Saffron SAP

Science-based Saffron for Mood Balance and Optimal Health

Saffron is a fragrant spice derived from the dried elongated stigmas and styles of *Crocus sativus* flower. The major bioactive compounds in saffron stigmas: crocins, crocetin, picrocrocin and safranal are indicated for the beneficial health properties of saffron. In addition, saffron also contains various other active components, including carotenoids, zeaxanthin, lycopene, beta-carotenes and polysaccharides. Saffron has been used in traditional medicine as an antidepressant, anticonvulsive, analgesic, aphrodisiac, antispasmodic, and expectorant. A plethora of preclinical and clinical studies suggest anti-inflammatory, antioxidant, antiplatelet and anticancer properties to saffron. Especially, substantial clinical evidence and randomized clinical studies support the potential benefits of saffron in managing depression, Alzheimer's disease, sexual function in men and women, premenstrual syndrome, glaucoma, macular degeneration and as an adjunctive support to cancer therapy and fibromyalgia.

Saffron SAP provides the highest quality clinically studied Saffron (*Crocus sativus L.*) stigma extract (affron™) for supporting optimal health. **Saffron SAP** can help alleviate depression and anxiety, improve cognitive function in Alzheimer's patients, enhance sexual function in men and women, alleviate premenstrual syndrome symptoms, promote eye health and provide adjunctive support to cancer therapy and fibromyalgia.

ACTIVE INGREDIENTS

Each capsule contains:
Saffron (*Crocus sativus L.*) stigma extract (affron™),
standardized to 3.5% Lepticrosalides™, providing crocins and safranal . . . . 14 mg

Other ingredients: Vegetable magnesium stearate, microcrystalline cellulose, and silicon dioxide in a vegetable capsule composed of vegetable carbohydrate gum and purified water.

This product is non-GMO and vegan friendly.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, or sugar.

Saffron SAP contains 60 capsules per bottle.

DIRECTIONS FOR USE

Adults and adolescents 12 years and over: Take 1 capsule twice daily or as directed by your healthcare practitioner.
Duration of use: Adolescents (12–17 years): Consult a healthcare practitioner for use beyond 8 weeks. **Adults (18 years and older):** Consult a healthcare practitioner for use beyond 12 weeks.

INDICATIONS

Saffron SAP may be used as an adjunct in cancer therapy and fibromyalgia, and can help:
- Manage depression and anxiety.
- Promote cognitive function in Alzheimer's disease.
- Enhance sexual function in men and women.
- Relieve PMS symptoms.
- Support eye health.

CAUTIONS AND WARNINGS

Consult a healthcare practitioner if symptoms persist or worsen, or if you are taking antidepressants. Consult a healthcare practitioner prior to use if you suffer from any psychological disorder and/or condition such as frequent anxiety or depression. Consult a healthcare practitioner if sleeplessness persists continuously for more than 4 weeks (chronic insomnia).
Contraindications: Do not use if you are taking blood thinners/anticoagulants or have a bleeding disorder. Do not use if you are pregnant or breastfeeding.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **Saffron SAP** lot numbers have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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Research Monograph

SAFFRON-CHEMISTRY AND TRADITIONAL USE

Saffron is a fragrant spice derived from the dried elongated stigmas and styles of the blue-purple saffron flower (*Crocus sativus L.*). [1] Four major bioactive compounds occur in saffron stigmas, namely: crocins (family of six mono-glycosyl or di-glycosyl polyene esters), crocetin (a natural carotenoid dicarboxylic acid precursor of crocin), picrocrocin (monoterpene glycoside precursor of safranal and a product of zeaxanthin degradation) and safranal. These compounds contribute to the colour, taste and aroma of saffron and are suggested for their beneficial health properties. In addition, saffron also contains various other active components, including carotenoids, zeaxanthin, lycopene, beta-carotenes and polysaccharides. [1] Saffron has been used in traditional medicine, as an antidepressant, anticonvulsive, analgesic, aphrodisiac, antispasmodic and expectorant and more recent pharmacological studies suggest anticancer, anti-inflammatory, antioxidant and antiplatelet attributes to saffron. [1] Especially, a number of human clinical trials have recently demonstrated the potential benefits of saffron in managing depression and anxiety, Alzheimer's disease, glaucoma, macular degeneration, dysmenorrhea and erectile dysfunction. [1]

