

Saffron

INTRODUCTION

Saffron is a spice derived from the dried stigmas of the *Crocus sativus* flower that is used traditionally as both a culinary spice and medicinal agent. It contains many bioactive compounds, including crocin and safranal, which have demonstrated antioxidant and anti-inflammatory activity as well as modulation of neurotransmitters in experimental models.¹ Several meta-analyses of randomized, controlled clinical trials suggest saffron improves symptoms related to stress, anxiety, and low mood, and improves multiple sleep parameters, including sleep quality and duration.²⁻⁴

What is affron®?

Affron is a well-studied saffron extract cultivated from saffron stigmas exclusively in Spain. It is standardized to provide ≥3.5% lepticosalides®, the bioactive compounds within saffron (including safranal and crocin), which are extracted via a chemical-free proprietary process. Pharmacokinetic studies in humans indicate that affron is both a bioavailable form of these active compounds, and that it is rapidly absorbed.⁵ Multiple controlled clinical trials have been conducted with affron at a dose of 28 mg per day, indicating its efficacy for improving symptoms related to stress, anxiety, low mood, and sleep quality in a variety of populations.⁶⁻¹¹

Mechanism of Action

Experimental models have demonstrated that saffron has multiple mechanisms of action, ranging from antioxidant and anti-inflammatory effects to modulation of the action of several neurotransmitters. Crocin, for example, is a natural carotenoid with antioxidant effects that may protect neurons from oxidative injury. It also has anti-inflammatory effects, including reducing the expression of nuclear factor-kappa B (NF-κB), tumour necrosis factor α (TNF-α), and cyclooxygenase-2 (COX-2).^{1,12} In addition, murine models indicate that saffron may have neuroprotective properties, in part mediated by an increase in brain-derived neurotrophic factor (BDNF) levels.^{13,14}

Additional experimental models show that saffron and its bioactive compounds modulate the levels of several monoamine neurotransmitters, including dopamine, norepinephrine, and serotonin. They may also act as antagonists for NMDA (N-methyl-D-aspartate) receptors, potentially leading to the clinical benefits for mood observed in clinical trials.¹⁵ The reduction in anxiety observed in clinical trials with saffron has been attributed in part to its effects on these neurotransmitters, along with agonism of the GABA_A receptor.¹⁶

In a randomized clinical trial, affron was shown to reduce negative mood and symptoms associated with stress and anxiety, including perceived stress and nervousness, tension, sadness, and fatigue, with benefits observed by four weeks among patients taking 28 mg per day compared to placebo, (but not at 22 mg per day).⁶ Similar benefits were also observed in an eight-week trial that enrolled adolescents (aged 12–16), including improvements in separation anxiety, low mood, and social phobia after taking

28 mg per day.⁷ Affron has been shown to improve clinician ratings of mood (Montgomery-Åsberg depression rating scale, [MADRS]) when combined adjunctively with standard therapies, at a dose of 28 mg per day.⁸ In a clinical trial of perimenopausal women, affron supplementation (28 mg per day) was found to improve symptoms of nervousness and mood, including improvements in the Greene climacteric scale (GCS) and the positive and negative affect schedule (PANAS) compared to a placebo.⁹ Supplementation with affron (14–28 mg per day) was also associated with an improvement in the sleep quality of participants with self-reported sleep problems, as well as an increase in evening melatonin levels.^{10,11}

ASSESSMENT

No absolute contraindications exist for affron supplementation. Saffron may lower blood pressure, but this is observed only at high doses and unlikely at the recommended dose.¹⁷ One case of possible interaction with a direct oral anticoagulant (rivaroxaban) has been reported; caution is advised with anticoagulant medications.^{17,18} Caution is also advised for patients taking anti-depressants, though a clinical trial with affron as add-on therapy among patients taking an SSRI (selective-serotonin reuptake inhibitors), SNRI (serotonin-noradrenaline reuptake inhibitors), or TCA (tricyclic antidepressant) documented clinician-rated improvement in symptoms, with a more favourable adverse effect profile than patients taking placebo.⁸

Some people may experience anxiety/nervousness, increased appetite, nausea, and/or headache, in which case discontinue use. Should be avoided during pregnancy/lactation. Careful screening and safety monitoring guidelines should be considered for any individual presenting with low mood and/or anxiety.¹⁹

GENERAL RECOMMENDATIONS AND DOSING

Recommended Dose: Adults (Mood, Symptoms of Stress, Nervousness, Sleep Quality): 1 capsule per day or as directed by a health care practitioner. Consult a health care practitioner for use beyond 12 weeks. For sleep quality, consult a health care practitioner for use beyond 4 weeks. **Adolescents Over 12 Years of Age (Mood):** 1 capsule per day or as directed by a health care practitioner. Consult a health care practitioner for use beyond 8 weeks.

SUMMARY

Numerous clinical trials have demonstrated saffron's safety and efficacy. It has been shown to improve multiple symptoms related to stress, anxiety, low mood, and poor sleep quality. Its multiple mechanisms of action, including antioxidant, anti-inflammatory, and neuroprotective effects, as well as modulation of neurotransmitters and their receptors, suggest it has broad potential to provide support for stress and its many impacts on mood and sleep. Affron provides a pure, bioavailable, and standardized amount of the active components of saffron, with several clinical trials supporting its use.

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