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REVIEW ON PHARMACOLOGICAL PROPERTIES OF SAFFRON (CROCUS SATIVUS)

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ABSTRACT

In this review different pharmacological properties of saffron petal such as antibacterial, antispasmodic, immunomodulatory, antitussive, antidepressant, antinociceptive, hepatoprotective, renoprotective, antihypertensive, antidiabetic and antioxidant activity have been introduced. Clinical trials conducted on women with premenstrual syndrome showed that saffron could reduce suf-fering symptoms more than the placebo and similar to standard treatments. Saffron contains chemicals that might alter mood, kill cancer cells, decrease swelling, and act like antioxidants. Their antidepressants effects are also very evident. Crocus sativus (saffron) may inhibit the aggregation and deposition of amyloid bin thehuman brain and may therefore be useful in Alzheimer‟s disease (AD). It originated in Greece, where it was revered for its medicinal properties. Furthermore, advanced research is needed to elabo-rate the role of saffron in health management and its mechanism of action in the modulation of biological activities. Thus the aqueous extract of saffron can improvefertility, which may be attributed to crocetin and/or flavonoids contents of the extract. According to the obtained results saffron-based beverage is a suitable medium for the growth of lactic acid bacteria and production of functional beverages.

INTRODUCTION

(Crocus sativus) is among the important herb which is used as medication for several centuries in different parts of the world such as India, China, Spain, Italy, Greece, and in Iran. The stigmas of saffron used as a flavoring spice in the cooking, in different parts of the world.[1]

A well-ordered food regime which embraces a consistent ingesting of probiotic microorganisms have many benefits including regulation of bowel function and intestinal micro-flora, inspiration of the body immune system, enhancement of lactose digestion, and protection against different pathogens. Saffron has also been used as a fabric dye, particularly in China and India, and in perfumery. Crocus sativus (saffron) Linn. Is belonging to Iridaceae family. Saffron(crocus sativus L) is a sterile triploid plant that is naturally propagated vegetatively by daughter corms developing on a mother corm. Hytochemical studies have shown saffron stigma is containing crocetin, crocin, picrocrocin and safranal.

C. sativus grows up to 20–30 cm height and has 5–11 true leaves that are shielded and covered by 5–11 non-photosynthetic and white leaves (cataphylls). World's annual production of saffron is estimated to be 300 tons. Saffron's also known as Zafaran taste and iodole form or hay-like fragrance result from the chemicals picro -crocin and safranal. It also contains a carotenoid pigment, crocin, which imparts a rich golden-yellow hue to dishes and textile. Beside its traditional usage as a spice, saffron has known as a stomach pain soother, antispasmodic, digestion aid, renal colic pains reliever, antidepressant, and appetizer agent in Iranian traditional medicine.

It was probably used as part of embalming rituals by the ancient Egyptians. The Mediterranean environment is recognized worldwide as the best region to produce saffron, with regards to its quality, which is attributed to many factor. In traditional medicine, it is used as an aphrodisiac, antispasmodic, expectorant, stomachache, relieving tension, depression and insomnia.[2]

The flower's natural fields are in the 30˚- 40˚ North latitude. Crocus sativus prefers friable, loose, low-density, well-watered, and well-drained clay-calcareous soils with high organic content. C. sativus extract has been studied in 8 anti-depressant clinical trials in comparison to placebo or some antidepressant drugs, in which saffron showed effectiveness as an antidepressant drug.

In India this high value aromatic spice is called Kum Kumin Sanaskrit and Kesar and in Kashmiri it is called Koung. The saffron is also called Golden crop because of its extreme high cash value and low volume and this great commercial activity is called as 'Golden Zest' in Indian Agriculture. Saffron extract was reported to be useful in the treatment of neurodegenerative disorders accompanying memory impairment. As saffron is a natural

product and, hence, saffron supplements are under less tight regulation regarding sale and dosage, this review is also intended to provideconcise information on dosage and potential side effects based on the available literature. Characterization of the transcription of saffron stigmas is vital for throwing light on the molecular basis of flavor, color biogenesis, genomic organization and the biology of the gynoecium of spices in general and saffron particularly.

Picrocrocinin is considered to be the main bitter principle of saffron. The method used in this work for the quality determination of saffron is high-performance liquid chromatography (HPLC) with PDA detector. This method is the most efficient analytical technique for the analysis of sensitive compounds in complex extracts of natural products. Pharmacological studies demonstrated that saffron extracts or its constituents hadantitumoral properties as well as blood lipid lowering and radicals cavenging properties. Saffron tastes bitter and contributes a luminous yellow-orange coloring to foods. The wild precursor of domesticated saffron crocus was likely Crocus cartwrightianus, which originated in Crete or Central Asia. The saffron produced in the region is of superior quality and can fetch as much as Rs 2,50,000 per kilogram in the market. Saffron also has trace amounts of thiamine and riboflavin. Saffron is a cold tolerant plant but temperate climate is better for its growth.

