

# St. John's Wort SAP

Science-based support for mood balance and relaxation\*

St. John's wort is a perennial plant grown primarily in Europe, Asia, and now the United States. It has been used traditionally for its astringent and sedative properties, in the treatment of depression, anxiety, and as a nerve tonic.\* The major constituents of St. John's wort are hypericin and hyperforin, which are considered to be largely responsible for its pharmacological effects.\* Recent clinical studies have contributed to the evidence of St. John's wort in the treatment of depression.\* St. John's wort has been shown to have efficacy and safety comparable to conventional antidepressants, providing a natural alternative to conventional drug therapies.\* Although the number of trials is limited, there are promising data that indicate menopausal symptoms such as hot flashes and depression may be alleviated by supplementation with St. John's wort extract.\* This may be the case with premenstrual symptoms of mood imbalance and physical discomfort, where further research is required to assert these claims.\*

**St. John's Wort SAP** provides a safe dose of St. John's wort extract to provide support in the management of depression and aid in calmness and relaxation.\*

## ACTIVE INGREDIENTS

Serving Size: 1 Capsule	Amount per serving	Servings: 60 % Daily Value
St. John's wort ( <i>Hypericum perforatum</i> ) herb top 8:1 extract providing 0.28% hypericin	300 mg	**

\*\* Daily value not established.

**Other ingredients:** Vegetable magnesium stearate, and silicon dioxide in a capsule composed of vegetable hypromellose and purified water.

**This product is non-GMO and vegan friendly.**

**St. John's Wort SAP** contains 60 capsules per bottle.

**Contains no:** Gluten, soy, wheat, corn protein, eggs, dairy, yeast, citrus, preservatives, artificial colours and flavours, starch, or sugar.

## DIRECTIONS FOR USE

**Adults:** Take 1-2 capsules daily or as directed by your healthcare practitioner.

**Duration of use:** Consult a healthcare practitioner for use beyond 18 weeks. Use for at least 1 week to see beneficial effects.

## INDICATIONS

**St. John's Wort SAP can help:**

- Relieve restlessness and nervousness.\*
- Promote healthy mood balance and relieve sleep disturbances associated with mood imbalance.\*
- Mitigate symptoms of depression.\*
- Improve symptoms of menopause.\*

## CAUTIONS AND WARNINGS

Avoid prolonged exposure to sunlight, or ultraviolet light (UV) therapy. Consult a healthcare practitioner if symptoms persist or worsen. Consult a healthcare practitioner prior to use if you are pregnant or breastfeeding, or if you are taking anti-anxiety or seizure medications, antihistamines, bronchodilators, muscle relaxants, and/or opiates.

## CONTRAINDICATIONS

Do not use this product if you are taking anti-cancer, antidepressant [e.g. selective serotonin reuptake inhibitors (SSRI)], cardiovascular, contraceptive medications, blood thinners, anti-HIV agents, and/or immunosuppressive medications.

## KNOWN ADVERSE REACTIONS

Some people may experience mild gastrointestinal disturbances, nausea, restlessness, and/or headaches. Stop use if hypersensitivity/allergy occurs.

**Do not use if seal is broken. Keep out of reach of children.**

## PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each St. John's wort SAP lot number have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.

\* 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.

Scientific Advisory Panel (SAP):  
adding nutraceutical research  
to achieve optimum health



351, Rue Joseph-Carrier, Vaudreuil-Dorion, Quebec, J7V 5V5  
T 1 866 510 3123 • F 1 866 510 3130 • nfh.ca

St. John's wort (*Hypericum perforatum* L.) is grown primarily in Europe and Asia and has also been cultivated in the United States for a long time. It is well known for its calmative and astringent benefits in traditional medicine. [1] These benefits have traditionally been applied for treatment of anxiety, depression, menopausal neurosis, sciatica, and as a general nerve tonic. [1] St. John's wort is composed of several phytochemical groups such as flavonoids, proanthocyanidins, phloroglucinols, and naphthodianthrones. Although the antidepressant activity of St. John's wort can be attributed to a combination of bioactives, the most common biomarkers that are also used for extract standardization are hyperforin, hypericin, and pseudohypericin. [2] There are several proposed mechanisms of action for the antidepressant activity of St. John's wort. Hypericin, certain flavonoids, and xanthenes may inhibit monoamine oxidase, thereby reducing the catabolism of neurotransmitters. [2,3] Other hypotheses explore the possibility of hyperforin reducing reuptake of serotonin, noradrenaline, and dopamine. [2,4] In either case, the antidepressant effect of St. John's wort, comparable to conventional drug therapy in terms of efficacy, have made it a popular choice of treatment for anxiety and depression.

