

## SAFFRON SPICE OF LIFE FOR MENTAL HEALTH

**Ellie Wright**

*Dr., EGW Research Institute LLC (USA)*

### Abstract

**Background:** Herbal medicine have been widely used to treat anxiety and depression since ancient times. Among the most researched botanical medicine for mental health are: St.Johns Wort, Valerian, Passionflower, and Saffron. This review aims to mainly assess Saffron (*Crocus Sativus*) efficacy for optimization of mental health. Even if antidepressants are the first line treatment for depression many people do not respond as expected to them which calls for finding alternative treatment to support population mental health needs. This study aims to compare safety and efficacy of botanical medicine including *Crocus Sativus* (Saffron) versus medical drugs in improving mental health symptoms.

**Objectives:** to assess the efficacy, tolerability, and safety of saffron (herbal, plant-derived) compared to placebo or conventional drugs for psychological conditions.

**Selection criteria:** from Medline (Pubmed) it was selected a list randomised, double-blind controlled trials, clinical trials from 2017 to 2022.

**Data collection and analysis:** this systematic review aimed to compare the efficacy and safety of pharmacological and non-pharmacological treatments for major depressive disorder (MDD), post partum depression, attention deficit/hyperactivity disorder, mild cognitive impairment, anxiety. Primary outcomes were efficacy (response rate) and safety (overall risk of adverse events) of botanical medicine.

**Main results:** a systematic review with network meta-analyses and randomised controlled trials were identified from published sources through searches in PubMed. The primary outcomes were efficacy (treatment response) and safety. In analyzing the interventions Saffron studies suggest improvements in mental health and overall health.

**Author conclusions:** Some patients do not respond well to pharmaceuticals and can not tolerate the side effects of drugs. In trying to find alternatives medications herbal medicine is considered. Literature reveals clinical evidence for various phytomedicine along with good safety. The potential benefits of saffron in mental health is suggested by several studies still more evidence is needed. The quality of evidence for does not provide concerns regarding potential harms and suggest safety in using Saffron.

**Keywords:** *Saffron, mental health, psychologic, anxiety, depression.*

---

### 1. Background

The number of people with depression and anxiety have been increased in the last couple of years and it is still a challenge to treat. Even if antidepressants are the first line treatment for depression many people do not respond as expected to them which calls for finding alternative treatment to support mental health needs. Moreover, we have an increased number of people who prefer a natural approach to mental health because of the concern of short term and long term side effects of the prescription drugs. At the same time, we have a large population that are not compliant with the anti- depression prescription. There is a continuing search in finding more alternative solutions support the needs of a genetically diverse population challenged with mental health issues.

The objective for this research was to assess the efficacy, tolerability, and safety of saffron (herbal, plant-derived) compared to placebo or conventional drugs for psychological conditions.

As criteria from Medline (Pubmed) it was selected a list randomized, double-blind controlled trials, clinical trials from 2017 to 2022. Search criteria key words include: *saffron, mental health, psychologic, anxiety, depression.*

The data collection and analysis aimed to compare the efficacy and safety of the non pharmacological treatments more exactly Saffron in major depressive disorder (MDD), post partum depression, attention deficit/ hyperactivity disorder, anxiety and mild cognitive impairment.

Several randomized double-blind studies were chosen from different settings, conditions and age groups challenged with anxiety and depression. For example, Saffron efficacy was tested after chemotherapy, in youth anxiety, in comparison of saffron vs fluoxetine in moderate postpartum depression, in cognitive function in elderly, in post-menopausal hot flashes, in saffron vs citalopram in major depressive disorder.

Saffron (*Crocus sativus* L.) is a medicinal plant, originally cultivated in the East and Middle East.

Saffron is collected from the stigmas of flower plant. The most important constituents are crocins and crocetin which are forms of carotenoids. Saffron has been valued for the antioxidant and anti-inflammatory properties. Saffron main constituents are Crocin (glycosylated carotenoids) which has been associated with neuroprotective effects. Some studies that Crocin have been reporting neuroprotective effects and depression protective. Some of the benefit effects have not been fully understood but still reported. It is suggested that the anti depressive effect of Crocin-I is due to the suppression of neuroinflammation (IL-1 $\beta$ ) in reducing the oxidative damage (Cerdá-Bernad et al., 2022). A study showed that crocin-I might play an antidepressant effects in a model of chronic corticosterone (CORT)-induced depression. It was found after the oral dose of Crocin-I of 40mg/kg induced accumulation of nicotinamide in the liver and improved synthesis of NAD<sup>+</sup> and SIRT3 deacetylase to increase superoxide dismutase 2 and glutathione reductase (Xiao et al., 2019).

