



Recent advances and Comparative Study of the taxonomic status, secondary metabolites ,Economic importance and Anti-cancerous properties of Crocus SativusL.,

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Abstract:-Saffron is obtained from the dried red stigmas of Crocus sativus L., an autumnal herbaceous flowering plant belonging to the Iridaceae family. It is largely cultivated in Iran, India, Afghanistan, Greece, Morocco, Spain and Italy. Saffron global production is estimated at 418 t y⁻¹ on 121,338 ha. It is known as the most expensive spice in the world and as beneficial for human health due to three main bioactive compounds: crocin, picrocrocine and safranal. The demand for saffron is increasing worldwide for its interesting role in cuisine, medicine and cosmetics. Saffron a perennial herb, well-known for its aroma and used for flavoring, is a culinary delight. It is an important commodity and is of great significance in the agricultural economics of Jammu and Kashmir. Saffron is popularly known as Red Gold(Kesar).India contributes 5% of the world's total production of which 90% is supplied only from its Jammu and Kashmir (J&K) regions. In India, the production of saffron from J&K is 3.83 tonnes whereas its annual demand is approximately 100 tonnes. Iran produces almost 90% of the total world production. The saffron market is expected to grow by 12.09% in the forecastperiod2020to2027regarding the medicinal effects of saffron.

Saffron is regarded as tonic andantidepressant and has been used in various ancient cultures f or strengthening digestion, relievingcoughs, smoothing menstruation, relaxing muscle spasms, calming anxiety and improve mood. In Jammu and Kashmir State, its cultivation is restricted to two districts only (Pulwama and Kishtwar). In the present review an attempt was made to highlight the Secondary metabolites and Economic importance of saffron, to discuss its distribution around the globe, to specify its taxonomic status, to enlist its chemical constituents, and to discuss its various beneficial usages and advances in research on the anticancer properties of saffron and its components

Keywords:- Crocus sativus ,Stigma,crocine,picrocrocine,safranal,Anticancerous ,Biomedical,Taxonomy,pharmacological extraction karewa soil.

Introduction:- *Crocus sativus* L. belongs to the Iridaceae family and is a perennial crop of monocotyledonous plants that form bulbs. It is planted around the end of summer in well-drained soil. The height of the flower stalk is approximately 100–150 mm, and it has six pale purple tepals, which grow to a size of approximately 30 mm in fall. The plant has three yellow stamens, a stigma, and a pistil of approximately 20, 20–40, and 60–100 mm in length, respectively. The stigma extending like a trumpet is divided into three parts and has a bright orange-red color. The dried stigma of this plant is commonly known as saffron which is derived from the Arabic word “Zafaran”, meaning yellow. In local language it is known as Koong . Persian word *zarparān* (زرپران) Saffron is known as one of the oldest cultivated plants, although its wild species is unknown. Historically, saffron has been traced back to cave arts in Mesopotamia, dating back at least 5,000 years It was cultivated from 2500 to 1500 B.C.E. (8). Although the origin of its cultivation is unclear, it is found to have been cultivated in Crete and Thera during the Minoan period (7,9). Saffron is believed to have originated from ancient Greece, Asia Minor, and Persia. The saffron spice and its cultivation later spread to India and China through the Silk Road across civilizations, cultures, continents, and countries. Saffron is currently cultivated in many countries including Iran, Spain, India, Italy, Afghanistan, Azerbaijan, China, and Uzbekistan. The major saffron-producing countries are Iran and Spain, which mainly export to Europe and Asia (10). In Jammu and Kashmir the main area of production has been Pulwama in Kashmir and Kishtwar in Jammu where the cultivated saffron is of good quality because the climatic conditions are suitable due to the karwas fertile soil and efficient topography of this area. In general, saffron is one of the most valuable spices and is used as a flavoring, coloring, and aroma agent in food and drinks worldwide. Saffron is consumed in the food industry and is also used in fragrances, cosmetics, and dyes Furthermore, saffron has been used in traditional medicine, crude drug, and folk medicine since ancient times because of its therapeutic properties . The attractive functions of saffron depend on its main secondary metabolic compounds as crocin, picrocrocin, and safranal Saffron is sometimes called “red gold” because it is one of the most expensive cash crops. It costs approximately 10 times more than vanilla and 50 times more than cardamom. Cultivation using non-mechanized agricultural systems, harvesting, and processing require complicated skills such as manual removal of the stigma on the day of harvest and approximately 400 h of work .Moreover, saffron is a very low-yield crop. Approximately 70,000–200,000 flower stigmas are required to produce 1 kg of saffron , one stigma formed by three filaments is obtained from each flower. Currently, there are many barriers against saffron usage to the widespread use of saffron in the food industry, such as low productivity cultivation methods, production difficulties, low yields, quality control, and food safety concerns. Therefore, it is necessary to provide and organize information on these issues from a broad food perspective. Therefore, this paper focuses on saffron in the food industry, its consumption as a spice, its effects on the economy, its ingredients, quality, safety, and its use in cooking. It also focus on plant discription and secondary metabolites found in *Crocus Sativa*.

