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File: ■ Saffron (*Crocus sativus*, Iridaceae)
■ C-reactive Protein
■ Systematic Review/Meta-analysis

HC 042056-655

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RE: Meta-analysis of Saffron Clinical Studies Show Positive Results on Mental Health Markers

Ghaderi A, Asbaghi O, Reiner Z, et al. The effects of saffron (*Crocus sativus* L.) on mental health parameters and C-reactive protein: A meta-analysis of randomized clinical trials. *Complement Ther Med*. January 2020;48:102250. doi: 10.1016/j.ctim.2019.102250.

Saffron (*Crocus sativus*, Iridaceae) dried stigmata is used to treat symptoms of mental health disturbances, such as depression and anxiety. However, conclusions from randomized clinical trials (RCTs) are equivocal. Hence, the purpose of this systematic review and meta-analysis was to summarize the data from RCTs and to evaluate the effects of saffron on parameters of mental health and C-reactive protein (CRP). C-reactive protein is a biomarker of inflammation, and it is elevated in people with major depressive disorder.

The following databases were searched from inception through July 30, 2019: PubMed, Scopus, ISI (Web of Science), Cochrane Central Register of Controlled Trials, EMBASE, and Google Scholar. References lists were also hand-searched. The following keywords were search terms: Crocus, colchicum, *Crocus sativus*, saffron, crocin, crocetin, safranal, depression, depressive symptoms, anxiety, beck depression inventory, BDI, beck anxiety inventory, BAI, Hamilton Rating Scale, Hamilton, Hamilton Rating Scale for depression, HDRS, HAMD, HDRS-D, Hamilton Rating Scale for anxiety, Pittsburgh sleep quality index, PSQI, inflammation, inflammation, inflammatory markers, C-reactive protein, and CRP. Included studies met the following criteria: human studies with a crossover or parallel design, and studies reporting data on the effects of saffron on parameters of mental health and CRP with standard deviation and a 95% confidence interval for both intervention and control groups. Excluded studies met the following criteria: in vivo animal studies, in vitro, case reports, observational, no control group, and very low quality. Study quality was assessed with the Cochrane collaboration risk of bias tool. The authors used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Data were extracted and a meta-analysis was conducted.

A total of 1873 articles were located, and 21 studies met all inclusion/exclusion criteria. Studies were conducted in Iran (21 studies) and Australia (two studies). In total, there were 1052 participants (563 treated with saffron and 489 treated with control), with each study including 28 to 81 participants with a mean age of 32-56 years. The participants had mild to moderate depression (two studies), premenstrual syndrome (one study), type 2 diabetes mellitus (one study), major depressive disorder (one study), "anxiety and depression" (one study), "major depression" (two studies), type 2 diabetes mellitus with mild to moderate anxiety and depression (one study), mild to moderate postpartum depression (one study), depression in metabolic syndrome (one study), "low mood but not diagnosed with depression" (two studies), generalized anxiety disorder (one study), coronary artery disease (two studies), metabolic syndrome (one study), patients undergoing coronary artery bypass grafting (one study), post-menopausal hot flashes and depression (one study), recovered methamphetamine consumers with HIV/AIDS (one study), and patients under methadone maintenance treatment (two studies). Saffron doses ranged from 22 to 1000 mg/day for 4-12 weeks. The products evaluated were not reported. All studies were judged as having high quality, and there was no evidence of publication bias.

The meta-analysis demonstrated that compared with control-treated participants, saffron-treated participants had a significant improvement on the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Pittsburgh Sleep Quality Index (PSQI) ($P < 0.001$ for all). There was no significant difference between treatment groups on Hamilton Depression Rating Scale (HDRS-D), Hamilton Anxiety Rating Scale (HARS-A), and CRP. A subgroup analysis showed that the effects of saffron on HDRS-D scores were greater in (1) non-depressed participants, (2) in studies with a duration ≥ 8 weeks, and (3) in participants aged < 50 years or > 50 years. The subgroup analyses had no effect on any other endpoint.

The authors conclude that saffron significantly reduced BDI, BAI, and PSQI scores, but did not affect HDRS-D, HARS-A scores, and CRP levels. The authors acknowledge that the results of the meta-analysis need to be taken with caution because the studies were very heterogeneous. They differed in mental health parameters, types of saffron (powder, extracts, and pure crocin), dosage, and treatment duration. Some researchers may argue that a meta-analysis should not be conducted on such a heterogeneous group. The authors declare no conflict of interest.

—Heather S. Oliff, PhD

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