Antimicrobial, antioxidant, and anticancer activities of saffron (*Crocus sativus*): a review

1Subreena Sidiq, 2 Dr. Purnima Shrivastava
1Research Scholar, 2 Head of Department
1Department of Botany,
1Bhagwant University, Ajmer, Rajasthan, India.

Abstract: *Crocus sativus* is a member of iridaceae family and its use in health management is in practice since ancient time. This study was designed through the search engines such as Pub Med, Scopus and Google Scholar. Saffron has accompanied all civilizations, whether for its culinary role, for its quality of dye or its ancestral virtues rooted in folk medicine. Different parts of *Crocus sativus,* such as stamen and corolla have been employed as a good source of antimicrobial agents. Cancer is one of the most feared diseases globally and there has been a sustained rise in its incidence in both developing and developed countries. Many common Indian spices and herbs in Indian ayurvedic medicine such as ginger, turmeric, cumin, basil, and saffron are known to have anticancer potential. Saffron is the dried stigmas of *Crocus sativus* L. plant. It consists of about 150 components out of which the more powerful phytochemicals are Crocin, Crocetin and Safranal. These carotenoids appear to suppress cell growth in neoplastic cells and offer direct protection against chemotherapy-induced DNA damage.

Index Terms - *Crocus sativus*; Antimicrobial activity; Antioxidant activity; Anticancer Activity; Traditional uses.

I. INTRODUCTION

Crocus sativus L. commonly known as saffron, belonging to Iridaceae family. This herbaceous perennial plant reaches 10 to 25 cm in height developing from its bulbs. The bulb, of sub-ovoid shape, is of variable size and forms. It has a massive structure and is covered by many concentric spathes. Each mother bulb produces from apical buds one to three large daughter bulbs and several small bulbs from lateral buds. Saffron has two types of roots: fibrous and thin roots at the base of the mother bulb, and contractile roots formed at the base of the lateral buds. The leaves vary from five to 11 per bud. They are very narrow and measure between 1.5 and 2.5 mm of dark green color. They measure 20 to 60 cm in length with a whitish band in the inner part and a rib on the outside. The flowers of *Crocus sativus* begin to appear at the beginning of autumn, towards the end of September of purple color composed of six tepals, three are internal, whereas the three others are external, which meet at the long tube that arises from the upper part of the ovary. At their appearance, the flowers are protected by whitish membranous bracts. The pistil is composed of an inferior ovary from which a thin style, 9 to 10 cm long, arises. The style ends with a single stigma composed of three filaments of intense red color whose length exceeds that of the tepals, which are the part of the plant interesting for the man from the point of view of culture.

It is widely cultivated in different parts of the world, particularly in Iran (Esmaeili, Ebrahimzadeh, Abdi & Safarian, 2011). Although the source of saffron is obscure, it is apparently originated from Asia Minor and Iran. The name of saffron is derived from Arabic word of za-faran meaning “be yellow” (Winterhalter & Straubinger, 2000; Cabellero-Ortega, Pereda-Miranda & Abdullaev, 2007). This exotic plant is a native of Southern Europe and now cultivated worldwide in many countries, particularly in Spain, Italy, France, Greece, Turkey, Iran and Jammu and Kashmir. This genus is represented in Turkish flora by 70 taxa. Its health management properties have been discussed in traditional prescriptions including Chinese, Ayurveda and Unani medicines. *Crocus sativus* has been reported its role as sedative, expectorant, anti-asthma, emmenagogue, and adaptogenic agent. Different plant parts like peels, fruits, seeds and rind of *Crocus sativus* contain various biochemically active ingredients such as crocin, crocetin, and safranal in different proportion.

