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Review Article

PHARMACOLOGICAL, PHARMACOGNOSTIC AND PHYTOCHEMICAL REVIEW OF SAFFRON

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Abstract

Since ancient times, herbal plants have been used throughout the world as a source of ayurvedic medicine. Over two millennia ago, the father of medicine Hippocrates mentioned and advised that "let food be your medicine and let medicine be your food". Currently the morbidity and mortality associated with cancer and depression are considerable and continue to increase. Cancer ranks second and depression stands fourth in mortality. Currently, the above strategies are very attractive and have earned serious consideration as a potential means of controlling these. So many health professionals showed increased interest in these fields and tend to develop a good formulation using an ayurvedic plant as active pharmaceutical ingredient. So, to meet the above needs a bulbous perennial plant called saffron (Crocus sativus .L) was selected and was tend to be used for the treatment of cancer as well as depression. Saffron contains more than 150 volatile and non-volatile components like safranal, crocin, picrocrocin and other carotenoids etc. Saffron is non toxic in animal studies (LD_{50}-20.7g/kg), non-cytotoxic in *in-vitro* studies (LD_{50}-200mg/kg), and 30mg/day of saffron yields anti–depressant effects. Saffron can be used effectively due to its less toxicity against different human health conditions which allows saffron as a potential medical drug in clinical trails. A vast growing body of research demonstrated that, saffron itself and its main constituents posses chemo preventive and anti-depressant effect. This review discusses recent literature data on different activities of saffron and its main ingredients.

Key words: Anticancer, Depression, Saffron.

Introduction:

Saffron is collected from dried stigmas of bulbous perennial plant called *Crocus sativus* belongs to the family Iridaceae[1]. Among the 85 species of *Crocus* genus, saffron is par excellent species due to its medicinal properties and outstanding feature of lilac to mauve colored flower with three stigmas which droop over the petals[1-2]. The word saffron is derived from the Arabic word Za'faran, which means "yellow" and is named due to its three yellow stamens, which lacks the active components and are not collected. Saffron is cultivated in the Middle Eastern Region of Eurasian continent, from Greece to Persia (Iran)[3].While Iran accounts for 70% of saffron worldwide, kashmiri saffron is widely considered superior due to its higher crocin content (Global press institute). The plant is propagated with the help of corms (bulbs) which divides to produce new plants. Each bulb produces one to seven flowers in which the stigmas are attached to the style[4]. The length of the stigmas is of 25-30 mm long. Hybridization of this plant produces an extra long stigmas and takes about 36,000 flowers to yield 1 pound of stigmas. World-wide, 190 tons of saffron are produced each year. Among 150 volatile and non-volatile components of saffron, approximately 40-50 constituents have been already identified and based on these data, we may justify that the pharmacological activity is due to the presence of a carotenoid called crocetin (mono and diglycosyl esters of polyene dicarboxylic acid) and crocin (digentiobiosyl ester of crocetin). The other constituent called picrocrocin is responsible for the bitter taste and volatile oil safranal is responsible for its characteristic honey like flavour[5-9]. Saffron is non toxic in animal studies (LD_{50}-20.7g/kg), non-cytotoxic in *in-vitro* studies (LD_{50}-200mg/kg), and 30mg/day of saffron yields mild to moderate anti–depressant effects and at this dose it has been found to be effective similar to Imipramine[10]. It was also found that the side effects like dry mouth and sedation with Imipramine can also be reduced by using saffron as an anti-depressant agent. Along with the above therapeutic effects, saffron has a multifarious applications as a biological specimen. The scientific classification of *Crocus sativus* was given in Table 1.

Table 1: Taxonomical classification of Crocus sativus.

Kingdom	Plantae
Divison	Magnoliophyta
Class	Liliopsida
Order	Asparagales
Family	Iridaceae
Sub-Family	Crocoideae
Genus	Crocus
Species	C.sativus

Synonyms

The names of this medicinal plant in 80 languages are mentioned below.

pharmaceutical	*Stigmata Croci*
Amharic	Safron
Arabic	زعفران زَعْفرَان Zafraan, Zafran
Armenian	Քըրքում, Քրքում Kerkoom, Kerkum
Assamese	জাফৰাণ, জাফৰান, কুঙ্কুম, কুংকুম Jafaran, Kunkum, Kungkum

