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Zafran (*Crocus sativus* L.): A Review on its Ancient Use in Unani Medicine and Recent Scientific Studies

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Abstract:

Background: *Zafran* is the dried stigmas of the flowers of saffron (Crocus sativus L.). *Zafran* has a rich history of medicinal applications, serving both as a food coloring and flavoring agent, as well as being utilized in traditional medicine for treating various ailments. The chief components of saffron are crocin, picrocrocin and safranal.

Aims and Objectives: This review is designed to provide a comprehensive summary of the potential health benefits of Crocus sativus (*Zafran* or saffron) in Unani medicine and to discuss its recent phytochemical and pharmacological studies.

Methods: The Unani classical literature was researched manually and online for this purpose. Various search engines Google Scholar advanced search, ResearchGate, PubMed, Web of Science, Scopus and AYUSH Research Portal etc. were searched by these search terms: "Saffron" OR "Crocus sativus" OR "*Zafran*" OR "C. sativus research paper" AND "Saffron and Unani system of medicine."

Result: In Unani Medicine, *Zafran* is used medicinally as an important medicine single as well as in compound formulations. Evidence based pharmacological studies revealed that it has important pharmacological properties e.g., Immunomodulator activity, Neuroprotective Activity, Anti-Depressant Activity, Cardioprotective and Antiatherosclerosis activity, Anticonvulsant activity etc. Various types of active phytoconstituents also have been searched and evaluated from C. sativus which are crocin, crocetin, picrocrocin, Safranal, the glucosyl ester of crocetin, β-carotene, Zeaxanthin etc. The presence of these phytochemicals may have contributed to the concerned pharmacological characteristics.

Conclusion: *Zafran* constituents show a wide spectrum of biological activities due to its phytoconstituents. It has the potential to function as a highly efficient natural remedy for various diseases. Therefore, further in vitro and in vivo investigations are necessary to explore the suggestions of USM and other traditional medicinal systems regarding the broad therapeutic benefits of Crocus sativus.

Keywords:

Zafran, *Crocus sativus*, Saffron, Kesar, Unani Medicine.

Introduction:

The connection between the evolution of mankind and the development of medicine is indeed profound and has evolved over millennia. Various indigenous systems of medicine, such as Unani, Ayurveda, Siddha, and Homeopathy, have played a crucial role in addressing human health and well-being. These systems often rely on natural resources, especially plants, to formulate remedies. Unani medicine, with its roots in ancient times, emphasizes a holistic approach to healthcare (Lone, 2012). This holistic perspective aligns with the idea that a person's overall health is interconnected and influenced by various factors (Lone, 2012; Anonymous, 2013). The estimated efficacy of herbal drugs falls between 70% and 90%, primarily due to the widespread utilization of traditional medicine by the majority of people in developing nations for addressing their healthcare requirements. Approximately 25% of all modern medications are estimated to come directly or indirectly from medicinal plants. This highlights the importance of preserving traditional knowledge about these plants and exploring their potential in modern drug development (Ekor, 2014). As societies continue to grapple with healthcare challenges, there is a growing recognition of the need to integrate traditional and modern approaches to achieve comprehensive and effective healthcare solutions. The synergy between traditional medicine and modern medical practices can contribute to a more holistic and patient-centered approach to health and well-being.

Zafran (Crocus sativus) from iridaceous genus is a well-known herbal medicine which has been widely employed as a drug to bolster health and combat illness from ancient time. It is regarded as a significant herb within the medical, cosmetic, and hygiene sectors. It is commonly used as a domestic spice in eastern and western cuisine. In cosmetics, Saffron extracts are included as fragrance ingredients, genuine saffron is worth its weight in gold. It is included in polyherbal formulation of Unani and ayurvedic medicine. Saffron is often used in several complementary medical practices, such as the Unani System of Medicine, Ayurveda, and Traditional Chinese Medicine, because of its wide range of medicinal uses in traditional systems of medicine (Farhan et al., 2020; Pullaiah, 2006). Extensive phytochemical and biochemical investigations have been conducted on saffron, revealing several constituents such as Crocin, Crocetin, and Safranal. Among these, Crocetin is predominantly responsible for its pharmacological effects. This paper aims to provide a comprehensive review of saffron on the basis of its description, botanical identification, habitat, cultivation and collection, recent phytochemical, therapeutic potential in various diseases and evidence based pharmacological studies.

