

Saffron

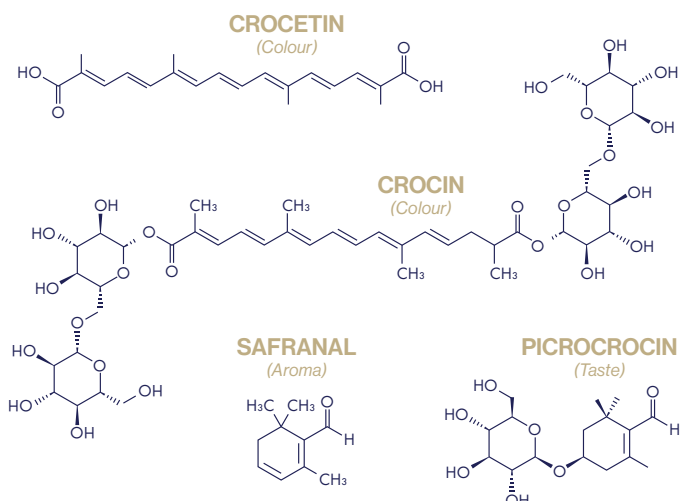
FOR THE MANAGEMENT OF MOOD, SLEEP AND PAIN



ARTICLE BY
DR ADRIAN LOPRESTI

Saffron is derived from the stigmas of the *Crocus sativus* flower. Each flower has three stigmas containing four major bioactive compounds: crocins, crocetin, picrocrocin, and safranal. Crocins and crocetin are responsible for the colour, picrocrocin for the taste, and safranal for the aroma. These compounds, along with the more than 150 volatile and non-volatile components, are responsible for the health enhancing properties of saffron.¹

Figure 1. Molecular structures of the bioactive substances



Saffron for mood support

Saffron has traditionally been used to treat eye, skin, respiratory, gastrointestinal, and genitourinary tract complaints. However, its mood-enhancing benefits have attracted the most interest over the last decade. Increasing research confirms that mood disorders are associated with several physiological disturbances, including disturbances in:

- Neurotransmitter activity
- Chronic, low-grade inflammation
- Excess oxidative stress
- Imbalances in the hypothalamic-pituitary-adrenal (HPA) axis
- Neurodegeneration²

Preclinical and clinical trials have shown that saffron can influence all these physiological pathways. For example, saffron seems to affect the activity of neurotransmitters such as serotonin and dopamine and has potent anti-inflammatory and antioxidant effects. Saffron can also modulate HPA axis activity by reducing cortisol concentrations and has neuroprotective effects.³

Saffron's antidepressant and anti-anxiety effects

A significant body of research has now accumulated demonstrating saffron's positive antidepressant and anti-anxiety effects. Findings from over 20 randomised controlled studies have regularly shown saffron can be an effective and safe treatment for mild-to-moderate depression.⁴ In randomised, double-blind, placebo-controlled studies, it regularly outperforms the placebo, typically working in 4 to 8 weeks.

In head-to-head studies with pharmaceutical antidepressants such as fluoxetine, imipramine, and citalopram, saffron has comparable efficacy with fewer side effects.⁵⁻⁷

In clinical trials my team have conducted, saffron reduced depressive and anxiety symptoms in teenagers⁹ and improved mood in women experiencing perimenopause.⁹ In another study that we conducted, saffron reduced depressive symptoms in adults taking a pharmaceutical antidepressant and tended to reduce adverse reactions associated with antidepressant use.¹⁰ In another study we conducted in 2021, saffron increased exercise enjoyment in recreationally-active males and increased their heart rate variability (a proxy measure of the stress response).¹¹ In all these studies, saffron was administered at 14mg twice daily.

Several systematic reviews and meta-analyses have now been published on the antidepressant and anxiolytic effects of saffron. These have all concluded that saffron is a promising natural agent to improve mood in people with depression and anxiety.^{3,4} In 2022, clinical guidelines for treating psychiatric disorders with nutraceuticals and phytochemicals were published by a taskforce of international expert.¹⁴ It was concluded that after St John's Wort, saffron had the largest body of evidence supporting its efficacy in treating unipolar depression. The taskforce provisionally recommended saffron as a stand-alone treatment for unipolar depression.