Azeri	Zəfəran Зәфәран
Basque	Azaparán, Hupa
Belarusian	Шафран Shafran
Bengali	জাফরাণ, জাফরান Japhran, Jafran
Bulgarian	Шафран Shafran
Catalan	Safrà
Chinese (Cantonese)	番紅花 [fàan hùhng fāa] Faan huhng faa
Chinese (Mandarin)	番紅花 [fān hóng huā], 藏红花 [zàng hóng huā] Fan hong hua, Zang hong hua
Croatian	Vrtni šafran
Czech	Šafrán
Danish	Safran
Dhivehi	ކުކުން Kukun
Dutch	Saffraan

Esperanto	Safrano
Estonian	Krookus, Safrankrookus, Safran
Farsi	زعفران Za'afaran, Zaafaran
Finnish	Sahrami
French	Safran
Gaelic	Crò, Cròdh, Cròch
Galician	Azafrán
Georgian	ზაფრანა Zaprana, Zaphrana
German	Safran
Greek	Κρόκος, Σαφράνι, Ζαφορά Krokos, Safrani, Zafora
Greek (Old)	Κρ□κος Krokos
Gujarati	કેસર Kesar
Hebrew	זעפרן זַעֲפְרָן Safran, Za'afran, Zafran

Hindi	केसर, ज़ाफ़रान Kesar, Zafran
Hungarian	Füszersáfrány, Sáfrány
Icelandic	Saffran
Indonesian	Kunyit kering, Kuma-kuma, Sapran
Irish	Chróch
Italian	Zaffarano, Zafferano
Japanese	蕃紅花 さふらん サフラン, バンコウカ Safuran, Bankōka, Bankoka
Kannada	ಅಗ್ನಿಶಿಖೆ, ಕುಂಕುಮ ಕೇಸರಿ, ಕೇಸರಿ Agnishikhe, Kunkuma kesari, Kesari
Kashmiri	کونگ, زعفران Kung, Zafaran
Kazakh	Зағыпаран, Запырангүл, Жауқазын Jawqazın, Zağıparan, Zapırangül
Khmer	Romiet
Korean	사프란, 샤프란

	Sapuran, Syapuran
Latin	Crocus, Safranum
Latvian	Safrāna krokuss, Safrānaugs
Lithuanian	Šafranas
Macedonian	Шафран Šafran
Malay	Koma koma
Malayalam	കാശ്മീരം, കുങ്കുമപൂ, >, കുങ്കുമപൂവ് Kashmeeran, Kungumampoovu, Kunkumapu
Maltese	Żagħfran, Żafran
Marathi	केशर Keshar
Nepali	केशर, कुंगकुम Kesar, Kung-kum
(Nepalbhasa)	Kesar
Norwegian	Safran
Oriya	କସେର, କୁଙ୍କୁମ ଫୁଲ Kesara, Kunkuma phul
Pahlavi	Kurkum
Pashto	Zaffaron

Polish	Krokus uprawny, Szafran
Portuguese	Açafrão, Açaflor
Provençal	Safran
Punjabi	ਕੇਸ਼ਰ, ਕੇਸਰ Keshar, Kesar
Romanian	ofran (Şofran)
Russian	Шафран Shafran
Sanskrit	Kumkuma, Kashmiirajan, Kashmiiran, Nagakeshara
Serbian	Шафран Šafran
Slovak	Šafrán siaty, Šafrán
Slovenian	Žafran
Spanish	Azafrán
Swahili	Zafarani
Swedish	Saffran
Tagalog	Kashubha
Tamil	குங்குமப்பூ Kungumapu, Kungumappu
Telugu	కుంకుమపువ్వు

	Kunkumapuvvu
Thai	หญ้าฝรั่น Ya faran
Tibetan	Gur-kum, Kha-che kye, Kunkum (uncertain)
Turkish	Safran, Zağferan
Ukrainian	Шафран, Крокус Shafran, Krokus
Urdu	کیسر ,زعفران Zafran, Kisar
Uzbek	Zafaron Зафарон
Vietnamese	Màu vàng nghệ, Quí nghệ, Nghệ tây Mau vang nghe, Qui nghe, Nghe tay
Yiddish	זאַפֿראָן, זאַפֿרען Zafren, Zafron

Origin and cultivation[11,14]