Methodology:

We performed a broad search about review and analysis of related articles published in various reputed journals using the phrases *"Zafran* or *Crocus sativus"*, *"Zafran* and Unani Medicine" *"Zafran* research paper", "Pharmacological activity of *Zafran"* in electronic searches of the Google Scholar advanced search, PubMed, Scopus, ResearchGate, Web of Science and AYUSH Research Portal. We also performed offline

search such as Hippocratic Journal of Unani Medicine, The Unani pharmacopoeia of India, The Wealth of India and Unani classical textbooks viz Al-Jam'i le-Mufradāt al-Advia wa al-Aghdhiyya, *Khazāīn al-adviā,* Muhīt-i A'zam, *Tankheeh-ul mufaradat,* Makhzan-ul Mufradāt etc., in the library of Govt. Nizamia Tibbi College and NRIUMSD, Hyderabad. All the botanical names are verified by The Plant List (www.theplantlist.org). Unani terms are used in accordance with the book "Standard Unani terminology" published by Central Council for Research in Unani Medicine (CCRUM), Ministry of AYUSH, Government of India and approved by World Health Organization.

TAXONOMICAL CLASSIFICATION: (Srivastava et al., 2010)

Kingdom	**Plantae**
Division	**Spermatophyta**
Class	**Monocotyledonae**
Order	**Liliales**
Family	**Iridaceae**
Genus	***Crocus***
Species	***C. sativus***

VERNACULAR NAMES: (Anonymous, 2003; Pullaiah, 2006; Srivastava et al., 2010)

Language	Name	Language	Name
Urdu	*Zafran*	Hindi	Kesar, *Zafran*
English	Saffron	Arabic	Kurkum
Sanskrit	Kara, Ghuia, Rakta	Marathi	Keshar

Persian	Zafarn	Kashmiri	Kong
Telugu	KunkumaPuvvu	France	Safran

Habitat and Distribution:

Saffron originates from southern Europe and is cultivated primarily in Mediterranean regions, notably in Spain, Austria, France, Greece, England, Turkey, and Iran. In India, it is grown in the Kashmir Valley, particularly in the Pampore Plateau at altitudes exceeding 1600m, as well as in Himachal Pradesh. The corms are planted in July or august in soil meticulously prepared during the previous autumn. The initial flowering occurs in September or October of the subsequent year. Following this, each corm reproduces, yielding one or more daughter corms, which multiply at least twofold, and are harvested in May or June (Anonymous, 2006; Farhan et al, 2020; Pullaiah, 2006; Srivastava et al, 2010.)

Collection: In November and December, flowers are gathered during the early morning hours. The stigmas and upper style portions are carefully removed by hand, and then the medicinal product is dried using artificial heat. It is stored in dry place (Anonymous, 2006.

Botanical Descriptions:

Macroscopic: A diminutive perennial plant that blooms in the autumn, characterized by its bulbous structure and large, fragrant blue or lavender flowers. These flowers possess trifid, orange-colored stigmas, which along with the style-tops yield the saffron of commerce. Leaves produced from the new bud, Sessile, 4-6 inches long, linear, smooth shining deep green, with a white depressed midrib. The sealing wax red stigmas in the dry condition are 20-40 mm long and when wet 35-50 mm long. The top part of the style to which the stigmas are attached is pale-yellow and not more than 5 mm in length. Odour is strongly aromatic and Taste is slightly bitter (Anonymous, 2003; Anonymous, 2009; Kritikar and Basu, 2012; Pullaiah, 2006;)

Microscopic: A diagrammatic transverse section passing through the center of the flattened stigma exhibits a horseshoe shape, revealing a rosette of vascular bundles nestled within the parenchymatous mesophyll tissue situated between the upper and lower epidermis. A detailed transverse section reveals an arrangement consisting of upper and lower epidermal layers, alongside 10-15 rows of parenchymatous mesophyll tissue containing orange-red colored pigments and traversing with conjoint collateral small vascular bundles (Anonymous, 2003; Anonymous, 2009.)