Saffron for sleep support

Throughout our studies, we received regular feedback of improved sleep, so we decided to examine the effects of saffron on sleep quality. We have conducted two randomised, double-blind, placebo-controlled trials examining the effects of saffron on sleep in people with unsatisfactory sleep. Again, positive results were identified.

Saffron improved sleep quality, mood after awakening, and restorative sleep.^{12,13}

We also found in one study that saffron increased evening melatonin concentrations.¹² This may be via its anti-inflammatory effects or its impact on neurotransmitter activity. In our first sleep study, saffron was administered at 14 mg twice daily. However, in the second study, it was administered at 14 mg or 28 mg one hour before bed. Results were comparable for all the doses, although mood upon awakening tended to be slightly higher with 28 mg dose.

Table 1. Dosages and research to support the use of saffron for mood and sleep disturbances

SAFFRON BENEFITS	TREATMENT
Depression and anxiety ⁴	14 mg, twice daily
Depression and anxiety in teenagers ⁸	
Mood support for perimenopausal women ⁹	
Depressive symptom reduction in people taking antidepressants ¹⁰	
Exercise enjoyment and improved heart rate variability ¹¹	
Melatonin production support ¹²	
Melatonin production support and improved mood upon waking ¹²	14-28 mg, one hour before bed

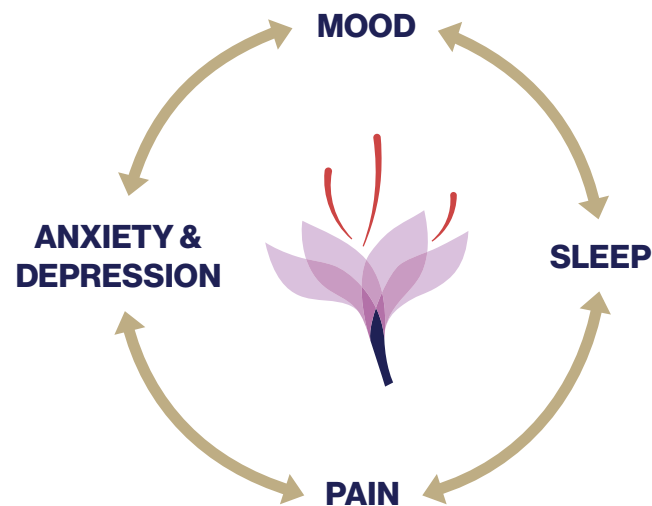


The association between sleep, mood and pain and the role of saffron

The positive effects of saffron on mood and sleep have important implications for all health conditions, as insomnia and depression are highly prevalent in most, if not all, disorders. For example, approximately one-third of people experiencing chronic pain suffer from depression, and about 50% suffer from insomnia.^{15,16} This has major treatment implications as suffering from comorbid chronic pain, depression, and/or insomnia can render pain and mood-related treatments less effective.

Research confirms that there is a bidirectional relationship between pain and sleep. In fact, some research has shown that sleep has a greater impact on pain than pain has on sleep.¹⁷

Therefore, treating sleep disturbances is imperative if someone presents with comorbid chronic pain and poor sleep. Saffron certainly presents as a good option. Although more research is required, there is some preclinical and animal research to suggest saffron can have analgesic and pain-relieving effects.^{18,19}



When it comes to saffron, quality is essential, as research confirms that because of its high cost, and the labour intensiveness associated with its cultivation, it is subject to adulteration. In fact, 1st-grade saffron in the market is rare.²⁰ Therefore, it is extremely important to choose high-quality extracts that have undergone clinical trials. So far, all my trials have been conducted on the patented saffron extract, affron®.

If you are looking to support clients with their mood and/ or sleep, saffron certainly presents as an evidence-based option. Obviously, it is not a magic pill and should be used as part of an integrative approach that targets a person's unique drivers of their mental or physical disturbances.