Saffron was cultivated from back more than 3000 years. It was originated from a wild precursor named *Crocus cartwrightianus*. Experts believe that saffron was first documented in 7th century BC. Mild winters with heavy snowfall and hot summers are excellent conditions for the plant's growth. Saffron grows well under temperate and dry climates; its vegetative growth coincides with cold weather and freezing condition. Annual rainfall requirement for saffron is about 300 mm. Saffron's maximum water requirement is in March and April of about 15 to 20 liters per m^2 per irrigation period. Saffron tolerates maximum of +45ºC and minimum of -18ºC. Planting is mostly done in june and corms are lodged 7-15 cm deep. Mother corms are planted deeper that yields high quality saffron but yields less flowers. *Crocus sativus* prefers loose, low density, well-watered and well-dried calcareous soils with high organic solvent. After a period of dormancy through the summer, harvesting is done at the time when flowers quickly wilt as the day passes. Few images of this plant are shown in Fig 1,2,3.

Fig-1 (Flower with stigmas)

Fig-2 (corms)

Fig-3 (Dried stigmas)

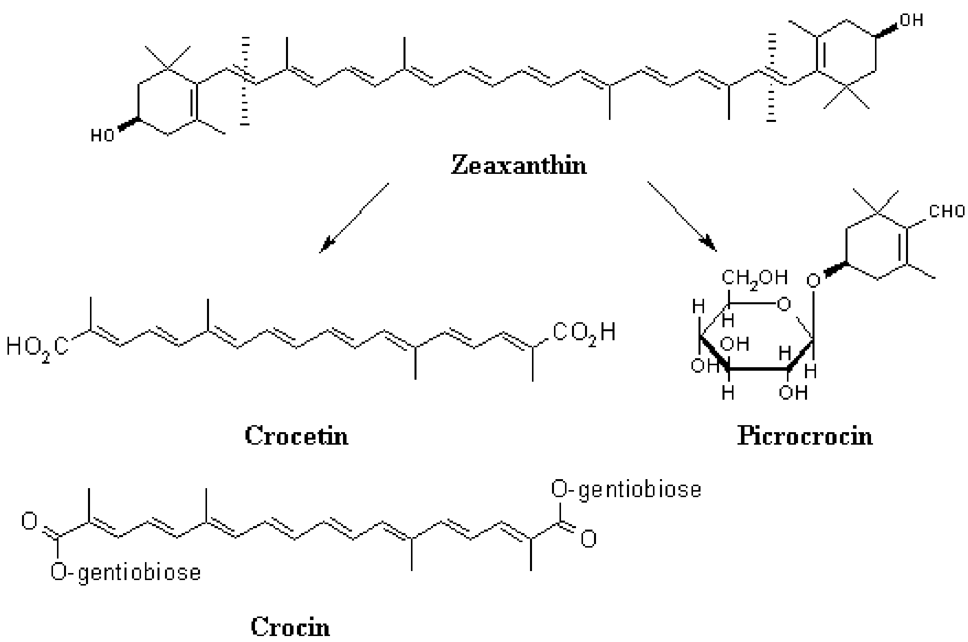
Phytochemical constituents[15-18]

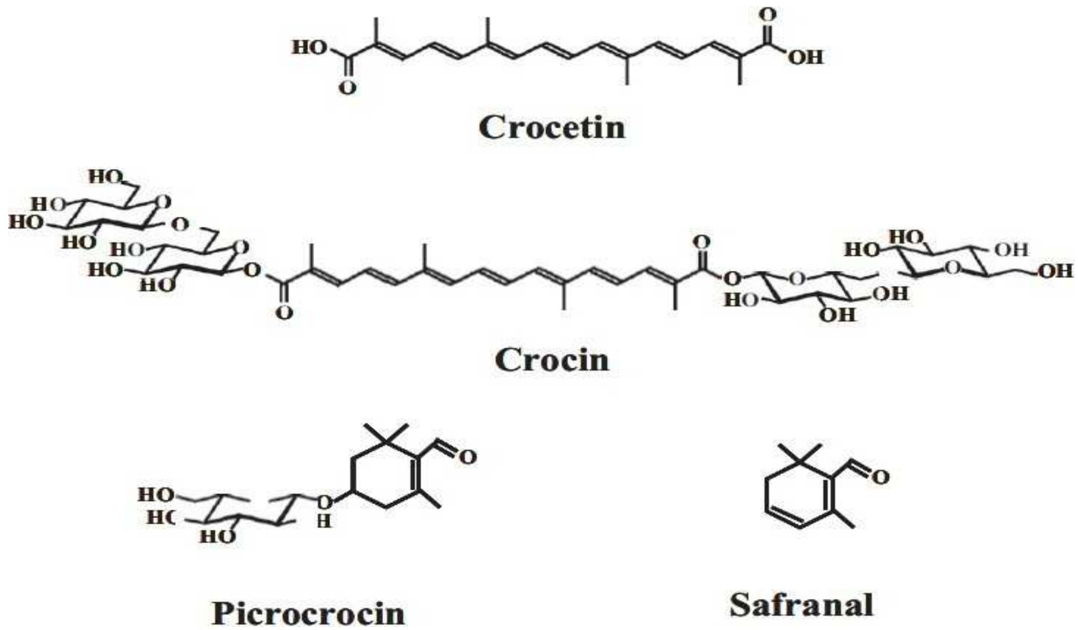
Saffron consists of a wide range of chemical constituents as shown in the Table 2.

