

## Saffron: Analytical and Therapeutic aspects

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### Abstract

This study followed 450 adults (20-65 years old) to evaluate the effects of saffron. More specifically, 200 individuals were evaluated for saffron's antidiabetic and antispasmodic activity in colon disorders, while 250 individuals were investigated for antidepressant and anti-inflammatory activity.

For the study, saffron was to be taken orally as a water preparation.

Method of preparation and use of saffron:

Threads of saffron are ground by pestle and mortar, about 30mg twice daily after meal or 20mg three times daily

Ground saffron is infused in a cup of hot water (70- 100ml) for 5-10 min until cool and taken orally

The daily intake is continued for about 3 weeks; the total dose is 1.200g.

For the investigation of saffron's antidepressant activity, clinical trials identified and screened 250 individuals selected randomly. Excluded: no depression symptoms (healthy or depression due to colon disorders or irregular menstrual cycle): n=170; with depression symptoms (evaluation in meta-analysis): n=80. Excluded: antidepressant control n=10.

Antidepressant drugs n=15, without drugs n=55. The total of people evaluated in the meta-analysis was n=70.

The results of the study showed that the use of saffron is a successful approach for treating MDD (major depressive disorder) in short-term use. It has also shown benefits in colon disorders and in patients with irregular menstrual cycles.

Absorption of Infrared spectroscopy and high-performance liquid chromatography (HPLC) techniques were employed to identify compounds.

**Keywords:** Saffron, antidepressant, antispasmodic, anti-diabetic, High Performance Liquid Chromatography, Infrared spectrophotometry.

## Introduction

The Primary Metabolite in Saffron, *Crocus sativus* Linné (1,2), a member of the Iridaceae family, is the source of saffron, a bright orange-red spice. It's often called the "Golden Condiment" because of its high price.

Several research studies have looked at the chemical makeup of *Crocus sativus* L. stigmas over the last two decades. The stigma of a *Crocus sativus* flower allegedly includes three primary metabolites:

Compounds in saffron's hue are called crocins (water-soluble carotenoids due to their high glycosyl contents). The bitter flavor in saffron comes from a compound called picrocrocin. The saffron scent comes from a volatile substance called safranal (3,4).

Crocetin, one of the components of saffron extract, is mostly responsible for the herb's medicinal effects. In addition, it contains a wide variety of carotenoids, including zeaxanthin, lycopene, and a host of - and -carotenes that are nonvolatile (fat-soluble) active components (5). Crocetin, picrocrocin, crocin, and safranal are all byproducts of the enzymatic breakdown of zeaxanthin. This crocin is a di-(-D-gentiobiosyl) ester of trans-crocetin.

Crocins are a class of hydrophilic carotenoids. They are crocetin polyene esters that may be either monoglycosyl or glycosyl. Crocetin is a conjugated polyene dicarboxylic acid, hydrophobic and hence oil soluble.

Two sugars called gentiobioses are esterified with crocetin to produce a product that is both water-soluble and water-soluble. The resulting carotenoid pigment, called -crocins, might account for more than 10% of the dry mass of saffron. Because it contains two esterified gentiobioses, -crocins is great for coloring rice dishes and other meals that are high in water content but low in fat (6)

The pigment zeaxanthin is broken down into picrocrocin., Picrocrocin, a monoterpene glycoside precursor of safranal, is hydrolyzed during the drying process to D-glucose and a free safranal molecule by enzymatic activity (enzyme glucosidase). The volatile oil safranal is responsible for most of the saffron's characteristic scent (7). Safranal is a less bitter volatile fraction of dried saffron than picrocrocin, and it may account for as much as 70% of the volatile fraction in certain samples. 2hydroxy-4,4'-trimethyl-2,5-cyclohexadien-1-one is another chemical responsible for the saffron scent (8). While it is present in smaller quantities than safranal, chemists discover it is the most potent contributor to the saffron scent. Chemically, dry saffron degrades swiftly in the presence of light and oxidizing chemicals, and it is also very sensitive to changes in pH (degrading rapidly at a pH of 3).

Isolated from both saffron and the cheaper Gardenia fruit was crocin, also known as Crocetin di-gentiobiose ester (9). One of the few naturally occurring carotenoids, crocin is a di-ester produced from the disaccharide gentiobiose and the dicarboxylic acid crocetin.

The ability to dissolve in liquid., Antioxidant, anticancer, and other pharmacological properties have been shown in crocin. drugs designed to improve memory and learning in the medical industry (10). Its orange-red pigment is notable not only for its strong antioxidant activity but also for various commercial uses, including those related to food coloring and textile dyes. A cosmetic preservative and anti-aging agent (11).

