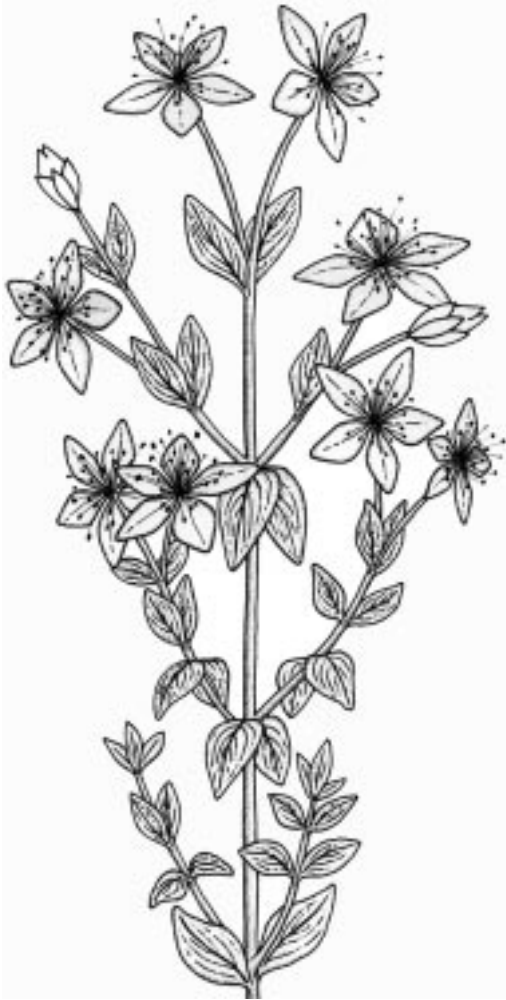


# Monograph



## Hypericum

### Description and Constituents

*Hypericum perforatum* (St. John's wort) is a five-petaled, yellow-flowered perennial weed common to the United States, Europe, and Asia. Small, dark red dots on the petals contain hypericin, one of many compounds found in this plant.

Hypericum contains numerous biologically active constituents, including hypericin and its derivatives, hyperforin, flavonoids (hyperoside, rutin, quercetin, etc.), catechin, epicatechin, procyanidin B2, amino acid derivatives (melatonin, GABA), and essential oils.

While it is not yet known definitively which constituent or constituents are responsible for Hypericum's anti-depressant effects, recent studies seem to indicate the compound hyperforin is at least in part responsible. Researchers found the concentration of this compound to significantly contribute, in a dose-dependent manner, to the anti-depressant effect of St. John's wort.<sup>1</sup> Another study, utilizing two behavioral assessments typically used to assess anti-depressant effects, found a positive correlation between hyperforin concentration and anti-depressant efficacy. The concentration of other constituents of several hypericum extracts were not found to be connected to their efficacy.<sup>2</sup>

### Mechanisms of Action

There are a number of proposed mechanisms of action for Hypericum's anti-depressant effect. It appears it may exert its effectiveness via several mechanisms involving a number of neurotransmitters and hormones. Initially, inhibition of monoamine oxidase (MAO) was believed to be the primary mode of action. More recent research indicates constituents of St. John's wort exert MAO inhibition only at concentrations higher than those typically found in commercially available extracts.<sup>3,4</sup>

Other researchers have found, in animal models, that Hypericum decreases serotonin re-uptake.<sup>5</sup> This is the mechanism of many commonly-used anti-depressants, such as Prozac. Further research found a decrease in post-synaptic receptors in the presence of Hypericum, resulting in a decrease in serotonin reuptake.<sup>6</sup>

Other researchers have found extracts of St. John's wort to be potent inhibitors of serotonin, dopamine, norepinephrine, GABA, and L-glutamate reuptake.<sup>2</sup>

### Clinical Applications

Mild to moderate depression: A meta-analysis of 23 studies involving over 1,500 individuals found significantly positive responses to St. John's wort based on analysis of the Hamilton Depression

Scale before and after treatment.<sup>7</sup> In a double-blind, placebo-controlled trial, 105 mildly depressed subjects were given a standardized extract of St. John's wort at a dose of 300 mg three times daily.<sup>8</sup> Significant improvements, using the Hamilton Depression Scale, were noted in depressive mood, sleep, and anxiety.

**Severe depression:** A randomized, placebo-controlled, crossover study of 72 patients with major depression found significant improvement in depression within the first two weeks of the trial in patients taking 300 mg three times daily of a standardized Hypericum extract.<sup>9</sup>

**Hypericum compared to standard anti-depressants:** A study compared 600 mg tid Hypericum standardized extract with imipramine 50 mg tid in 209 severely depressed patients.<sup>10</sup> The results were similarly positive in both groups, although the Hypericum group experience significantly fewer side-effects (34.6% compared to 81.4% in the imipramine group). Hypericum also compares favorably to maprotiline<sup>11</sup> and amitriptyline.<sup>12</sup>

**Seasonal affective disorder (SAD):** Twenty patients suffering from SAD were given either 300 mg tid standardized hypericum extract along with bright light or the same dose Hypericum with dim light (apparently not enough to affect SAD). Both groups experienced a significant reduction in Hamilton Depression Scale scores, with no difference between the bright and dim light groups.<sup>13</sup>

**Antiviral effects:** Although extracts of Hypericum, particularly hypericin, have been found to have *in vitro* antiviral effects against HIV, HSV and other viruses,<sup>14-16</sup> this antiviral activity may not occur *in vivo*, as some research indicates hypericin's antiviral effects are dependent on exposure to light, which may not occur in the body.<sup>17</sup> However, a small pilot study confirms potential benefit of Hypericum *in vivo*. Eighteen people with HIV/AIDS were treated intravenously with a Hypericum preparation twice weekly in addition to oral doses (undisclosed dosage) of Hypericum. Sixteen of 18 showed stable or increased CD4 values over a 40-month period. Improvement in CD4/CD8 ratios were observed in the majority of subjects. In addition, only two of the 16 positive responders experienced an opportunistic infection during the 40-month observation period.<sup>18</sup>

**Wound healing:** Hypericum has long been used both orally and topically for healing of wounds and burns, due in part to its antimicrobial effects. In a study of second and third degree burns, burns treated with a topical Hypericum ointment healed at least three times faster and keloid formation was prevented when compared to burns treated with conventional methods.<sup>19</sup> In another study, a tincture of Hypericum was compared to a topical application of Calendula. The wound healing effect of oral Hypericum was more pronounced than the effect of topical Calendula for the healing of incision, excision, and dead space wounds.<sup>20</sup>

## Dosage and Toxicity

Hypericin has been identified as a phototoxic substance which may cause photosensitization in fair-skinned individuals. People exposed to the sun may burn or tan faster after oral consumption of Hypericum. One study found 600 mg three times daily reduced tanning time by 21 percent.<sup>21</sup> In a multicenter study of 3,250 patients, adverse effects were noted in 2.4 percent of subjects, the most common effects being gastrointestinal irritation, restlessness, tiredness, and allergic reactions.<sup>22</sup>

Typical dosages of standardized Hypericum extracts (0.3% hypericin) range from 300 mg three times daily for mild-to-moderate depression to 600 mg three times daily for severe depression.

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