The other active components are essential oils (volatile oil) in 0.3- 1.5%, crocin derived from crocetin about 2%, carotenes 8%, picrocrocin and safranal 4%. The active constituents present are the degradative products of zeaxanthin and to a small extent from lycopene and beta-carotene. The degradative products from zeaxanthin formed from bio-oxidative cleavage are shown in the graphical abstract below.

Table 2: Chemical Constituents of *crocus sativus.*

Substance	Proportion
Simple sugars	12–15%
Water	9–14%
Proteins, amino acids, other nitrogen compounds	11–13%
Cellulose (fiber)	4–7%
Fats	3–8%
Minerals (measured as acid soluble ash)	1–1.5%
Other non-nitrogen (mainly complex sugars)	about 40%





Structures of active chemical constituents

Pharmacology studies

Toxicity:[19]

No toxic effect was seen on human body with saffron consumption. But excess consumption leads to narcotic effects in the body.

Alzheimer's disease:[20,21]

Saffron at the dose of 30 mg/day (15 mg twice per day) or donepezil 10 mg/day (5 mg twice per day) was found to be effective similar to donepezil in the treatment of mild-to-moderate alzheimer's disease after 22 weeks.

Anti-depressant effect[7, 22-23]

Antidepressants activity is due to increment in brain serotonin, norepinephrine and dopamine concentration. Some investigators have proposed that the extract may induce its anti-depressant activity via interaction with serotonin. 30mg/day of saffron yields mild to moderate anti–depressant effects and at this dose it has been found to be effective similar to Imipramine. It was also found that the side effects like dry mouth and sedation with Imipramine can also be reduced by using saffron as an anti-depressant agent.

Anti-oxidant effect[24,25]

It was shown that, antioxidant activity of saffron carotenoids is more effective than safranal. However, the synergistic effect of all the bioactive constituents gives to saffron spice a significant antioxidant activity. The antioxidant activity of saffron compounds can protect DNA and tRNA from harmful chemical reactions in these ligand–polynucleotide complexes but in order to have a solid proof for that, further experimental work has to be performed in order to prove that the oxidation products of the saffron compounds does not harm DNA/tRNA.

Anti-inflammatory effect[26,27]

Microglial cells play critical roles in the immune and inflammatory responses of the central nervous system (CNS). Crocin or crocetin represses microglial activation. Crocin and crocetin were shown to be effective in the inhibition of LPS-induced nitric oxide (NO) released from cultured rat brain microglial cells. These compounds reduced the LPS-stimulated productions of tumor necrosis factor-α, interleukin-1β, and intracellular reactive oxygen species. These compounds also effectively reduced LPS-elicited NF-κB activation. In addition, Crocin reduced NO release from microglia stimulated with interferon-γ and amyloid-β. In organotypic hippocampal slice cultures, both crocin and crocetin blocked the effect of LPS on hippocampal cell death. These results suggest that crocin and crocetin provide neuroprotection by reducing the production of various neurotoxic molecules from activated microglia.

Bactericidal effect[28-30]

Safranal and crocin, the main compounds responsible for the flavouring and colouring are capable of exhibiting bactericidal effect in the order of 8-16 mg/mL and 64-128 mg/mL for safranal and crocin, respectively. These data suggest that these compounds, and probably their chemical relatives, are involved in the antibacterial activity of saffron, and that this effect can significantly reduce the risk of food contamination with Salmonella by this spice.