Saffron stigmas contain numerous volatile compounds and ingredients including crocin, picrocrocin and safranal and these compounds are accountable for color, taste and odor of saffron respectively. Safranal is the major coloring constituent of saffron, so saffron is used as a flavoring and coloring agent. In addition to these compounds, saffron also contains little amounts of other pigments like anthocyanin, α-carotene, β- carotene, and zegxantin. Since one dry stigma in saffron plant weighs about 2 mg and each flower contains three of them, approximately 150,000 saffron flowers must be carefully picked for the production of 1 kg of the spice. Harvesting the flowers and separating the stigmas is very time consuming. Consequently, saffron is still the world's most expensive spice (Winterhalter & Straubinger, 2000; Melnyk et al., 2010). Saffron petal is the main by-product of saffron harvesting which is not usable for the farmers. The amount of saffron petal is more than 10000 tons each year (Kafi, Kakhki & Karbasi, 2000). Nowadays, saffron petals are only used for dye extraction, which is not flourished yet.

Chemical analysis of *C. sativus* stigmas has shown the presence of about 150 volatile and nonvolatile compounds; fewer than 50 constituents, however, have been identified so far. The volatiles consist of more than 34 components that are terpenes, terpene alcohols, and their esters among which safranal is the main component. Nonvolatile compounds comprise crocins, crocetin, picrocrocin safranal, and flavonoids (quercetin and kaempferol). Particularly, crocins, glucosyl esters of crocetin, are watersoluble carotenoids and are responsible for saffron's characteristic colour. Picrocrocin, glycoside of safranal, is responsible for the bitter taste of the spice and is precursor of safranal. Safranal, the main component of the distilled essential oil, is a monoterpene aldehyde, responsible for its characteristic aroma.

Clasification of Crocus sativus

Kingdom	Plantae (Angiosperms, Monocots)
Order	Asparagales
Family	Iridaceae
Subfamily	Crocoideae
Genus	*Crocus*
Species	*C. sativus*

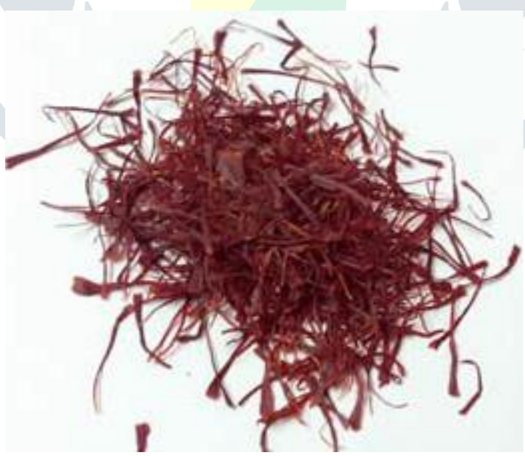

Fig 1: Dried stigmas of saffron

II. MAIN PHYTOCHEMICAL COMPONENTS OF SAFFRON

Chemical analysis of *C. sativus* stigmas has shown the presence of about 150 volatile and non-volatile compounds. Fewer than 50 constituents, however, have been identified so far. The three main biologically active compounds are

1. Crocin, a carotenoid pigment responsible for the yellow-orange color of the spice.
2. Picrocrocin, bringing saffron flavor and bitter taste.
3. Safranal, a volatile compound responsible for the aroma and smell so specific to saffron.

III. ANTIMICROBIAL ACTIVITY

Multi-drug resistant microorganism to antibiotics is alarmingly rising worldwide. As a treatment module against microorganism, natural products or derivatives of medicinal plants represent a symbol of good source of antimicrobial agents without any adverse side effect. Different parts of *Crocus sativus*, such as stamen and corolla have been employed as a good source of antimicrobial agents. Extracts of *Crocus sativus* against various bacterial strains have confirmed an improved activity against bacteria and fungi used as test organisms. In addition, antibacterial effects of other blends like aqueous, ethanolic and methanolic extracts of petal were measured against the food borne pathogens and the results have confirmed that such extracts show antimicrobial activity against most of the pathogenic bacteria.

IV. ANTIOXIDANT ACTIVITY

The imbalance between reactive oxygen species (ROS) production and antioxidant level is directly linked to the pathogenesis of diseases. The enhancement of antioxidant level or reduction of reactive species level is maintained through antioxidant properties of plants or their derivatives. Natural products or derivatives of medicinal plants usually contain various components including flavonoids which show a pivotal role as antioxidants and free radicals scavenging activity. Numerous studies based on *in vivo* and *in vitro* have confirmed that *Crocus sativus* has a significant antioxidant activity.