**Bioavailability and Absorption of Crocin:** Extensive research has shown that the body does not absorb crocin. It was also discovered that crocin is not absorbed after being taken orally, either once or repeatedly. It has been found that crocins are first hydrolyzed to crocetin before being absorbed orally and that the absorbed crocetin is partly converted to mono- and di-glucuronide conjugates (12). When crocin is ingested, it is largely eliminated by the bowels.

**Saffron's Secondary Metabolites and Their Role in its Chemistry** Saffron comprises 5% fat, 10% water, 5% minerals, 12% protein, 5% crude fiber, and 63% carbohydrates (% dry weight). Saffron contains more than 150 volatile chemicals, including terpenes, alcohol, terpenes, and their esters, as well as Anthocyanins, flavonoids, vitamins (particularly riboflavin and thiamine), and minerals. Saffron's distinctive coloring comes from carotenoids, the primary pigments in the spice's stigmas and soluble in either water or lipids.

Water-soluble apocarotenoid crocetin ester derivatives include one or more sugar molecules; the most significant is the trans crocetin (digentibiosyl) ester. Fat-soluble carotenoids include lycopene, - and -carotene, and zeaxanthin. In addition, -crocetin and -crocetin are members of this class of minor components. As a result, there is a decreased level of inflammation. Because of their widespread availability and few side effects, natural product-based therapies for migraine, pain, inflammation, and arthritis are quite popular in conventional medicine. *C. sativus* has shown efficacy as an anti-inflammatory in this context as well. Extracts from the stigma and petals of saffron were tested for their anti-inflammatory effects, and the findings indicated they were effective (13). Crocin and safranal, two components of saffron, were shown to reduce the amount of neutrophils and the inflammatory pain response in a separate investigation.

**An Effect on the Kidneys (Nephrotoxicity, Magnitude, Crocin,** which can be extracted from saffron, has also been tested by certain researchers to determine its effectiveness in combating renal issues. Scientists have shown that this chemical prevents acute renal failure and oxidative stress in animal experiments (14). The antioxidant properties of safranal have been investigated, and the results suggest that it may mitigate nephrotoxicity.

**Efficacy against diabetes:** Both mildly and severely diabetic rats showed a decrease in fasting blood glucose after being given saffron extract (15).

Saffron doses of 40 and 80 mg/kg were also shown to dramatically elevate body weight and serum TNF- while lowering blood glucose and glycosylated serum protein levels (16).

A methanolic extract of saffron, crocin, and safranal significantly lowered fasting blood glucose and hemoglobin A1c levels; crocin, for its part, has been shown in further research to drastically lower blood glucose levels (17, 18).

When comparing disease control groups and diabetic rats, it was shown that diabetic rats whose bodies were orally administered saffron extract gained much more weight and had normalized blood insulin levels (19).

Arousing pursuits, such as adding saffron to your diet, are great ways to boost your libido and fertility. Crocin and its aqueous extract, especially at dosages of 160-320 mg/kg b.w., enhanced mounting and erection frequency behaviors and decreased ejaculation, intromission, and mount latency characteristics (20).

Anti-anxiety effects Crocin, a component of saffron, was studied to see whether it had any anxiolytic properties. It was shown that the latency to enter the dark compartment was significantly lengthened by either crocin, which did not affect the animals' motor activity or diazepam.

The Effect of Anticonvulsants: The anticonvulsant effects of safranal and crocin were tested in mouse models, with safranal showing a shorter seizure duration, a later commencement of convulsions, and protection against mortality (21).

### **Substances and Techniques**

Ingredient: about 500 grams of Qaenat Razavi saffron (Khorasan, Iran)

Saffron's preparation and usage (**Figure 1**):



**(Figure 1) : Saffron: glass of saffron water preparation, 30mg with 70- 100ml water.**

Saffron threads are pounded in a mortar and pestle; recommended dosages are 30mg twice day after eating and 20mg three times daily (every 8 hours)

A cup of hot (temperature: 70-80°C) water (70-100ml) is infused with powdered saffron for 5-10 minutes till cool and then consumed orally.

The recommended dosage is 1,200 milligrams (mg), taken once daily for three weeks.

### **Analysis of Saffron's Efficacy**

We tracked 450 adults (20-65 years old) during the course of the trial. Two hundred people were tested for saffron's anti-diabetic and antispasmodic effects on people with colon diseases, and two hundred and fifty people were studied for its potential anti-depressant and anti-inflammatory properties. We used random effects modeling approaches to determine the average impact of saffron water preparation vs patients without medicines and saffron water preparation versus antidepressant (e.g., fluoxetine and imipramine) group.

