

St. John's Wort (Hypericum perforatum) as an Alternative Treatment for Depression

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Abstract

Depression is one of the most common mental disorders worldwide that has a significant impact on the quality of life of individuals and society. Depression has recently become one of the mental health illnesses that many people in Indonesia experience, but Indonesian people do not yet have concerns about the treatment of depression, especially mild depression. Conventional depression treatments that already exist, such as selective serotonin reuptake inhibitor (SSRI) antidepressants, have been proven effective, but have side effects, so people are afraid to undergo treatment. St. John's Wort (*Hypericum perforatum*) is one of the alternative treatments for depression that is popular throughout the world, but in Indonesia, no herbal medicine industry company has developed this plant as a treatment for mild depression with herbs. This review aims to review the effectiveness and safety of St. John's Wort as a treatment for depression, as well as discuss its potential benefits and limitations. Based on a literature review, St. John's Wort is effective in reducing symptoms of depression in patients with mild to moderate depression. However, of course, it still needs to be used with caution because of the potential for side effects and interactions with other drugs. Thus, St. John's Wort can be an alternative treatment for depression with new herbs in Indonesia that are effective, but it needs to be used under strict supervision.

Keywords: Antidepressant, Herbal plant, *Hypericum perforatum*

INTRODUCTION

Depression is one of the most common mental disorders worldwide, with a significant impact on the quality of life of individuals and communities. According to the World Health Organization (WHO, 2017), depression is a leading cause of disability and premature death worldwide. Conventional treatments for depression, such as selective serotonin reuptake inhibitor (SSRI) antidepressants, are effective in reducing depressive symptoms, but have side effects and limitations (Gelenberg et al., 2019). Many individuals with depression experience side effects such as nausea, headaches, and sexual dysfunction, reducing their quality of life (Mohsin, 2019).

Furthermore, some individuals may not respond to conventional treatments or have medical conditions that prevent them from using them. Therefore, many individuals seek more natural and safe alternative treatments. One popular alternative abroad is St. John's Wort (*Hypericum perforatum*), an herbal plant that has been used for centuries to treat depression (Forsdike, 2019).

St. John's Wort has been used in traditional medicine in various countries, including Europe and Asia, to treat a variety of conditions, including depression, anxiety, and insomnia. This plant contains various active compounds, including hyperforin and hypericin, which are believed to have antidepressant effects (Jerome, 2024). However, treating depression using this plant is not yet popular in Indonesia. This review aims to assess the effectiveness of St. John's Wort as an alternative treatment for depression, as well as discuss its potential benefits and limitations. Therefore, this review is expected to provide an overview of St. John's Wort as an alternative psychiatric/neurological treatment, including as an antidepressant.

METHODS

This journal review process was conducted through an internet search using the keywords "St. John's Wort," "Herbal Treatment for Neurological and Psychiatric Diseases," "*Hypericum perforatum*," and "Herbal Treatment for Depression." The primary data sources obtained included 16 national and international journals. These journals were then screened. Inclusion criteria were journals published within the last seven years. Other sources came from other journals related to herbal treatment for neurological and psychiatric diseases..

RESULTS

Depression is a complex mental disorder that can affect anyone, regardless of age, gender, or background (WHO, 2017). Depression can manifest itself in a variety of ways, including feelings of sadness, loss of interest in previously enjoyed activities, changes in appetite, sleep disturbances, and fatigue (WHO, 2017). Depression can significantly impact an individual's quality of life, social relationships, and work productivity (Salawi, 2003). If not treated appropriately, depression can lead to disability and even premature death (WHO, 2017).

Selective serotonin reuptake inhibitors (SSRIs) are commonly used to treat depression. Fluoxetine is the most commonly used SSRI. SSRIs work by inhibiting serotonin reuptake at synapses, thereby increasing serotonin levels in the synaptic cleft.

Serotonin is a neurotransmitter that plays a role in regulating emotions and behavior. By increasing serotonin levels, SSRIs can help reduce symptoms of depression, such as feelings of sadness, loss of interest, and changes in appetite. Antidepressants such as SSRIs are also used to treat perinatal depression, or depression that occurs in pregnant and postpartum women (Zepeda, 2023). While SSRIs can be effective, they carry risks to the fetus and newborn. Therefore, many women seek alternatives such as herbal remedies (Zepeda, 2023).

Several herbal remedies have been traditionally used to treat various psychiatric and neurological conditions. St. John's Wort (*Hypericum perforatum*) has been used to treat mild to moderate depression with promising results (Linde et al., 2008). Kava (*Piper methysticum*) (Pittler & Ernst, 2000), Ginkgo biloba (Kennedy & Wightman, 2011), and Ashwagandha (*Withania somnifera*) (Cooley et al., 2018) have also been used to treat neurological and psychiatric conditions with proven effectiveness.

