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## “ST. JOHN'S WORT: THE HERBAL HOPE FOR DEPRESSION - A REVIEW.”

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### ABSTRACT:

This abstract presents an overview of St. John's Wort (*Hypericum perforatum L.*), highlighting its pharmacognostic characteristics, bioactive constituents, antidepressant activity, adverse effects, marketed preparations, and uses. Pharmacognostically, St. John's Wort is identifiable by its distinctive yellow flowers and perforated leaves. Its bioactive constituents, including hypericin, hyperforin, and flavonoids, are responsible for its antidepressant activity through the inhibition of neurotransmitter reuptake. While effective in managing mild to moderate depression and anxiety, St. John's Wort exhibits adverse effects such as gastrointestinal disturbances and photosensitivity, along with potential drug interactions. Various commercial preparations, including capsules, tablets, extracts, and teas, are available in the market, differing in concentrations of bioactive constituents. Despite its therapeutic benefits, caution is warranted in its use due to adverse effects and interactions. In conclusion, St. John's Wort represents a promising herbal remedy for mood disorders, necessitating careful consideration of its safety profile and standardization of formulations to ensure optimal therapeutic outcomes.

**KEYWORDS:** St. John's Wort, *Hypericum perforatum L.*, pharmacognosy, bioactive constituents, antidepressant activity, adverse effects, marketed preparations, uses.

## INTRODUCTION:

St. John's Wort (*Hypericum perforatum*) has a rich historical background as a medicinal herb, dating back to ancient Greece and widely recognized for its diverse therapeutic applications. Native to Europe, it has also found its place in various regions, including the United States and Canada.

One of its primary uses lies in the treatment of depression, where it is believed to modulate neurotransmitter levels in the brain, particularly serotonin, dopamine, and norepinephrine, crucial for mood regulation. Studies indicate its efficacy in managing mild to moderate depression, often comparable to standard antidepressants but with fewer side effects. Beyond depression, St. John's Wort is employed for an array of ailments, including anxiety and certain skin conditions like wounds and eczema, attributed to its anti-inflammatory and antibacterial properties.

Available in multiple forms such as capsules, tablets, liquid extracts, and teas, standardized products ensure consistent levels of active ingredients. Typically, a dosage of 300 mg thrice daily is recommended for depression, although individual variations and condition-specific formulations may exist. While generally deemed safe for short-term use in adults, caution is warranted due to potential interactions and side effects. St. John's Wort interacts with numerous medications, including antidepressants, oral contraceptives, and anticoagulants, compromising their efficacy. Moreover, adverse effects like gastrointestinal symptoms and heightened photosensitivity are noted. Special populations, including children, pregnant or breastfeeding women, and individuals with bipolar disorder, are advised against its usage due to potential exacerbation of their conditions.

St. John's Wort (*Hypericum perforatum*) is a well-known herbal remedy with a long history of use for various ailments. This review aims to explore its bioactive constituents, antidepressant activity, uses, and adverse effects. The plant contains several bioactive compounds, including hypericin, hyperforin, and flavonoids, which are believed to contribute to its pharmacological effects.

One of the most studied properties of St. John's Wort is its antidepressant activity. Research suggests that it may be effective in the treatment of mild to moderate depression, possibly due to its ability to inhibit the reuptake of neurotransmitters such as serotonin, dopamine, and norepinephrine. However, the mechanism of action is not fully understood until.



Figure 1 St. John's Wort Flower

**PHARMACOGNOSTIC ACCOUNT:**

Aspect	Description (1)
Generic Name	St. John’s Wort
DrugBank Accession	DB01323
Type	Biotech
Groups	Approved, Investigational, Nutraceutical
Synonyms	Common St John’s Wort flowering top, Hyperici herba, Saint John’s Wort, St. John’s Wort, and more
Uses	Traditional medicine: used for centuries in herbalism; Medical research: studied for depression
Interactions	Can interfere with various drugs, affecting their metabolism and efficacy(2)
Side effects	Include stomach pain, fatigue, restlessness, photosensitivity, skin irritation, and mood swings.

