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Saffron: An Insight of Important Medicinal and Nutritional Values

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ABSTRACT

Saffron (Crocus sativus) is costliest spices in the world due to high nutritional values. It has also been used in traditional medicine for treatment of different types of illnesses since ancient times. Many of these medicinal properties of saffron can be attributed to a number of bioactive compounds like safranal, crocin, picrocrocin and crocetin as well as highly active antioxidants. This review is aimed to explore the nutritional and medicinal values of saffron and highlight the recent advances in the field.

1. Introduction

Herbs and spices have been at the forefront of history since the beginning of time and have been one of the most sought items since antiquity courtesy their wide range of properties. Apart of being additive to enhance the taste, flavour and aroma of cuisine, spices have been in forefront for their medicinal properties [1, 2]. Abundant anecdotal information documents the historical use of herbs and spices for their health benefits. There is a long list of manuscripts in Ayurveda as well as ancient Chinese, Unani, Egyptian and Korean medicine system, where use of spices in therapeutics in well recorded [3, 4]. Spices were used from a general therapeutic purpose e.g. application of turmeric on external injuries or cloves and cardamom were wrapped in betel-nut leaves and chewed after meals to increase the flow of saliva and aid digestion; to the extensively specified purpose like preservation of mummies [5].

Saffron is one of the major spices, specifically known for its high richness of culinary, nutritional as well as medicinal values, which makes it the costliest spices in the world. Though, saffron has been in dietary and therapeutic uses such as treating cold and fever, treatment of menstrual disorders, boosting libido and gastric problems since ages; but recent studies have paved the way for a more specified and effective use of saffron for a better nutritional and medicinal aspects. This review explains about the medicinal properties and nutritional values of saffron and recent advances in this domain.

1. Saffron

Brief Description

Saffron (Crocus sativus) a member of family Iridaceae, also called Kesar in Hindi, Safran in German, Hong Hua in Chinese and Zaferen in Turkish; is a spice derived from the flower of the plant. The commercial part crimson stigma and styles, called threads, are collected and dried for use mainly as a seasoning and colouring agent in food, cosmetics, medicine and spices blends etc.

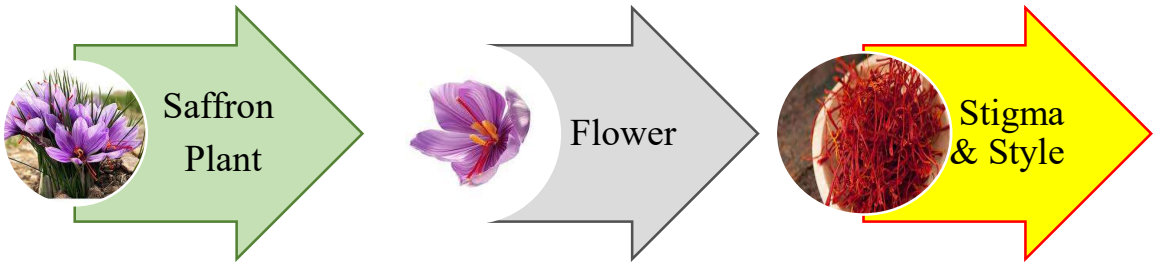


Figure 1. Saffron and its commercially useful parts

The typical aroma and fragrance of saffron is due to the presence of bioactive compounds picrocrocin, safranal; while the colour is result of a carotenoid pigment, crocin [6, 7].