Standards for admission and rejection:

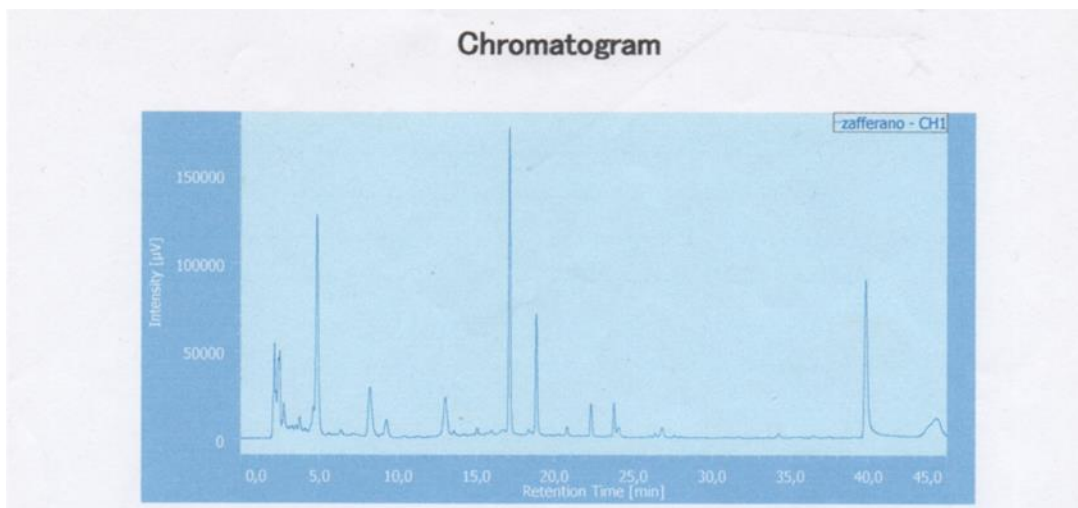
Study inclusion criteria included the following:

- depressed adults (aged 20-65)
- study design: a randomized controlled trial
- Saffron water's impact on mood disorders is investigated.
- Regarding the second set, we used data from randomized controlled trials to randomly choose N=250 participants.
- Excluded: N=170 individuals with no depressive symptoms; N=80 individuals with depressive symptoms evaluated in a meta-analysis.
- 10 people were taken out of the antidepressant control group.
- 15 people took antidepressants, and 55 people did not. Seventy participants in the evaluation based on a meta-analysis.

### **Components**

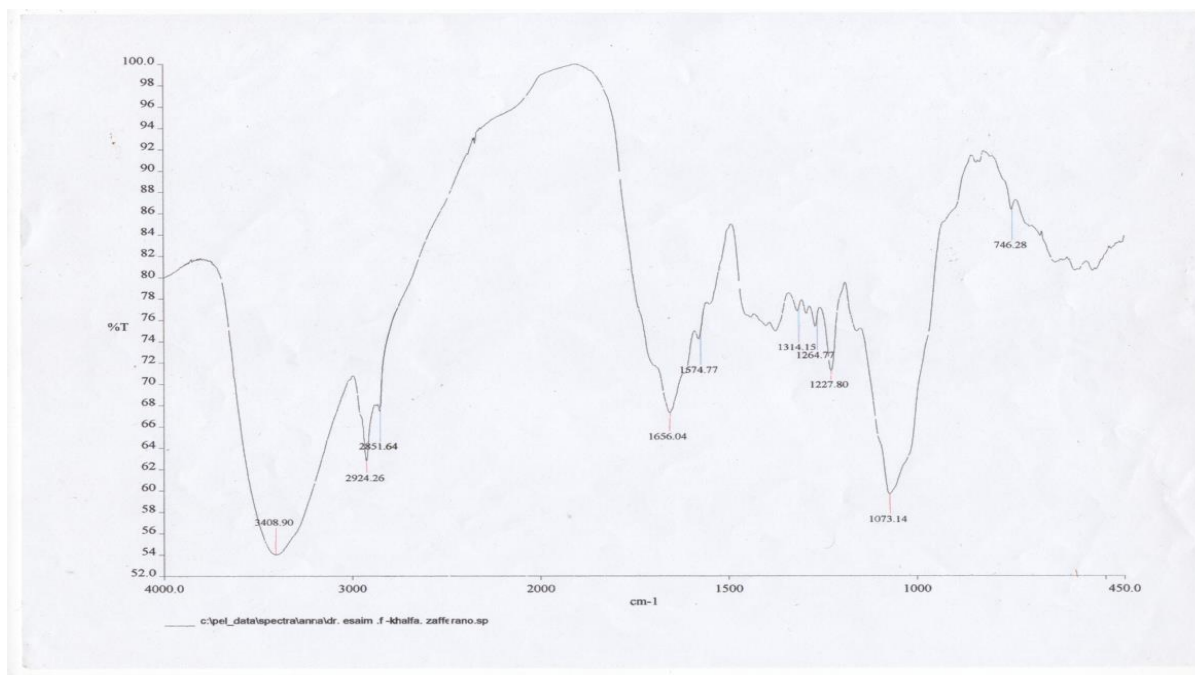
(**Figure 2**) show HPLC, a sensitive and easy high-performance liquid chromatography approach, was devised to determine saffron. The chromatography was performed on a reversed-phase hypersil C18 column. Methanol and water were used as the mobile phase in a 50:50 (v/v) ratio. UV detectors set at 220 nm and a 1 ml/min flow rate were used to monitor the saffron.