*Table 1 Pharmacognostic table of the St. John’s Wort Flower*

Description	A perennial flowering plant that grows up to one meter tall, featuring many yellow flowers with black glands around their edges, long stamens, and three pistils.(3)
Origin	Possibly a hybrid between <i>H. attenuatum</i> and <i>H. maculatum</i> originating from Siberia. Native to temperate regions across Eurasia and North Africa.
Distribution	Found worldwide, introduced to East Asia, Australia, New Zealand, North and South America. Considered a noxious weed in non-native areas.
Bioactive Compounds	Produces chemicals like hypericin and hyperforin which have various medical uses, including acting as antidepressants.(4)
Traditional Medicine	Used since at least the first century AD, often as a cure-all. Modern times focus has been on its use as an antidepressant.(5)
Environmental Impact	Densely covers open areas excluding native plants, and considered poor grazing material. Biocontrol methods have been introduced to control its spread.(6),(7),(8)

*Table 2 Pharmacognostic description of the St. John’s Wort Flower*

**BIOACTIVE COMPOUNDS:**

<b>Compounds</b>	<b>Class</b>	<b>Biological activity</b>
Hypericin	Naphthodianthrone	Antidepressant, anticancer, antiviral)(9),(10),(11)
Pseudohypericin	Naphthodianthrone	Antidepressants (12)
Hyperforin	Acylphloroglucinol	Antidepressant, anti-inflammatory, antimicrobial (13),(14),(15)
Adhyperforin	Acylphloroglucinol	Antidepressants (16)
Quercetin	Flavonol	Antioxidant, anti-inflammatory, anticancer (17),(18),(19)
<b>Rutin</b>	Flavonol glycoside	Antioxidant, anti-inflammatory (20),(21)
<b>Chlorogenic</b>	Phenolic acid	Antioxidant, anti-inflammatory, antidiabetic (22),(23),(24)
<b>Caffeic acid</b>	Phenolic acid	Antioxidant, anti-inflammatory (25)

*Table 3 Main bioactive compounds of St. John's Wort Flower*

St. John's wort contains a diverse array of bioactive compounds, with the major ones being the naphthodianthrone hypericin and pseudohypericin, the acylphloroglucinols hyperforin and adhyperforin, and various flavonoids and phenolic acids

These compounds exhibit a wide range of pharmacological activities, including antidepressant, anticancer, antiviral, anti-inflammatory, antimicrobial, antioxidant, and antidiabetic effects. The antidepressant activity is attributed mainly to hypericin, pseudohypericin and hyperforin.

The flavonoids quercetin and rutin, as well as the phenolic acids chlorogenic acid and caffeic acid, contribute significantly to the antioxidant and anti-inflammatory properties of St. John's wort extracts. Chlorogenic acid also shows potential antidiabetic effects.

Following are the chemical structure(26):

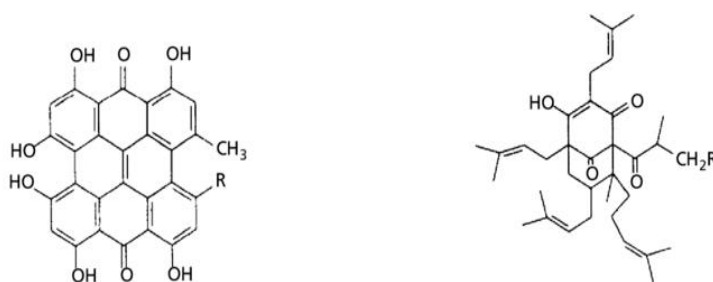
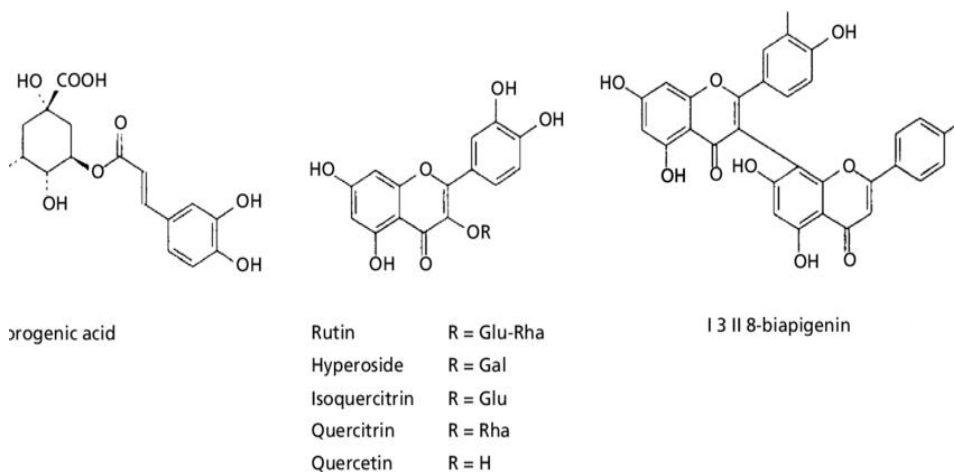