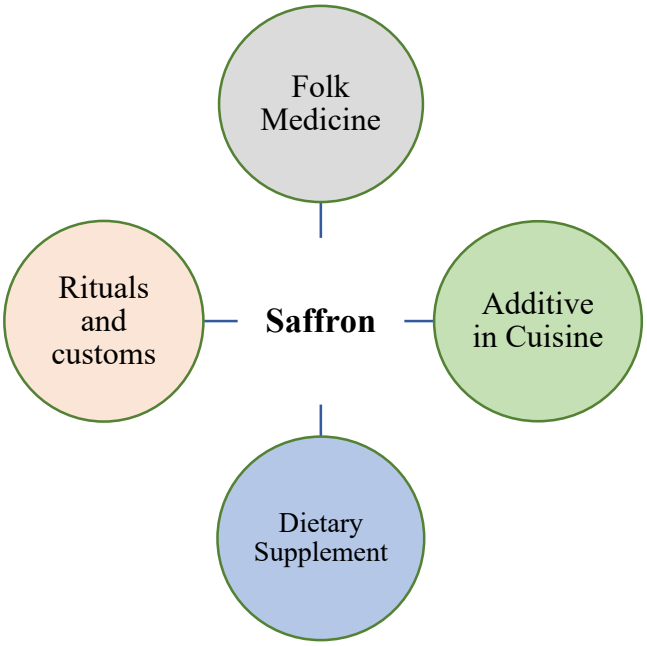


Figure 2. Uses of Saffron at a Glance

Approximately 150000 flowers are needed for one kilogram of dried saffron; an inferior and less expensive qualities include also the yellow stamina (male sexual organ), which do not have any taste of their own.

Traditional Uses

As discussed earlier, saffron has been used as a folk medicine in different medicine system of various parts of the world like Ayurveda, Unani, Korean, Egyptian and Chinese. It was widely used against gastric issues, asthama, menstrual problems and epidermal problems [8]. Saffron has also been used as a principal constituent in the preparation different opioid, which were used as analgesic during 16th-19th centuries in Europe [9].

Bioactive Compounds of Saffron

Chemical profiling of saffron had showed presence of more than 150 compounds, among them coloured carotenoids (crocin and crocetin), volatile compounds (safranal and picrocrocin), monoterpene aldehydes, ethanolic compounds and non-glycosylated carotenoids like β-carotene, lycopene and zea-xanthin are major one [10, 11, 12]. Although saffron contains some conventional carotenoids (α- and β-carotene, lycopin and zeaxanthin); intensive

colour of saffron is due to carotenoid type pigments and its staining capability is mostly caused by crocetine esters. Crocetin is a dicarboxylic acid with a C18 backbone, formed from carotenoid precursors (diterpene carotenoid) [13, 14].

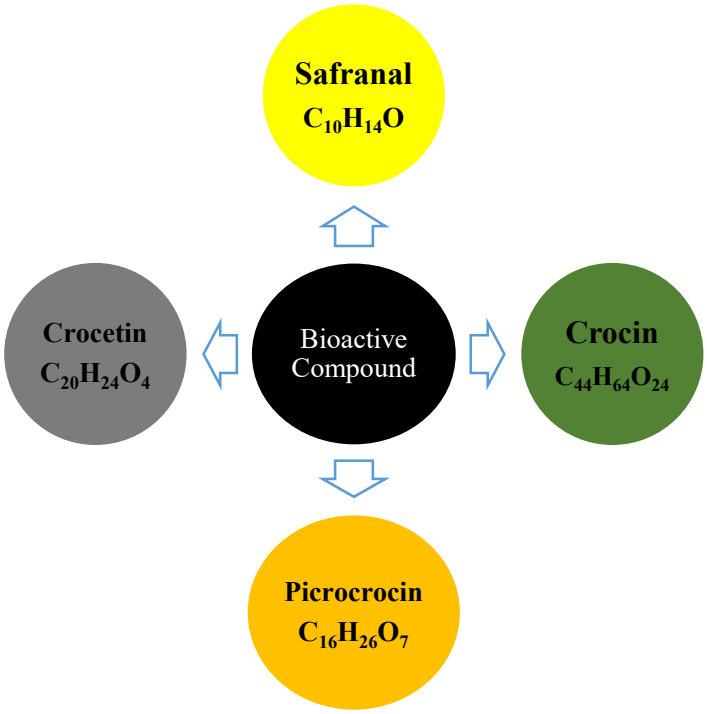


Figure 3. Important Bioactive Compounds in Saffron

Crocin is a carotenoid compound; a diester formed from the disaccharide gentiobiose and the dicarboxylic acid crocetin, is the single most important saffron pigment. The component underlying saffron's aroma is α-crocin (it composes more than 10% of dry saffron's mass): trans-crocetin di-(β-D-gentiobiosyl) ester; structurally known as 8, 8-diapo-8, 8-carotenoic acid [15, 16].