Preparation of the saffron solution: 2mg in 10ml water, heat until dissolved, conduct centrifuge for a few minutes until full dissolution, and lastly, produce a dilution. Injection Volume:20.00µl. The time to acquire was 45 minutes. Crocetin (17.0 rt), Crocetin-like (18.8), Crocin (22.3 rt), and Crocin (23.8 rt), Absorption of Infrared Radiation Spectrophotometry (**Figure 3**): A few milligrams of saffron powder is placed within the device.



(Figure 2) : Saffron: HPLC Technique is used for the determination of molecules.

Chromatography was accomplished with a reversed- phase hypersil C18 column. Mobile phase consisted of Methanol – water (50:50, v/v), Injection Volume (20.00 Micro L), Acquisition time (45.0 min).



(Figure 3) : Infra-red Absorption Spectrophotometry.

## Results

The results shown in the Tables (1-5) and (Figure 4).

The initial sample size of 200, 20 showed a reduction in blood glucose, 140 showed an antispasmodic effect, and 40 showed no effects. This meta-analysis looked at clinical studies

including persons with depression disorder (to compare the saffron water preparation to medications), healthy people, and those with colon problems to quantify the effects of frequent consumption of the saffron water preparation on depressed symptoms.

Saffron's antidepressant properties were investigated, and the results suggested it might be useful in treating depression in people with MDD. Saffron's effects were shown to be much greater than those of the no-drug control group.

Those who were treated with both saffron and an antidepressant (either fluoxetine or imipramine) showed significantly greater improvement in their depression symptoms than those who were treated with only one. The findings are consistent with those of previous studies in the literature (22,23).

There were no discernible differences (same effect) between the long-term use of saffron and the antidepressant medicine imipramine; nevertheless, the use of saffron was linked to a greater number of side effects, including nausea, vomiting, and headache (24).

**Table (1) Sample preparation Compared with and without drug**

<b>Sample preparation</b>	<b>Compared With condition</b>	<b>Sample number</b>	<b>Age(years)</b>	<b>Result</b>
<b>Adult with mild to moderate depression</b>	<b>With drug</b>	<b>15</b>	<b>25-55</b>	<b>Relive symptom of depression similar effect</b>
<b>Adult with mild to moderate depression</b>	<b>Without drug</b>	<b>55</b>	<b>25-45</b>	<b>Relive symptom of depression</b>

**Table (2) Adverse event Compared with age and Sample number**

<b>Adverse event</b>	<b>Age(years)</b>	<b>Sample number</b>	<b>Result</b>
<b>Women (20-45 y) with menstrual cycle cramps</b>	<b>20-45</b>	<b>30</b>	<b>Relive symptom</b>
<b>Insomnia</b>	<b>30-50</b>	<b>50</b>	<b>Also</b>
<b>Respiratory disorder</b>	<b>20-2</b>	<b>35</b>	<b>Also</b>

**Table (3) Adverse event with saffron and antidepressant**

<b>Adverse event</b>	<b>Saffron</b>	<b>Antidepressant</b>
<b>Headache</b>	<b>14</b>	<b>8</b>
<b>Sedation</b>	<b>6</b>	<b>9</b>
<b>Anxiety</b>	<b>8</b>	<b>14</b>
<b>Decreased appetite</b>	<b>15</b>	<b>9</b>
<b>Vomiting</b>	<b>13</b>	<b>4</b>
<b>Dry mouth</b>	<b>1</b>	<b>7</b>