Figure 2 Chemical Structure of bioactive compounds

## ANTIDEPRESSANT ACTIVITY OF DRUG:

St. John's wort (*Hypericum perforatum*) is a flowering plant that has been used for centuries to treat a variety of ailments, including depression. The main bioactive compounds responsible for its antidepressant activity are hypericin, pseudohypericin, hyperforin, and various flavonoids.

### ➤ Mechanism of Action

The exact mechanism by which St. John's wort exerts its antidepressant effects is not fully understood, but several mechanisms have been proposed.

1. Inhibition of serotonin, dopamine, and noradrenaline reuptake: St. John's wort inhibits the synaptosomal uptake of these neurotransmitters, similar to the mechanism of action of selective serotonin reuptake inhibitors (SSRIs). (27),(28)
2. Activation of GABA and glutamate receptors: St. John's wort has been shown to have significant affinity for adenosine, GABA(A), GABA(B), and glutamate receptors, which may contribute to its antidepressant effects. (29)
3. Downregulation of beta-adrenergic receptors and upregulation of serotonin 5-HT(2) receptors: In vivo studies have shown that St. John's wort extract leads to these changes in receptor expression in the rat frontal cortex. (30)
4. Regulation of hypothalamic-pituitary-adrenal axis function: Recent studies suggest that St. John's wort is involved in the regulation of genes that control the HPA axis, which is often dysregulated in depression. (31)



### ➤ Efficacy

Several studies have demonstrated that St. John's wort is more effective than a placebo and comparable to standard antidepressants in treating mild to moderate depression. In fact, some research has shown the supplement to be as effective as several prescription antidepressants, such as SSRIs. (32)

In a meta-analysis of 29 studies involving 5,489 patients with depression, St. John's wort was found to be superior to placebo and similarly effective as standard antidepressants, with a lower incidence of side effects. (33)

### ➤ Dosage and Administration

The recommended dosage of St. John's wort for the treatment of depression is 900 mg per day, taken in three divided doses (300 mg three times daily). It may take 2 to 4 weeks for the full clinical effect to manifest, as plasma levels continue to rise gradually over several weeks. (34)

### ➤ Safety and Tolerability

St. John's wort is generally well-tolerated, with an overall side-effect rate of 2.4% in clinical trials. The most common side effects include gastrointestinal upset, increased anxiety, minor palpitations, photosensitivity, fatigue, restlessness, dry mouth, headache, and increased depression.

Transient photosensitivity is the most common side effect and occurs more frequently at higher dosages. St. John's wort should be used cautiously in patients with bipolar disorder due to a few case reports of St. John's wort-related mania. (35),(36)

### ➤ Drug Interactions

St. John's wort can interact with a wide range of medications due to its ability to induce cytochrome P450 3A4 activity. This can lead to decreased effectiveness of many drugs, as at least half of all marketed medications are metabolized via this pathway.(37)

Some of the medications that may interact with St. John's wort include oral contraceptives, anticoagulants, anticonvulsants, antidepressants, antifungals, antiretrovirals, antitumor agents, cardiovascular drugs, immunosuppressants, and opioid analgesics. Patients should be advised to consult with their healthcare provider before using St. John's wort in combination with any other medications. (38)