In the essential oil (max. 1%), several terpene aldehydes and ketones are found; among them the most abundant constituent is safranal i.e. 2, 6, 6-trimethyl 1, 3-cyclohexadiene-1-carbaldehyde (contribute 50% or more); another olfactorily important compound is 2-hydroxy 4, 4, 6-trimethyl 2, 5-cyclohexadien-1-one [17, 18].

The bitter taste is attributed to picrocrocin, the glucoside of an alcohol structurally related to safranal (4-hydroxy 2, 4, 4-trimethyl 1-cyclohexene-1-carboxaldehyde); and undergoing the process of deglucosylation, picrocrocin yields safranal [19, 20]. A wide range of anthocyanins e.g. delphinidin and petunidin and flavonol glycosides e.g. kaempferol have also been isolated and identified from blue perianth segments and flowers [21, 22].

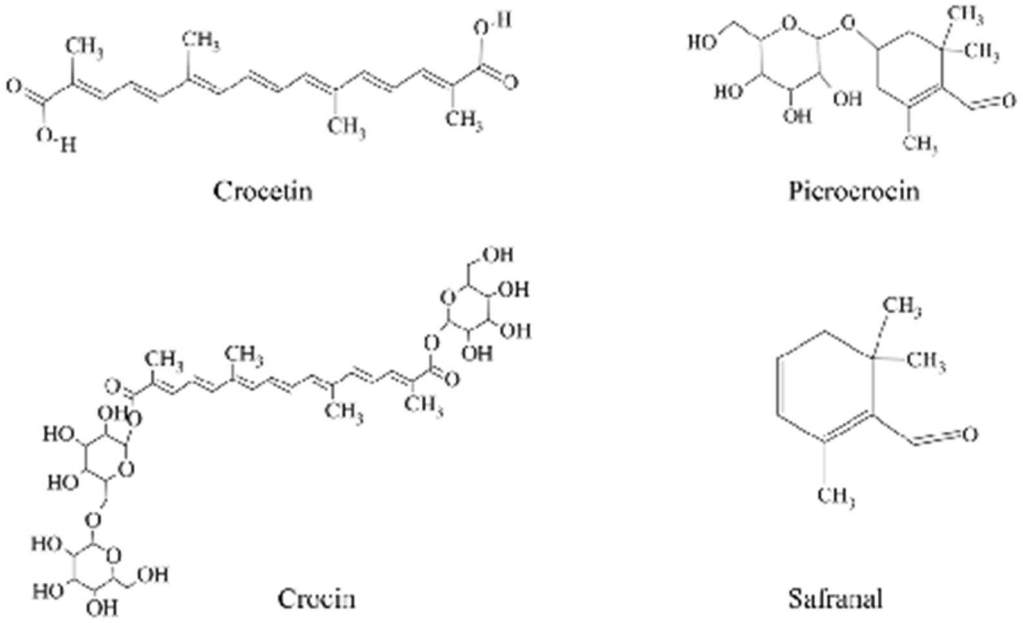


Figure 4. Chemical Structure of Bioactive Compounds of Saffron

2. Pharmacological activities

Saffron is a noteworthy medicinal and spicy plant because of its bioactive compounds and medicinal uses of saffron (Crocus sativus Linnaeus) have a long history beginning in Asian countries since the Late Bronze Age. Recent studies have validated its potential to lower the risk of several diseases. There have been clinical trials on therapeutic effects of saffron potential therapeutic applications of saffron on hypolipidemic, antidiabetic activities, antitumor, anticancer, antidepressant, antioxidant, neurodegenerative disorder, cardiovascular disease and antibacterial effects and many others [23, 24].