## 2. Conclusion

The potential benefits of saffron in mental health is suggested by several studies and still more evidence is needed. The quality of evidence for does not provide concerns regarding potential harms and suggest safety in using Saffron. Crocin is one of the main glycosylated carotenoids of saffron, studies suggest beneficial activities and has been reported to be associated with neuroprotective effects. In this paper the biological action of crocin was explored for the on depression-like through investing the mechanisms of actions including but not limited to neuroinflammation and oxidative damage. It is suggested that the antidepressant activity of crocin-I was probably achieved through the suppression of neuroinflammation (IL-1 $\beta$ ) and oxidative stress in the mouse hippocampus. Some studies suggests crocin-I could reduce the levels of oxidative damage markers (reactive oxygen species and malonaldehyde) to rescue impaired mitochondrial function. However, still the full mechanism of action is not fully understood and more studies are needed (Cerdá-Bernad et al., 2022).

## References

- Akhondzadeh, S., Mostafavi, S. A., Keshavarz, S. A., Mohammadi, M. R., Hosseini, S., & Eshraghian, M. R. (2020). A placebo controlled randomized clinical trial of *Crocus sativus* L. (saffron) on depression and food craving among overweight women with mild to moderate depression. *Journal of clinical pharmacy and therapeutics*, 45(1), 134–143. <https://doi.org/10.1111/jcpt.13040>
- Asadollahi, M., Nikdokht, P., Hatef, B., Sadr, S. S., Sahraei, H., Assarzaghan, F., & Pirzad Jahromi, G. (2019). Protective properties of the aqueous extract of saffron (*Crocus sativus* L.) in ischemic stroke, randomized clinical trial. *Journal of ethnopharmacology*, 238, 111833. <https://doi.org/10.1016/j.jep.2019.111833>
- Cerdá-Bernad, D., Valero-Cases, E., Pastor, J. J., & Frutos, M. J. (2022). Saffron bioactives crocin, crocetin and safranal: effect on oxidative stress and mechanisms of action. *Critical reviews in food science and nutrition*, 62(12), 3232–3249. <https://doi.org/10.1080/10408398.2020.1864279>
- Cicero, A. F., Bove, M., Colletti, A., Rizzo, M., Fogacci, F., Giovannini, M., & Borghi, C. (2017). Short-Term Impact of a Combined Nutraceutical on Cognitive Function, Perceived Stress and Depression in Young Elderly with Cognitive Impairment: A Pilot, Double-Blind, Randomized Clinical Trial. *The journal of prevention of Alzheimer's disease*, 4(1), 12–15. <https://doi.org/10.14283/jpad.2016.10>
- Ghajar, A., Neishabouri, S. M., Velayati, N., Jahangard, L., Matinnia, N., Haghighi, M., Ghaleiha, A., Afarideh, M., Salimi, S., Meysamie, A., & Akhondzadeh, S. (2017). *Crocus sativus* L. versus Citalopram in the Treatment of Major Depressive Disorder with Anxious Distress: A Double-Blind, Controlled Clinical Trial. *Pharmacopsychiatry*, 50(4), 152–160. <https://doi.org/10.1055/s-0042-116159>
- Kashani, L., Eslatmanesh, S., Saedi, N., Niroomand, N., Ebrahimi, M., Hosseinian, M., Foroughifar, T., Salimi, S., & Akhondzadeh, S. (2017). Comparison of Saffron versus Fluoxetine in Treatment of Mild to Moderate Postpartum Depression: A Double-Blind, Randomized Clinical Trial. *Pharmacopsychiatry*, 50(2), 64–68. <https://doi.org/10.1055/s-0042-115306>