DEPRESSION AND ANXIETY

One of the most extensively studied aspects of saffron is its role in the treatment of depression and anxiety. Studies on saffron range from major depressive disorders (MDD) and also in treating mild to moderate depression. [2] A systematic review that combined data from 12 clinical trials evaluating the effectiveness of saffron on psychological and behavioral outcomes, showed that saffron may improve the symptoms and the effects of depression, sexual dysfunction, and excessive snacking behaviors. [2]

Another meta-analysis reviewing data from six randomized placebo-controlled trials concluded that saffron had large treatment effects and, when compared with antidepressant medications, exhibited similar antidepressant efficacy. Saffron's antidepressant effects potentially are due to its serotonergic, antioxidant, anti-inflammatory, neuro-endocrine, and neuroprotective effects.[1] In a study with 60 patients with anxiety and depression randomized to receive a 50 mg saffron (dried stigma) capsule or a placebo capsule twice daily for 12 weeks, saffron supplementation significantly improved symptoms in comparison to placebo with almost no side effect. [3] In a randomized, double-blind, placebo-controlled, pilot clinical study, the efficacy of 30 mg/day of crocin was studied as an adjunctive treatment (along with an SSRI fluoxetine/ sertraline/ citalopram) for 4 weeks on 40 MDD patients. Crocin combined with the SSRI demonstrated a significant reduction in depression. [4]

In a meta-analysis by Hausenblas et al, it was shown that saffron supplementation significantly reduced depression symptoms compared to the placebo condition and that saffron supplementation was equally effective as antidepressant therapy in reducing depression symptoms. [5] A number of other studies have corroborated the adjunctive utility of saffron with antidepressant drugs (imipramine and fluoxetine), especially in patients with mild to moderate depression including postpartum depression and post percutaneous coronary intervention patients. [6, 7]

Administration of saffron and its constituents has been known to increase glutamate and dopamine levels in the brain in a dose-dependent manner. Saffron and its constituents also interact with the opioid system to help manage withdrawal syndrome. [8]

COGNITIVE FUNCTION IN ALZHEIMER'S DISEASE

Clinical explorations have been made to evaluate the potential of saffron in the treatment and management of Alzheimer's disease (AD). Saffron has been suggested to potentially inhibit the aggregation and deposition of amyloid β in the human brain and may therefore be useful in AD. In a 16-week double-blind study in 46 patients with mild to moderate AD, administration of 30 mg/day of saffron extract (containing 0.26–0.30mg of safranal and 3.70–3.50 mg of crocin) had resulted in a significantly better outcome on cognitive function than the placebo with no adverse events reported.[9] In another 22-week multicenter, randomized, double-blind study, 54 adults (aged 55 years and above), received either 30 mg/day of saffron extract (providing 0.26–0.30mg of safranal and 3.70–3.50 mg of crocin) or donepezil 10 mg/day. The study results showed that saffron extract was effective similar to donepezil in the treatment of mild-to-moderate AD. [10]

SEXUAL FUNCTION

Saffron has been used traditionally to promote sexual function and a number of clinical studies support the clinical utility of saffron in treating sexual dysfunction. In a randomized double-blind placebo-controlled study, researchers evaluated the safety and efficacy of saffron on selective serotonin reuptake inhibitor-induced sexual dysfunction in women. In this study, 38 women with major depression who were stabilized on fluoxetine 40 mg/day for a minimum of 6 weeks, and had experienced subjective feeling of sexual dysfunction, were randomly assigned to saffron extract (30 mg/daily), providing 0.26–0.30mg of safranal and 3.70–3.50 mg of crocin or placebo for 4 weeks. Female sexual function index (FSFI) was used as the measure performed at baseline, week 2, and week 4. At the end of the fourth week, patients in the saffron group had experienced significantly more improvement in total FSFI, arousal, lubrication, and pain aspects of FSFI, however, not in desire, satisfaction, or orgasm aspects. [11]