Here in this section, we will discuss about the pharmacological properties of saffron, recent advances and developments in detail.

Effects on Nervous System Disorders

Saffron has been reported to be effective against hypertension, memory impairment,

antigenotoxic and cytotoxic activities. Clinical studies have shown promising results when saffron extracts were used in the treatment of mild to moderate depression, Alzheimer's disease [25, 26, 27], with a median lethal doses (LD50) of Crocus sativus recorded to be 200 mg/ml and 20.7 g/kg in vitro and in animal studies. Saffron is known to intereact with opioid system and helps to reduce withdrawal syndrome; it is also showed that administration of the Crocus sativus and its constituents may help to increase the level of glutamate and dopamine subject to the dose [28, 29, 30].

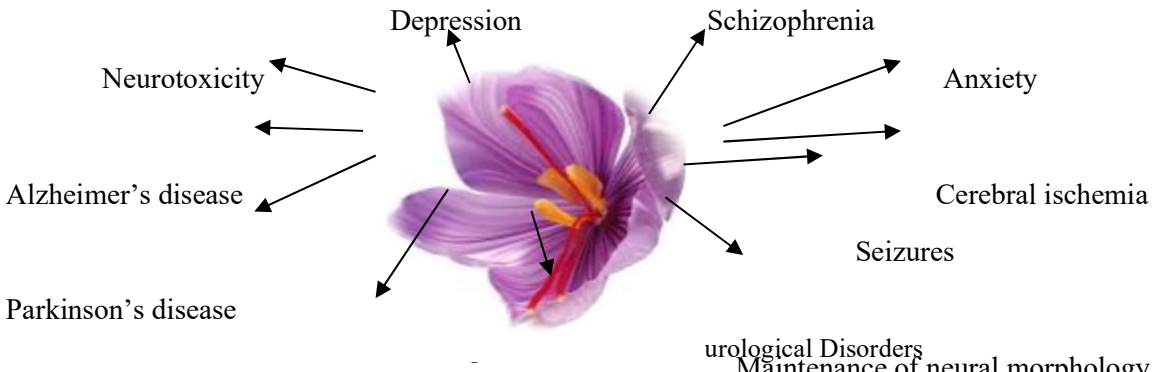
Studies conducted by Hoyle and Burnstock (1991) showed that administration of saffron extract can modulate the nor adrenaline and adenosine triphosphate (ATP) release as co-transmitters from sympathetic nerves; which is responsible for electrical field stimulated induction of contractions of vas deferens in rats [31, 32]. Safranal is also reported for to have inhibitory effect on histamine (H1) receptors, stimulatory effect on β2-adrenoreceptors, blocking effect of safranal on muscarinic receptors [33, 34]. It is also shown by in vitro studies that the neuro-protective effects of saffron and its constituents in amnesic and ischemic rat models [35, 36]; it also have significant role in improved learning and memory [37]. Saffron has a

noteworthy as anticonvulsant effects; Sunanda and co (2014) showed that 400 and 800 mg/kg dosage of saffron have significant impact on antiepileptic activity in pentylenetetrazole (PTZ) induced seizure, however a dose of 200 mg/kg did not showed similar effects [38, 39].

Saffron and its active ingredients and derivatives have shown encouraging results when administered for treatment of Alzheimer's disease. Study showed that aqueous ethanolic (50:50, v/v) extract of stigma of saffron has inhibitory effects on Aβ fibrillogenesis; and the principal factor in this mechanism was trans-crocin-4, which is a digentibiosyl ester of crocetin [40, 41]. Studies using rodents as model animal to for Alzheimer's disease had showed, that 3 weeks of treatment using saffron extract (30 mg/kg) improves the cognition deficit in rat and has an antagonizing effect on the STZ-induced cognitive deficits in rats [42, 43, 44, 45]. Akhondzadeh and co. (2010) reported that dose of saffron limited to 30mg/day administered twice a day (i.e. 15g mg/dose), was as effective as donepezil for treatment of mild-to-moderate AD case of patients 55 years and older; and the treatment lasting for 16 weeks showed better results than placebo.