- Lopresti, A. L., & Drummond, P. D. (2017). Efficacy of curcumin, and a saffron/curcumin combination for the treatment of major depression: A randomised, double-blind, placebo-controlled study. *Journal of affective disorders*, 207, 188–196. <https://doi.org/10.1016/j.jad.2016.09.047>
- Lopresti, A. L., & Smith, S. J. (2022). An examination into the mental and physical effects of a saffron extract (affron®) in recreationally-active adults: A randomized, double-blind, placebo-controlled study. *Journal of the International Society of Sports Nutrition*, 19(1), 219–238. <https://doi.org/10.1080/15502783.2022.2083455>
- Lopresti, A. L., Drummond, P. D., Inarejos-García, A. M., & Prodanov, M. (2018). affron®, a standardised extract from saffron (*Crocus sativus* L.) for the treatment of youth anxiety and depressive symptoms: A randomised, double-blind, placebo-controlled study. *Journal of affective disorders*, 232, 349–357. <https://doi.org/10.1016/j.jad.2018.02.070>
- Lopresti, A. L., Smith, S. J., Hood, S. D., & Drummond, P. D. (2019). Efficacy of a standardised saffron extract (affron®) as an add-on to antidepressant medication for the treatment of persistent depressive symptoms in adults: A randomised, double-blind, placebo-controlled study. *Journal of psychopharmacology (Oxford, England)*, 33(11), 1415–1427. <https://doi.org/10.1177/0269881119867703>
- Kashani, L., Esalatmanesh, S., Eftekhari, F., Salimi, S., Foroughifar, T., Etesam, F., Safiaghdam, H., Moazen-Zadeh, E., & Akhondzadeh, S. (2018). Efficacy of *Crocus sativus* (saffron) in treatment of major depressive disorder associated with post-menopausal hot flashes: a double-blind, randomized, placebo-controlled trial. *Archives of gynecology and obstetrics*, 297(3), 717–724. <https://doi.org/10.1007/s00404-018-4655-2>
- Salek, R., Dehghani, M., Mohajeri, S. A., Talaei, A., Fanipakdel, A., & Javadinia, S. A. (2021). Amelioration of anxiety, depression, and chemotherapy related toxicity after crocin administration during chemotherapy of breast cancer: A double blind, randomized clinical trial. *Phytotherapy research : PTR*, 35(9), 5143–5153. <https://doi.org/10.1002/ptr.7180>
- Tajaddini, A., Roshanravan, N., Mobasseri, M., Aeinehchi, A., Sefid-Mooye Azar, P., Hadi, A., & Ostadrahimi, A. (2021). Saffron improves life and sleep quality, glycaemic status, lipid profile and liver function in diabetic patients: A double-blind, placebo-controlled, randomised clinical trial. *International journal of clinical practice*, 75(8), e14334. <https://doi.org/10.1111/ijcp.14334>
- Tabeshpour, J., Sobhani, F., Sadjadi, S. A., Hosseinzadeh, H., Mohajeri, S. A., Rajabi, O., Taherzadeh, Z., & Eslami, S. (2017). A double-blind, randomized, placebo-controlled trial of saffron stigma (*Crocus sativus* L.) in mothers suffering from mild-to-moderate postpartum depression. *Phytomedicine : international journal of phytotherapy and phytopharmacology*, 36, 145–152. <https://doi.org/10.1016/j.phymed.2017.10.005>
- Wauquier, F., Boutin-Wittrant, L., Pourtau, L., Gaudout, D., Moras, B., Vignault, A., Monchoux De Oliveira, C., Gabaston, J., Vaysse, C., Bertrand, K., Abrous, H., Capuron, L., Castanon, N., Vauzour, D., Roux, V., Macian, N., Pickering, G., & Wittrant, Y. (2022). Circulating Human Serum Metabolites Derived from the Intake of a Saffron Extract (Safir'Inside™) Protect Neurons from Oxidative Stress: Consideration for Depressive Disorders. *Nutrients*, 14(7), 1511. <https://doi.org/10.3390/nu14071511>
- Xiao, Q., Xiong, Z., Yu, C., Zhou, J., Shen, Q., Wang, L., Xie, X., & Fu, Z. (2019). Antidepressant activity of crocin-I is associated with amelioration of neuroinflammation and attenuates oxidative damage induced by corticosterone in mice. *Physiology & behavior*, 212, 112699. <https://doi.org/10.1016/j.physbeh.2019.112699>