Effect on coronary artery disease[31]

Fifty milligrams of saffron dissolved in 100 ml of milk was administered twice a day to human subjects as reported in an Indian study published in 1998. The significant decrease in lipoprotein oxidation susceptibility in patients with coronary artery disease (CAD) indicates the potential of saffron as an antioxidant.

Effect on learning behavior and long-term potentiation[32-37]

Several Japanese studies have reported that 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. These results suggest that oral administration of saffron may be useful as treatment for neurodegenerative disorders and related memory impairment. Recently, it was shown that crocin isolated from saffron exhibits anti-apoptotic action in PC-12 cells treated with daunorubicin. These findings suggest that crocin inhibits neuronal death induced by both internal and an external apoptotic stimulus in highly differentiated cells (neurons). This selective behavior suggests important therapeutic implications, related to the fact that programmed cell death is reduced in cancer and increased in neurodegenerative disease.

Anti cancer activity[38-48]

Different hypotheses for the modes of anticarcinogenic and antitumor actions of saffron and its components have been proposed. One of the mechanisms for the antitumor or anticarcinogenic action of saffron and its components is the inhibitory effect on cellular DNA and RNA synthesis, but not on protein synthesis. A second suggested mechanism for the antitumor action of saffron and its constituents is the inhibitory effect on free radical chain reactions, because most carotenoids are lipid-soluble and might act as membrane-associated high-efficiency free-radical scavengers, which is connected with their antioxidant properties. A third proposed mechanism by which the saffron extract exerts its antitumor effect is the metabolic conversion of naturally occurring carotenoids to retinoids, but recently, it was reported that conversion carotenoids to vitamin A is not a prerequisite for anticancer activity . A fourth suggested mechanism is that the cytotoxic effect of saffron is connected with interaction of carotenoids with topoisomerase II, an enzyme involved in cellular DNA-protein interaction. Recently, several other mechanisms for the antitumor effect of saffron and its constituents have also been proposed. It was demonstrated that a novel glucoconjugate, isolated from corm and callus extract of saffron, caused swelling and local plasma membrane evagination, and it was suggested that cytotoxicity is mediated via extracellular fluid uptake. It was also reported that saffron contains lectins, and it might also be suggested that antitumor activity of saffron is mediated via lectins. Treatment of tumor cells with saffron resulted in an increase in the level of intracellular sulphydryl compounds, and this could be one explanation for the potentiation of saffron cytotoxicity. Another suggested mechanism is that cytotoxic effect of carotenoids from saffron is mediated via apoptosis. Interesting studies indicate that encapsulation in amorphous polymer matrices of saffron extracts or saffron carotenoids greatly improves their stabilities and enhances their antitumor effects. More recently, it was shown that γ-irradiation, necessary for microbial decontamination, did not produce significant qualitative changes of volatile essential oil constituents of saffron, but induced a slight decrease in glycosides and an increase in aglycone content in carotene constituents of saffron. This relative stability of saffron to irradiation should also be taken to account in the search for an explanation of the chemopreventive potential of this spice. Thus, although several hypotheses have been put forward, the exact mechanism(s) of anticarcinogenic and antitumor effects of saffron and its main constituents are not clear at present.

Anticonvulsant effect[49]

In Iranian traditional medicine, saffron had been used as an anticonvulsant remedy. Recently, in experiments with mice using maximal electroshock seizure (MES) and pentylenetetrazole (PTZ) tests, Iranian scientists have demonstrated that the aqueous and ethanolic extracts of saffron possess anticonvulsant activity. These authors suggested that saffron extracts might be beneficial in both absence and tonic clonic seizures.

Ophthalmic[50,51,52]

In vitro experiments demonstrated a concentration-dependent protective effect of the carotenoid, crocin and its analogs on animal retina. Increased blood flow in the retina and choroid has been demonstrated. As a dietary supplement, saffron extract prevented retinal damage in rats, and it may have a role in the treatment of ischemic retinopathy and age-related macular degeneration.

Other uses

Saffron is also used for treating various skin ailments, skin fairness, indigestion, diarrhea, nausea, vomiting, body pains, nerve weakness, dysurea, impotency, erectile dysfunction, menstrual disturbances, fever, psoriasis[53] etc.