Methods: This review article was constructed from published scholarly papers obtained from various web databases, including PubMed, Google Scholar, Science Direct, and Springer, as well as from websites and published books. My search period for this article was from October 2023



to January 2024.

Chemistry of Saffron

Saffron contains more than 150 volatile and aroma-yielding compounds. It also has many nonvolatile active components,[29] many of which are carotenoids, including zeaxanthin, lycopene, and various α - and β -carotenes. However, saffron's golden yellow-orange colour is primarily the result of α -crocin. This crocin is trans-crocetin di-(β -D-gentiobiosyl) ester; it bears the systematic (IUPAC) name 8,8-diapo-8,8-carotenoic acid. This means that the crocin underlying saffron's aroma is a digentiobiose ester of the carotenoid crocetin. Crocins themselves are a series of hydrophilic carotenoids that are either monoglycosyl or diglycosyl polyene esters of crocetin (Alipour Eskandani, 2013). Crocetin is a conjugated polyene dicarboxylic acid that is hydrophobic, and thus oil-soluble. When crocetin is esterified with two water-soluble gentiobioses, which are sugars, a product results that is itself water-soluble. The resultant α -crocin is a carotenoid pigment that may comprise more than 10% of dry saffron's mass. The two esterified gentiobioses make α -crocin ideal for colouring water-based and non-fatty foods such as rice dishes. The bitter glucoside picrocrocin is responsible for saffron's flavour. Picrocrocin (chemical formula: $C_{16}H_{26}O_7$; systematic name: 4-(β -D-glucopyranosyloxy)-2,6,6-trimethylcyclohex-1-ene-1-carboxaldehyde) is a union of an aldehyde sub-element known as

safranal (systematic name: 2,6,6-trimethylcyclohexa-1,3-diene-1-carboxaldehyde) and a carbohydrate. It has insecticidal and pesticidal properties, and may comprise up to 4% of dry saffron. Picrocrocin is a truncated version of the carotenoid zeaxanthin that is produced via oxidative cleavage, and is the glycoside of the terpene aldehyde safranal. The reddish-coloured zeaxanthin is, incidentally, one of the carotenoids naturally present within the retina of the human eye (Alipour Eskandani, 2013). When saffron is dried after its harvest, the heat, combined with enzymatic action, splits picrocrocin to yield D-glucose and a free safranal molecule. Safranal, a volatile oil, gives saffron much of its distinctive aroma. Safranal is less bitter than picrocrocin and may comprise up to 70% of dry saffron's volatile fraction in some samples. A second element underlying saffron's aroma is 2-hydroxy-4,4,6-trimethyl-2,5-cyclohexadien-1-one, which produces a scent described as saffron, dried hay-like. Chemists find this is the most powerful contributor to saffron's fragrance, despite its presence in a lesser quantity than safranal. Dry saffron is highly sensitive to fluctuating pH levels, and rapidly breaks down chemically in the presence of light and oxidizing agents. It must, therefore, be stored away in air-tight containers to minimize contact with atmospheric oxygen. Saffron is somewhat more resistant to heat (Golmohammadi, 2012).

Nutritents components and Energy composition of Saffron:-

<u>Components</u>	Compositions/100 g dry weight)	<u>Components</u>	Compositions/100 g dry weight)
Energy(kcal.)	381.2	Minerals	Traces amount
Moisture	3.84	DietaryFibres	13.8 Soluble:- 6.0 In-Soluble:-7.8
Ash	6.60	Glucose	7.40
Proteins	13.63	Fructose	3.09
Lipids	8.76	Inositol	0.33
Carbohydrates	62.0	Sorbitol	0.20
Reducing Sugar	16.5	Enzymes	Traces

Table1:- Depicts the nutrients, components and Composition of Saffron.

