St. John's Wort

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NUTR 547

Learning Objectives

- Identify health claims associated with St. John's Wort.
- Name the two substances in St. John's Wort that are shown to have biological activity.
- Describe the prevalence of depression in America.

Learning Objectives

- Describe the effect of St. John's Wort on mild to moderate depression compared to placebo.
- Describe the main concern of St. John's Wort intake with regard to drug interactions.

St. John's Wort
Hypericum Perforatum

- Claims:
  - Treatment of mild to moderate depression.
  - Relieves anxiety, insomnia, and headaches.
  - Used on first degree burns and healing of other wounds.

History

- Native to Europe & Asia.
- Called St. John's Wort because it flowers around St. John's day and wort is an Old English term for plant.
- Plant name: *Hypericum Perforatum*
- Traditional Uses:
  - Anti-inflammatory, Sedative, Diuretic, Anti-malarial, Vulnerary

Composition

- Contains at least 10 substances including hypericin & hyperforin, which are shown to have biological activity.

Formulation & Dosage

- *Colorado Nutrition* 900 mg .3% hypericin – take 2 daily.

- *Nature's Way* 350 mg .3% hypericin – take 2 daily.

Depression Criteria

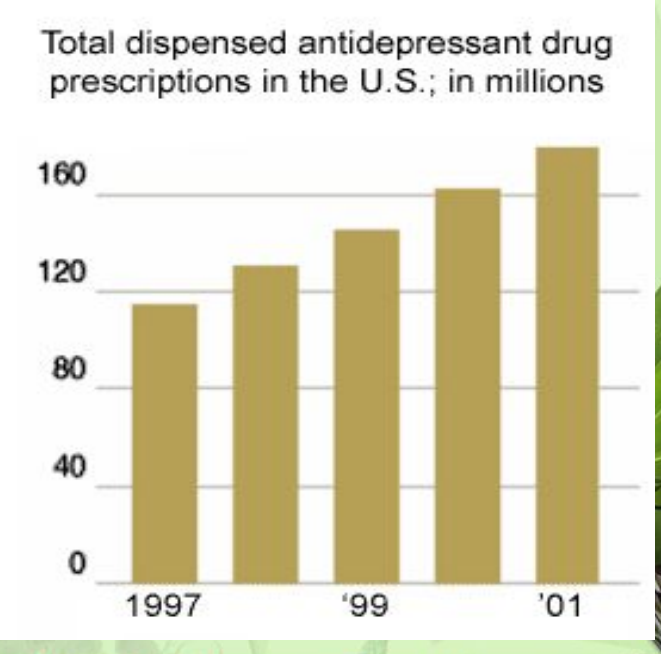
- DSM-IV Criteria for major depression
  - Period of at least 2 weeks during which there is either depressed mood or the loss of interest or pleasure in nearly all activities and 4 additional symptoms:
    - Change in appetite or weight
    - Change in sleep
    - Change in psychomotor activity
    - Decreased energy
    - Feelings of worthlessness or guilt
    - Difficulty thinking, concentrating, or making decisions
    - Recurrent thoughts of death

Depression Criteria

- Dysthymia – mild to moderate
  - Chronic disturbance involving depressed mood and at least 2 other symptoms with history of depressed mood for at least 2 years.

Prevalence of Depression

- Effects estimated 17 million Americans every year.
- Twice as common in women than men.
- Costing the nation 44 billion/year.

