



History of saffron

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Abstract: In this review, we present a brief summary on the history of saffron and its use. The main purpose of this paper is to show how modern medical science can use saffron on the basis of old descriptions. When preparing this review PubMed database, Wikipedia.org and Google Scholar were searched and based on old descriptions references to saffron in our university libraries' herbal books and mine personal old botanical books were used. Saffron has been one of the most expensive spices since Ancients Times. There are several myths and legends regarding its origin and utilization. The dried stigma of the *Crocus sativus* L. flowers has been used for 4,000–5,000 years as a dye, seasoning, perfume, medicinal plant, respectively. In Ancient Cultures (Akkadian, Mesopotamia, Greece, Rome), it was equally a symbol of wealth. Saffron was the dye of some old wall paintings and royal garments. It is mentioned even in the Bible (Old Testament). Several data in old pharmaceutical books like Avicenna's Book of Canon, the Persian Aghili, Galenus dealt with its medicinal use. They applied it for healing, in the treatment of depressive mood. It was considered as well as a remedy against some pain and fever related to malaria. In the late Middle Ages, it was believed that saffron is one of the most effective phytotherapeutic agents against some serious infectious diseases such as plague or cholera. Based on the old medicinal data it seems that saffron, together with some other medicinal plants, can be a good source to develop modern pharmaceutical products for example against some cardiovascular diseases. related to malaria. Experiences demonstrated the possibility that some of the saffron's components would have been used as cardio protector drugs. Recently, it has been introduced as an element of a diet proposed in a protocol to patients with severe acute respiratory disease, such as COVID, as it may reduce the COVID infection for it may reduce the progression of COVID caused pulmonary damages.

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Introduction

The aim of the present review is to provide information to the readers about the long history of saffron not only its medical points of view but its role in the different cultures over many centuries. It is a relatively short review, but I hope it will still arouse general and medical interest for saffron*.

Saffron is one of the most expensive spices (*Crocus sativus*, or real saffron). There were centuries when saffron

was much more expensive than gold. This is a special variety because it is a triploid: it doesn't grow in the wild and does not reproduce without human intervention.

It has the highest price/quantity because it is difficult to cultivate, and it requires significant manual work while harvesting by hand in autumn. The ideal climate to cultivate saffron must have cold winter and dry, hot summer. The soil must be rich in nutrient and well cultivated. This is why there have been few regions where the saffron grew

* Personal comment from the author: I am living in Budapest (capital of Hungary) in the 11th district. Very near to our house (about 2 km.) there is quarter where the streets have been named after some flowers including saffron (Sáfrány) street.

naturally. Usually in early October (1), it blooms within two or three days (early morning) only and the harvesting work must be finished within 2–3 hours before sunrise. The workers have to collect as many flowers as they could within this short time frame. They have to take off the stigmas only and let them dry. Only stigmas of the orange-red flowers should be collected (2). About 90,000–100,000 flowers of fresh saffron have about 5.0 kg stigmas which become 1.0 kg when dried. This difficult cultivation and harvest explain the higher prices. An indoor experiment was conducted on Oita prefecture, Japan approximately hundred years ago but proved to be unsuccessful and therefore abandoned (Y. Shoyama's, personal information).

The first botanical description on saffron had been written by Dioscorides, the Greek physician in Asia Minor, who wrote a five-volume treatise concerning medical matters, entitled *Περὶ ὅλης ἰατρικῆς* in Greek or *De Materia Medica* in Latin. *De Materia Medica* was the first extensive pharmacopeia (3). This is why Dioscorides was considered as the first pharmacologist. His “pharmacopeia” was used from the 1st century A.D. for more than eight-nine centuries (4) and translated to Latin and Arabic, until Avicenna's work was available (9th–10th century A.D.) (5). It gave detailed descriptions on different “useful” plants including the saffron. In Middle Ages codices and later, when printed books were available, botanical textbooks and taxonomy books (6–9) contained colorful images on plants including the *Crocus* species.