In this revie Crocin w, we focus on the studies dealing with the interactions of morphine reward and dependent with saffron extract.

CHEMICAL CONSTITUTION

Crocin, Picrocrocin, safranal, flavanoles, PH-5.8 to 7.8.

HISTORY

Saffron was first documented in a 7^{th} – century BC Assyrian botanical reference complied under Ashurbanipal. Since then, documentation of saffron's use over a span of 4.000 years in the treatment of some ninely illnesses has been uncovered. Saffron slowly spread throughout much of Eurasia, later reaching parts of North Africa, North American, and Oceania. Saffron is native to Southwest Asia. Iran at present is the world's largest producer of saffron. According to some authors the saffron first originated in Iran and Kashmir from where Phoenicians introduced it to Greek and Roman world. Later it was brought by Arabs and Moors to the Spain The word saffron is derived from the Arabic word za'fraan, which translates to yellow 5. The term in ancient Greek is Korikos, the Romans used the term Crocum; English, Saffron; Italian, Zafferano; French, safran; Spanish, Azafran; German,

Saffran; Russian, Shafran; Turkish, Zaferen 11, 13. In Sanskrit it bears the name of kumkuma and is described as charu (fair), vara (suitor), agnishikha (having a crest of fire), saurabh (fragrant).[3]

1. **Saffron in Egypt** -In ancient Egypt, (3100 BC – 476 AD) saffron was imported from Crete and one of its important uses was in medicine and was mentioned in 'The Ebers Papyrus'
2. **Indian Saffron** -Some belive that saffron was first introduced to India by ancient Persians its exact date is unknown, but Wan Zhen (a Chinese medical writer), described Kashmiri saffron by 3rd century AD. A Buddhist legend dates saffron plantation there back to the 5th century.[4]
3. **Spanish saffron-** Modern saffron cultivation in Europe began in Spain in the 10th century AD after Muslim campaigns in 712 AD. After conquering Iran, Muslims brought the knowledge of cultivating saffron from Persia to Spain.
4. **Modern saffron cultivation in Europe** -Saffron cultivation in Europe declined after the fall of Western Roman Empire (5thcentury AD) and for several centuries saffron cultivation was rare. Saffron came back to Europe by the Muslim in 10th century AD.

Saffron

Saffron crocus, Crocus sativas, with its vivid Saffron "threads" plucked from crocus flower crimsons stigma and styles. and dried.

VARIETIES OF SAFFRON

1. Sargol Iranian Variety
2. Mancha Spain
3. Rio Spain
4. Sierra Spain
5. Indian Saffron
6. Italian Variety
7. Iranian Standard Variety

PHARMACOLOGICAL PROPERTY

1. Antidepressant
2. Antinociceptive
3. Anti tussive
4. PMS improvement
5. Anti tumor
6. Anti bacterial
7. Anti spasm
8. Immunomodulator
9. Anticancer Activity
10. Antioxidant Activity
11. Anti Alzheimer Activity
12. Anti diabetic Activity
13. Antihyperlipidemic Activity

1. **Antidepressant:-** Depression is a psychological disorder which influences thought, behavior, and moof.[5]
2. **Antinociceptive:-** Antinociception also known as nocioception/nociperception is the body's response to potentially toxic stimuli, like harmful chemicals (e.g., capsaicin, formalin), mechanical injury (e.g., cutting, crushing), or adverse temperatures (heat and cold) by the sensory nervous system.
3. **Anti tussive:-** The antitussive activity of C. sativus (stigma and petal) and it active ingredients (safranal and crocin) was investigated in guinea pigs using nebolized solution of citric acid 20%.