Rank	Country	Estimated Annual production(metric tonne)
01	Iran	190
02	India	6-7
03	Greece	3-4
04	Morocco	1.5-2

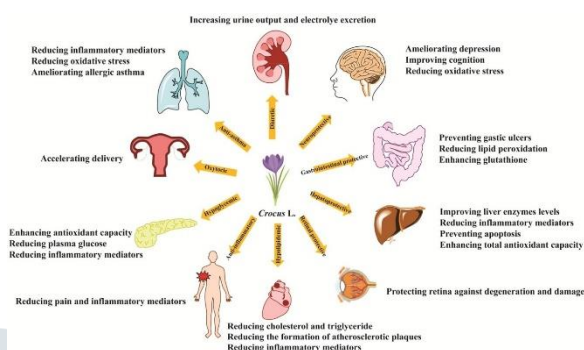
Table2:-Depicts the Top ranking of Saffron production

Botany:-the taxonomic classification of *C. sativus* series is as follows:

1. Division:-Spermatophyta
2. Sub-division:- Angiospermae
3. Class:- Monocotyledonae
4. Sub-class:- Liliidae
5. Order:- Liliales
6. Family:- Iridaceae
7. Genus:- *Crocus*
 - a. Sub-genus: Anthers with extrose dehiscence
 - b. Section *Crocus*: Scape subtended by a membranous prophyll
 - c. Series *Crocus*: Corm tunics finely fibrous, usually reticulate; flowers autumnal; leaves rather numerous, usually 5–30, appearing with the flowers or shortly after; bracts flaccid, usually not closely sheathing the perianth-tube, membranous, white or transparent with no marking; anther yellow; style branches 3, usually red and often expended at the apex, entire or at most fimbriate; seed coats covered with dense mat of papillae. $2n = 12, 14, 16, 26$.

Geographical Distribution of Saffron:- The origins of *C. sativus* is not clearly known, some author suggest eastern Mediterranean as its endemic place and some consider its Iranian origin. As per the archaeological and historical data, the domestication of *C. sativus* is very old (2,000 to 1,500 years BC) . The *C. Sativus* reported to be cultivated in Afghanistan, Azerbaijan, China, Egypt, France, Greece, India, Iran, Iraq, Israel, Italy, Japan, Pakistan, Morocco, Spain, Switzerland, Turkey, United Arab Emirates since ancient times and recently Australia also have started its cultivation

Harvesting:-The high retail value of saffron is maintained on world markets because of labour-intensive harvesting methods, which require some 440,000 hand-picked saffron stigmas per kilogram (200,000 stigmas/lb) – equivalently, 150,000 crocus flowers per kilogram (70,000 flowers/lb). Forty hours of labour are needed to pick 150,000 flowers. One freshly picked crocus flower yields on average 30 mg of fresh saffron or 7 mg dried; roughly 150 flowers yield 1 g ($\frac{1}{32}$ oz) of dry saffron threads; to produce 12 g ($\frac{7}{16}$ oz) of dried saffron, 450 g (1 lb) of flowers are needed; the yield of dried spice from fresh saffron is only 13 g/kg (0.2 oz/lb).



Pharmacological Extracts of Saffron :-Shown in the form of mindmap

Medicinal properties of Saffron:-

Medicinal plants are the most natural remedy for man's disease and sicknesses which has been bestowed on human by nature. Though man has made a great improvements in the field of pharmacology, yet the great and remarkable role of medicinal plants in healing and relieving the pain cannot be ignored. The effectual raw material existing in medicinal plants has been used by man for a long time and they do not seem to be replaced by man made products.

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Saffron (*Crocus sativus* L.) is a plant of the iridaceae family. The dried intact stigmas of saffron are widely used as a condiment, medicinal plant and food additive in the different countries. Recently, saffron extract was found to have anti-cancer activities against different carcinoma cells. Many of these medicinal properties of saffron can be attributed to a number of its compounds such as crocins, phenolic, flavonoid and other substances having strong antioxidant and radical scavenger properties. The importance of antioxidants in maintaining health and

protection from cancer is of great interest in revealing the antioxidant compounds of spice or herb plants.