Saffron is still harvested by hand, even today, as no sophisticated machinery has been developed to fit the refined harvesting needs. Therefore, saffron remains highly priced in our times. Only the true saffron (*Crocus sativus*) can be used. It shouldn't however be confused with *Crocus vernalis*. We have history of false saffron being sold, which is actually a mixture with marigold (*Calendula officinalis*), or with safflower (*Carthamus tinctorius*) (10), although all frauds can be easily detected. In our age Iran produces about 85% of the world's saffron (data from UN Food and Agriculture Org.).

During centuries the saffron has been used for the following purposes:

- ❖ Dye (for both wall painting, of cave painting, and for textile coloration, royal garments, woven carpets, funeral shrouds, etc.).
- ❖ For worships.
- ❖ Perfume (cosmetics, fragrance).
- ❖ Spice (seasoning, teas, food color e.g., in meat soup).
- ❖ Medicinal plant.

❖ Else (e.g., to show one's wealth).

The origin of saffron is questionable. Traces of naturally grown saffron can be found across the Mediterranean shores of Asia Minor and in the valley between Tigris and Euphrates rivers (11). Cultivation and use of saffron, probably came from the ancient Greece or Crete or Persia (Iran) (11). It has been believed that it is originated from South-East Asia and/or India. According to literary data (12), it hadn't been known in East or in India before Alexander the Great's war of conquest. His troops took saffron with them (see further) and brought it to Far East and India.

Probably its name came from Persia (zarparan: having golden stigmas) or Za'feran (Arabic word for yellowish). The Latin name: safranum can be the origin of the old French word: safran.

The scientific name of saffron (*Crocus sativus*) is of Latin origin. The famous Latin (Roman) poet Ovidius in his work: “*Metamorphoses*” wrote the following:

.....modo vir, modo femina Sithon
te quoque, nunc adamas, quondam fidissime parvo,
Celmi, Iovi largoque satos Curetas ab imbri
et Crocon in parvos versum cum Smilace flores
praetereo dulcique animos novitate tenebo.
Unde sit infamis, quare male fortibus undis
Salmacis enervet tactosque remolliat artus,
(*Crocus* and *Smilax* may be trun'd to flow'rs
And the Curetes spring from bounteous show'rs
I pass a hundred legends stale, as these
And with sweet novelty your taste to please.)
(Translated by Rolfe Humphries).

The old Greek legend (which is written in Ovidius' poem) is practically a “love story”. *Crocus*, a handsome youth met with the nymph *Smilax* and very soon she disappeared. When after a long search he met her again *Smilax* transformed him into a fine, purple colored flower: the saffron (13).

Saffron is as old as humanity. It has been used since the Stone age. Traces of saffron pigment were proved by modern methods in a prehistoric cave in Iraq and in wall painting in Santorini (Greece) (14,15). These Fresco paintings in Santorini, are 3,000–5,000 years old, show saffron scenes. On a picture three women are seen, one with embroidered crocus flowers on sleeve, another wearing a necklace made of crocus statements and a third put her wounded foot on crocus flower (14).

Saffron is mentioned in the Old Testament (16), in the Hebrew Tanakh. In the Songs of Song (in Hebrew: Shir-ha-Shirim, meaning: the most beautiful song) by Solomon

(4:14) it is written the following:

“Your lips drop sweetness like boneycomb.....Your cheeks are an orchard of pomegranates, an orchard full of rare fruits, spikenard and saffron, sweet cane and cinnamon”.

In Persia, in Isfahan and Khorasan the saffron was cultivated as far as the 10th century BC (17). The saffron threads were woven, and the textiles offered to divinities (18). They used it as dye, perfume, medicine, and body washes, respectively. saffron threads mixed into hot tea was drunk as a curative drug against melancholy.

Saffron as a symbol of wealth

During the 10th century BC, the Persian saffron threads were interwoven into Persian royal carpets and funeral shrouds. With modern methods (spectrometry and chromatography) Han and coworkers (18) were able to prove that textile dyes were frequently used in ancient China, as well.