Antioxidant activity of saffron has been observed in extract of stigma and such extract shows role in the reduction of chlorophyll damage, lipid per oxidation, and protein oxidation. Similarly, other finding has confirmed that saffron stigma contains superior antioxidant activity. Earlier findings have demonstrated that active and inactive constituents of saffron extract have high antioxidant activity and saffron petal extract showed antioxidant activity. Another study demonstrated that constituent of saffron such as crocin has a potent antioxidant activity. Lebanon based finding demonstrated that saffron notably decreased lipid per oxidation as well increased superoxide dismutase activity when compared to control group. Crocin, constituent of saffron showed role in the inhibition of lipid per oxidation and restored SOD activity and stigmas of *Crocus sativus* contains more antioxidant activity as compared to tomatoes and carrots.

V. ANTICANCER ACTIVITY OF SAFFRON

Cancer is defined by uncontrollable division of cells that destroy body tissue. According to World Health Organization (WHO) that, cancer major cause of death or morbidity in human population (Globocan, 2016). The death toll because of cancer has increased from 7.4 million in 2004 to 8.2 million in 2012 worldwide as reported by the International Agency for Research on Cancer (IARC). (Globocan, 2016) [7]. Incidences of cancer are being observed to increase, recently and this is mainly attributed to urbanization, industrialization, lifestyle changes, increased population and increased elderly population. (Zanardi *et al.*, 2016). Recently great emphasis has been given on alternative medicines as the existing treatments for cancer like, radiotherapy and chemotherapy are not very promising and have various side effects. Now a day's traditional knowledge has also been utilized for the development of new effective medicines. Many common Indian spices and herbs in Indian ayurvedic medicine such as ginger, turmeric, cumin, basil, and saffron are known to have anti-cancer potential. (C.M. Kaefer and J.A. Milner, 2011).

Cancer is one of the most feared diseases globally and there has been a sustained rise in its incidence in both developing and developed countries. It is one of the major non communicable diseases posing a threat to world health. Unfortunately, enhancements
in socioeconomic circumstances are generally associated with increased cancer incidence. China, India, and Russia, which share rapidly rising cancer incidence, have cancer mortality rates that are nearly twice as high as in the UK or the USA. Vast geographies,
growing economies, aging populations, increasingly westernized lifestyles, relatively disenfranchised subpopulations, serious contamination of the environment, and uncontrolled cancer causing communicable infections have all contributed to its rapid rise in incidence. Under Indian circumstances cancer could lead to severe social and economic consequences, frequently causing family hardships and societal inequity. In a population of ~1.2 billion, nearly > 1 million new cases of cancer are diagnosed every

year causing ~600,000e700,000 deaths in 2012.