Shahmansouri and co. (2014) reported that has bioactive compounds which are highly effective against depression; as evident by the administration of saffron (30 mg/day) capsules for six weeks, which was found as efficient as the administration of fluoxetine (40 mg/day) for same period [46, 47, 48].

Saffron and its components, are effective in the treatment of neurological disorders such as Parkinson's disease, Alzheimer's disease, Schizofrenia and depression; because they bioactive compounds specially the safranal, crocin and crocetin, have inhibitory effect on fibrillation of apoalpha lactalbumin and suppresses the formation of toxic amyloid structure (which is related to neural disorders) [49, 50, 51].



Saffron has also been found very effective to combat the neurotoxicity, administration of saffron extract dosage 200 mg/kg co-ppt with honey syrup (500 mg/kg) for 45 days showed significant reduction in neurotoxicity caused by aluminium chloride. Actually crocin up to concentration level of 10 μM, act as inhibitor in formation of peroxidized lipids in pheochromocytoma cells (PC12); it helps to restore superoxide dismutase activity and maintained neurons morphology [52, 53, 54]. Saffron has also been found effective against withdrawal symptoms in drug addiction, defective neurotransmission, morphine-induced inhibition of spatial learning and memory and retension of memory by different researchers [55, 56, 57, 58].

Anti-tumour Effects

Tumours are groups of abnormal cells that form lumps or growths. They can start in any one of the trillions of cells in our bodies. Tumours grow and behave differently, depending on whether they are cancerous (malignant), non-cancerous (benign) or precancerous. Tumours are results of defective and disruptive cell division/growth caused by breakdown of orderly process.

Saffron, owing to its bioactive compounds, is known to play important role in critical phases of cell division and apoptosis through various mechanisms and helps in inhibition of tumour development and progression [59, 60]. The animal model based studies showed that administration of 10 μM of crocin helps to suppress the tumour necrosis factor alpha (TNF-

α)-induced expression of proapoptotic mRNA, which releases cytochrome c from mitochondria [61, 62]. It was also documented that crocin with a dose of 50 mg/kg arrests/prevents the retinalganglion cells (RGCs) apoptosis after retinal ischemia/reperfusion injury via phosphatidylinositol 3-kinase/AKT (PI3K/AKT) signalling pathway [63].

Studies have shown that crocetin plays an important and critical role in the reversal of pathological modifications in cancerous cells and administration of aqueous extract of saffron acts as an inhibition agent against the growth of both transitional cell carcinoma and normal cell lines [64,65]. One of the study showed that crocin has antiproliferative and treatment with saffron results in the reduced telomerase activity of HepG2 cells. It is also found that crocetin helps to reduce the cytotoxicity in case of aflatoxin B1 in the fibroblast cells and inhibits the DNA-adduct formation of microsomes [66, 67].

It is also reported that bioactive ingredients of saffron are able to modulate and alter the morphology of cell and can significantly affect the apoptosis. Crocin has been found to actively inhibit the tumour weight and size of xenografts in mice; it has also showed critical inhibitory effects on cell proliferation and induced apoptosis and arrested the cell division at G0/G1 phase [68, 69].

Anti-microbial & Anti-inflammatory Effects

Folk medicine has been very common use during traditional days for the treatment of epidermal like skin infections as well as internal microbial infections like food poisoning, pain, inflammation, arthritis etc, and saffron has been one of them. In this regard, saffron has been reported to be in use among wide section of society. Clinical research has shown that crocin and safranal suppressed inflammatory pain response and decreased the number of neutrophils; and extracts of stigma and petal of saffron exerts anti-inflammatory activity [70, 71].