Medicine men (physicians) in ancient Egypt used the saffron as royal perfumes. The Egyptians imported saffron from Syria, Babylon, and Crete, respectively although there were times (during the reign of Ramses II and later in the 12th- early 11th century BC) when it couldn't had been very expensive as saffron was found in Menepthah pharaoh (the 13th son of Ramses II) (19) workers' buildings ruins

Queen Cleopatra put saffron into the milk when she had a bath, believing that she would find more pleasure in making love. In ancient Rome saffron became a symbol of wealth. They scattered the saffron in public spaces, royal halls, courts. When Nero made his entry in Rome the main street was sprinkled with saffron in his respect (16).

Other non pharmaceutical relations

Medieval illuminated manuscripts often used dyes for yellow and orange colors. E.g., in the 13th century depiction of Thomas Becket's assassination, the yellow color is due to the use of saffron (20).

The herbalist Wan Zhen wrote that

“the habitat of saffron is in Kashmir, where people grow it principally to offer it to the Buddha.” In China saffron was included in the Bencao Gangmu in 1578 for spiritual uses (21).

In India, they grew it to offer to Buddha. A monolith statue, the *Babubali*, made between 978–993, was carved with saffron pictures and since it has been washed with Indian saffron every twelve years. Buddhist priests have

colored their robes with saffron (12).

In England the town of Walden was renamed as Saffron-Walden because for more than two centuries (15th–16th centuries AD.) saffron was successfully cultivated on the fields around the town (22). Saffron became a valuable gift to the visitors in a high position of Saffron Walden. E.g., Queen Elisabeth the First's attorney general in 1546 was given a high amount of saffron from the town's principal. Later, when the demand for saffron decreased and its cultivation was very difficult the production came to its end in Saffron-Walden and all over in England.

The saffron use in cooking has equally a long history. It is used to color the dishes (like soup) or for seasoning. In ancient Iran (Persia) only the royal cook was allowed to use saffron while preparing the dishes. The Kurdish culinary culture used *Crocus* for centuries, mainly in nomadic pastoralism (23). It also means that in the Middle East the plant has been used for centuries, alike in India and in Spain. “There is no paella in Spain without saffron!”

Uses of saffron in medicine and pharmacology

For several millennia saffron (*Crocus sativus*) has been used for medicinal purposes as a phytotherapeutic agent against different diseases. The first authentic phytotherapeutic document of its use are the wall paintings in Thera (Santorini) (1800 BC.) on which a woman is seen when she treats her wounded foot with saffron (14).

In the Akkadian empire the city of Azupiranu was referred in Ancient History texts as Saffron City because it's king, Sargon of Akkad was cured there, as they believed, by the saffron (24).

According to ancient Persian records, saffron arrived in China by the Mogul invaders around 300–200 BC. The saffron is mentioned in ancient Chinese medical texts like *Shennong Bencaojing*, written around the 3rd century BC. to cure bad memory functions and dementia (25).

In Persia saffron threads mixed in hot tea was a drink serving as a curative drug against melancholy.

Sumerians used wild saffron, (*Crocus cartwrightianus*), as a remedy and in potions believed to have magical powers. For example, the perfumer of king Gilgamesh made a salve to the king against his aching legs (around 2600 BC.) (26).

Egyptians also used it for different gastrointestinal ailments, and to heal wounds. Urinary tract diseases in men were treated with saffron emulsion by Egyptian healers. They applied a saffron contained ointments through the skin and expected that it would clean the inner organs of

the body by entering through the venous system (27). In the medieval Cairo (11th–13th century) healers described practical use of herbal drugs (saffron included), few of which have survived even in the 20th century (28).

During Alexander the Great's war (340–330 BC.) the emperor and his chief commanders have had made saffron infusion and poured into their baths for its curative purposes in battle wounds. One of the preferred “cocktails” of Alexander was a mixture of wine and saffron for he believed that it would give him more force on the battleground as well as in bed (as an aphrodisiac). This is why Greek hetaerae (courtesans) used it in their bath and as well as for potpourri (11).

Aulus Cornelius Celsus in the 1st century AD. prescribes saffron as a medicine for wounds, cough, colic, scabies. In the late Byzantine Empire (13th century) Myrepsos wrote a book focused on herbal antidotes (29). In his book among the most frequently used plants it is also mentioned. This book can be a good source to find old herbal recipes and to translate it into our modern ages.