In another 4-week randomized double-blind placebo-controlled study, 36 male patients with MDD whose depressive symptoms had been stabilized on fluoxetine and had subjective complaints of sexual impairment were randomly assigned to saffron extract (15 mg twice per day), providing 0.26–0.30mg of safranal and 3.70–3.50 mg of crocin or placebo. International Index of Erectile Function scale was used to assess sexual function at baseline and weeks 2 and 4. The study results showed that saffron extract significantly improved erectile function and intercourse satisfaction domains compared to the placebo. These results suggest that saffron could be used efficaciously for the treatment of fluoxetine-related erectile dysfunction. [12] Interesting results from an open-label pilot study in 20 male patients with erectile dysfunction who were supplemented with a tablet containing 200 mg of saffron extract (containing 3.9 mg of crocin and 0.05 mg of safranal) showed a significant improvement on sexual function with increased number and duration of erectile events even after taking it for only ten days. [13] The study had some limitations including no participant blinding and lack of control and a small sample size. However, the results suggest a potential role of saffron for ED and future well controlled clinical trials are required to confirm the observations from this pilot study.

PREMENSTRUAL SYNDROME

A double-blind and placebo-controlled study in women aged 20-45 years with regular menstrual cycles and experience of premenstrual syndrome (PMS) symptoms were randomly assigned to receive saffron extract capsules 30 mg/day (15 mg twice a day) or placebo for two menstrual cycles. Women administered saffron extract experienced a significant relief in symptoms of PMS in cycles 3 and 4 as well as a reduction in the Hamilton Depression Rating Scale. These results are encouraging in supporting the use of saffron as an alternative treatment for PMS. However, more studies are warranted to confirm these findings. [14]

EYE HEALTH

A number of studies support the beneficial effects of saffron in improving eye health. In a prospective, comparative, randomized interventional pilot study, the clinical use of saffron as an adjunct in improving intraocular pressure (IOP) in eyes in patients with primary open-angle glaucoma (POAG) was evaluated. In this study, 34 clinically stable POAG patients receiving treatment with timolol and dorzolamide eye drops were randomized to receive 30 mg/day aqueous saffron extract orally (17 patients) or placebo (17 patients) for one month as an adjunct. Researchers observed that IOP was significantly decreased compared to placebo after 3 weeks of treatment. Even at four weeks, IOP was still significantly lower in the saffron group. Noteworthy, none of the patients experienced side effects during the study. [15] Saffron was studied for its efficacy in improving early age-related macular degeneration (AMD) in a study where 25 patients with AMD were randomly assigned to oral saffron stigma 20 mg/day or placebo supplementation over a 3-month period. It was found that saffron administration improved retinal flicker sensitivity in early AMD. [16] These beneficial properties could be attributed to the various carotenoids such as zeaxanthin and lycopene present in saffron.

CANCER

Several preclinical studies have suggested the potential use of saffron in the adjunctive treatment of cancer. Studies in animal models and with cultured human malignant cell lines have demonstrated antitumor and cancer preventive activities of saffron. [17] A small randomized, double blind, placebo-controlled clinical study in 13 patients suffering from liver metastases where along with standard chemotherapy regimen, patients in one group were administered with saffron capsule (50 mg, twice daily) during chemotherapy periods whereas patients in another group just received a placebo. The study results showed that in the saffron-treated group, two patients showed partial and complete response (50%), whereas in the placebo group no response was seen. Also, two deaths in placebo and one in saffron group occurred. However, due to the low number of participants in the study, further investigations with larger sample size are required. [18]

FIBROMYALGIA

In a study, 54 patients with fibromyalgia (FM), aged 18-60 years were randomly assigned to take one capsule containing 30 mg duloxetine or one capsule containing 15 mg saffron extract (providing 0.13–0.15mg of safranal and 1.65–1.75 mg of crocin) daily during the first week. Patients then took two capsules of duloxetine or saffron daily during the second week and continued at that dose through a total of 2 months. Primary outcomes were changes in Hamilton Rating Scale for Depression score, Fibromyalgia Impact Questionnaire score, and Brief Pain Inventory pain score from baseline to eight weeks. Secondary outcomes were changes in VAS pain score, fatigue assessments, and Hospital Anxiety and Depression scores from baseline to eight weeks. Mean scores for all outcome assessments improved after eight weeks in both the saffron and duloxetine groups and were not statistically significantly different from each other. There were no significant differences in the number of adverse events across groups. These results certainly provide good preliminary evidence of a measurable level of improvement in symptoms of fibromyalgia. Lack of a placebo arm, small sample size and shorter study duration were weaknesses of the study, but the results are encouraging to consider saffron as part of a treatment strategy for those suffering from fibromyalgia. [19]

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