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Phytochemistry and Pharmacology of Saffron, the Most Precious Natural Source of Colour, Flavour and Medicine

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Abstract

Saffron (*Crocus sativus* L.), primarily a Mediterranean herb has been valued since antiquity not only as a culinary condiment, but also as a source of dye, perfume and medicine. It is well known for its diverse uses such as a food additive and a palliative agent for many human diseases. Medicinally, Saffron is regarded as tonic and antidepressant and has been used in various ancient cultures for strengthening digestion, relieving coughs, smoothing menstruation, relaxing muscle spasms, calming anxiety and improving mood. Phytochemical investigation of Saffron has led to the isolation and characterization of a number of active chemical constituents.

Pharmacological studies have only validated the traditional medicinal claims of Saffron but also discovered further therapeutic efficacies. In view of its diverse therapeutic efficacy, saffron can be a promising candidate with potentials for new drug design. Phytochemical, pharmacological varied uses and quality control aspects of saffron are reviewed in this paper..

Key Words: Saffron, Traditional Uses, Phtochemistry, Pharmacology, Quality control

Saffron – An Introduction

The red Saffron filaments are actually the dried stigmas of the coloured flowers of Saffron, which is a perennial spicy herb of Iridaceae family. The plant is botanically known as *Crocus sativus* L. and recognized as Red Gold in producer countries. The word saffron is originated from the French term *Safran*, derived from the Latin word *Safranum* that comes from the Arabic word as far that means ‘yellow’. Etymologically, the word *Crocus* has its origin from the Greek word ‘*Croci*’ which means the weft, thread used for weaving on a loom. *Sativus* means cultivated, possibly a reference that it no longer grows wild¹. The Arabs called it, *Zahafaran* from which the name saffron appears to be derived. In Hindi it is called *Keshar*, in Sanskrit *Kumkuma* or *Kashmiirajan* and in Tamil *Kungumapu*. The flower of *C. sativa* is light purple, but it is the thread-like reddish-coloured stigma of the flower that is valued both as a flavouring and fragrance material and as a natural colorant. The three stigmas (25-30 mm long) of saffron flowers, drooped over the petals are picked from each flower by hand. It takes about 36,000 flowers to yield just 1 pound of stigmas². Over 200,000 dried stigmas (obtained from nearly 70,000 flowers) yield 500 g of pure saffron which cost as much as \$30 per ounce in the American market³. Besides, its short blooming season (~3 weeks in the fall) and labour-intensive harvest make it the world’s most precious and expensive cultivated herb in the world⁴. Saffron is very intensively fragrant, slightly bitter in taste and produces a bright yellow-orange solution when soaked in warm water. Since time immemorial, Saffron is often used, both for its bright orange-yellow colour and intense flavour and aroma.

Origin and History

Its origins, like those of so many plants that have been in cultivation since antiquity, are

lost to history. The genus *Crocus* comprising about 80 species of hardy corms (as well as many forms or varieties) is native to regions from the Mediterranean to western China and southwest Asia where it has been cultivated for its dye since ancient times⁵. There is indication that this plant was grown in Palestine in the time of Solomon for saffron. A sterile triploid cultivated variety *Saffron crocus* possibly developed from the wild *Crocus* of Greece. Saffron had been one of the most beloved and expensive spices of ancient Greeks, Egyptians and Romans for its aroma, colour and supposed aphrodisiac properties. Around 2400 BC, there were evidences of its use in coloring tunics in Castile-la-Mancha region of Spain. Saffron became more renowned in Mesopotamia with the development of Babylonian culture. Several texts speak of its use as a condiment during the reign of Hammurabi (1800-1700 BC). Saffron finds its name in the oldest text (5th century BC) of Kashmir⁶. Iran, Kashmir and Spain are the major saffron producing countries of the world. Hippocrates and his contemporary Greek physicians like Dioskourides and Galinos mentioned *Crocus* as a therapeutic herb. It was considered a rare pharmaceutical plant of ancient Greece with unique properties. The herb is referred throughout ancient history and mentioned in several medical writings of the classical Greek and Roman times all the way to the Middle Ages. In ancient times in and around Persia, saffron was used in the preparation of high quality paper, but more commonly it was used as ink, a practice that continued for centuries. Saffron ink of various shades of colour (from light yellow to blood red) was used for writing the address in the letters and edicts of kings and rulers, rubrics and headings in books and documents, and decoration and illustrations in texts. Saffron ink was also used for the writing of holy prayers and making charms, amulets and talismans, on paper, cloth and sometimes shrouds⁷. In a translation of the Zoroastrian text '*Bandihesh*' saffron is described as an aromatic plant, while in another translation of the same text, it is considered a colourant. There is evidence that it was used by the Sumerians, more than 5000 years ago, indicating its hoary past. According to mythological Roman poet *Publius Ovidius Naso* the plant took its name from the youth *Crocus*, who after witnessing in despair the death of fair Smilax was transformed into this flower.