## **MARKETED PREPARATIONS:**

St. John's Wort, we had investigated into its marketed preparations, which typically center around the plant's medicinal properties, particularly its potential as a natural remedy for depression and anxiety. Marketed preparations often include extracts derived from the flowers, leaves, and stems of the St. John's Wort plant, standardized to contain specific concentrations of active compounds like hypericin and hyperforin. These preparations commonly come in various forms such as capsules, tablets, liquid extracts, and topical oils. While St. John's Wort is widely available and used by many seeking alternative treatments for mood disorders, its efficacy and safety remain subjects of ongoing research and debate within the scientific community, particularly concerning its potential interactions with other medications. Therefore, as a research student, exploring the nuances of these marketed preparations, including their composition, dosage, and clinical evidence supporting their use, would be crucial for gaining a comprehensive understanding of St. John's Wort and its therapeutic potential. Following are some marketed preparations.



Figure 3 Tablets



Figure 4 powder



Figure 5 Tablets



Figure 6 Capsules

**ADVERSE EFFECTS:**

1. Toxicological effects

Toxicological studies on Herka extract LI 160 have shown that the ineffective dose in mice and rats is greater than 5000 mg/kg. Long-term toxicity studies in rats and dogs found only non-specific symptoms such as weight loss. In vivo and in vitro studies, did not show significant mutagenic properties of the herb. One bacterial study found genotoxicity in Salmonella typhimurium and attributed the effect to quercetin.

2. Effects on pregnancy and lactation

Although there are reports of human exposure to the herb during pregnancy, insufficient data are available. recommended for use during pregnancy or breastfeeding. In animal experiments, giving St. John's wort to mice before or during pregnancy did not significantly affect the cognitive functions of their offspring. In a recent study of a woman with postpartum depression who used St. John's wort, breast milk samples were taken not detected. adverse effects on mother or child. Only the hyperforin component of the herb was excreted in breast milk in measurable amounts.

3. General Adverse Effects

In published studies, the herb was generally well tolerated at recommended doses for up to 1-3 months. The most common side effects were gastrointestinal symptoms, skin reactions, fatigue and restlessness, restlessness

or anxiety, dizziness, headache, and dry mouth concluded that the number of side effects is comparable to placebo patients and less than with standard antidepressant treatment. Data from observational studies showed that side effects may occur in 3% of patients. A review of adverse events in patients treated with 1.08 mg/day hypericin between 1991 and 1999, including approximately 8 million individuals, documented 95 adverse events. A European pharmacovigilance study in which 3250 patients received 1.08 mg/day hypericin included the total. 4% of 2 side effects.

In a post-marketing study of Aristoforat, the incidence of side effects was documented to be 1% in 2,404 outpatients over 4-6 weeks. Plasma concentrations of the drug up to 300 ng/ml are tolerated. (39)

## USES:

St. John's Wort is commonly used to treat depression, anxiety, and mood disorders. It is also used for its anti-inflammatory, antioxidant, and antimicrobial properties. Additionally, it has been studied for its potential benefits in conditions such as menopausal symptoms, premenstrual syndrome (PMS), and skin disorders.

While St. John's Wort is generally considered safe for short-term use, it can cause adverse effects and interactions with other medications. Common side effects include gastrointestinal symptoms, dizziness, and photosensitivity. It can also interact with a wide range of medications, including antidepressants, anticoagulants, and oral contraceptives, leading to potentially serious effects.

## COUNTERPOINT:

St. John's Wort should not be used in children, pregnant or breastfeeding women, or individuals with bipolar disorder, as it may worsen these conditions. It should also be used with caution in individuals with certain medical conditions, such as liver disease or a history of substance abuse.

## CONCLUSION:

After delving into the introduction of St. John's Wort, it's evident that this herb holds significant potential in pharmacognosy due to its rich history of traditional use and modern scientific exploration. The exploration of its bioactive constituents has uncovered compounds like hyperforin and hypericin, which contribute to its antidepressant activity through various mechanisms. However, it's crucial to acknowledge the potential adverse effects associated with its use, such as photosensitivity and interactions with other medications. Despite this, the diverse uses of St. John's Wort in alleviating symptoms of depression, anxiety, and other mood disorders cannot be overlooked. In conclusion, while St. John's Wort offers promising antidepressant effects, its usage warrants careful consideration and monitoring due to potential adverse effects and interactions with other drugs.