Crocus sativus L. (family Iridaceae) is an important crop cultivated for its red stigmatic lobes that constitute the high valued saffron of commercial use. Saffron is a perennial autotriploid vegetatively propagated plant where breeding is generally difficult. In recent years application of tissue culture for the large scale propagation and genetic improvement of saffron has been emphasized. Compared with the traditional method, plant tissue culture offers a great potential for callus induction.

Saffron (*Crocus sativus* L.) is a triploid, sterile, monocot plant belongs to the family Iridaceae, sub family Crocoideae. *C. sativus* only bloom once a year and should be collected within a very short duration, the stigmas of Saffron flowers are harvested manually and subjected to desiccation then have been used as a spice. It has been also used as a drug to treat tumor, cancer, chronic uterine hemorrhage, insomnia, scarlet fever, small pox, colds and cardiovascular disorders. It has been shown that saffron is a protective agent against chromosomal damage. Saffron has been vegetative propagated by corm, each mother corm produce 7-8 cormlet each year. The main colors of saffron, crocetin and crocetin glycosides, and the main flavors, picrocrocin, Safranal is the main component of aroma and its bitter taste is related to Glycoside picrocrocin that are derived from the oxidative cleavage of the carotenoid zeaxanthin which cleavage by zeaxanthin cleavage dioxygenase (ZCD).

Saffron (*Crocus sativus* L.) is a valuable medicinal plant whose product is varied under different types of stresses. Several studies demonstrated the antimicrobial effects of red stigmas of saffron flowers but because of the high expense of the stigma the use of this part of the plant as antimicrobial agent is not economical. Therefore, in this study the antibacterial activity of the total methanol extract of the petals and stamens of Saffron flowers against five food borne strains were evaluated.

Saffron (*Crocus sativus* L.) belongs to the Iridaceae family. Its valuable dried spice that accumulates in the stigmas is widely used for coloring and flavoring many foods. It has a long medicinal history as part of traditional healing; several modern research studies have hinted that the spice has possible anticarcinogenic (cancer-suppressing), anti-mutagenic (mutation preventing), immunomodulating, and antioxidant-like properties.

Saffron is dried stigmas of *Crocus sativus* L. and member of Iridaceae family which is propagated with means of corms, because it is a sterile plant and can't produce seeds. Each mother corm produces 8-9 cormlet every year. Corms are faced with much stress, such as water deficiency,

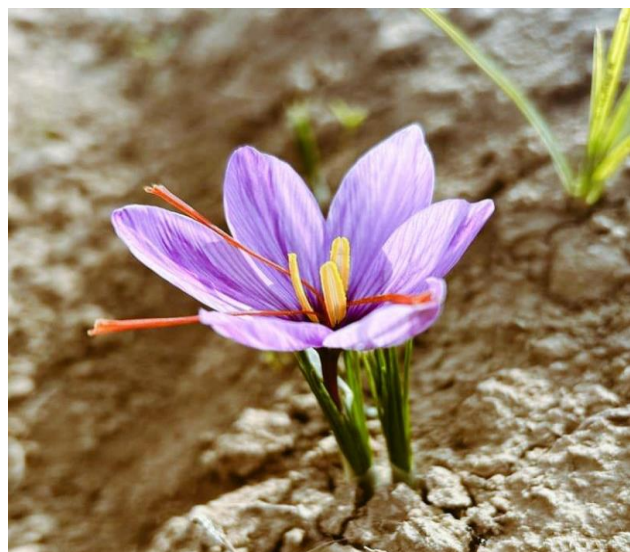
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Use of Saffron:- Saffron's aroma is often described by connoisseurs as reminiscent of metallic honey with grassy or hay-like notes, while its taste has also been noted as hay-like and sweet. Saffron also contributes a luminous yellow-orange coloring to foods. Saffron is widely used in Indian, Persian, European, Arab, and Turkish cuisines. Confectioneries and liquors also often include saffron. Common saffron substitutes include safflower (*Carthamus tinctorius*, which is often sold as "Portuguese saffron" or "açafraão"), annatto, and turmeric (*Curcuma longa*). Saffron has also been used as a fabric dye, particularly in China and India, and in perfumery.[84] It is used for religious purposes in India, and is widely used in cooking in many cuisines, ranging from the Milanese risotto of Italy to the bouillabaisse of France to the biryani with various meat accompaniments in South Asia (Alipour Eskandani, 2013). Saffron has a long medicinal history as part of traditional healing; several modern research studies have hinted that the spice has possible anticarcinogenic (cancer-suppressing), anti-mutagenic (mutation-preventing), immunomodulating, and antioxidant-like properties. Saffron stigmas, and even petals, may be

helpful for depression. Early studies show that saffron may protect the eyes from the direct effects of bright light and retinal stress apart from slowing down macular degeneration and retinitis pigmentosa. (Most saffron-related research refers to the stigmas, but this is often not made explicit in research papers.) Other controlled research studies have indicated that saffron may have many potential medicinal properties.