Parts Used:

Dried stigmas and tops of styles (Anonymous, 2009; Beta'ar, 1999; Ghani, 2011.)

***MIZAJ* (Temperament):**

Hot (2O) and Dry (1O) (Anonymous, 2009; Beta'ar,1999; Ghani, 2011; Khan, 2013; Usmani, 2008.

***AFA'L* (Actions):**

Muqawwi-e-Jigar (Liver tonic), *Muqawwi-e-Alaat-e-Tanaffus* (Tonic to respiratory organ), *Musakkin* (Sedative), *Muqawwi-e-Qalb* (Cardiac tonic), *Daf-e-Taffun* (Anti-septic), *Mujalli-e-Basr* (Improves eyesight), *Mufarreh* (Exhilarant), *Mufatteh* (Deobstruent), *Mudirr-e-Haiz* (Emmengogue), *Mudir-e-Baul* (Diuretic), *Muharrik-e-Bah* (Sexual Stimulant), *Mulaiyin* (Laxative), *Muqawwi-e-Ahsha* (Tonic to visceral organs), *Muhallil* (Resolvent), *Muhallil-e-Riyah* (Carminative), *Dafa-e-Tashannuj* (Anti-Spamsmodic), *Muqawwi-e-Dimag* (Brain tonic) (Anonymous, 2009; Ghani, 2011; Beta'ar, 1999; Khan, 2013; Usmani, 2008.)

Therapeutic Uses:

According to Tabari, *Zafran* is described as warm, moderate, and dry which suggest that *Zafran* is believed to have properties that can balance the humors in the body. The description of *Zafran* as resolvent and bitter indicates its potential to address liver obstructions. Razi has described "*Zafran* is a digestive drug with astringent properties. It cleanses the stomach". In the context of digestion, astringents help in toning the stomach (Javadi, Sahebkar and Emami, 2013).

Razi also suggested that "Ingestion of 6 to 7 grams of *Zafran* induces the labor. I myself prescribed it for many times and the results were always successful" (Ghani, 2011; Javadi, Sahebkar and Emami, 2013). Jurjani has stated that "*Zafran* is astringent and resolvent and its fragrance can strengthen these two effects. Hence, its action on enlivening the essence of the spirit and inducing happiness is great". *Zafran* serves as a heart tonic. It has been used to promote cardiovascular health and alleviate palpitations (Beta'ar,1999; Javadi, Sahebkar and Emami, 2013). Traditionally, Zafran has been recommended to enhance respiratory function, alleviate asthma symptoms, and act as a tonic for the lungs (Beta'ar I., 1999; Ghani, 2011; Khan, 2013, Javadi, Sahebkar and Emami, 2013; Usmani, 2008). Ibn Sina has mentioned that "Local application of *Zafran*, combined with beeswax or egg yolk and olive oil is effective in treating uterine malignancies". *Zafran* is employed in the preparation of a special eye remedy known as Kohl, aimed at addressing various ophthalmic disorders including cataracts and conjunctivitis, as well as enhancing vision. It is also used as a prophylactic during waba (Anonymous, 2009; Beta'ar 1999; Ghani, 2011; Usmani, 2008; Khan, 2013.)

***MUZIR* (Adverse effects):**

Muqi (Emetic), *Muzife Ishteha* (Decreases appetite), *Musda'a* (Cephalgic), *Muzirre Kulliya* (Adverse effect on Kidneys), *Muzife Riya* (Higher doses show adverse effects on lungs). At high doses, *Zafran* can induce narcotic and euphoric effects, causing excessive pleasure that may ultimately result in temporary paralysis (Beta'ar 1999; Farhan et al., 2020; Ghani, 2011; Khan, 2013; Usmani, 2008.)

***MUSLEH* (Correctives):**

Anisoon, Usarah Zariskh with *Jawarish Safarjali*. (Beta'ar,1999; Ghani 2011; Khan, 2013; Usmani, 2008.)

***BADAL* (Substitutes):**

Equal quantity of *Darchini*, Equal quantity of *Qust*, Equal Quantity of *Tukhm-e-Turanj*, Fourth part of *Sumbul-ut-Teeb* (Beta'ar,1999; Ghani 2011; Khan, 2013; Usmani, 2008.)