## REFERENCES:

1. Rahimi, R., & Abdollahi, M. (2012). An update on the ability of St. John's wort to affect the metabolism of other drugs. *Expert Opinion on Drug Metabolism and Toxicology*, 8(6), 691–708. <https://doi.org/10.1517/17425255.2012.680886>
2. Russo, E., Scicchitano, F., ... B. W.-P., & 2014, undefined. (n.d.). *Hypericum perforatum: Pharmacokinetic, Mechanism of Action, Tolerability, and Clinical Drug–Drug Interactions*. *Wiley Online Library*. Retrieved May 14, 2024, from <https://onlinelibrary.wiley.com/doi/abs/10.1002/ptr.5050>
3. Mehta, S. (2012). *Pharmacognosy of St. John's Wort*. <http://pharmaxchange.info/press/2012/12/pharmacognosy-of-st-johns-wort/>



4. WHO. (2002). WHO Monographs on Selected Medicinal Plants. In *WHO monographs on selected medicinal plants* (Vol. 2). World Health Organization. <https://archive.org/details/medicinal-plants/who-monographs-on-selected-medicinal-plants-vol-2/page/149>
5. Apaydin, E. A., Maher, A. R., Shanman, R., Booth, M. S., Miles, J. N. V., Sorbero, M. E., & Hempel, S. (2016). A systematic review of St. John's wort for major depressive disorder. *Syst Rev*, 5(1), 148. <https://doi.org/10.1186/s13643-016-0325-2>
6. Apaydin, E. A., Maher, A. R., Shanman, R., Booth, M. S., Miles, J. N. V., Sorbero, M. E., & Hempel, S. (2016). A systematic review of St. John's wort for major depressive disorder. *Syst Rev*, 5(1), 148. <https://doi.org/10.1186/s13643-016-0325-2>
7. Dhayabaran, V., Pharmacognosy, A. M.-J. of P. &, & 2017, undefined. (2017). Nanoparticulated formulations of St. John's wort (*Hypericum perforatum* L.) as smart drug delivery system combating depression incited in mice models. *Redalyc.Org*, 5(3), 187–199. <https://www.redalyc.org/pdf/4960/496053943006.pdf>
8. Zeliou, K., Kontaxis, N., ... E. M.-... of chromatographic, & 2017, undefined. (n.d.). Optimized and Validated HPLC Analysis of St. John's Wort Extract and Final Products by Simultaneous Determination of Major Ingredients. *Academic.Oup.ComK Zeliou, NI Kontaxis, E Margianni, C Petrou, FN LamariJournal of Chromatographic Science, 2017•academic.Oup.Com*. Retrieved May 14, 2024, from <https://academic.oup.com/chromsci/article-abstract/55/8/805/3792897>
9. Alahmad, A., Alghoraibi, I., Zein, R., Kraft, S., Dräger, G., Walter, J.-G., & Scheper, T. (2022). Identification of Major Constituents of *Hypericum perforatum* L. Extracts in Syria by Development of a Rapid, Simple, and Reproducible HPLC-ESI-Q-TOF MS Analysis. *ACS Publications*, 7(16), 13475–13493. <https://doi.org/10.1021/acsomega.1c06335>
10. Caldeira, G., Gouveia, L., Serrano, R., Plants, O. S.-, & 2022, undefined. (2022). *Hypericum* genus as a natural source for biologically active compounds. *Mdpi.Com*. <https://doi.org/10.3390/plants11192509>
