complications	Ephedrine
Mushrooms				
Mexico, U.S., South America, Southeast Asia, Europe	Eating or drinking	Hallucinations, nausea, alterations in perception	Possible hepatotoxicity	Psilocybin, psilocin

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Herb-drug interactions

Many herb-drug interactions can be explained through inhibition or inducement of P450 microenzymes.⁸ For example, St. John's Wort is a potent inducer of 3A4 and an inhibitor of several others (1A2, 2C9, 2C19, 2D6, and 3A4).⁹ St. John's Wort is particularly worrisome given the interactions with anticoagulants, digoxin, antidepressants, and protease inhibitors.^{10,11} In one case series, St. John's Wort was reported to cause mania.¹²

Lack of regulation of plant products could mean that patients may not even be consuming the plant listed on the product label. For example, preparations of ginseng may contain substantially more or less ginseng than labeled as well as varying quantities of other, unrelated, but active substances.¹³ Thus, if there is a question of a herb/drug interaction, it is important to stress to the patient the necessity of discontinuing all herbal supplements.

Herb and plant misuse is yet another overlooked issue (Table 2). This can be more important in certain cultures than others. Because many commonly abused plants are not regulated by government agencies, they are more freely available even if they are not native to one's country. Some plants, such as betelnut, may leave telltale traces of their use, such as staining of the teeth and gums or oral ulcerations, which may become cancerous. Others offer no such signs.

Conclusion

You advise Ms. P that St. John's Wort may interfere with her levels of coumadin and arrange for her to have her blood drawn for INR and PT levels, which were therapeutic. You advise her to discontinue the St. John's Wort and arrange for Ms. P to undergo weekly group and individual cognitive behavioral therapy. Two months later she reports that she is doing well. 

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