***MIQDAR-E-KHURAQ* (Dose):**

1 gm to 3 gm (Beta'ar,1999; Ghani HN, 2011; Khan, 2013)

Compound Formulations:

Table 1: Some important compound formulations and its Therapeutic Uses

Sl. No.	Formulations	Actions	Therapeutic Uses
1.	*Habb-e-Jawahar* (Anonymous, 2006)	*Muqawwi-e-Aza-e-Raeesa*	*In Zof-e-Aza-e-Raeesa*
2.	*Habb-e-Khas* (Anonymous, 2006)	*Muqawwi-e-Asab, Muqawwi-e-Bah and Muqawwi-e-Aza-e-Raeesa*	*In Zof-e-Asab, Zof-e-Bah and Zof-e-Aza-e-Raees*
3.	*Habb-e-Hamal* (Anonymous, 2006)	*Muqawwi-e-Rahem*	*Uqr, Zof-e-Rahem.*
4.	*Habb-e-Jadwar* (Anonymous, 2006)	*Muwaiiid-e-Mani, Mughalliz-e-Mani, Moharrik-e-Asab*	*Zof-e-Asab, Nazla Muzmin. Zof-e-Bah, Riqqat-e-Mani, Surat-e-Inzal.*
5.	*Habb-e-Nazla* (Anonymous, 2006)	*Muqawwi-e-Dimagh and Asab*	*Nazla, Suda, Zof-e-Dimagh and Asab*
6.	*Qurs Musallas* (Anonymous, 2006)	*Musakkin-e-Alam*	*Dard Shaqeeqa and Suda*
7.	*Jawarish Jalinoos* (Anonymous, 2006)	*Muqawwi-e-Meda, Muqawwi-e-Masana*	*Zof-e-ishteha, zof-e-meda, Balghami khansi, Bawaseer*
8.	*Jawarish Zarooni Sada (Anonymous, 2006)*	*Mudirr-e-Baul, Mufattit-e-Hasat, Kasir-e-Riyah.*	*Zof-e-Kuliya, Hasat-e-Kuliya, Hasat-e-Masana, Waj ul-Qutn.*
9.	*Khamira Abresham Hakim Arshad Wala (Anonymous, 2006)*	*Muqawwi-e-Aza-e-Raeesa*	*In Khafqan and Zof-e-Badan*
10.	*Majun Azaraqi (Anonymous, 2006)*	*Muqawwi-e-Aasab*	*In Zof-e-Aasab, Falij, Laqwa and Waja-ul-Mafasil*
11.	*Majun Dabid-ul-Ward (Anonymous, 2006)*	*Mudirr-e-Baul and Mohallil-e-Waram*	*In Waram Jigar, Waram Meda, Waram Reham, Zof-e-Jigar and Zof-e-Meda*

12.	*Majun Muqawwi-e-Reham* (Anonymous, 2006)	*Muqawwi-e-Reham, Sailan-e-Reham*	*In Zof-e-Reham*
13.	*Majoon-e-Falasfa* (Anonymous, 2006)	*Muqawwi-e-Meda, Hazim, Mushtahi.*	*Salas-ul-Baul, Zof-e-Ishteha, Nisyan, Usr-ul-Baul, Waj-ul-Mafasil, Zof-e-Bah.*
14.	*Majoon-e-Salab* (Anonymous, 2006)	*Muqawwi-e-Bah, Mughalliz-e-Mani.*	*Zof-e-Bah, Riqqat-e-Mani.*
15.	*Majun Piyaz* (Anonymous, 2006)	*Muqawwi-e-Bah and Mumsik*	*In Zof-e-Bah, increased sperm count*
16.	*Majoon-e-Buqrat* (Anonymous, 2006)	*Muqawwi-e-Kuliya, Muqawwi-e-Kabid, Muqawwi-e-Meda, Muqawwi-e-Bah, Kasir-e-Riyah*	*Zof-e-Kabid, Zof-e-Meda, Zof-e-Ishteha, Kirm-e-Ama, Nafkh-e-Shikam.*
17.	*Mufarreh Azam* (Anonymous, 2006)	*Muqawwi-e-Aaza-e-Raeesa and Muqawwi-e-Meda*	*In Zof-e-Aaza-e-Raeesa, Zof-e-Meda and Tabkheer-e-Meda*
18.	*Mufarreh Barid* (Anonymous, 2006)	*Muqawwi-e-Asab.*	*Zof-e-Qalb, Zof-e-Asab, Khafqan.*
19.	*Halwa-e-Salab* (Anonymous, 2006)	*Muqawwi-e-Bah, Muwallid-e-Mani, Muqawwi-e-Aam*	*Zof-e-Bah, Qilat-e-Mani, Zof-e-Badan*
20.	*Tiryaq-e-Afayee* (Anonymous, 2006)	*Daf-e-Sumoom, Man-e-Asarat-e-Waba.*	*Humma-e-Wabayee, Laza-e-Hashrat*