About the Plant

Saffron is a stemless perennial herb with a round sub-soil corm of 3-5cm diameter. Each corm produces 6 to 8 leaves similar to grass weeds. The short sprinkle roots grow at the base and circumference of the corm; the first part to appear is the flower which blooms in fall, winter and early spring. However, in the first year after planting, because the corms are too weak and not properly established in the deep soil yet, the flower buds are not strong enough to develop and even the leaves come out later than usual. The flower consists of three sepals and three petals of the same lilac colour, which makes them hardly distinguishable. There are three stamens with filaments twice as long as the anthers. Out of the single-ovule ovary in the center of the flower grows a long thin style of a light yellow colour, which ends in a triple stigma of 2-3 cm length, and bright orange red colour⁵. The stamen, the yellow pollen-producing organ, is not the source of Saffron, as it is often made out to be, but the long, crimson stigmas are the source of Saffron. On account of being triploid, saffron is necessarily sterile, and its beautiful flowers cannot produce any seeds, thus propagation is possible only by means of corms⁷.

Chemical Composition

Saffron is a noteworthy medicinal and spicy plant because of its powerful odour and intensive natural yellow colour. Considering its wide range of medical uses, saffron has undergone extensive phytochemical and biochemical studies and variety of biologically active ingredients has been isolated. Phytochemical investigations have revealed that the stigmas of the saffron flower contain a number of chemical substances including carbohydrates, minerals, musilage, vitamins B₁ & B₂ and pigments, crocin, crocetin, carotene, lycopene and zigzantin⁸. In addition, it contains small amounts of the pigment anthocianin, oil soluble pigments including alphacarotene, betacarotene and zexgantin⁹. The colour is mainly due to the degraded carotenoid compounds, crocin. The flavour come from the carotenoid oxidation products, mainly safranal and the distinctive flavour comes from glucoside, picrocrocin¹⁰. Saffron has a strong aroma, which is produced by specific essential oils. Safranal, the major principle of *C. sativus* is a carboxaldehyde volatile compound constituting around 70% of total essential oil is formed by

de-glucosylation of picrocrocin¹⁰. Several terpene aldehyds and ketones are also found in the essential oil. The most abundant constituent is safranal, 2,6,6-trimethyl 1,3-cyclohexadiene-1-carboxaldehyd (>50%); another olfactorically important compound is 2-hydroxy-4,4,6-trimethyl 2,5-cyclohexadien-1-one. Furthermore, terpene derivatives, pinene and cineol have been identified. Phytochemical studies also indicated that the presence of flavonoids such as rutin, quercetin, luteolin, hesperidin, bioflavonoids, tannins and anthocyanins in flower petals may be responsible for its antinociceptive¹¹ and anti-inflammatory¹² and blood pressure lowering¹³ effects.