## Depression

Randomized, double-blind, placebo-controlled trials have helped establish the safety and efficacy data of St. John's wort in the support of minor or major depression symptoms. In a randomized, double-blind, placebo-controlled trial conducted with 47 participants, administration of 900 mg/day of St. John's wort (0.3% hypericin) for 6 days increased the capacity to remember positive words and reduced recognition of disgust and fear in facial expressions. [5] The antidepressant effect is exerted at lower doses as well. Another trial (n=200) supplementing with 600 mg/day of St. John's wort extract (0.17% hypericin) for 8 weeks showed reduced scores of anxiety, depression, and overall clinical global impression scores, in patients suffering from atypical depression. [6,10] The efficacy of St. John's wort has also been tested against major depression, where patients (n=332) experienced reduction in depression scores with administration of 600 mg/day of extract for 6 weeks. Higher remission rates were observed when the dose was increased to 1200 mg/day. [7]

## St. John's Wort vs Fluoxetine

The potential use of St. John's wort as a natural therapeutic alternative has prompted comparison studies with commonly used antidepressants. Fluoxetine is a selective serotonin reuptake inhibitor, a mechanism that has been attributed to St. John's wort as well. Several studies have compared the dose and efficacy of these treatments. In a randomized, double-blind, placebo-controlled trial (n=70), dose of 150 mg/day (0.45 mg/day hypericin) for 6 weeks achieved 83% of the efficacy of 20 mg/day of fluoxetine. [8] The results were more pronounced with 900 mg/day of St. John's wort (0.17% hypericin) compared to the same dose of fluoxetine, where St. John's wort was tolerated significantly better with fewer adverse events, and successful reduction in depression scores, in a multicenter, randomized double-blind, placebo-controlled trial (n=72). [9,10] This trend was observed even in the treatment of major depressive disorder. In a randomized, single-blind, placebo-controlled trial (n=135), supplementation of 900 mg/day of St. John's wort (0.17% hypericin) extract for 12 weeks showed higher reduction in symptoms of depression compared to 20 mg/day fluoxetine in patients suffering from major depressive disorder. [10,11]

## St. John's Wort vs Sertraline

Sertraline is another serotonin uptake inhibitor that has been compared with St. John's wort extract. A comparison of sertraline and St. John's wort shows promising results in terms of clinical safety and efficacy. A randomized, double-blind, placebo-controlled trial (n=30) showed that administration of 600 mg/day for 1 week, followed by 900 mg/day (0.17% hypericin) of St. John's extract for 6 weeks, had a similar effect in reducing severity of depression compared with 75 mg/day of sertraline. [10,12] Another randomized, double-blind trial (n=87) showed similar results, where administration of 900 mg/day of St. John's wort (0.3% hypericin) for 4 weeks showed similar reduction in depression scores compared with 50 mg/day of sertraline. The doses were increased for non-responders for both treatments, with St. John's wort at 1800 mg/day and sertraline at 100 mg/day for 12 weeks, producing similar effects. [13] A multicenter trial has corroborated these results, where 241 participants were given 612 mg/day of St. John's wort extract (0.21% hypericin) or 50 mg/day sertraline for 12 weeks. Both treatments had similar effects in terms of reducing depression scores with fewer adverse events observed in St. John's wort group compared to sertraline. [14,15]

## St. John's wort Effect on Sleep

St. John's wort has been used in traditional medicine as a calmative and sedative, however these claims need further clarification and understanding with robust clinical data. Certain conventional antidepressants have sedative effects as well, and it has been hypothesized that St. John's wort may exert its antidepressant effect through similar mechanisms. Two double-blind, placebo-controlled crossover trials have tested this theory. The first trial (n=11) administered 0.9 mg/day while the second administered 1.8 mg/day of hypericin from St John's wort extract for 14 days. Sleep recordings and polysomnograms showed an increase in REM sleep latency with treatment, comparable to conventional antidepressants. [16] A randomized, double-blind, placebo-controlled trial (n=173) administering 600 mg/day of St. John's wort (0.17% hypericin) for 6 weeks showed improvement in efficacy measures of somatoform scales in treatment of somatoform disorders. [10,17] Further well-designed clinical trials with standardized extracts are required to substantiate this evidence.

## St. John's wort for Premenstrual and Menopausal Symptoms

Although the evidence is preliminary, St. John's wort appears to be among the list of herbs that can provide a natural therapeutic alternative in the management of premenstrual and menopause symptoms. A randomized, double-blind, placebo-controlled, crossover trial (n=36) showed that supplementation with 900 mg/day of St. John's wort (0.18% hypericin) for 2 menstrual cycles can improve physical and behavioral symptoms accompanying premenstrual syndrome. [18] The antidepressant activity of St. John's wort helps in management of menopausal symptoms, too. A randomized, double-blind, placebo-controlled trial (n=80) showed that dose of 0.99 mg/day of St. John's wort extract for 8 weeks can help reduce severity and frequency of hot flashes and manage depression. [19] Another randomized, double-blind, placebo-controlled trial (n=47) with a dose of 900 mg/day (0.3% hypericin) for 3 months showed improvement in menopause related quality of life, and fewer sleep problems. [20] Further research should help corroborate this evidence.