Chemical Constituents:

More than 150 compounds have been identified in saffron stigma including coloured carotenoids (e.g. crocins and crocetin as glycosidic derivatives), volatile agents (e.g.picrocrocin and safranal which are the bitter components), colourless monoterpene aldehydes, etc. The traces of non-glycosylated carotenoids unrelated to crocetin are β-carotene, lycopene and zeaxanthin. Crocetin and Crocin isolated from saffron are two principal chemicals responsible for the red colour of saffron. Crocetin makes up about 0.3% of the total weight of the saffron stigma (Anonymous, 2003; Anonymous, 2006; Farhan et al., 2020; Pullaiah, 2006; Srivastava et al., 2010; Kritikar and Basu, 2012; Maqbool et al., 2022).

Crocin belongs to a group of natural carotenoid commercially extracted from the dried stigma of *C. sativus*. It is the main pigment of saffron (approx. 80% of pigment content). Crocin is not absorbed orally. Before or during intestinal absorption, crocins undergo hydrolysis to crocetin, and the absorbed crocetin is partially metabolized into

mono- and diglucuronide conjugates.

The other colour compounds of saffron are carotenoids and glycosidic, alpha and beta-carotene, Zeaxanthin gentiobioside, lycopene, glycoside, gentio-glycoside, gama-crocetin and beta-crocetin di-glycoside (Anonymous, 2006; Khazdair, 2015).

Safranal (which is fat soluble) and pigments of the crocetin carotenoid are bitter, but picrocrocin is the primary responsible for Zafran's bitter taste. Saffron lipophilic carotenoids are alpha- and betacarotene, lycopene and zeaxanthin. Kaempferol has also been found in alcoholic extract of saffron petals. Flavonoids especially lycopene, proteins, starch, amino acids, resins and other compounds have also been shown to be present in saffron. Saffron contains small traces of thiamine and riboflavin as well (Pullaiah, 2006; Anonymous, 2006; Maqbool et al 2022; Khazdair, 2015.)

Table.2. Main phytochemicals from Zafran (C. Sativus)

Phytochemicals	Active Compounds
Carotenoids	*α-carotene, β-Carotene, crocins and crocetin*
Monoterpene	Safranal and picrocrocin
Isophorones	Isophorone
Minerals	Calcium, iron, magnesium, phosphorus and potassium
Vitamins	A, B1, B2, B6, and C