Precisely, the aroma, flavour and colour are primarily due to the three chemicals, safranal, picrocrocin and crocin respectively. The major colouring compound, crocin (C₄₄H₆₄O₂₄) which is responsible for strong colour imparting trait of Saffron is one of the few naturally occurring carotenoids easily soluble in water. Its high water solubility is one of the reasons for widely preferred application of Saffron as a colourant in food and medicine¹⁴. The principal element giving saffron its special flavour is picrocrocin (C₁₆H₂₆O₇) which is stable in fresh saffron but as a result of heat and the passage of time it decomposes thereby releasing the volatile aldehyde safranal. In the food processing industry saffron is used as a colourant and flavouring agent in sausages, margarine, butter, cheese and alcoholic and non-alcoholic beverages. It is also used for colouring and flavour in ice cream and sauces and dressings¹⁵.

Traditional Medicinal Uses

Since ages, saffron has been considered to have a number of therapeutic properties. The Ebers papyrus (1550 B.C.) mentions saffron as an ingredient in the cure for kidney problems¹⁶. During 16th to 19th centuries, Saffron was used in various opioid preparations for pain relief¹⁷. In folk medicine and Ayurvedic healthcare system, Saffron is regarded as sedative, tonic, stomach stimulant, expectorant, anti-asthma, emmenagogue, and adaptogenic agent and has been used in the treatment of ailments such as dysentery, measles, enlargement of the liver and gallbladder and urological infections. In the recent times, it is being used as a remedy for catarrhal

infections, for melancholia, to treat liver enlargement, as a nerve sedative, as a carminative, diaphoretic, and emmenagogue¹⁸. Modern pharmacological studies have demonstrated that saffron extract or its constituents have antidepressant¹⁹, anti-inflammatory²⁰, anti-tumor effects, radical-scavenging, learning and memory improving properties^{21,22}. Saffron extract also has chemoprotective properties and protects from genotoxin-induced oxidative stress in mice^{23,24,25}. Anticonvulsant effects have been reported in both PTZ and maximal electroshock (MES) models in mice²⁶.

Pharmacological Attributes

Saffron has been pharmacologically investigated and clinically trailed for its efficacy against a number of ailments. Aqueous and ethanol extracts of *C. sativus* petals have been found to reduce blood pressure in a dose-dependent manner²⁷. Clinical trials conducted for evaluating the efficacy of saffron in mild-to-moderate depression reported it to be more effective than placebo and at least equivalent to therapeutic doses of imipramine and fluoxetine^{28,29}. Anti-nociceptive and anti-inflammatory activities were reported from stigmas and petals of saffron²⁰. The relaxant effects of *C. sativus*, stimulatory effect of aqueous-ethanolic extracts and one of its constituent, safranal, indicated a relatively potent stimulatory effect of the extract from *C. sativus* partially due to its constituent, safranal³⁰.

As a dietary supplement, saffron extracts reported to prevent retinal damage in rats and found to have a role in the treatment of ischemic retinopathy and age-related macular degeneration^{31,32}. A notable decrease in cholesterol and triglyceride levels and reduction in vascular damage were observed when hyper-lipidemic rabbits were treated by crocetin. The aphrodisiac activities of *C. sativus* stigma aqueous extract and its constituents, safranal and crocin, were evaluated in male rats that exhibited an aphrodisiac activity of saffron aqueous extract and its constituent crocin. Safranal however did not show aphrodisiac effects³³. In addition, an anti-oxidant effect was observed in human platelets together with the inhibition of lipid peroxidation³⁴. Potential role of saffron extracts in cancer therapy has been investigated and as per report saffron appears to be a selective cytotoxic plant but its mechanism is not clearly determined³⁵. Saffron extract and two

of its main ingredients, crocin and crocetin have been reported to improve memory and learning skills in ethanol-induced learning behaviour impairments in mice and rats. Oral administration of saffron found to be useful in the treatment of neurodegenerative disorders and related memory impairment³⁶. Crocin analogs isolated from saffron significantly increased the blood flow in the retina and choroid as well as facilitated retinal function recovery and it could be used to treat ischemic retinopathy and/or age-related macular degeneration³⁷. The saffron component safranal was found responsible for co-mutagenic effect. In the *in vitro* colony-forming test system, saffron displayed a dose-dependent inhibitory effect only against human malignant cells³⁸. Saffron itself, as well as its carotenoid components, reported to be potential cancer chemopreventive agents³⁹. *Crocus sativus* stigma extract and its major constituent crocin found to possess significant antiproliferative properties against human prostate cancer⁴⁰. Carotenoid ingredients of saffron demonstrated cytotoxic activity against *in vitro* tumor cells. Saffron crocin derivatives possessed a stronger inhibitory effect on tumor cell colony formation⁴¹.