11. *The chemical structures of the main active constituents of St John's wort.* | *Download Scientific Diagram*. (n.d.). Retrieved May 14, 2024, from [https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort\\_fig1\\_7416464](https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort_fig1_7416464)
12. Rychlewski, P., Kamgar, E., Mildner-Szkudlarz, S., Kowalczewski, P. Ł., & Zembrzuska, J. (2023). Determination of the contents of bioactive compounds in St. John's wort (*Hypericum perforatum*): Comparison of commercial and wild samples. *Open Chemistry*, 21(1). <https://doi.org/10.1515/CHEM-2022-0347/MACHINEREADABLECITATION/RIS>
13. Alahmad, A., Alghoraibi, I., Zein, R., Kraft, S., Dräger, G., Walter, J.-G., & Scheper, T. (2022). Identification of Major Constituents of *Hypericum perforatum* L. Extracts in Syria by Development of a Rapid, Simple, and Reproducible HPLC-ESI-Q-TOF MS Analysis. *ACS Publications*, 7(16), 13475–13493. <https://doi.org/10.1021/acsomega.1c06335>
14. Caldeira, G., Gouveia, L., Serrano, R., Plants, O. S.-, & 2022, undefined. (2022). *Hypericum* genus as a natural source for biologically active compounds. *Mdpi.Com*. <https://doi.org/10.3390/plants11192509>
15. *The chemical structures of the main active constituents of St John's wort.* | *Download Scientific Diagram*. (n.d.). Retrieved May 14, 2024, from [https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort\\_fig1\\_7416464](https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort_fig1_7416464)
16. Caldeira, G., Gouveia, L., Serrano, R., Plants, O. S.-, & 2022, undefined. (2022). *Hypericum* genus as a natural source for biologically active compounds. *Mdpi.Com*. <https://doi.org/10.3390/plants11192509>
17. Alahmad, A., Alghoraibi, I., Zein, R., Kraft, S., Dräger, G., Walter, J.-G., & Scheper, T. (2022). Identification of Major Constituents of *Hypericum perforatum* L. Extracts in Syria by Development of a Rapid, Simple, and Reproducible HPLC-ESI-Q-TOF MS Analysis. *ACS Publications*, 7(16), 13475–13493. <https://doi.org/10.1021/acsomega.1c06335>
18. Kuo, C., Chou, Y., Liao, K., Shieh, C., *Molecules*, T. D.-, & 2020, undefined. (n.d.). Optimization of light intensity, temperature, and nutrients to enhance the bioactive content of hyperforin and rutin in St. John's wort. *Mdpi.Com*. <https://doi.org/10.3390/molecules25184256>
19. *The chemical structures of the main active constituents of St John's wort.* | *Download Scientific Diagram*. (n.d.). Retrieved May 14, 2024, from [https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort\\_fig1\\_7416464](https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort_fig1_7416464)