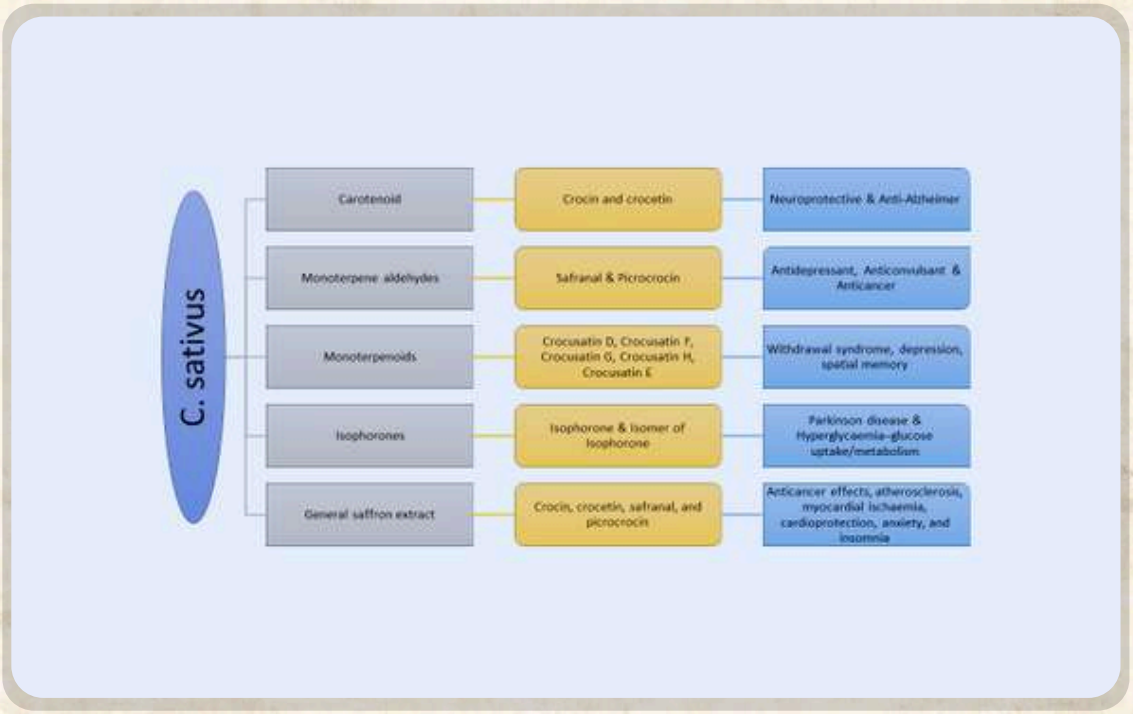

Fig. 1. Pharmaceutical properties of *Zafran (C. sativus)*

Evidence Based Pharmacological Studies:

Immunomodulator Activity:

In this study, *C. sativus* was given orally at dose of 50 mg/kg, and the result of the study showed that it stimulates both cellular and humoral immune responses.

C. sativus significantly increased neutrophil adhesion, attenuated cyclophosphamide-induced neutropenia, and increased the phagocytic index in a test for cellular immunity called the carbon clearance assay (Khajuria et al., 2010.)

Radical Scavenging Activity:

The study was designed to evaluate the DPPH radical scavenging activity of extract from *C. sativus,* and some of its bioactive constituents i.e., crocin and safranal.

Crocin demonstrated significant radical scavenging activity, followed by Safranal (Assimopoulou et al., 2005).

Effect on Respiratory system:

A preclinical study revealed, the relaxant effect of *C. sativus* on smooth muscle in guinea pig tracheal chain experiment. The results were comparable to, or even higher than, the relaxation achieved with theophylline, indicating potential for its utilization in treating various respiratory disorders such as asthma (Saadat et al., 2019).

Anti-Depressant Activity:

The aqueous extracts of C. sativus manifests conquering antidepressant effect in rats and the mechanism of its antidepressant effect may be due to elevating the levels of VGF, BDNF, CREB and P-CREB in rat. The FST (forced swim test) was performed on the days 1st and 21st and was compared with Imipramine. The findings from the Forced Swim Test (FST) indicated a significant reduction in immobility time with C. sativus treated rats. The protein levels of BDNF, CREB and p-CREB were significantly increased in C. sativus treated rats (Ghasemi et al., 2014).

Anti-diabetic activity:

In an experimental study, the results showed significant increase in serum insulin level in diabetic rats treated with C. sativus extract. There was significantly reduced in blood glucose levels. In addition, administration of saffron extract at a dose of 600 mg/kg resulted in improvements in hypertrophy and hyperplasia of cells within the islets of Langerhans associated with pyknosis of their nuclei in alloxan induced diabetic rats (Elgazar et al., 2013).

Anti-Gastric Ulcer Activity:

The effects of the C. sativus constituents Safranal is compared with lansoprazole against gastric ulcer induced by indomethacin in rats. Gastric contents volume and pH were measured. Histological changes were assessed using a light microscope. Safranal and lansoprazole normalized gastric volume and pH, decreased the area of gastric ulcers, and provided gastric protection (Tamaddonfard et al., 2019).