Besides these pharmacological activities, improvement of ethanol-impaired memory in mice, impact on learning behaviour and neuronal cell death, and psoriasis management are reported^{42,43}. Saffron is generally not toxic when ingested in culinary amounts, but a lethal dose at 20g and an abortifacient dose at 10g have been recorded¹⁷. Adverse reactions such as rhinoconjunctivitis, bronchial asthma, cutaneous pruritus, and anaphylaxis have been reported^{17,44}.

Processing and Quality Control

Proper drying is the most important part of saffron processing as moisture is the main adversary that shortens the shelf life and quality of the saffron. Cutting the stigmas apart prior to drying, lead to the complete removal of moisture even from inside the saffron stigma. However, if the stigmas attached to each other are left intact, moisture is trapped inside the stigma. Moist saffron tends to develop a musty smell instead of saffron's distinct clean aroma⁴⁵. In fact, it is the drying process that activates the chemical compounds, which release aroma, colour and flavour. Storage conditions including relative air humidity, temperature of the surroundings, direct sunlight, oxygen, and quality of packages are other important factors that cause decomposition or reduce

the quality include. Dry saffron is highly sensitive to fluctuating pH levels and rapidly breaks down chemically in the presence of light and oxidizing agent⁴⁶. It must, therefore, be stored in air-tight containers in order to minimize contact with atmospheric oxygen. The volatile oil of saffron is preferably obtained by super-critical fluid (ScCO₂) extraction. The distillate is separated with ether, which is then removed by heat. The oil obtained is a yellow liquid with a strong aroma of saffron⁴⁷. This oil is composed of terpenes, which is highly susceptible to oxidization and must be stored under special conditions.

One of the most important quality determining parameters of saffron is its colouring power which is the only measuring tool that assures one of consistent saffron quality. It is determined by measuring the amount of colouring constituents present as per standard procedure. The general range of saffron colouring strength could be from 110-250+. True saffron should easily dissolve in aqueous phase and spread the special odour of saffron. If the water extract of true saffron is dried and a rod dipped in sulphuric acid is drawn across the surface, a blue colour appears and turns purple or reddish-brown. Other detection methods include colour reactions, microscopic study, TLC and HPLC analyses⁴⁸. Good quality Saffron should be free from other yellow or white plant parts (style) mixed in with the red threads (stigma), of the saffron crocus plant. Further, detection of artificial colours, such as naphthol yellow, tartrazine, quinoline yellow, sunset yellow, in saffron is carried out exclusively by UV-Vis spectrometry, when crocetin is precipitated⁴⁹ or in combination with HPLC procedures⁴⁸.

Conclusion

C. sativus is an important medicinal food plant growing widely and also cultivated for nutritional and economic purpose. It has long been used in traditional medicine around the world, and modern scientific study suggests that saffron could also have a role to play in fighting disease. The active constituents in saffron could help alleviate gastric problems, heart disease, insulin resistance, depression, premenstrual syndrome, insomnia and anxiety. The carotenoid compounds responsible for saffron's striking colour (safranal, crocetin, crocin) could play a part in inhibiting the growth of tumours. Eating saffron also appears to help vision by retarding the

degeneration of the retina that occurs with age. Saffron is the most expensive spice in the world and its high price is due to its labour-intensive cultivation, harvesting, handling and high demand⁴. However, cultivated of saffron is limited to only few countries with old civilization⁵⁰. Recent reports on present and potential therapeutic properties of Saffron and its demand for various phytochemical and biotechnological researches have led to frequent adulteration and frauds⁴. Determination of chemical composition of saffron is another crack for preventing the saffron adulteration. It is, therefore, certification of the origin and quality of saffron through modern phytochemical and molecular techniques has become imperative.

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