References

- Gohari, A.R., S. Saeidnia, and M.K. Mahmoodabadi, An overview on saffron, phytochemicals, and medicinal properties. *Pharmacognosy reviews*, 2013. 7(13): p. 61-6.
- Fries, G.R., et al. Molecular pathways of major depressive disorder converge on the synapse. *Mol Psychiatry*, 2023. 28(1): p. 284-297.
- Lopresti, A.L. and P.D. Drummond, Saffron (*Crocus sativus*) for depression: a systematic review of clinical studies and examination of underlying antidepressant mechanisms of action. *Hum Psychopharmacol*, 2014. 29(6): p. 517-27.
- Marx, W., et al., Effect of saffron supplementation on symptoms of depression and anxiety: a systematic review and meta-analysis. *Nutr Rev*, 2019.
- Kashani, L., et al., Comparison of Saffron versus Fluoxetine in Treatment of Mild to Moderate Postpartum Depression: A Double-Blind, Randomized Clinical Trial. *Pharmacopsychiatry*, 2017. 50(2): p. 64-68.
- Ghajar, A., et al., *Crocus sativus* L. versus Citalopram in the Treatment of Major Depressive Disorder with Anxious Distress: A Double-Blind, Controlled Clinical Trial. *Pharmacopsychiatry*, 2017. 50(4): p. 152-160.
- Akhondzadeh, S., et al., Comparison of *Crocus sativus* L. and imipramine in the treatment of mild to moderate depression: a pilot double-blind randomized trial [ISRCTN45683816]. *BMC complementary and alternative medicine*, 2004. 4: p. 12.
- Lopresti, A.L., et al., 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. *J Affect Disord*, 2018. 232: p. 349-357.
- Lopresti, A.L. and S.J. Smith, The Effects of a Saffron Extract (affron®) on Menopausal Symptoms in Women during Perimenopause: A Randomised, Double-Blind, Placebo-Controlled Study. *J Menopausal Med*, 2021. 27(2): p. 66-78.
- Lopresti, A.L., et al., 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. *J Psychopharmacol*, 2019. p. 26988119867703.
- Lopresti, A.L. and S.J. Smith, An examination into the mental and physical effects of a saffron extract (affron®) in recreationally-active adults: A randomized, double-blind, placebo-controlled study. *J Int Soc Sports Nutr*, 2022. 19(1): p. 219-238.
- Lopresti, A.L., S.J. Smith, and P.D. Drummond, An investigation into an evening intake of a saffron extract (affron®) on sleep quality, cortisol, and melatonin concentrations in adults with poor sleep: a randomised, double-blind, placebo-controlled, multi-dose study. *Sleep Med*, 2021. 86: p. 7-18.
- Lopresti, A.L., et al., Effects of Saffron on Sleep Quality in Healthy Adults With Self-Reported Poor Sleep: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Clin Sleep Med*, 2020.
- Sarris, J., et al., Clinician guidelines for the treatment of psychiatric disorders with nutraceuticals and phytochemicals: The World Federation of Societies of Biological Psychiatry (WFSBP) and Canadian Network for Mood and Anxiety Treatments (CANMAT) Taskforce. *World J Biol Psychiatry*, 2022. 23(6): p. 424-455.
- Roughan, W.H., et al., Comorbid Chronic Pain and Depression: Shared Risk Factors and Differential Antidepressant Effectiveness. *Front Psychiatry*, 2021. 12: p. 643609.
- Finan, P.H., B.R. Goodin, and M.T. Smith, The association of sleep and pain: an update and a path forward. *J Pain*, 2013. 14(12): p. 1539-52.
- Koffel, E., et al., The bidirectional relationship between sleep complaints and pain: Analysis of data from a randomized trial. *Health Psychol*, 2016. 35(1): p. 41-9.
- Safaklah, H.A., et al., Role of Muscarinic Receptors in Hypoalgesia Induced by Crocin in Neuropathic Pain Rats. *ScientificWorld-Journal*, 2020. 2020: p. 4046256.
- Ait Tassit, M., et al., Safety Assessment and Pain Relief Properties of Saffron from Taliouine Region (Morocco). *Molecules*, 2022. 27(10).
- Khilare, V., et al., Multiple tests on saffron find new adulterant materials and reveal that 1st grade saffron is rare in the market. *Food Chem*, 2019. 272: p. 635-642.