Cardioprotective and Antiatherosclerosis Effect:

In 2021 Yu L et.al, designed the study and showed the cardio-protective effect of C. sativus constituents Crocetin against vitamin D3 and high fat induced atherosclerosis in rats. The rats were received oral administration of crocetin and simvastatin for 30 days. Crocetin dose-dependently abridged the level of total cholesterol, VLDL, LDL,

triacylglycerol and increased the level of HDL. Additionally, Crocetin significantly reduced the level of malonaldehyde and increased the level of superoxide dismutase, catalase, reduced glutathione and glutathione peroxidase. Furthermore, Crocetin significantly decreased the levels of pro-inflammatory cytokines and inflammatory mediators (Yu et al., 2021).

Hepatoprotective Activity:

Preclinical study was designed with the aim to investigate the protective effects of hydroalcoholic extract, remaining from C. sativus petals (CSP) against acetaminophen-induced hepatotoxicity in male rats. The acetaminophen treatment resulted in higher levels of AST, ALT, bilirubin, lower total protein and albumin concentration along with severe inflammation and necrosis in histopathology than the control group. The administration of CSP with a dose of 20 mg/kg result in lower levels of ALT, AST and bilirubin, with a significant increase in concentration of total protein and albumin. The histopathological results regarding liver pathology, revealed that low doses of CSP showed hydropic degeneration with mild necrosis in centrilobular areas of the liver, while the high doses of CSP appeared to have only mild hepatocyte degeneration (Omidi et al., 2014).

Nephroprotective Activity:

Administration of C. sativus at 40 mg/kg/day and 80 mg/k/day significantly reduced the Gentamicin-induced increases in BUN S. Cr and MDA level and histological injury. Results suggested that the C. sativus treatment reduces gentamicin-induced nephrotoxicity and this effect seems to be dose dependent (Ajami et al., 2010).

Anticonvulsant Activity:

Crocus sativus stigma components safranal and crocin were tested for anticonvulsant activity in rats using PTZ-induced convulsions. Safranal (0.15 and 0.35 ml/kg, i.p.) reduced seizure duration, delayed the beginning of tonic convulsions, and saved rat from deaths. Crocin (200 mg/kg, i.p.) showed no anticonvulsant effect (Hosseinzadeh and Talebzadeh, 2005).

Antihypertensive Activity:

The study was done to examined the impact of C. sativus stigma aqueous extract and two active constituents, crocin and safranal, on blood pressure of normotensive rats and those induced with desoxycorticosterone acetate-induced hypertension.

The aqueous extract obtained from saffron stigma, along with safranal and crocin, exhibited a dose-dependent reduction in Mean Arterial Blood Pressure (MABP) in both normotensive and hypertensive anaesthetized rats (Imenshahidi, Hosseinzadeh and Javadpour, 2010).

Anti-inflammatory and Antioxidant Activity:

The study was designed to evaluate anti-inflammatory and antioxidant effect of C. sativus extract (25, 50, 100mg/kg b.w.) towards adjuvant induced arthritic mice for 47 days. Significant decrease in TNF-α and IL-1β levels were noted in mice belonging to the CSE-2 and CSE-3 groups compared to arthritic mice. However, mice in the CSE-1 group showed no significant changes in these levels. The findings suggest that CSE effectively regulates pro-inflammatory molecules and acts as a potent scavenger of free radicals. Consequently, it exhibits the capability to alleviate inflammation and

oxidative stress during the disease (Rathore, 2015).

Anti-Alzheimer Activity/ Effect on Learning and Memory Behaviour:

In this study, the effect of C. sativus component crocins on sporadic Alzheimer's disease induced by intracerebroventricular streptozocin in male rats was investigated. Crocin (30 mg/kg)-treated STZ-injected rats exhibited more correct choices and decreased errors in the Y-maze compared to STZ-injected rats treated with vehicle alone. In addition, crocin in the mentioned dose could significantly effected learning and memory impairment in treated STZ-injected group in passive avoidance test. These results demonstrate the effectiveness of crocin (30 mg/kg) in antagonizing the cognitive deficits caused by STZ in rats and its potential in the treatment of neurodegenerative diseases such as Alzheimer's disease (Khalili and Hamzeh, 2010).