4. **PMS improvement:-** In a double blind clinical study, the women (20-45 years) who experienced PMS symptoms for at least t least 6 months, received saffron petal Twice a day.
5. **Antitumor:-** Antitumor activity of saffron (Crocus sativus) extract a commonly used spice in India was studied against intraperitoneally transplanted sarcoma-180 (S-180), Ehrlich ascites Carcinoma (EAC) and Dalton's lymphoma ascites (DLA) tumours in mice.
6. **Anti bacterial:-** Comparison of the antibacterial effects of saffron extract with antibiotics shows that antibiotics can be replaced by this plant. For example, the effect of saffron extract on s. aureus is similar with antibiotic erythromycin.
7. **AntiSpasm:-** As an antispasmodic, saffron is used for stomach pain by helping digestion and improving appetite.
8. **Immunomodulator:-** The most of herbal medicines have immunomodulatory effects and alter immune function.
9. **Anticancer Activity**:- Recent scientific findings have been encouraging, uniformly showing that saffron and its derivatives can affect carcinogenesis in a variety of in vivo and in vitro models particularly crocin and crocetin have significant anticancer activity in breast, lung, pancreatic and leukemic cells. Saffron has selective toxicity against cancer cells, through inhibition of RNA and DNA synthesis and increasing apoptosis. The mutagenic, antimutagenic and cytotoxic effects of saffron and its main components were studied on the growth of different human malignant cells in vitro.Crocin has been considered as the most important anticancer agent of saffron that plays a role in gene expression and apoptosis in cancer cells. We have recently reported that saffron (SE) and crocin (CR) exhibit anticancer activity by promoting cell cycle arrest in prostate cancer (PCa) cells. The need for anticancer drugs with high efficacy and low toxicity has led to studies evaluating putative antineoplastic factors in fruits, vegetables, herbs, and spice. The anti-proliferative effect of Crocus sativus extract and its major constituent, crocin, was studied on three colorectal cancer cell lines. The anticancer activity of saffron extract (dimethyl-crocetin) against a wide spectrum of murine tumors and human leukemia cell lines was studied.
10. **Antioxidant Activity:-** Oxidative stress plays an important role in many cardiovascular diseases, and its uncontrolled chain reaction is related to myocardial injury.
11. **Anti-Alzheimer Activity:-** The main carotenoid constituent, trans-crocin-4, the digentibiosyl ester of crocetin, inhibited A-beta fibrillogenesis in Alzheimers disease.

12. **Anti-diabetic Activity**-Crocetin, the active constituent of saffron was found to possess anti diabetic activity in fructose-fed rats as it alleviated free fatty acid induced insulin insensitivity and dysregulated mRNA expression of adiponectin, TNF-alpha and leptin in primary cultured rat adipocytes suggesting the possibility of crocetin treatment as a preventive strategy of insulin resistance and related diseases.Streptozotocin (STZ) is a toxic compound for pancreatic beta cells. This compounds damages pancreatic beta cells and leads to lower insulin level and elevates blood glucose. Saffron at 40 and 80 mg/kg significantly increased body weight and serum TNF-α and decreased blood glucose levels, glycosylated serum proteins, and serum advanced glycation endproducts (AGEs) levels which triggered oxidative reaction.[6]
13. **Antihyperlipidemic activity:-** Crocin, one of the constituents of saffron was shown to produce mohypolipidemic effect in the dose range of 25 mg/kg to 100 mg/kg body weight in diet-induced hyperlipidemic rats by inhibiting pancreatic lipase thereby leading to malabsorbtion of fat and cholesterol producing hypolipidemic effect.

***The effects of Saffron on nervous system diseases** -Neurodegenerative diseases of the central nervous system are often associated with impairment of memory and other cognitive functions. In conclusion, according to the studies it seems that the saffron and its constituents (especially crocin) improve the memory function in patients suffering from memory disorders and antagonize the external degeneration of the memory.

***Effect on ocular blood flow and retinal function -**It as been found in an in vitro study that saffron may protect the photoreceptors from oxidative stress.it seems that saffron and its constituents (especially crocin and crocetin) can play role as an eye protection. These effects can be contributed to the antioxidant and anti-inflammatory properties, and inhibition of apoptosis by saffron and its constituent

***Anticonvulsant effect -**This study has shown that the saffron extract may be useful in the treatment of absence and tonic-clonic seizures.Khosravan in 2002 has found that after inducing artificial seizure by maximum electroshock (MES) and pentylene tetrazol (PTZ), aqueous and alcoholic extracts of saffron (at doses of 0.8 and 2g/kg respectively) have shown anticonvulsant effects.

***Effect on depression-** More specifically, a saffron extract might inhibit serotonin reuptake in synapses. Inhibiting synaptic serotonin reuptake keeps serotonin in the brain longer, thereby enhancing its positive effects while combating depression.

***Effect on blood pressure** -saffron extract and its constituents, especially crocin and safranal, have some blood pressure modulating properties. However, its need additional investigations to find effective dose and mechanism of action, the effect may be contributed to antioxidant properties of saffron and its constituents.

***Effect on Premenstrual syndrome-**A study was conducted to investigate whether saffron (stigma of Crocus sativus L.) could relieve symptoms of premenstrual syndrome (PMS). Women aged 20–45 years with regular menstrual cycles and experience of PMS symptoms for at least 6 months was taken for the study.

***Effect on Respiratory system-**The relaxant effect of Crocus sativus on smooth muscle was evident as shown in guinea pig tracheal chain experiment. The relaxation produced with the aqueous-ethanolic extract and safranal in comparison with saline as negative control, and theophylline, was comparable to or even higher than that relaxation produced with theophylline suggesting its use in the treatment of various respiratory disorders like asthma etc.