20. Kuo, C., Chou, Y., Liao, K., Shieh, C., *Molecules*, T. D.-, & 2020, undefined. (n.d.). Optimization of light intensity, temperature, and nutrients to enhance the bioactive content of hyperforin and rutin in St. John's wort. *Mdpi.Com.* <https://doi.org/10.3390/molecules25184256>
21. *The chemical structures of the main active constituents of St John's wort.* | Download Scientific Diagram. (n.d.). Retrieved May 14, 2024, from [https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort\\_fig1\\_7416464](https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort_fig1_7416464)
22. Alahmad, A., Alghoraibi, I., Zein, R., Kraft, S., Dräger, G., Walter, J.-G., & Scheper, T. (2022). Identification of Major Constituents of *Hypericum perforatum* L. Extracts in Syria by Development of a Rapid, Simple, and Reproducible HPLC-ESI-Q-TOF MS Analysis. *ACS Publications*, 7(16), 13475–13493. <https://doi.org/10.1021/acsomega.1c06335>
23. Rychlewski, P., Kamgar, E., Mildner-Szkudlarz, S., Kowalczewski, P. Ł., & Zembrzuska, J. (2023). Determination of the contents of bioactive compounds in St. John's wort (*Hypericum perforatum*): Comparison of commercial and wild samples. *Open Chemistry*, 21(1). <https://doi.org/10.1515/CHEM-2022-0347/MACHINEREADEABLECITATION/RIS>
24. *The chemical structures of the main active constituents of St John's wort.* | Download Scientific Diagram. (n.d.). Retrieved May 14, 2024, from [https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort\\_fig1\\_7416464](https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort_fig1_7416464)
25. Rychlewski, P., Kamgar, E., Mildner-Szkudlarz, S., Kowalczewski, P. Ł., & Zembrzuska, J. (2023). Determination of the contents of bioactive compounds in St. John's wort (*Hypericum perforatum*): Comparison of commercial and wild samples. *Open Chemistry*, 21(1). <https://doi.org/10.1515/CHEM-2022-0347/MACHINEREADEABLECITATION/RIS>
26. *The chemical structures of the main active constituents of St John's wort.* | Download Scientific Diagram. (n.d.). Retrieved May 14, 2024, from [https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort\\_fig1\\_7416464](https://www.researchgate.net/figure/The-chemical-structures-of-the-main-active-constituents-of-St-Johns-wort_fig1_7416464)
27. Butterweck, V. (2003). Mechanism of action of St John's wort in depression: What is known? *CNS Drugs*, 17(8), 539–562. <https://doi.org/10.2165/00023210-200317080-00001/METRICS>
28. LAWVERE, S., & MAHONEY, M. C. (2005). St. John's Wort. *American Family Physician*, 72(11), 2249–2254. <https://www.aafp.org/pubs/afp/issues/2005/1201/p2249.html>
29. Butterweck, V. (2003). Mechanism of action of St John's wort in depression: What is known? *CNS Drugs*, 17(8), 539–562. <https://doi.org/10.2165/00023210-200317080-00001/METRICS>
30. Butterweck, V. (2003). Mechanism of action of St John's wort in depression: What is known? *CNS Drugs*, 17(8), 539–562. <https://doi.org/10.2165/00023210-200317080-00001/METRICS>
31. Butterweck, V. (2003). Mechanism of action of St John's wort in depression: What is known? *CNS Drugs*, 17(8), 539–562. <https://doi.org/10.2165/00023210-200317080-00001/METRICS>
32. *St. John's wort - Mayo Clinic.* (n.d.-a). Retrieved May 14, 2024, from <https://www.mayoclinic.org/drugs-supplements-st-johns-wort/art-20362212>
33. Maciej Serda, Becker, F. G., Cleary, M., Team, R. M., Holtermann, H., The, D., Agenda, N., Science, P., Sk, S. K., Hinnebusch, R., Hinnebusch A, R., Rabinovich, I., Olmert, Y., Uld, D. Q. G. L. Q., Ri, W. K. H. U., Lq, V., Frxqwu, W. K. H., Zklfk, E., Edvhg, L. V., ... فاطمی, ح. (2013). Synteza i aktywność biologiczna nowych analogów tiosemikarbazonowych chelatorów żelaza. *Uniwersytet Śląski*, 7(1), 343–354. <https://doi.org/10.2/JQUERY.MIN.JS>
34. LAWVERE, S., & MAHONEY, M. C. (2005). St. John's Wort. *American Family Physician*, 72(11), 2249–2254. <https://www.aafp.org/pubs/afp/issues/2005/1201/p2249.html>
35. LAWVERE, S., & MAHONEY, M. C. (2005). St. John's Wort. *American Family Physician*, 72(11), 2249–2254. <https://www.aafp.org/pubs/afp/issues/2005/1201/p2249.html>
36. *St. John's wort - Mayo Clinic.* (n.d.-b). Retrieved May 14, 2024, from <https://www.mayoclinic.org/drugs-supplements-st-johns-wort/art-20362212>
37. GORDON, J. B. (1998). SSRIs and St. John's Wort: Possible Toxicity? *American Family Physician*, 57(5), 950–953. <https://www.aafp.org/pubs/afp/issues/1998/0301/p950.html>
38. *St. John's wort - Mayo Clinic.* (n.d.-b). Retrieved May 14, 2024, from <https://www.mayoclinic.org/drugs-supplements-st-johns-wort/art-20362212>
39. Hammerness, P., Basch, E., Ulbricht, C., Barrette, E. P., Foppa, I., Basch, S., Bent, S., Boon, H., & Ernst, E. (2003). St. John's Wort: A Systematic Review of Adverse Effects and Drug Interactions for the Consultation Psychiatrist. *Psychosomatics*, 44(4), 271–282. <https://doi.org/10.1176/APPI.PSY.44.4.271>