



# Psychotropic Effects of Saffron: A Brief Evidence-based Overview of the Interaction Between a Persian Herb and Mental Health

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Saffron is the dried stigma of a plant named *Crocus sativus L.* and has been known as the world's most expensive spice and a widely used medicinal plant. Indeed, saffron is a Persian herb with a history as long as Persian Empire (1). Saffron could be found throughout the world; however, Iran accounts for 90% of the world's whole saffron and is the origin of the most researches conducted on the potential medical utilities of this expensive spice (2). Beyond the traditional uses of saffron for treating some conditions such as stomachache or impaired digestion, this spice has shown hypolipidemic, hypotensive, anti-inflammatory, antioxidant, neuroendocrine, and neuroprotective effects (3,4). Moreover, it has been exhibited that saffron and its active constituents can increase the reuptake inhibition of dopamine and norepinephrine, antagonize N-methyl-D-aspartate (NMDA) receptors, and agonize Gamma Aminobutyric Acid (GABA) receptors (5). There is mounting evidence proposing psychoprotective properties of saffron in different neurological and psychiatric settings.

## Alzheimer's disease

Few medications are currently available for treatment of mild to moderate Alzheimer's Disease (AD), which is a worldwide concern due to its high prevalence among old age population. Saffron and its bioactive derivatives might be appropriate alternatives to present therapeutics as they improve cognitive performance, learning behavior, and spatial memory through various mechanisms, including protection against neurodegeneration and neurotoxicity; inhibition of  $\beta$ -amyloid aggregation; prevention of neurofibrillary tangle and senile plaques formation; suppression of the acetylcholinesterase activity; and neuroinflammation reduction (6). Taken together, it seems that saffron and its derivatives could promote the recovery in patients with neurodegenerative diseases through multiple pathways. The effectiveness of saffron in management of AD has been reflected by a significant number of clinical trials (7-9). Additional trials are warranted to confirm the neuroprotective properties of this spice.

## Depression

A number of randomized placebo-controlled clinical trials have indicated the alleviating effects of saffron petal, stigma, or hydro-alcoholic

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extract in depression. When it comes to treating mild to moderate depression, saffron was as effective as several well-established antidepressants, including fluoxetine (10-13), imipramine (14), citalopram (15), and sertraline (16). Safety of saffron was also acceptable since it was tolerated better or as well as other antidepressants. The antidepressant effects of saffron has been attributed to its several mechanisms of action such as inhibiting reuptake of monoamines, antagonizing NMDA, and facilitating Brain-Derived Neurotrophic Factor (BDNF) signaling.

### **Obsessive-compulsive disorder**

Active constituents of saffron, crocins, showed promising beneficial effects in an animal model of Obsessive-Compulsive Disorder (OCD) *via* a functional interaction with the serotonergic system (17). Later on, the results of the animal study were supported by a

randomized clinical trial where saffron was as effective and safe as fluvoxamine in treatment of mild to moderate OCD (18). Finally, a recent 8-week randomized clinical trial has reported that crocin exerts similar beneficial effects with fluoxetine on patients with mild to moderate OCD (19).

### **Attention-Deficit/Hyperactivity Disorder**

There is growing interest in nonstimulant strategies for treatment of ADHD due to possible absence of complete response to stimulants as well as safety issue. Herbal medicine is considered as one of the main alternative options because of better safety profile and cultural acceptability. In this respect, a recent randomized, double-blind clinical trial showed that saffron alleviates ADHD symptoms as well as methylphenidate in a safe manner (20). Further clinical trials of saffron seem necessary to confirm these findings.

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