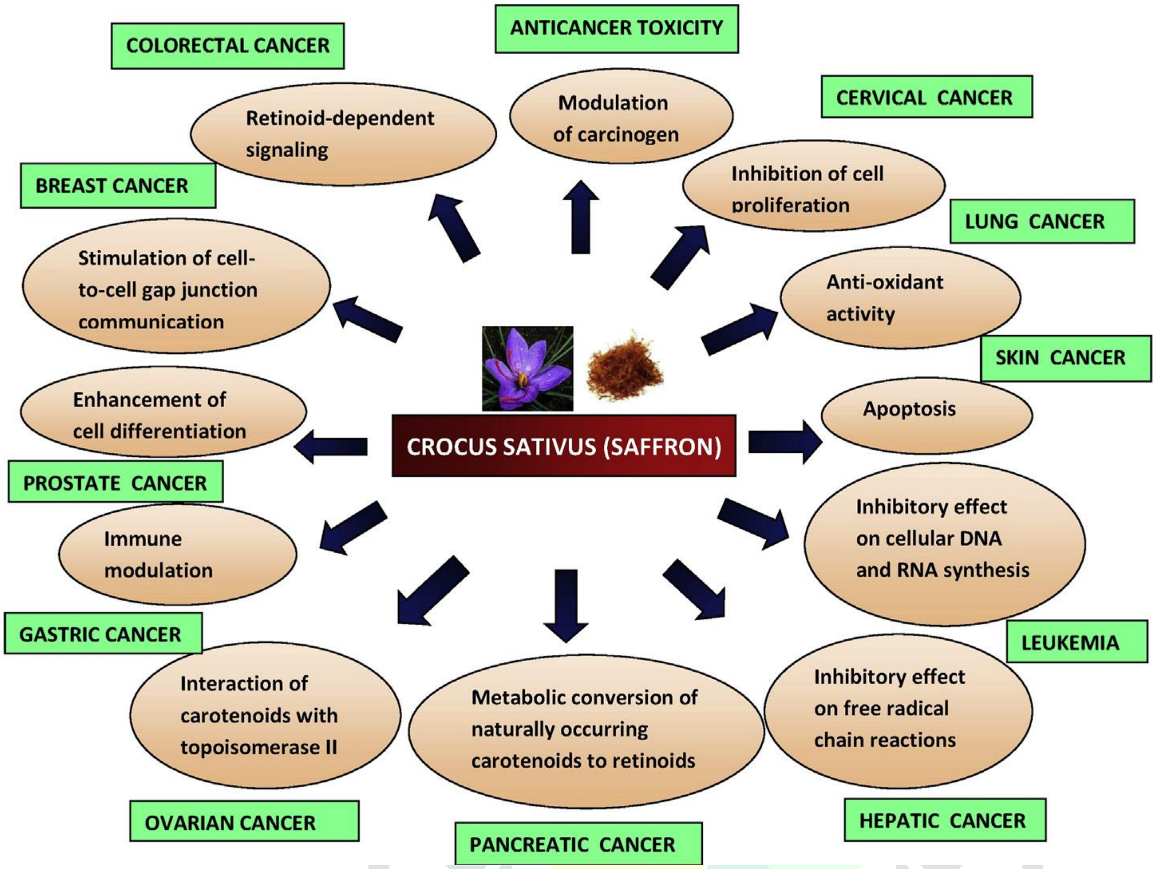

Fig 2: **CROCUS SATIVUS ANTICANCER MACHANISMS**

VI. TRADITIONAL USES OF SAFFRON

In traditional Iranian medicine, saffron can improve the complexion and can be used to treat erysipelas. In traditional Greek medicine, it can refresh the skin of the face and is used to relieve the liver of the domination of bile and to treat acne, skin diseases and wounds. In addition, the body may look younger and brighter]. In another category, Hindu women used saffron to make the bindi, the yellow dot on the forehead. It is, in a way, a third eye symbolizing good fortune and conscience. Nowadays, saffron tepals have been studied in several studies as being rich in crocin and kaempferol, thus representing an important source of bioactive compounds for potential cosmetic formulations. Beside the antioxidant properties, saffron presents multiple interests for cosmetic applications. The most promising activities are listed hereafter.

Saffron is known to reduce the pigment called melanin. Thus, it is very effective as a lightening agent for the skin. The formulation containing *C. sativus* extract caused significant depigmentation and anti-rhythmic effect on human skin. Melanocytes produce melanin in skin as a mixture of two pigments eumelanin and phaeomelanin, which are (brown black) and (red yellow) respectively. Prolonged exposure to the sun is extremely harmful because it puts the skin in contact with UV rays, known to cause serious lesions. Saffron is known to have anti-sun effects that can protect the skin from harmful UV rays. Studies show that saffron lotion may be a better sunscreen than homosalate (an organic compound used in some sunscreens). Thus, saffron can be used as a natural UV absorbing agent. In traditional herbal cosmetics uses, saffron can be soaked with a few basil leaves to treat blemishes such as acne. A mixture of soaked saffron strands and virgin coconut oil, or olive oil, and a bit of raw milk is an effective way to exfoliate and improve blood circulation face skin. Saffron is known to reduce a skin condition called erythema, characterized by inflammation, redness or rash.