***Effect on Cerebral ischemia –** The neuroprotective activities of saffron have been demonstrated in experimental models of cerebral ischemia. Saffron biocompounds are capable of attenuating all the alterations induced byischemia, most likely due to its antioxidant properties

POST – HARVEST HANDALING METHOD OF SAFFRON

Traditional postharvest practices being followed in Kashmir is main reason for quality deterioration and recovery loss. There are different methods of handling such as picking, drying, decontamination, packing.[7]

1. **Picking and sorting:-** In Kashmir, flower picking is not usually done daily. Flowers should be carried in clean baskets. A Delay in flower picking from the date of flower open-ing and a delay in separation of the stigma from the flower contribute to the drop in crocin content. In order to comply with ISO specifica-tions it is a good idea to repeat sorting 2–3 times per batch.

2. **Drying:-** According to the statutory standards of Zhejiang, saffron used for TCM should be dehydrated at low temperatures (<60°C). However, there are different drying processes including microwave drying, vacuum oven drying, and electric oven drying where the drying temperature is higher than 60°C. Drying is a critical step in saffron processing. Drying brings about the physical, biochemical and chemical changes necessary for imparting the desired attributes to saffron. Picrocrocin, the bitter constituent, decreases during drying. Samples dried in shade or under accelerated conditions had a better flavour profile that coincided with higher amounts of safranal (550-680 g kg-1) and lower levels of 4-□-hyd-roxysafranal (140-200 g kg-1).
3. **Decontamination:-** Spices may be highly contaminated with moulds, yeasts and bacteria, either as vegetative cells or spores coming from plants, soil, or the faeces of birds, rodents, insects, etc. In Kashmir, no decontamina-tion practices ate followed, as decontamination by chemical treatment (ethylene oxide, propylene oxide and methyl bro-mide) or irradiation leave toxic residues and adversely affect organoleptic properties (Sjöberg et al. 1991).
4. **Packing:-** Dried saffron is vulnerable to moisture ingression, light and air (photo-oxidation). Packaging of a dried product is normally done in poly bags by farmers and later (between 1-6 months) sold to wholesale traders. In Iran Institute of Standard and Industrial Research Organiza-tion (ISIROI) has released "Control Points of Harvesting and Processing of Saffron" with the aim to introduce suita-ble methods of harvest.

ADAPTIONS

1. **Climate** -Saffron thrives best in warm sub-tropical climate and can be grown at 2000 meters of mean sea level. Spring rain is considered favourable for corm production, while rain immediately before flowering encourages high flower yield. During the summer rest period, maximum temperatures of 30–4OC can be tolerated as well. Saffron prefers direct sun exposure, even though in India it is cultivated together with almond trees.[8]
2. **Soil** -The Crocus sativus grows in many different soil types but thrives best in calcareous, humus-rich and well-drained soil with a pH between 6 and 8. Good soil pH ranges from neutral to slightly alkaline.[9]

AGRICULTURAL PRACTICES

1. **Planting and harvesting of crop –** Planting cycle, planting time, planting method and seed rate are the critical factors for saffron productivity. Planting cycle have 10 – 12 years

duration.Every month from January–September plough is carried out to keep the field clean. Plough is done with Bullock drawn plough.[10]

2. **Irrigation** -Saffron is grown in arid and semi-arid regions in Iran in late autumn, winter and late spring with rainy season. It should be irrigated by supplemental basin irrigation. … In areas with a seasonal rainfall of 600 mm a post- flowering irrigation of about 50 mm is adequate for economical yield. Irrigation is not a necessary practice.
3. **Crop Rotation**- Saffron cultivation needs to be included in a crop rotation.[11]
4. **Fertilization** -The application of about 20–30 tons per ha of organic manure is the most common fertilisation practice all over the world. Dalfard 15® is a specific fertilizer for saffron plants which is used in many saffron farms in some parts of Iran, especially South Khorasan province, usually by foliar spraying.
5. **Weed and Rodent Management –** Weeds are probably the main problem for saffron since it is unable to compete, above all because of its very low height. Weeds are managed by hand in annual crops in Italy, while in perennial crops a good chemical control is generally achieved with 10 kg/ha of Simazine (Gesatop 50%) or Atrazine (Gesaprim 50%).
6. **Pests and diseases -** Rabbits, rats and birds can cause problems in saffron fields by eating or lifting the corms. Fungal attacks are mostly promoted by humid conditions. Diseases: 2.1 Dry rot (Thrips sp.) (Rhizoglyphus sp) – 2. 2.2 Bulb rot (Sclerotium spp).[12]

CONCLUSION

From an agronomic point of view, saffron is a very unusual plant for its agrological and ecophysiological characteristics. In conclusion, it seems that saffron. and its active constituents (crocin, crocetin and safranal) play a protective and therapeutic role in the nervous system, cardiovascular and gastrointestinal diseases.

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