Table 1. St. John's Wort journal research results

Research Result	Author
SJW has potential as a neuroprotective and antinociceptive agent by reducing inflammation, oxidative stress, and pain..	Sarıyıldız, 2023
St. John's Wort has potential benefits in managing neuropathic pain.	Khaled,2025
St. John's Wort effectively treats depression in mice by increasing	Bussmann, 2024

LPE levels in the hippocampus, which has the potential to be a new biomarker for depression therapy.

Chitosan-based hypericin nanoemulsion has potential as a future treatment for depression..

Perinatal depression in pregnant and postpartum women can affect child development. St. John's Wort is an alternative treatment, but its safety and effectiveness require further research.

St. John's Wort is effective in treating mild to moderate depression and has a good safety profile, making it an attractive treatment option..

Long-term administration of *Hypericum perforatum* causes cognitive impairment, possibly due to decreased levels of neurotrophic factors, especially in female rats.

SJW is effective for mild to moderate depression, but is underused due to limited knowledge and concerns about drug interactions.

Further education and product standardization are needed to increase its use.

SJW is an effective and safer alternative treatment for mild to moderate major depressive disorder, but there is insufficient evidence for its use in severe depression. Additional research with better reporting quality is needed.

SJW is a potential alternative for treating mild to moderate MDD. Product quality control, side effect monitoring, and further research are needed.

Research on curcumin and *Hypericum perforatum* suggests potential antidepressant effects, but further research is needed for confirmation.

The safety and effectiveness of SJW in treating depression still require further research and strict regulation to ensure its safe use.

Salawi, 2023

Zepeda, 2023

Canenguez, 2022

Valvassori, 2018

Forsdike, 2017

Apaydin, 2016

Adadzi, 2024

Shamabadi, 2021

Mohsin, 2019

reducing inflammation, oxidative stress, and pain, thus potentially managing neuropathic pain (Sarryildiz, 2023). Research has also shown that SJW is effective in treating depression in mice by increasing LPE levels in the hippocampus, which has the potential to be a new biomarker for depression therapy. Furthermore, chitosan-based hypericin nanoemulsion has potential as a future treatment for depression (Salawi, 2023).

Perinatal depression in pregnant and postpartum women can affect child development, and SJW is an attractive treatment alternative (Zepeda, 2023). Although SJW is effective in treating mild to moderate depression and has a good safety profile, its safety and effectiveness require further research, especially in long-term use (Canenguez, 2022).

SJW is effective for mild to moderate depression, but is underutilized due to limited knowledge and concerns about drug interactions (Apaydin, 2016). Further education and product standardization are needed to increase its use. SJW is an effective and safer alternative treatment for mild to moderate major depressive disorder, but there is insufficient evidence for its use in severe depression (Jerome, 2024).

Research and *Hypericum perforatum* show potential antidepressant effects, but further research is needed for confirmation (Mohsin, 2019). Therefore, the safety and effectiveness of SJW in treating depression require further research and strict regulation to ensure its safe use. Therefore, SJW could be a potential alternative treatment for mild to moderate depression with product quality oversight, side effect monitoring, and further research.

CONCLUSION

Depression is a complex mental disorder that can affect anyone and significantly impacts the quality of life. While SSRIs can be effective in treating depression, they carry risks to the fetus and newborn, leading many women to seek alternatives such as herbal remedies. St. John's Wort (SJW) has shown potential as a neuroprotective and antinociceptive agent, and is effective in treating mild to moderate depression. However, the safety and effectiveness of SJW require further research, particularly in long-term use. Therefore, SJW may be a potential alternative for the treatment of mild to moderate depression with product quality control, side effect monitoring, and further research.

OFFERING THANKS

St. John's Wort (SJW) has shown potential as a neuroprotective and antinociceptive agent by

In writing this article review, the author would like to thank Mr. Apt. Wempi Budiana, M.Si, as a lecturer in the Herbal Medicine course at Bhakti Kencana University.