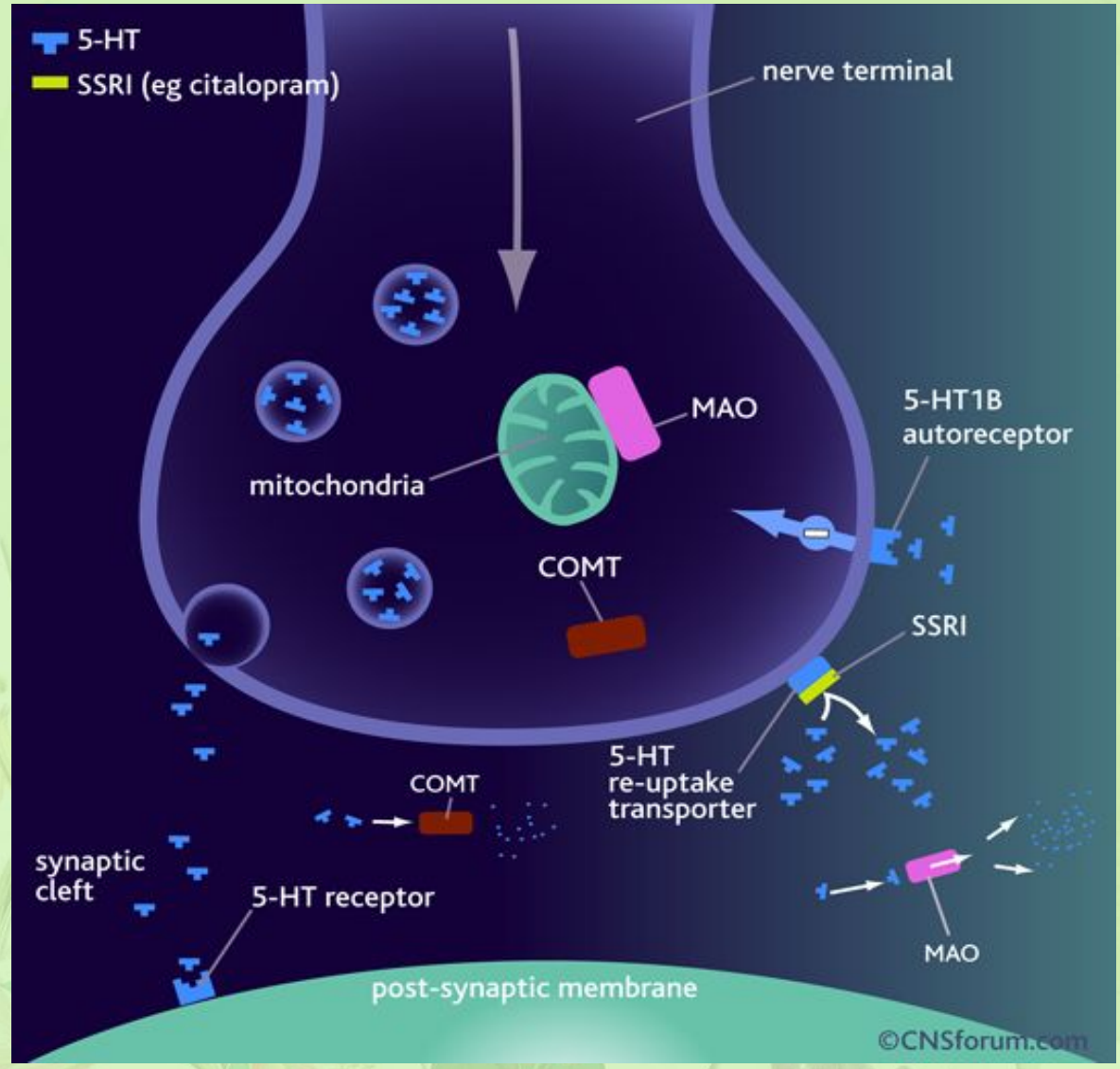


Mechanism of controlling depression

- Depression is caused by a deficiency of serotonin or norepinephrine
- Substances having positive effects on depression should impact levels of these neurotransmitters

Mechanism of action

- MAO inhibition occurs with high concentrations of SJW.
- Inhibits serotonin uptake in post-synaptic receptors from a reduction in serotonin receptors.
- Decreased uptake of dopamine and norepinephrine by SJW has been observed.


5-HT
SSRI (eg citalopram)
nerve terminal
MAO
5-HT1B
autoreceptor
mitochondria
COMT
SSRI
5-HT
re-uptake
transporter
COMT
synaptic
cleft
5-HT receptor
MAO
post-synaptic membrane
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SJW vs. prescription anti-depressants

- Anti-depressant side effects:
  - Headache, GI upset, nervousness, sexual dysfunction, fatigue, and insomnia.
- Symptoms not as common with SJW.
- SJW is less expensive

Hypericum Treatment of Mild-Moderate Depression in a Placebo-Controlled Study. A Prospective, Double-Blind, Randomized, Multicentre Study
Human Psychopharmacology (1998) 13

- Specific Aim

  Evaluate the clinical efficacy of hypericum extract against placebo.

- Study Design

  Prospective, double-blind, randomized, placebo-controlled, multicenter study

- Subjects
  - 162 patients (54 men, 108 women)
  - >18 years old
  - With mild to moderate depression (16-24 HAMD score)

Hypericum Treatment of Mild-Moderate Depression in a Placebo-Controlled Study. A Prospective, Double-Blind, Randomized, Multicentre Study
Human Psychopharmacology (1998) 13

- Treatment
  - 2 x 250 mg/day ZE117 .5mg hypericin or placebo
  - 6 weeks
- Compliance
  - Monitored by providing medication in a MEMS-4 container, which has a built in computer chip to record opening dates and times.
- Outcome Measures
  - Hamilton Depression Score – improvement of 50% from baseline or a total score of 10 or less.

Hypericum Treatment of Mild-Moderate Depression in a Placebo-Controlled Study. A Prospective, Double-Blind, Randomized, Multicentre Study
Human Psychopharmacology (1998) 13

- Results
  - Compliance rate of 88.9%
  - Mean HAMD Scores
    - Placebo group 18.76 → 17.89
    - Active group 20.13 → 10.53
- Demonstrates that hypericum extract is an effective treatment for mild to moderate depression.

