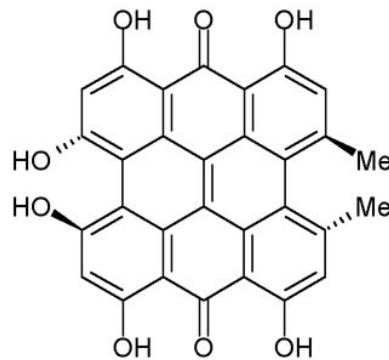
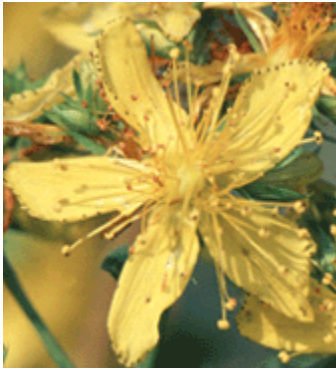


St. John's Wort (*Hypericum perforatum*)



Hypericin
(major constituent)

Background

- *Hypericum perforatum* L. belongs to the Hypericaceae family and is mostly found in Europe, Asia, Northern Africa, and in North America.
- “Hypericum” derived from the Greek and means “over an apparition”, a belief that the herb was so intolerable to evil spirits that a whiff of it would scare them away.
- “perforatum” derived from the Latin “perforated” as the leaves, when held in light, reveal translucent dots giving the impression that the leaf is perforated.
- Saint John's wort (SJW) is in reference to its yellow flowers traditionally gathered for the feast of St John the Baptist; “wort” is the old English word for plant.
- Active ingredients are extracted from dried leaves and the flowering tops.
- Traditionally SJW has been used both externally and internally for a wide range of medical conditions.
- Most common modern day use of SJW is treatment of depression.
- SJW is an over-the-counter product, but is not recommended for use without the supervision of a physician.

Benefits

- SJW has shown to produce fewer side effects compared to synthetic antidepressants therefore exhibiting better patient tolerability.
- Applied to the skin, SJW shows antibacterial and anti-inflammatory actions

Functions

- Mild to Moderate Depressive disorders
- Anxiety disorders
- Atopic dermatitis
- Obsessive-compulsive disorder (OCD)
- Peri-menopausal symptoms (i.e. Hot flashes)
- Premenstrual syndrome (PMS)
- Seasonal affective disorder (SAD)
- Somatoform disorders

Mechanism of Action

- SJW's mechanism is still not completely understood.
- SJW has weak inhibitory effects on type A monoamine oxidase (MAO)
- The possible mechanism with the most support is that SJW inhibits reuptake of serotonin (5-HT1), norepinephrine (NE), and dopamine (DA) accounting for its antidepressant effects and also playing a role in most other proposed uses.
- Hypericin and Hyperforin are major constituents of SJW that are responsible for its effects.

Research:

Mild to Moderate Depression

- Short term studies (1 to 3 months) suggest SJW more effective than placebo and equally effective as tricyclic antidepressants (TCAs) and SSRIs in mild to moderate depression.
- SJW has shown to lack the major side effects seen from other antidepressants allowing SJW to be known as a well tolerated and safe antidepressant.
- Studies have shown SJW to reduce aggressive behavior, enhance physical activity, and improve sleeping time, all relating to its antidepressant activity.
- Long term use or treatment for severe depression has not been studied.

Anxiety

- Studies have shown benefit using SJW to reduce anxiety symptoms (restless feeling, trouble concentrating, irritability, etc).
- One study compared a combination herbal product (St. John's wort and valerian root) with the benzodiazepine diazepam in patients with moderately severe anxiety and noted significant benefit. It is important here to realize that valerian root is commonly used for anxiety so benefit cannot be solely attributed to SJW.
- Anxiety is a common symptom of depression so it is important to determine exactly what the SJW is treating.

Atopic Dermatitis

- Hyperforin containing SJW cream and pure hyperforin exert an inhibitory effect on epidermal Langerhans cells proving to show benefit in the treatment and aftercare of subacute eczema.
- Hypericin is the constituent that exhibits photosensitivity whereas hyperforin does not. When a topical form of SJW is needed, a hypericin-free cream should be used to avoid this side effect.
- Hyperforin cream can also inhibit the growth of multiresistant strains of *Staphylococcus aureus* giving it an antibacterial effect.
- Hypericum cream may be an effective herbal remedy for the treatment of mild to moderate atopic dermatitis if corticosteroids are unwanted and photosensitivity is an issue.

Side Effects

- | | |
|----------------------------------|----------------------|
| ○ Gastrointestinal symptoms | ○ Headache |
| ○ Skin reactions (rash, itching) | ○ Dry mouth |
| ○ Fatigue and sedation | ○ Photosensitivity |
| ○ Restlessness or anxiety | ○ Serotonin Syndrome |
| ○ Mania | ○ Frequent urination |
| ○ Dizziness | ○ Decreased libido |

Dosage

Oral:

300 mg SJW, standardized to 0.3% hypericin extract, three times daily
(may be standardized to 2-5% hyperforin as well)

Topical:

Standardized 1.5% hyperforin cream applied to skin once daily

Interactions

- As a result from recent studies, the main concern with SJW is its potential to induce the metabolism of co-administered medications that are broken down by enzymes of the cytochrome P450 (CYP450) enzyme system.
- SJW is a potent inducer of the isozyme CYP3A4 which is responsible for metabolizing majority of medications in the liver. This raises a lot of concern because SJW can potentially decrease blood concentrations of medications, foods, and other herbals metabolized by CYP3A4, therefore decreasing their effect.
- Another reason for concern with interactions is due to the possible additive effects the two drugs can have if they exhibit similar actions, leading to adverse reactions.

Drugs to Watch for Interactions

- Irinotecan (Camptosar)
- Carbamazepine (Tegretol)
- Amitriptyline (Elavil)
- Sertraline (Zoloft)
- Nefazodone (Serzone)
- Paroxetine (Paxil)
- Warfarin (Coumadin)
- Indinavir (Crizivan)
- Nevirapine (Viramune)
- Tolbutamide (Orinase)
- Cyclosporine
- Tacrolimus (Prograf, Protopic)
- Digoxin (Lanoxin)
- Methadone
- Loperamide
- Oral contraceptives
- Alprazolam (Xanax)
- Midazolam (Versed)
- Nifedipine (Procardia)
- Antibiotics causing photosensitivity
- Aminolevulinic acid
- Phenobarbital
- Meperidine (Demerol)
- Fenfluramine (Pondimin)
- Nortriptyline
- Phenytoin (Dilantin)
- Pentazocine (Talwin)
- Reserpine
- Tramadol (Ultram)

Herbs, Supplements, and Food to Watch for Interactions

- Red Yeast Rice
- Foxglove
- Oleander
- Tyramine-containing foods (i.e. cheeses, red wine)
- Iron
- Capsaicin
- Valerian root

Safety

- Be aware that the US Food and Drug Administration does not strictly regulate herbs and dietary supplements. There is no guarantee of strength, purity or safety of products containing or claiming to contain St. John's wort.

- FDA suggests that patients with HIV/AIDS on protease inhibitors or non-nucleoside reverse transcriptase inhibitors avoid taking St. John's wort due to the serious interactions. This also applies to patients receiving an organ transplant.
- Read labels clearly and only consider products that specifically state the amount of hypericin or hyperforin. Inform your physician of all medications, herbs, and supplements you are taking.

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