Once dried, the spice releases a pleasant aroma described by Aristophanes as a "sensual smell" (Clouds 51) admired by the Greeks. It is from safranal, which is the main odoriferous compound of saffron that we obtain the note "saffron". In ancient Greece (around 2000 to 146 BC), saffron was a royal dye and was used as a perfume in salons, courts, theaters and bathrooms. Later, its use spread among ordinary people. Historically, plant pigments such as curcumin, beet anthocyanins, carotenoids from peppers, chlorophyll from green leaves and saffron, have been used to color food and cosmetics, for centuries. Nowadays, many commercially used cosmetics are made with the synthetic colorants, which can cause side effects due to prolonged use. However, the current trend matches towards healthy natural ingredients incorporated within these cosmetic products. In cosmetics, saffron has been used at low levels due to its high cost. It has been used as a substitute for turmeric where light exposure would cause fading of turmeric. It also used as a substitute for tartrazine.

From antiquity to the present day, and all over the world, most of the saffron produced was, and is still used, in cooking. Its aroma is described by chefs and saffron specialists as resembling honey, but with metallic notes. Saffron is used in India, Iran, Spain and other countries as a condiment for rice. In Spanish cuisine, it is used in many dishes such as Paella Valenciana, a specialty made from rice, and zarzuela, made from fish. Saffron is also used in French bouillabaisse, a spicy fish soup, Italian Milanese risotto and saffron cake. Iranians use saffron in their national dish—chelow kabab. Indian cuisine uses saffron in its biryanis, traditional dishes made from rice. It is also used in some candies such as gulabjaman and kulfi. In Morocco, saffron is used in tea instead of mint, but also as a spice in the preparation of various traditional dishes including koftas (meatballs and tomatoes) or mrouzia (a sweet-salty dish made from mutton or dill). Saffron is also a central ingredient in the blend of chermoula herbs that perfume many Moroccan dishes.

The harmful effect of synthetic food dyes has led to their banning in some countries and the return to natural dyes. The use of saffron as much as an alternative dye is advantageous in the field of agro-food thanks to the high solubility of crocine in water. Thus, the powerful dyeing power of saffron—which could also be used in cosmetic—has been used for a long time to color butter, pasta, cheeses, and oleomargarines. The golden yellow color of saffron is used in painting, textiles. The saffron solutions remain largely stable in alkaline and acidic medium. This property is due to crocin pKa (acid dissociation constant), dicarboxylic acids, esters, and nitrogen compounds. Saffron buffers solutions reduce the oxidation of cellulose. Saffron continues to dye the clothes of Buddhist monks, silk, wool, and Oriental carpets. Natural dyes have better biodegradability and compatibility with the environment, lower toxicity and less allergenic than some of the synthetic dyes.

VII. CONCLUSION

Saffron is the most valuable medicinal food product because of its importance in the sustainable development of the production areas of this spice. The dried stigmas of the plant *Crocus sativus* (Iridaceae) are used in saffron as a well-known spice

that has other significance in the pharmaceutical industries, textile dyes, and especially cosmetics; nowadays, the latter is ubiquitous and based on the incorporation of healthy and natural ingredients. Worldwide researchers are working on the correlation of

saffron with lowering risk of many types of cancers They are also investigating the contribution of the large number of phytochemicals in saffron. Among these phytochemicals, Crocins, Crocetin, and Safranal are considered the most pharmacologically advantageous as they affect cell growth regulation, and modulate gene expression in cancer cells. Saffron, a spice obtained from the flower of *Crocus sativus*, is rich in carotenoids. Two major natural carotenoids of saffron, crocin and crocetin, are responsible for its color. It could be concluded that saffron petal as the main by-product of saffron production possessed considerable phenolic compounds which showed high antioxidant power and antimicrobial activity. Therefore, taking into account that saffron petal is discarding more than thousands tons each year, phenolic compounds extracted from this solid waste might be used as natural antioxidant.

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