Efficacy of St. John's wort extract WS 5570 in major depression: A double-blind, placebo-controlled trial
The American Journal of Psychiatry (2002) 159:8

- Specific Aim
  - Investigate the antidepressant efficacy and safety of Hypericum perforatum extract.
- Study Design
  - Double-blind, placebo-controlled, multi-center trial.
- Subjects
  - Age 18 to 65
  - Had a current major depressive episode meeting the DSM-IV criteria
  - HAMD score between 18 and 25
  - 375 patients

Efficacy of St. John's wort extract WS 5570 in major depression: A double-blind, placebo-controlled trial
The American Journal of Psychiatry (2002) 159:8

- Treatment
  - 3 x 300 mg/day .12-.28% hypericin or placebo
  - 6 weeks
- Outcome Measures
  - HAMD 50% lower than at baseline

Efficacy of St. John's wort extract WS 5570 in major depression: A double-blind, placebo-controlled trial
The American Journal of Psychiatry (2002) 159:8

- Results
  - Percent of responders was significantly higher for St. John's Wort (52.7%) than for placebo (42.3%).
- Adverse Effects
  - SJW: 30% Placebo: 37%

Effect of Hypericum perforatum in Major Depressive Disorder A Randomized Controlled Trial
JAMA (2002) 287:14

- Specific Aim
  - To test the efficacy and safety of a well characterized Hypericum Perforatum extract in major depressive disorder.
- Study Design
  - Randomized, double-blind, parallel group, outpatient trial of hypericum, sertraline, or placebo treatment.
- Subjects
  - Outpatients meeting DSM-IV criteria
  - Minimum score of 20 on HAMD
  - 340 patients

Effect of Hypericum perforatum in Major Depressive Disorder A Randomized Controlled Trial
JAMA (2002) 287:14

- Treatment
  - 900 mg/day .12-.28% hypericin or
  - Sertraline or
  - Placebo
  - 8 weeks
  - Could receive increased amounts after weeks 3 or 4 if CGI score was above 3 or 4.
- Outcome Measures
  - Clinical Global Impressions Scales for Severity (CGI) score of 1 or 2 and
  - Decrease in HAMD score at least 50% and
  - HAMD score of 9 to 12

Effect of Hypericum perforatum in Major Depressive Disorder A Randomized Controlled Trial
JAMA (2002) 287:14

- Results
  - Full response rates at acute phase exit did not differ between placebo and either hypericum or sertraline.
  - Study fails to support efficacy of H Perforatum in moderately severe major depression.

St John's wort for depression-an overview and meta-analysis of randomized clinical trials British Medical Journal (1996)

- Objective
  - To investigate if extracts of St. John's wort are more effective than placebo in the treatment of depression, are as effective as standard antidepressive treatment and have fewer side effects than standard antidepressant drugs.
- Trials
  - 23 randomized trials including total of 1757 outpatients with mild or moderately severe depressive disorders. 15-placebo controlled, 8-compared with another drug treatment.

St John's wort for depression-an overview and meta-analysis of randomized clinical trials British Medical Journal (1996)

- Treatment
  - Hypericin varied .4 to 2.7 mg
  - 300 mg to 1000 mg
  - 4 to 8 weeks

St John's wort for depression-an overview and meta-analysis of randomized clinical trials British Medical Journal (1996)

- Hypericum vs. Placebo
  - HAMD: significant effect of hypericum over placebo. Average 4.4 points better.
- Hypericum vs. Standard Antidepressants
  - HAMD scores slightly better with hypericum than standard

St John's wort for depression-an overview and meta-analysis of randomized clinical trials British Medical Journal (1996)

- Side Effects
  - Hypericum 19.8%
  - Standard 52.8%
- Conclusion
  - Good evidence that hypericum is better than placebo. Insufficient evidence that SJW works as well as antidepressants.

Adverse Effects

- Increased sensitivity to light
- Dry mouth
- Dizziness
- GI symptoms
- Fatigue
- Headache
- Sexual dysfunction

Herb-drug Interactions

- St. John's Wort inducer of various drug metabolizing enzymes
- Urgent bulletin to physicians from Committee on Safety of Medicine

Herb-drug Interactions: Committee on Safety of Medicine

- HIV Medications
  - Reduced blood levels with possible loss of HIV suppression
- Warfarin
  - Reduced anticoagulant effects and need for increased dose
- Cyclosporin
  - Reduced blood levels with risk of transplant rejection

Herb-drug Interactions: Committee on Safety of Medicine

- Oral Contraceptives
  - Reduced blood levels with risk of unintended pregnancy
- Anticonvulsants
  - Reduced blood levels with risk of seizures
- Digoxin
  - Reduced blood levels and loss of control of heart rhythm or heart failure

Herb-drug Interactions: Committee on Safety of Medicine

- Theophylline
  - Reduced blood levels and loss of control of asthma
- Triptans & SSRIs
  - Increased serotonergic effects with increased incidence of adverse reaction

Summary & Recommendations

- St. John's Wort appears to be more effective than placebo in treating mild to moderate depression.
- Assess potential herb-drug interactions.
- Strongly encourage SJW usage to be monitored by a physician.