Biomedical Properties of Saffron:- Saffron's biomedical properties have attracted the interest of researchers during the last decades (see reviews of Basker and Negbi, 1983; Abdullaev (1993), Abdullaev (2002); Ríos et al., 1996; Souret and Weathers, 1999). Hartwell (1982) reported that in ancient times **saffron** was used as an anticancer agent, and he described the use of preparations containing **saffron** extracts against different kinds of tumours and cancers. Thus, liver, spleen, kidney, stomach and uterus tumours have been treated with pharmaceutical preparations of **saffron**. In the early 1990s, some authors demonstrated that crude **saffron** extracts presented antitumour and anticarcinogenic activities, as well as cytotoxic and antimutagenic effects. The aim of the present review is to summarize the recent research on the active anticancer constituents present in the **saffron** plant, their potential therapeutic applications, and the biotechnological production of these substances. besides some of the proven biomedical properties are as under

- **Antidepressant effect:-** A number of recent preclinical and clinical studies indicate that stigma and petal of *C. sativus* have antidepressant effect. The antidepressant effect of *C. sativus* petal as well as stigma aqueous and ethanolic extracts has been shown in mice by Karimi et al. (2001). It was reported that two constituents of saffron, safranal and crocin, also have antidepressant activity in mice Hosseinzadeh et al. (2004) Akhondzadeh Basti (2007) Moshiri (2006). Hosseinzadeh et al. (2007) results indicate that the saffron petal component, kaempferol, may be of valuable agent in the treatment of depression.
- **Effects on ocular blood flow and retinal function:-** Dementia is a mental disorder characterized by loss of intellectual ability (judgment or abstract thinking) which invariably involves impairment of memory. The most common cause of dementia is Alzheimers disease (AD), which is a progressive neurodegenerative disorder associated with loss of neurons in distinct brain areas and cord. The saffron extract and two of its main ingredients crocin and crocetin, improved memory and learning skills in ethanol-induced learning behavior impairments in mice and rats. Oral administration of saffron may be useful as treatment for neurodegenerative disorders and related memory impairment (Jagdeep et al., 2009; Abe and Saito, 2000; Abe, 1994; Sigura et al., 1995).

- **Effect on blood pressure:-** Aqueous and ethanol extracts of saffron reduced the blood pressure in a dose dependent manner. EFS of the isolated rat vas deferens also were decreased by these saffron extracts (Fatehi et al., 2003).
 - **Anti-inflammatory effects :-**Saffron stigma and petal extracts exhibited antinociceptive effects in chemical pain test as well as acute and/or chronic anti-inflammatory activity and these effects might be due to their content of flavonoids, tannins, anthocyanins, alkaloids and saponins (Hosseinzadeh and Yiounesi, 2002).
 - **Antiparkinsonian effect:-** Crocetin, which is an important ingredient of saffron, may be helpful in preventing Parkinsonism (Ahmad, 2005)
 - **Improving learning and memory skills**
Akhondzadeh, et. al. (2010a; b) proposed saffron may inhibit the aggregation and deposition of amyloid beta in the human brain. This property of saffron was assessed in the treatment of mild to moderate Alzheimer's diseases. Saffron extract and crocins had shown to prevent spatial learning and memory impairment caused by the effect of chronic induced stress (Ghadroost, et al., 2011). The correlation between the antioxidant activity of saffron and impairment caused by oxidative stress, was one of the proposed mechanisms for saffron having preventive property against memory impairment. A positive correlation between the enhancement of cognitive function and increase in total brain antioxidant activity supported by animal model (Papandreou, et al., 2011) clearly demonstrated the role of saffron. Furthermore, observation of attenuated scopolamine induced spatial memory performance in mice upon the treatment with 15 and 30mg/kg of crocin, supported the effectiveness of saffron in cognitive function (Pitsikas, et al., 2007)
- Other Therapeutic uses of Saffron:-**