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## INDICATION SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety have been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias, etc) assessed and have been rated using a 5 star ★ rating classification.

\* 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.

Indication	Suggested dosage	Supporting evidence and study outcomes	Study design	Outcomes measures/ selection criteria for studies	Safety	Evidence quality rating
<b>Depression (Compared with Placebo)</b>						
Depression <sup>1</sup>	3 capsules/day for 6 days	Reduced recognition of facial expressions of disgust and fear.* Increased remembering capacity of positive words*	Randomized, double-blind, placebo-controlled trial (n=47); dose = 900 mg/day St. John's wort (0.3% hypericin) extract for 6 days	Beck depression inventory, Snaith-Hamilton Pleasure Scale, State-Trait Anxiety Inventory, Positive and Negative Affect Schedule, visual analog scale and personality questionnaire	Mild to moderate side effects. 1 participant reported severe side effects and discontinued after 1 day	★★★★
Atypical depression <sup>2,6</sup>	1 capsule/day for 8 weeks	Reduction in scores of anxiety, depression in patient health questionnaire, and clinical global impression scores*	Randomized, double-blind, placebo-controlled trial (n=200); dose = 600 mg/day St. John's wort extract (0.17% hypericin) for 8 weeks	HAMD, Patient health questionnaire, clinical global impression scale, Hamilton anxiety scale	Mild to moderate adverse events, 16 out of 23 fully remitted by the end of study. Gastrointestinal, musculoskeletal, and respiratory system related effects	★★★★
Major depression <sup>3</sup>	2 capsules/day for 6 weeks, OR 4 capsules/day for 12 weeks depending on response.	Reduction in HAMD-17 scores.* Higher remission rates experienced in the 1200 mg/day group compared to 600 mg/day group*	Randomized, double-blind, placebo-controlled, multicenter trial (n=332); dose 600 mg/day (for 6 weeks) or 1200 mg/day (for 12 weeks) St. John's wort extract. Hypericin content of extract not known	HAMD-17, responder and remission rates, Clinical Global Impressions Scale (CGI), the Montgomery-Asberg Depression Rating Scale (MADRS), Beck Depression Inventory (BDI)	Low incidence of adverse events (mainly gastrointestinal distress), 3 serious adverse events, but could not be attributed directly to treatment	★★★★
<b>St. John's Wort vs Fluoxetine in Depression</b>						
Mild to moderate depression <sup>4</sup>	1 capsule/day for 6 weeks	St. John's wort achieved 83% of the efficacy of fluoxetine.* Comparable reduction in depression scores with both treatments.* Same number of adverse reactions with both treatments*	Randomized, double-blind, controlled trial (n=70); dose = 150 mg/day of St. John's wort extract (0.45-0.49 mg total hypericin) for 6 weeks compared with 20 mg/day fluoxetine	Hamilton depression scale (HAMD), von Zerssen depression scale, Clinical Global Impression scale	Mild to moderate adverse events in 2 patients (anxiety and nausea)	★★★★
Mild to moderate depression <sup>5,6</sup>	6 capsules/day for 4 weeks (symptoms and adverse reactions should be monitored)	St. John's wort tolerated significantly better than fluoxetine, reduction in depression observed with both treatments*	Randomized, double-blind, multicenter, placebo-controlled trial (n=72); dose = 900 mg/day of St. John's wort extract (0.17% hypericin) for 4 weeks compared with 20 mg/day fluoxetine or placebo.	HAMD-21 scale, Montgomery-Asberg Rating Scale, Clinical Global Impression	Higher incidence of adverse events in fluoxetine group compared to St. John's wort. 4 subjects in St. John's wort treatment withdrew from study. No serious adverse events	★★★★
Major depressive disorder <sup>7</sup>	3 capsules/day for 12 weeks (symptoms and adverse reactions should be monitored)	Higher reduction in depression in St. John's wort group compared to fluoxetine or placebo group*	Randomized, single-blind, placebo-controlled trial (n=135); dose = 900 mg/day of St. John's wort extract (0.17% hypericin) for 12 weeks, compared with 20 mg/day fluoxetine or placebo	HAMD-17 depression scores	Mild adverse effects - headache, nausea, dry mouth, gastrointestinal upset, sleepiness	★★★★
<b>St. John's Wort vs Sertraline</b>						
Depression <sup>8</sup>	4 capsules/day for 1 week, followed by 6 capsules/day for 6 weeks	Reduced severity of symptoms in both groups, similar effect of both treatments*	Randomized, double-blind, trial (n=30); dose 600 mg/day, or 50 mg/day sertraline for 1 week, followed by 900 mg/day of St. John's wort extract (0.17% hypericin) for 6 weeks, compared with 75 mg/day sertraline	HAM-D, Clinical global impressions scale	2 patient drop-outs due to headache, dizziness, and numbness. 2 patients dropped out due to sertraline treatment	★★★★