Modern pharmacological findings found similarities which were described in Ibn Sina's (Avicenna) Canon of Medicine as a good remedy against depression and anti-inflammatory, bronchodilator agent (17,30). In Avicenna's Canon as well as in Traditional Persian Medicine there are descriptions on herbal remedies to cure “cardiac” diseases with medicinal plants including saffron (31). Parvizi (32), based on Avicenna's book recommended topical medications against cutaneous leishmaniasis in modern phytotherapy, too.

In the Middle Ages the economic power of saffron increased during the Black Plague. It was believed that saffron-containing medications would cure the plague. Pirates would even invade Venetian and Genoese ships for saffron. In Nuremberg (presently in Germany) a Safranschou law was ratified, codifying that saffron theft led to fines, imprisonment and even execution, if found guilty (33).

Between 1347–1350, the plague (Black Death) spread throughout in Europe, and hit Austria, too. It was said that the plague could be prevented by saffron infusion and saffron remedies. Thus, the kingdom needed Saffron too. The town of Basle ordered from Persia saffron for the same purposes. Near the town of Basle, Austrian nobles hijacked and confiscated the saffron shipment (nearly 400 kg) from the merchants of Basle. A war started between Leopold of Austria and the bishop of Basle: The Saffron War. Finally, saffron was returned to the town but the bishop had to pay a great amount of money to the nobles (33).

There were recipes in Galen's' book which included saffron ointment. Galen proposed saffron remedies, as well (33). The administration of plants in veterinary and human medicine goes back to several thousand years. as mentioned above, Scientific analyzes were already available in the to extract active substances from plant and use them in therapy. Recently the components of *Crocus sativus*: crocin, safranal, crocetin, picrocrocin have been isolated (see details within the papers in this special issue). It has been proved that the major ingredient of saffron, crocin, is a good antioxidant and may help as anti-inflammatory, anti-diabetic drug (34). Modern analytical methods identified, that *Crocus sativus* has bioactivity and bioavailability (35). Kaiser (36) posted that the active substance/s of saffron may help the cure of rheumatoid pain.

Phytotherapy, including saffron had been proposed against dementia already several hundred years ago. Recently: Tsarbopoulos, and Sarris and others (37–39) have shown that medicinal plants, like saffron may prevent dementia because of “anti-aging” and cognitive enhancing properties. It seems that saffron can help in the treatment of major depressive disorders, as well. They conclude that phytochemicals can be effective in different psychiatric diseases, but there is a need for more detailed studies. Crocus improved mild depression after coronary interventions (40). It has been changed that saffron capsules have a good antidepressant effect in such interventions. Chalatsa and coworkers (41) proposed that crocin and crocetin have therapeutic potentials for different neurodegenerative diseases thus promising tools in the prevention of Alzheimer's disease.

It has been demonstrated that *Crocus sativus* has an important effect in improving the blood circulation (42). The possibility of saffron's anticarcinogenic activity could also be taken into consideration (39).

A very recent study (43) has shown that crocin can be effective to limit the progression of the current pandemic disease: SARS-Covid 19. The authors demonstrated that crocin has an antioxidant property and helps in acute pulmonary infection. Crocin equally may can reduce the oxidative stress caused by viral infection. They propose that more clinical investigations are needed to study this component of saffron to help COVID patients. In accordance with this, Moslemifard and coworkers (44) proposed a phytotherapy diet protocol which should include saffron for hospital patient having severe respiratory infection like COVID19. It seems that such diet helps in the subacute phase of these patients.

General conclusions

Medicinal plants have been used for different purposes since millennia. When looking back at the history of saffron it is obvious that it was largely used to heal lot of ailments. It was given a magic power and curative properties. The modern medical and pharmaceutical research revealed that old therapies are valuable source even nowadays for phytotherapy and on the base of old applications it would be possible to find new drug for different diseases. Recent, modern sophisticated investigations on saffron's components give perspectives to find new potent drugs in the treatment of cardio-vascular diseases, in cancer therapy, wound healing, as pain killer or its use in infectious respiratory syndromes. Naturally more intense, detailed experiments and clinical analyses should be done. When we are looking through the history saffron usage it is evident that the continuous development of saffron's applications in medicine and pharmacy have to be carry on.

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