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# HerbClip™



**File: ■ Saffron (*Crocus sativus*, Iridaceae)**
**■ Inflammation**
**■ Antioxidant**
**■ Immunomodulation**

**HC 051746-581**

**Date: November 30, 2017**

**RE: Review of Pharmacology of Saffron and Its Constituents**

Boskabady MH, Farkhondeh T. Anti-inflammatory, antioxidant, and immunomodulatory effects of *Crocus sativus* L. and its main constituents. *Phytother Res*. July 2016;30(7):1072-1094.

Saffron (*Crocus sativus*, Iridaceae) is cultivated in mild, dry climates as a food flavoring and colorant, perfume ingredient, and medicinal herb. Widely used in Iran, its common name comes from the Arabic *zafaran* (yellow), for the high carotenoid pigment content of its flower stigmas. Based on traditional use and modern research, saffron and its compounds may be useful in neurodegenerative disorders, coronary artery disease, respiratory diseases, gastrointestinal (GI) problems, and urinary disorders.

Saffron's over 150 volatile and non-volatile compounds include proteins, carbohydrates, minerals, vitamins, and pigments. Volatile components include over 34 terpenes and their esters, among which safranal, a monoterpene aldehyde responsible for saffron's characteristic aroma, predominates. Non-volatile compounds include carotenoid crocins, crocetin, picrocrocin, quercetin, and kaempferol. Crocetin and crocins provide saffron's yellow color. Picrocrocin, a crystalline terpene-glucoside, is safranal's precursor and gives saffron its taste. In flower petals, glycoside derivatives of quercetin and kaempferol are the major flavonoids. Saffron and its constituents reportedly have anticancer, antimicrobial, antimutagenic, and anti-genotoxic effects.

Saffron is considered a safe spice with very low toxicity. Stigma and petal extracts have been tested for toxicity, both showing very little; however, stigma extracts had greater toxicity than petal extracts. α-Crocin, dimethylcrocetin, and safranal also have been studied for toxicity. In vivo, after safranal exposure for 21 days at a sub-acute dose, there were no toxic effects on heart, liver, or spleen, but pathological changes were seen in kidneys and lungs. In a safety study with 100 healthy human subjects who took 200 or 400 mg saffron stigma tablets daily for one week, minor clinical and laboratory parameter changes were seen but no major adverse events (AEs). Patients with various chronic diseases have taken saffron safely. An antidepressant effect of saffron has been reported without AEs, and a study of saffron for premenstrual syndrome (PMS) found only mild, tolerable AEs. Some studies have reported that 1.2-2 g saffron caused nausea, vomiting, diarrhea, and bleeding. It may not be safe in pregnancy.

The authors searched electronic databases from 1990 to 2015 for information on anti-inflammatory, antioxidant, and immunomodulatory effects of saffron and its main constituents. Inclusion criteria are not given. They searched for studies, articles, reviews, and editorials. Mostly in vitro and in vivo studies are referenced. Anti-inflammatory studies found benefits of saffron and safranal on total and differential white blood counts, inflammatory mediators, swelling and edema, lung pathology, cough frequency, and tracheal responsiveness, and of α-crocin on airway inflammation. Results suggest therapeutic use in respiratory illnesses. Benefits in pain relief including neuropathic pain and neurotoxicity are also reported to rest on anti-inflammatory effects. Possible benefits in inflammation-related GI tract and cardiovascular disorders, arthritis, and diabetes are also mediated by anti-inflammatory mechanisms. These anti-inflammatory effects are related to saffron's immunomodulatory and antioxidant properties.

Modulatory effects of hydroethanolic plant extract and of safranal on interleukin (IL)-4, interferon-γ (IFN-γ), and IL-4/IFN-γ ratios in vivo and in vitro in human lymphocytes, as well as increased T-helper 1/T-helper 2 balance in sensitized animals, are reported. Crocetin protected against lipopolysaccharide-induced lung injury by modulating IL-6, monocyte chemoattractant protein-1, and tumor necrosis factor-α, suggesting therapeutic potential in immune-related respiratory disorders such as asthma. Benefits in encephalomyelitis and neurotoxicity are also related to immunomodulation. In vivo, safranal inhibited venom-induced pro-inflammatory cytokines, platelet aggregation, and neutrophil apoptosis through immunomodulatory effects; in vitro in human neutrophils, venom-induced apoptosis was neutralized by α-crocin.

Antioxidant effects of saffron and its constituents have been well researched. Results make up a large portion of this report. Saffron and its compounds stabilize cellular membranes, scavenge reactive oxygen species, and reduce peroxidation of unsaturated membrane lipids, suggesting therapeutic value in aging, anti-inflammatory, and wound-healing processes. Benefits in in vivo models of nervous system disorders have been found to result from antioxidant activities. Antioxidant effects of the hydroethanolic plant extract on heart tissue damage; of α-crocin on induced vascular toxicity, heart histopathological damage, and hepatotoxicity; and of crocetin on angiotensin II-induced vascular cell adhesion molecule-1 (VCAM-1) expression, monocyte-endothelial cell adhesion, cardiovascular damage, and cardiac hypertrophy have been demonstrated in vivo and/or in vitro, suggesting a therapeutic use in heart diseases. Antioxidative effects of ethanolic and aqueous extracts of saffron, safranal, and α-crocin underlie their benefits in urogenital disorders. Ethanolic and aqueous plant extracts, safranal, α-crocin, and crocetin also exhibit beneficial antioxidant effects in GI system problems. Among these extracts and compounds, α-crocin is the most-studied and best-documented antioxidant.

While its exact mechanisms of action are poorly described and understood, saffron consumption is positively related to lower risks of various diseases. Preclinical and clinical studies indicate its possible usefulness in mild to moderate depression and PMS. However, there are remaining concerns about saffron's potential toxicity. More safety studies and well-designed clinical trials are needed to confirm its benefits.

*—Mariann Garner-Wizard*

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