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NUTRITION AND HEALTH INFO SHEET

St. John's Wort

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In recent years a significant amount of public interest in alternative medicines has focused on the use of St. John's wort as an antidepressant. Consumers may be attracted to this product because it is available over the counter and is perceived as safe or natural.¹ St. John's wort is one of the most extensively studied herbal medications available. Research has examined its safety, mechanism of action, product purity, and efficacy in comparison with conventional antidepressants. (Only a clinical physician, however, should diagnose and treat depression.)

What is St. John's wort?

St. John's wort, also known by the Latin name *Hypericum perforatum*, is a plant with bright yellow-orange flowers. Both leaves and flowers may be incorporated into medicinal preparations.²

Is St. John's wort an effective antidepressant?

Clinical trials of St. John's wort usually compare it with placebo (sugar pill) or a tricyclic antidepressant. Tricyclic antidepressants (TCAs) are synthetic antidepressants often used to treat mild to moderate depression.²

For treatment of mild to moderate depression

Studies of patients experiencing mild to moderate clinical depression have generally concluded that short-term use of St. John's wort is more effective than placebo, and that it is as effective as low doses of TCAs. Additionally, studies have found that short-term use of St. John's wort produces fewer side effects than TCAs, which may result in increased patient compliance.³

For treatment of major depression

In addition to the large number of studies investigating mild or moderate depression, a few studies have examined the efficacy of St. John's wort in treating major depression.⁴ These studies have not found significant treatment effects, and researchers have therefore concluded that patients with major depression do not benefit from St. John's wort. Synthetic antidepressants (such as selective serotonergic reuptake inhibitors, or SSRIs) are significantly more effective than St. John's wort for the treatment of major depression.

How does St. John's wort work?

The antidepressant mechanism of St. John's wort is not well understood. Hyperforin and hypericin are two compounds contained in this herb that are thought to have pharmacological activity. Several compounds in St. John's wort may be acting synergistically to produce the drug's effects, with no single compound being solely responsible for antidepressant activity.⁵ The antidepressant effect is thought to result from selective inhibition of serotonin, dopamine, and norepinephrine reuptake in the central nervous system.⁶

Does the use of St. John's wort produce side effects?

Newly pregnant women and those attempting to conceive should be advised to discontinue use of St. John's wort, as damage to reproductive eggs may occur with use of high dosages, and sperm motility may be inhibited in men. Pregnant women with normal hormonal mood swings, and women with a history of postnatal depression are advised to ask maternity staff about its use. No adverse events have been seen with St. John's wort and breast-feeding; however, no long-term studies have been conducted regarding the effects the herb may have on infants.⁷ When used as a monotherapy, the reported incidence of side effects for St. John's wort is lower than for synthetic antidepressants. In clinical trials, mild side effects have included headache, fatigue, gastrointestinal upset, and restlessness.³ Potentially serious side effects of St. John's wort include photosensitivity, which is rare, and induction of manic symptoms in predisposed patients.⁶

Is it safe to combine St. John's wort with other medications?

When combined with other medications, St. John's wort can pose serious health concerns. This is because it increases the rate of metabolism of several types of synthetic drugs. Plasma levels of a variety of drugs can be decreased as a result.

What are some of the drugs affected by St. John's Wort (SJW)?

Drug(s) affected	Purpose of affected drug(s)	Adverse effects documented when combined with SJW	Reference
Warfarin, Coumarin, Phenprocoumon	anticoagulants	lowering of serum warfarin and phenprocoumon levels; reduced response to warfarin	8, 9, 10
Oral contraceptives	contraceptive, regulator of menstrual cycle	breakthrough bleeding; (no unwanted pregnancies documented)	9, 12
Amitriptyline, nortriptyline	antidepressants	lowering of serum amitriptyline and nortriptyline levels by 22–40 percent	8
Digoxin	anti-arrhythmic, cardiotonic	lowering of serum digoxin levels	8, 9
Indinavir	HIV protease inhibitor	lowering of serum indinavir levels	13
Cyclosporin	immunosuppressant (prevent rejection of organ transplant)	lowering of serum cyclosporin levels; acute heart transplant rejection	8, 9, 14
SSRIs (selective serotonin reuptake inhibitors)	antidepressants	symptoms of central serotonin excess, especially in elderly patients	15

Patients who are stabilized on treatment regimes that combine St. John's wort with other medications should not discontinue their St. John's wort without medical supervision, as this could cause dangerous changes in the pharmacokinetics of their other medications.¹¹ In addition, since St. John's wort affects a variety of enzymes and transporters involved in drug metabolism, the drugs whose metabolism could potentially be changed by St. John's wort extend far beyond those listed in the table. Patients should consult a knowledgeable physician before combining St. John's wort with any other medications.

Are St. John's wort products quality-controlled?

St. John's wort is classified as a dietary supplement under the Dietary Health Education and Supplement Act of 1994. Supplements are not subject to the same regulatory procedures as conventional drugs.¹⁶ Since St. John's wort products are prepared from extracts of plant matter, the dose of active compounds present in each preparation is uncertain. Thus, the potency of St. John's wort supplements varies significantly from manufacturer to manufacturer and between batches prepared by the same manufacturer.⁵

What can we conclude about St. John's wort?

In general, clinical trials have found that St. John's wort is an effective antidepressant for persons experiencing mild to moderate depression, with an efficacy similar to tricyclic antidepressants and significantly greater than placebo. However, St. John's wort has been found ineffective for those suffering from major depression. St. John's wort has fewer side effects than tricyclic antidepressants, which may improve patient compliance with this antidepressant regimen. The most serious safety concerns related to the use of St. John's wort are its ability to modify the metabolism of other medications and the lack of standardization in the levels of active compounds in St. John's wort products, which makes accurate dosing difficult.

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