saffron to treat menstrual disorder (Ríos, et al., 1996) was supported by the psychological and physiological effect of saffron odor in women to treat premenstrual syndrome, dysmenorrhea and irregular menstruation (Fukui, et al., 2011). This study speculated that saffron odor may interfere with the level of sex steroid hormones to achieve anti-stress action. Saffron effect on the endocrine system was further supported by observation of reducing metabolic and behavior signs of stress in saffron treated rodents (Hooshmandi, et al., 2011). Relating with the anti-stress function of saffron, it had been reported that saffron extract and crocin would improve erectile dysfunction (ED) and sexual behavior in male (Hosseinzadeh, et al., 2008). The outcome of this study benefited in improvement of ED function by saffron. The effect was noted to be equivalent to sildenafil which is clinically used for the treatment of ED due to its arterial vasodilation enhancement (Shamsa, et al., 2009). At the same time its hypotensive property had been further supported with the effect in lowering of blood pressure of rats by saffron and its constituents, safranal and crocin (Imanshahidi et al 2009)

As far as the anti-cancerous properties of saffron is concerned ,some of the Major studies on the anticancer effects of saffron extract and its major ingredients in cell lines and animal models of cancer

Bioactive Compounds	Cell line	Suggested mechanism of action	REFERENCES
Saffron ethanol extract	Breast cancer cells MCF-	Caspase activation, upregulation of Bax expression. Apoptosis. Downregulation of VEGFR expression. Cell proliferation and angiogenesis inhibition	Mousavi et al., 2009 Mousavi and Baharara, 2014
Safranal, crocin	Myelogenous leukemia cells K-562	Downregulation of Bcr-Abl expression	Geromichalos2014
Safranal, crocetin, crocin	Breast cancer cells MCF-7, MDA-MB 231	Cell proliferation inhibition	Chryssanthi et al., 2007
Crocetin	Breast cancer cells MCF-7, MDA-MB 231	Downregulation of metalloproteases expression. Cell invasion inhibition, apoptosis	Paper et al., 2000
Crocetin	Colon cancer cells SW480	Arrest of cells in the S phase, upregulation of P21 expression. Cell proliferation inhibition	SLi et al., 2012
Crocetin	Leukemia cells HL60, K-562, L1210, NB4, P388	Activation of the intrinsic apoptotic pathway	Moradzadeh et al., 2019
Crocetin, crocin	Lung adenocarcinoma	Upregulation of the p53 and Bax mRNA levels;	Chen et al., 2015

	cells A549, SPC-A1	downregulation of the f Bcl-2 mRNA levels. Apoptosis	
Crocin	Breast cancer cells MCF-7	Caspase-8,9 and activation, Bax/Bcl-2 ratio increase, mitochondrial membrane potential disruption, cytochrome c release. Cell proliferation inhibition, apoptosis	Bakshi et al., 2016
Crocin	Breast cancer cells HCC70, HCC1806	Microtubules depolymerization. Cell proliferation inhibition	Hire et al., 2017
Crocin	Ovarian cancer HO-8910 cells	Arrest of cells in the G0/G1, upregulation of p53, Fas/APO-1, and Caspase-3 expression. Apoptosis	Xia et al., 2015
Crocin	Gastric cancer cells AGS	p53 dependent and independent mechanisms. Apoptosis	Hoshyar et al., 2017
Crocin	Gastric cancer cells AGS	Downregulation of OCT4, KLF, SOX2, NANOG, and Nucleostemin expression. Apoptosis	Akbarpoor et al., 2020
Saffron aqueous extract	4T1 cells were xenografted in mice	Changes in p53 expression. Inhibition of tumor progression	Nezamdoost et al., 2020

Conclusion:- Saffron has shown its role in disease prevention and treatment and its importance in disease cure . The role of saffron including crocin ,Picrocrocin and crocetin in the management of numerous diseases has proven. Saffron has also been reported to exhibit an anti-tumour effect through inactivation or activa-tion of different molecular cascades. As a therapeutic plant, saffron (*C. sativus* L. is a promising herb of pharmaceutical industry due to its varied medicinal properties ranging from mild fever to cancer and DNA repair.

Conflict of Intrest:-The author declares no conflict of Intrest.

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