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File: ■ Saffron (*Crocus sativus*, Iridaceae)
■ Efficacy and Safety
■ Oxidative Stress

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RE: Saffron of Potential Benefit in Certain Cognitive, Mood, Vision, and Menstrual Conditions and Apparently Safe in Therapeutic Doses

Broadhead GK, Chang A, Grigg J, McCluskey P. Efficacy and safety of saffron supplementation: current clinical findings. *Crit Rev Food Sci Nutr*. April 15, 2015; [epub ahead of print]. doi: 10.1080/10408398.2013.879467.

Saffron (stigmas of *Crocus sativus*, Iridaceae) is used widely as a traditional medicine and spice. Several compounds in saffron have been shown to be bioactive; specifically, crocetin, crocin, and safranal have demonstrated antioxidant activity. Also, crocin is considered to be the compound providing saffron's color, and safranal is likely the compound contributing to the herb's aroma. This review covers the efficacy and safety of saffron for the potential treatment of several health conditions associated with chronic oxidative stress, as assessed in human clinical studies and supported by preclinical research.

Alzheimer's disease progresses, in part, due to nervous system damage from oxidative stress. In an in vitro study, crocin prevented both amyloid plaque formation and neurofibrillary tangles, markers of Alzheimer's disease pathology. Memory improvements in normal rats, rats with induced memory problems, and rat models of both diabetic cerebral disease and Alzheimer's disease, were seen with saffron consumption. Mechanistic studies suggest that both safranal and crocetin share a similar anticholinesterase mechanism of action as standard Alzheimer's disease pharmaceuticals. In a small clinical trial with Alzheimer's disease patients, 30 mg of saffron daily for 16 weeks resulted in better cognition; another study using the same dosage suggested that saffron was comparable in efficacy to donepezil, a standard pharmaceutical for this condition.

With in vivo studies addressing mood, crocetin has been shown to interact with central nervous system receptors, suggesting molecular modulation. Significant alleviation of depression was observed in those suffering from mild to moderate depression (30 mg/day of saffron for six weeks) in two small clinical studies. Another study found that 30 mg/day of saffron for nine weeks was comparable in efficacy to the pharmaceutical imipramine in those with mild to moderate depression.

During in vivo studies investigating vision, topical saffron showed positive impacts on retinal blood flow in rabbits, and cataracts were prevented in a rat model via increased endogenous antioxidant defense. Another in vivo study with a rat model showed potential benefits of saffron supplementation in retinitis pigmentosa, perhaps due to antioxidant bioactivity. In a small clinical study, saffron consumption positively impacted aspects of age-related macular degeneration, including visual acuity.

Saffron has also been studied for possible effects in reproductive issues. A clinical study in women reported that 30 mg/day of saffron during two menstrual cycles significantly improved premenstrual syndrome (PMS) symptoms as compared with placebo ($P<0.001$). In women exposed to saffron aroma, levels of 17-beta-estradiol were increased and the stress hormone cortisol was reduced. Two small clinical trials with men and women showed that saffron supplementation reduced fluoxetine-induced sexual dysfunction.

In animal models of cardiovascular disease, saffron was found to modulate cellular markers of myocardial infarction and attenuate nuclear factor-kappa B (NF-κB) signaling involved with inflammation and apoptosis. In addition, other in vivo studies in diabetic and hyperlipidemic models have shown saffron and crocin decrease cholesterol and triglyceride concentrations. In both healthy subjects and patients with coronary artery disease consuming 50 mg of saffron daily for six weeks, a significant decrease in lipoprotein oxidation susceptibility was observed ($P<0.001$), though not with control subjects.

In toxicity investigations, no adverse side effects were observed at a crocin dosage of 20 mg/day for one month in healthy subjects; it is mentioned that certain blood parameters including prothrombin time were lowered in this study. Another study using 400 mg/day of saffron for one week reported no impacts on multiple blood coagulation parameters. Elevations of immunoglobulins G and M (markers of the immune system) were observed in healthy male subjects taking 100 mg of saffron daily for three weeks; these markers were at normal concentrations following another three weeks of supplementation. There has been one case of anaphylaxis associated with saffron, but overall its allergic potential is considered low.

In conclusion, it is stated that saffron and its bioactive components are effective in alleviating cellular oxidative stress damage. Both in vivo and clinical trials (limited by small size and short follow-up) suggest the use of saffron in multiple health conditions and chronic diseases where excessive reactive oxygen species are a factor. Further clinical investigations of saffron that are underway will hopefully substantiate its therapeutic benefits and ideally identify mechanisms of action in disease states, verifying its use for a variety of conditions.

—Amy C. Keller, PhD

The American Botanical Council has chosen not to include the original article.