

Saffron

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Handling Editor:

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Saffron (*Crocus sativus* L.; Iridaceae) is a perennial herb that produces purple flowers with drooping red stigmas. The plant is indigenous to south-western Asia and southern Europe and now cultivated in many other countries, including Afghanistan, China, India, Iran and New Zealand. The red stigmas are the part used medicinally (after drying), and as a spice and colouring agent in food. Saffron has a long history of traditional use for treatment of abdominal pain, fever, and to stimulate or increase menstrual blood flow; uses in traditional Chinese medicine, include for treatment of haematoma, melancholia, convulsions, as a sedative, for 'blood stasis' after childbirth, and eruptions in infectious diseases.

Saffron is extremely expensive as more than 150 000 flowers are required to produce 1 kg of stigma material. For this reason, intentional financially motivated adulteration of saffron occurs and may be widespread. Known adulterants of saffron include other plant materials, such as the tepals (often incorrectly described as 'petals') of saffron flowers, stigmas of safflower (*Carthamus tinctorius*) and calendula (*Calendula officinalis*), and powdered curcuma (*Curcuma longa* L.) rhizome, animal material, chalk, synthetic dyes and other substances.

Common names

Saffron, red gold [*English*]; fan honghua, xi honghua, zanghonghua [*Chinese*]; zafran [*India*] and many others.

Preparations

Traditional preparations of saffron were often tinctures and teas, as well as topical formulations, such as ointments, and poultices. Contemporary preparations are sold as solid-dose forms (usually capsules) of extracts of saffron stigma, formulated as single- and multi-ingredient products with other herbal and non-herbal ingredients.

Received: 8 June 2022

Accepted: 9 June 2022

Published: 27 June 2022

Cite this:

Barnes J
Journal of Primary Health Care 2022;
14(2): 189–190.
doi:[10.1071/HC22067](https://doi.org/10.1071/HC22067)

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Summary message

Evidence from preclinical studies of saffron and/or its major constituents supports several pharmacological effects, including anti-tumour, anti-inflammatory, immunomodulatory, anti-diabetic, antidepressant (eg serotonergic) and anxiolytic activity. Clinical research with saffron preparations has focussed on the treatment of mild-to-moderately severe depression, and sleep disorders, but at present there is no definitive evidence for efficacy in these conditions; many existing studies have methodological limitations, including low participant numbers, short study duration and use of poorly defined extracts of saffron stigma. Robust, longer-term studies using well-described saffron extracts that meet accepted standards for pharmaceutical quality are required. Food use of saffron is generally safe. Contact dermatitis has been reported with occupational exposure to saffron. Saffron is toxic at total daily doses of 5 g or higher. Caution is advised with concomitant use of saffron and antiplatelet or anticoagulant medicines. Comprehensive investigation of the clinical safety profile of saffron and its important constituents when used in a pharmaceutical/medicinal context is required.

Manufacturers' claims

Saffron products are promoted/marketed for managing appetite and controlling weight, for mood and emotional support, to support eye health, and as an antioxidant, among other claims.

Active constituents

The important active constituents of saffron are carotenoid derivatives and include crocetin, crocin (an ester of crocetin), picrocrocetin and safranal; other bioactive compounds are present, including kaempferol, quercetin, flavones (eg luteolin) and anthocyanins (eg delphinidin).

Evidence for efficacy

Preclinical studies have provided some evidence for anti-tumour, anti-inflammatory, immunomodulatory, anti-diabetic, antioxidant, anti-platelet, antidepressant (eg serotonergic) and anxiolytic effects for saffron and its constituents, as well as for inhibitory activity in pathology associated with cognitive impairment.

Clinical research with saffron preparations has focussed on the treatment of mild-to-moderately severe depression, and sleep disorders, but at present there is no definitive evidence for efficacy in these conditions. A recent meta-analysis included 12 clinical studies of saffron extracts 30 mg/day for 6–12 weeks in adult patients with symptoms of mild-to-moderately severe depression. Saffron was more effective than placebo, and as effective as conventional medicines (fluoxetine, four studies; citalopram, one study), in improving symptoms of depression. However, the studies included in the meta-analysis involved very small numbers of participants, used different extracts of saffron (including two trials using extract of saffron 'petals') and all were conducted in one country (Iran). Larger trials are required, involving patients sampled from other population groups, and using tightly defined extracts of saffron stigma that meet accepted standards for pharmaceutical quality.

Another meta-analysis of 8 trials involving healthy adults, patients with insomnia and other conditions, including type-2 diabetes mellitus, reported that saffron had a beneficial effect on sleep quality. Controlled clinical trials

investigating the effects of saffron preparations in patients with allergic asthma, cognitive impairment, type-2 diabetes mellitus, delayed-onset muscle soreness, visual disorders, male infertility, erectile dysfunction and metabolic syndrome have also reported some beneficial effects. However, many of these studies had methodological limitations and further trials are required to confirm or refute these findings.

Adverse effects

Saffron is used in foods and is generally regarded as safe when consumed in usual quantities in this context. However, comprehensive investigation of the clinical safety profile of saffron and its important constituents when used in a pharmaceutical/medicinal context is required. Very limited data from clinical trials indicate that the frequency and types of adverse events reported for saffron are similar to those reported for placebo and standard antidepressants (fluoxetine, citalopram) used as comparators. Spontaneous reports of adverse reactions associated with saffron include rash, flushing, hyperhidrosis, vomiting, malaise, and insomnia; causality has not necessarily been established in these cases. Contact dermatitis has been reported in saffron workers. Saffron is toxic at total daily doses of 5 g or higher.

Interactions

The clinical relevance of the effects of saffron on platelet activity and blood coagulation reported in preclinical studies is unclear. Caution is advised with concomitant use of saffron and antiplatelet or anticoagulant medicines.

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Data availability. Data sharing is not applicable as no new data were generated or analysed for this article.

Conflicts of interest. JB is a co-author/co-editor of books on scientific aspects of herbal medicines and receives/has received royalties from Pharmaceutical Press, Elsevier, and Springer Nature/MacMillan Education.

Declaration of funding. This research did not receive any specific funding.

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