Saffron is also known to possess very potent antimicrobial properties; studies using bacteria and fungi as test organisms have shown that extracts of Crocus sativus is highly effective against various bacterial strains [72]. It is also revealed that blends like aqueous, ethanolic and methanolic extracts of petal of saffron are highly potent against food borne bacterial infections. Different parts of Crocus sativus, such as stamen and corolla have been employed as a good source of antimicrobial agents [73, 74].

Hepato & Cardio-protective Effects

Wide ranges of medicinal plants are used for various purposes; fumes, vapours and extracts from their floral parts, leaves and roots have specifically been used for better health of heart and liver. In this regard, saffron has also been checked as traditional as well as clinical medicine for its synergistic effects on functional health of heart and liver.

Clinical tests have produced results which have affirmed the saffron as potential medicine for liver ailments. Studies have showed that extract of saffron petals can regulate the levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) [75, 76]. These enzymes are normally predominantly contained within liver cells and to a lesser degree in the muscle cells. If the liver is injured or damaged, the liver cells spill these enzymes into the blood, raising the AST and ALT enzyme blood levels and signaling liver disease.

Crocin has showed positive results against cardio-toxicity through reducing lipid peroxidation as well as alleviating apoptosis; cardio-protective effect of saffron active constituents including crocin has been confirmed through regulation of oxidative stress [77, 78]. Clinical tests using rat as model organisms have showed that saffron and constituent compounds are effective in reduction of the myocardial lipid peroxidation as well as levels of serum creatine kinase (CK) and lactate dehydrogenase (LDH) [79].

Anti-diabetic, Anti-obesity & Anxiolytic Effects

Evidences from traditional medications and documents, clinical studies on model organisms as well as recent findings have proved the effects to combat the diabetes and obesity. Findings have demonstrated that administration of saffron doses 40 and 80 mg/kg significantly lowers the level of blood glucose levels and glycosylated serum protein [80]; while other study

conducted on rats showed that extract of saffron can reduce the blood sugar in mild and severe diabetic conditions [81]. Studies have revealed that if saffron extract is administered orally, it significantly the serum insulin level in diabetic rats as compared to disease control groups [82].

A study conducted in rats showed that safranal at higher dosage demonstrated anxiolytic effects and furthermore, safranal increased the total sleep time dose dependence [83, 84]; while crocin induces the anxiety relieving effects. Crocin has been found effectively controlling the total fat deposition, rate of body weight gain and regulates the weight ratio of epididymal fat to body [85]. Earlier investigations concluded on obese rats showed that saffron has anti-obesity and anorectic effects; it reduces the fat mass and increases insulin sensitivity and also reduces leptin level [86].

3. Nutritional Properties

Saffron has been in use for a number of purposes like dietary consumption, blended drinks like saffron kahwa, medicinal uses, garnishing and topping of cuisines, aesthetic pruposes, traditional ritual and customs on auspicious occasions and many more.

Saffron is source of dietary fibres, a number of vitamins, amino acids, minerals and essential macro and micro nutrients. Dried saffron is 65% carbohydrates, 6% fat, 11% protein (table) and 12% water. In one tablespoon (2 grams; a quantity much larger than is likely to be ingested in normal use) manganese is present as 29% of the daily value. Consumption of saffron can provide the required dietary dosages of vitamin A, thiamine, riboflavin, niacin, folate, vitamin B9, B12 and vitamin D [87].

Chemical profiling of saffron pollen showed its highly enriched aspects in terms of nutritional values. Pollen of saffron is a good source of minerals such as potassium (57,460 ppm), magnesium (3,357.5 ppm), sodium (1,100 ppm), calcium (600 ppm), zinc (100.75 ppm), iron (194 ppm), copper (53.2 ppm) and manganese (48.5 ppm) [88]. Studies have also shown a very good content of crude fiber (7.4 percent), crude fat (5.8 percent), and crude protein (23.6 percent) in saffron [89].

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References to the work should follow the 7th APA style and carefully checked for accuracy and consistency. Please ensure that every reference cited in the text is also present in the reference list and vice versa.

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