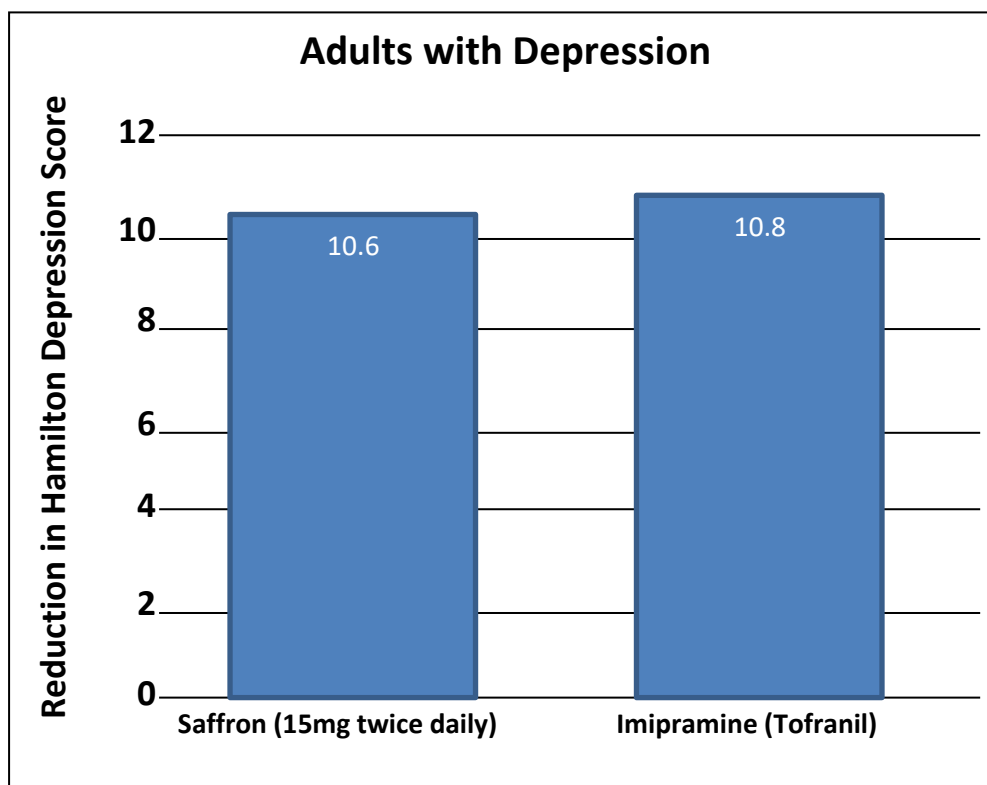
**Table (4) Sample preparation Compared with and without drug fluoxiten**

<b>Sample preparation</b>	<b>Compared with condition</b>	<b>Sample number</b>	<b>Age(years)</b>	<b>Result</b>
<b>Adult with mild to moderate depression</b>	<b>With drug fluoxiten</b>	<b>15</b>	<b>25-55</b>	<b>Relive symptom of depression Similar effect</b>
<b>Adult with mild to moderate depression</b>	<b>Without drugs</b>	<b>55</b>	<b>25-45</b>	<b>Relive symptom of depression</b>

**Table (5) Adverse event Compared with age and Sample number**

<b>Adverse event</b>	<b>Age(years)</b>	<b>Sample number</b>	<b>Result</b>
<b>Woman (20-45 y) with irregular menstrual cycles</b>	<b>20-45</b>	<b>30</b>	<b>Relive symptom</b>
<b>Colonic patient</b>	<b>30-50</b>	<b>75</b>	<b>Also</b>
<b>Respiratory disorder</b>	<b>30-50</b>	<b>20-27</b>	<b>10</b>





(Figure 4) : Comparative between Saffron and Tofranil in Adults with Depression

## Discussion

The field of medicine is becoming more interested in the use of treatments based on alternative medicines. Crocin and crocetin, two active components in saffron, have been shown to have a role in illness management by modulating several physiological and biochemical processes.

According to the results of the included studies in this meta-analysis, using saffron as a short-term treatment for MDD is effective. It is a tranquilizer of the nervous system and helps those who have problems with their intestines or menstrual cycle. Saffron, which has depressive, antispasmodic, and antidiabetic properties, is recommended in a water solution (dose: 30mg twice a day for three weeks in a month, without sugar). Some people should not consume saffron, thus it's important to heed the cautions and warnings around its use.

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