Moderate depression <sup>9,10</sup>	2 capsules/day for 12 weeks (additional 12 weeks depending on assessment)	Decreased depression scores, almost same with both treatments, improvement in mood scores and clinical global impression scores.* Fewer adverse events in St. John's wort group compared to sertraline*	Randomized, double-blind, multicenter trial (n=241, 200 treated for 12 weeks, 81 for additional 12 weeks); dose = 612 mg/day St. John's wort extract (0.21% hypericin) or 50 mg/day sertraline for 12 weeks	HAMD-17 depression scores	12 patients with St. John's wort treatment - reaction linked to treatment. 5 discontinued study. Dry mouth, nausea, heartburn, sweating, increase in liver markers. Headache, dizziness in 1 patient	★★★★
Depression <sup>11</sup>	3 capsules/day for 4 weeks, followed by 6 capsules/day for 12 weeks for low responders (patients should be monitored for adverse reaction at higher dose)	Similar reduction in depression scores by 12 weeks for both treatments*	Randomized, double-blind, trial (n=87); dose 900 mg/day of St. John's wort or 50 mg/day sertraline for 4 weeks. For non-responders at 4 weeks - 1800 mg/day St. John's wort extract (0.3% hypericin) or 100 mg sertraline for 12 weeks	HAMD, Beck Depression Inventory	1 adverse reaction with 1800 mg dose - acute manic reaction. More side effects recorded in sertraline group compared to St. John's group	★★★★

### Sleep Disorders

Sleep disorders <sup>12,3</sup>	4 capsules/day for 6 weeks.	Improvement in primary efficacy measures of somatoform scales, treatment was safe and well-tolerated in treating somatoform disorders*	Randomized, double-blind, placebo-controlled trial (n=173); dose = 600 mg/day St. John's wort extract (0.17% hypericin) for 6 weeks	Wei Lachin test - Somatoform disorders screening instrument (SOMS-7), somatic subscore of Hamilton anxiety scale (HAMA), Symptom checklist 90-R (SCL-90-R), Clinical global impressions scale, global judgement of efficacy	Safety and tolerability comparable to placebo. 1 adverse event related to treatment (nightmares)	★★★★
Sleep modification comparable to antidepressants <sup>13</sup>	1 capsule/day for 14 days	Increase in REM sleep latency, comparable to conventional antidepressants*	2 trials - Double-blind, placebo-controlled crossover trials. First - (n=11); dose = 0.9 mg/day of hypericin from St. John's wort extract. Second - (n=10); dose = 1.8 mg/day of hypericin from St. John's wort extract for 14 days. Extract amount not known	Sleep recordings, polysomnograms.	No adverse events reported	★★★

### Menopause Symptoms

Postmenopausal symptoms <sup>14</sup>	1 capsule/day for 8 weeks.	Reduced frequency and severity of hot flashes, reduced intensity of depression*	Randomized, double-blind, placebo-controlled trial (n=80); dose 0.99 mg/day of St. John's wort extract for 8 weeks. Extract potency not known	Hamilton scale, frequency and severity of hot flashes	No adverse effects reported	★★★
Hot flashes and quality of life <sup>15</sup>	3 capsules/day for 3 months	Improved menopause-specific quality of life, fewer sleep problems*	Randomized, double-blind, placebo-controlled trial (n=47); dose = 900 mg/day (0.3% hypericin) for 3 months	Hot flash severity and frequency, quality of life questionnaire	Constipation, lethargy main side effects	★★★★

### Premenstrual Symptoms

Premenstrual syndrome symptoms <sup>16</sup>	2 capsules/day for 2 menstrual cycles	Improvement in physical and behavioral symptoms*	Randomized, double-blind, placebo-controlled, crossover trial (n=36); dose = 900 mg/day (0.18% hypericin) for 2 menstrual cycles.	Daily symptom report, State Anxiety Inventory, Beck Depression Inventory, Aggression Questionnaire and Barratt Impulsiveness Scale. Plasma hormone levels, inflammatory markers	Mainly digestive and respiratory symptoms, almost equal between treatment and placebo. 1 adverse event (chest pain) occurred, but not associated with treatment	★★★★
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