REFERENCES

1. Abdelrahman, K. M., & Hackshaw, K. V. (2021). Nutritional Supplements for the Treatment of Neuropathic Pain. *Biomedicines*, 9(6), 674. <https://doi.org/10.3390/biomedicines9060674>
2. Apaydin, E. A., Maher, A. R., Shanman, R., Booth, M. S., Miles, J. N., Sorbero, M. E., & Hempel, S. (2016). A systematic review of St. John's wort for major depressive disorder. *Systematic reviews*, 5(1), 148. <https://doi.org/10.1186/s13643-016-0325-2>
3. Bussmann, H., Bremer, S., Hernier, A. M., Drewe, J., Häberlein, H., Franken, S., Freytag, V., Boonen, G., & Butterweck, V. (2024). St. John's Wort Extract Ze 117 and Escitalopram Alter Plasma and Hippocampal Lipidome in a Rat Model of Chronic-Stress-Induced Depression. *International journal of molecular sciences*, 25(23), 12667.
4. Canenguez Benitez, J. S., Hernandez, T. E., Sundararajan, R., Sarwar, S., Arriaga, A. J., Khan, A. T., Matayoshi, A., Quintanilla, H. A., Kochhar, H., Alam, M., Mago, A., Hans, A., & Benitez, G. A. (2022). Advantages and Disadvantages of Using St. John's Wort as a Treatment for Depression. *Cureus*, 14(9), e29468. <https://doi.org/10.7759/cureus.29468>
5. Cooley, G., et al. (2018). Effects of ashwagandha (*Withania somnifera*) on cortisol levels in stressed individuals: A systematic review. *Journal of Alternative and Complementary Medicine*, 24(3), 236-245.
6. Forsdike, K., & Pirota, M. (2019). St John's wort for depression: scoping review about perceptions and use by general practitioners in clinical practice. *The Journal of pharmacy and pharmacology*, 71(1), 117–128. <https://doi.org/10.1111/jphp.12775>
7. Gelenberg, A. J., et al. (2019). Practice guideline for the treatment of patients with major depressive disorder. American Psychiatric Association. World Health Organization. (2017). Depression and Other Common Mental Disorders: Global Health Estimates
8. Jerome Adadzi, Nicholas A. Kerna. (2024). St. John's Wort (*Hypericum perforatum*) in Major Depressive Disorder: Efficacy, Safety, Clinical Implications, and Its Role as an Herbal Alternative or Complementary Treatment. Authorea. DOI: 10.22541/au.172782161.12647676/v1
9. Kennedy, D. O., & Wightman, E. L. (2011). Herbal extracts and phytochemicals: Plant secondary metabolites and the enhancement of human brain function. *Advances in Nutrition*, 2(1), 32-50.
10. Linde, K., et al. (2008). St John's Wort for major depression. *Cochrane Database of Systematic Reviews*, (4), CD000448.
11. Mohsin Ahmed, Rownak Jahan, and Mohammed Rahmatullah (2021). "St. John's Wort (*Hypericum perforatum*): A Review of its Potential Antidepressant Efficacy and Safety", *Australian Herbal Insight*, 4(1),1-6,10003
12. Nobakht, S. Z., Akaberi, M., Mohammadpour, A. H., Tafazoli Moghadam, A., & Emami, S. A. (2022). *Hypericum perforatum*: Traditional uses, clinical trials, and drug interactions. *Iranian journal of basic medical sciences*, 25(9), 1045–1058. <https://doi.org/10.22038/IJBMS.2022.65112.14338>
13. Otero, M. C., Ceric, F., Miranda-Rojas, S., Carreño, C., Escares, R., Escobar, M. J., Saracini, C., Atala, C., Ramírez-Barrantes, R., & Gordillo-Fuenzalida, F. (2024). Documentary Analysis of *Hypericum perforatum* (St. John's Wort) and Its Effect on Depressive Disorders. *Pharmaceuticals (Basel, Switzerland)*, 17(12), 1625
14. Pittler, M. H., & Ernst, E. (2000). Kava extract for treating anxiety. *Cochrane Database of Systematic Reviews*, (2), CD003383.
15. Salawi, A., Almoshari, Y., Sultan, M. H., Madkhali, O. A., Bakkari, M. A., Alshamrani, M., Safhi, A. Y., Sabei, F. Y., Al Hagbani, T., Ali, M. S., & Alam, M. S. (2023). Production, Characterization, and In Vitro and In Vivo Studies of Nanoemulsions Containing St. John's Wort Plant Constituents and Their Potential for

- the Treatment of Depression. *Pharmaceuticals* (Basel, Switzerland), 16(4), 490. <https://doi.org/10.3390/ph16040490>
16. Sarıyıldız, A., Kaplan, H. M., Şingirik, E., & KOZANOĞLU, E., (2023). Modulatory effects of *Hypericum perforatum* extract on sciatic nerve injury-induced peripheral neuropathy: an experimental study on mice. *Cukurova Medical Journal*, vol.48, no.2, 513-521.
 17. Shamabadi, A., & Akhondzadeh, S. (2021). Advances in Alternative and Integrative Medicine in the Treatment of Depression: A Review of the Evidence. *Archives of Iranian medicine*, 24(5), 409–418. <https://doi.org/10.34172/aim.2021.59>
 18. Valvassori, S. S., Borges, C., Bavaresco, D. V., Varela, R. B., Resende, W. R., Peterle, B. R., Arent, C. O., Budni, J., & Quevedo, J. (2018). *Hypericum perforatum* chronic treatment affects cognitive parameters and brain neurotrophic factor levels. *Revista Brasileira de Psiquiatria* (São Paulo, Brasil: 1999), 40(4), 367–375. <https://doi.org/10.1590/1516-4446-2017-2271>
 19. World Health Organization. (2017). *Depression and Other Common Mental Disorders: Global Health Estimates*.
 20. Zepeda, R. C., Juárez-Portilla, C., & Molina-Jiménez, T. (2023). St. John's Wort usage in treating perinatal depression. *Frontiers in behavioral neuroscience*, 16, 1066459. <https://doi.org/10.3389/fnbeh.2022.1066459>