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RE: Saffron Supplementation Improves Clinical Signs and Markers of Inflammation and Oxidative Stress in Patients with Rheumatoid Arthritis


Symptoms of rheumatoid arthritis (RA) include inflammation, pain, swelling, morning stiffness in synovial joints, bone destruction, and functional deformity. The pro-inflammatory cytokines interleukin-1 and tumor necrosis factor-alpha (TNF-α) are involved in the pathophysiology of the disease. Several animal studies have reported that saffron (*Crocus sativus*, Iridaceae) relieves acute and chronic pain because of its anti-inflammatory effects. In animal and in vitro studies, the main constituents of saffron (crocetin, crocin, and safranal) have been shown to reduce oxidative stress and inflammation by decreasing malondialdehyde (MDA) and increasing glutathione peroxidase, superoxide dismutase, and catalase levels. Results of studies on the effects of saffron on inflammation in humans are contradictory. These authors conducted a randomized, double-blind, placebo-controlled clinical trial to investigate the effects of saffron on clinical outcomes and on markers of inflammation and oxidative stress in female patients with RA.

Sixty-six non-smoking, non-pregnant female patients older than 18 years were recruited from the Rheumatology Clinic of Shariati Hospital and Rasoul-e-Akram Hospital in Tehran, Iran, from July 2017 to October 2018. The patients had been diagnosed with RA at least two years earlier and had active disease. The patients had no history of acute cardiovascular disease, renal failure, or liver dysfunction. During the previous three months, they had not taken any supplements other than those prescribed for RA, contraceptives, or anticoagulants.

Thirty-three patients took one saffron tablet daily for three months. The other 33 patients took one placebo (hydroxyl propylmethyl cellulose) tablet daily for three months. The Pharmaceutical Research Center of Tehran University produced the saffron tablets by converting 500 g of Sargol saffron (Saharkhiz Saffron Company; Masshad, Iran) into 100 mg tablets. The placebo tablets matched the saffron tablets in color, shape, and smell. Anthropometric, clinical, and biochemical assessments were conducted at baseline and after three months of intervention. Primary outcomes included changes in the inflammatory markers high-sensitivity C-reactive protein (hs-CRP), TNF-α, erythrocyte sedimentation rate (ESR), and interferon gamma (IFN-γ), and changes in the disease activity score (DAS).
Secondary outcomes were changes in biomarkers of oxidative stress—total antioxidant capacity (TAC) and MDA levels.

Of the 66 patients, 32 in the saffron group and 31 in the placebo group completed the study. In the placebo group, one patient withdrew from the study, and one patient did not attend the final follow-up visit. In the saffron group, one patient withdrew from the study.

No significant between-group differences were observed in baseline characteristics. The only adverse effect reported during the study was stomach pain, which was reported by one patient in each group.

At the end of the study, significant decreases in tenderness and swelling in the joints, pain intensity based on a visual analogue scale, and DSA were observed in the saffron group compared with the placebo group and compared with baseline (P < 0.001 for all). At the end of the study, the Physician Global Assessment scores were significantly improved in the saffron group compared with the placebo group (P = 0.002). Compared with baseline, significant improvements in IFN-γ (P = 0.037), hs-CRP (P = 0.004), and ESR (P=0.018) levels were observed in the saffron group compared with baseline. Improvements in the levels of TNF-α, IFN-γ, ESR, hs-CRP, MDA, and TAC were greater in the saffron group compared with the placebo group; however, the between-group differences were not significant.

Limitations of this study include the small sample size and the lack of assessment of other inflammatory and oxidative stress biomarkers and gene expression of immunity factors, which would help explain the mechanisms of action. Future studies should compare the efficacy of saffron with anti-inflammatory drugs and examine its effects when used for other inflammatory diseases.

"According to the results, saffron supplements could positively and significantly improve clinical outcomes in RA patients," the authors conclude.

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—Shari Henson

**Peer Reviewer Comments**

The researchers did not provide the details of saffron content. Crocins and safranal changes in different regions where saffron is cultivated for commercial purposes, and there are variations with seasonal harvesting and processing of saffron. The researchers did not report any details of adverse events monitoring which is a vital component of a randomized controlled trial design.

The TNF-α initial levels were 1,472.20 ± 2,875.90 (57.49–2,618.56) and post treatment these were 1,327.60 ± 2020.70 (411.30–1974.68). If the lower results are seen, 57.49 and 411.30, the same are not explained by authors.

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