Abortifacient Activity:

This study was carried out to evaluate the claimed antifertility effect of *C. sativus* extract in proven fertile female Wistar Rats at the doses 50 mg/kg b.w./day for 30 days. Different parameters were studied in female wistar rats including effect of Abortifacient study, Anti-implantation, Reproductive outcome, Estrogenic and Anti-estrogenic activity. In the group treated with *C. sativus* extract, there was an increase in percentage of resorption index, indicating a failure in embryo development. The reduction in implantation may be due to estrogenic or anti-estrogenic activity. The control rats showed good number of litters (Zargar, 2020).

Antitussive Activity:

Using a nebulized 20% citric acid solution in guinea pigs, the antitussive activity of *C. sativus* stigma and petal extracts and its constituents, safranal and crocin, were assessed. Safranal (0.25-0.75 ml/kg) and the ethanolic extract of *C. sativus* (100-800 mg/kg) both led to a reduction in the number of coughs. The ethanolic and aqueous extracts *C. sativus* of petal and crocin lacked antitussive activity (Hosseinzadeh and Ghenaati, 2006).

Effect on Premenstrual Syndrome:

This randomized triple-blind controlled clinical trial was carried out to identify *C. sativus* effect on the severity of premenstrual syndrome among female students. The intervention group was administered with capsules containing 30 mg of dried saffron stigma extract once daily, while the control group received placebo capsules for two menstrual cycles. By the conclusion of the study, notable disparities were observed between the two groups regarding alterations in the mean severity of PMS symptoms over the study duration. These findings indicate that saffron may decrease the severity of PMS symptoms (Beiranvand et al., 2016).

Conclusion:

In present scenario, there is consequently rises in the demand and uses of alternative medicines e.g., Unani, Ayurvedic, Yoga, Siddha and Homeopathic systems with their popularity and worldwide acceptability. Therefore, it is essential to critically evaluate alternative medicine from a scientific perspective in order to provide the world new sources for treating, preventing, and curing a wide range of illnesses. Zafran (C. sativus) is a well-known plant-based medication that has been used for a very long

time in Unani and other traditional systems of medicine for its pharmacological effects. The Present review article revealed the information about Zafran (C. sativus) which includes its introduction, nomenclature, vernacular names, taxonomical classification, habitat and distribution, collection, macroscopic and microscopic descriptions, chemical constituents, therapeutic actions and its uses, therapeutic importance of Zafran as evident by research performed on it. Evidence based pharmacological studies revealed that it has important pharmacological properties e.g., Immunomodulator activity, Radical Scavenging Activity, Anti-Depressant Activity, Effect on respiratory system, Cardioprotective and Antiatherosclerosis activity, Nephroprotective effect, Hepatoprotective activity, Anticonvulsant activity, Antihypertensive activity, Anti-inflammatory and antioxidant Activity, Anxiolytic Activity, Anti-Alzheimer Activity, Abortifacient Activity, Antitussive Activity, Effect on Premenstrual syndrome. Various types of active phytoconstituents also have been searched and evaluated from C. sativus which are crocin, crocetin, picrocrocin, Safranal, the glucosyl ester of crocetin, (4R)-4-hydroxy-3,5,5-trimethylcyclohex-2-enone and (4S)-4-hydroxymethyl-3,5,5-trimethylcyclohex-2-enone, crocetin-(β-gentiobiosyl)-(β-neapolitanosyl) ester, the crocinoid, 13-cis-crocin, tetrahydrolycopene, β-carotene,Zeaxanthin and a number of aroma constituents of C. sativus. The presence of these phytochemicals may have contributed to the concerned pharmacological characteristics. Crocus sativus has warm and dry Mizaj and acts better when it is fresh. Because of its aromatic characteristics and its ability to induce contraction, Crocus sativus strengthens the spirit, and expands, freshens and brightens it and has a great effect on the movement of spirit. The ancient Unani physicians and scholars employed C. sativus widely as a single and compound formulations for multiple pharmacological activities in various illnesses, however some of these still need to be validate using modern scientific methods. In this review, we had tried to compile all the available information from both Unani and other published scientific papers and textbooks regarding the medicinal uses and pharmacological activities of C. sativus, which we believe, will be fruitful for researchers to design the further scientific studies to discover and to extend the spheres of its therapeutic application.

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