Conclusion:

Nature has gifted our planet earth with millions of species of the plants which are scientifically important. One among them being *Crocus sativus.* This plant is a boon to the human society. Therefore, the herbs are to be used for the treatment of any diseases and proper researches has to be carried out to prove it less harmful than the allopathic medicines. In this review, we have tried to present the important and the most recent findings on the uses of the plant, *Crocus sativus*.

References

1. Abdullaev, F.I. 1993. Biological effects of saffron. BioFactors. 4: 83-86.

2. Abdullaev, F.I. 2004. Biomedical properties of saffron and its potential use in cancer therapy and chemoprevention trials. Cancer Det. Preven. 28 (6):426-432.

3. Shultes RE. The kingdom of plants. In: Thomson WAR, editor. Medicines from the earth. New York, NY: McGraw-Hill Book Co.; 1978. p. 208.

4. Rios JL, Recio MC,Giner RM, Manez S. an update review of saffron and its constituents, 1996;10:189-93.

5. Duke, JA. Handbook of Medicinal Herbs. Boca Raton, Florida: CRC Press, 1985.

6. Deo, B. (2003). Growing saffron — The world's most expensive spice. Crop & Food Research, 20, 1−4.

7. Akhondzadeh S, et al., Comparison of Crocus sativus and imipramine in the treatment of mild to moderate depression: a pilot double-blind randomized trial, Biomed Central Complementary and Alternative Medicine 2004; 4(1): 12.

8. Hill, T. (2004). The contemporary encyclopedia of herbs and spices: Seasonings for the global kitchen. Hoboken: John Wiley & Sons, Inc.
9. ISO Technical Specifications 3632-1/2. (2003). Saffron (Crocus sativus L.). Part 1: Specifications and Part 2: Test methods.
10. Noorbala AA, Hydro-alcoholic extract of Crocus sativus versus fluoxetine in the treatment of mild to moderate depression: a double-blind, randomized pilot trial, Journal of Ethnopharmacology 2005; 97(2): 281–284
11. Bucheker, R.; Eugster, C. H. Absolute configuration of picrocrocin. Helv. Chim. Acta 1973, 56, (3), 1121-1125.
12. Cadwallader, K.R.; Back, H.H.; Cai, M.; ACS Symposium Series, No. 166 (Spices), American Chemical Society, Pub., Washington DC, 1997, pp.66-79.
13. Teale; Stephen A.; Webster; Francis X.; Zhang; Aijun, New aggregation pheromone for the bark beetle Ips pini and uses thereof , United States Patent 5,167,955, December 1, 1992
14. Aslami, H.M. 2006. Saffron from Planting to Harvesting to Processing. 1st National Conference on Saffron, Heart, Afghanistan.
15. Rios, J. L., Recio, M. C., Giner, R. M., & Manez, S. (1996). A update review of saffron and its active constituents. Phytotherapy Research, 10, 189−193.
16. Alonso, G. L., Salinas, M. R., Garijo, J., & Sanchez-Fernadez, M. A. (2001). Composition of crocins and picrocrocin from Spanish saffron (Crocus sativus L.). Journal of Food Quality, 24(3), 219−233.
17. Carmona, M., Zalacain, A., Salinas, M. R., & Alonso, G. L. (2007). A new approach to saffron aroma. Critical Reviews in Food Science and Nutrition, 47, 145−159.
18. Maggi, L., Carmona, M., del Campo, C. P., Kanakis, C. D., Anastasaki, E., Tarantilis, P. A., et al. (2009). Worldwide market screening of saffron volatile composition. Journal of the Science of Food and Agriculture, 89(11), 1950−1954
19. Martin, G. 2002. Evaluation of the developmental toxicity of crocetin on *Xenopus* Food Chem. Toxicol . 40(7):959-964.

20. Becker RE, Greig NH (2008) Alzheimer's disease drug development in beyond: problems and opportunities. Curr Alzheimer Res 5:346–357.
21. Tsuno N (2009) Donepezil in the treatment of patients with Alzheimer's disease. Expert Rev Neurother 9:591–598.
22. Akhondzadeh Basti, A., Moshiri, E., Noorbala, A., Jamshidi, A., Abbasi, S. H., & Akhondzadeh, S. (2007). Comparison of petal of Crocus sativus L. and fluoxetine in the treatment of depressed outpatients: A pilot double-blind randomized trial. Progress in Neuro-Psychopharmacology & Biological Psychiatry, 31(2), 439−442.
23. Akhondzadeh, S., Fallah-Pour, H., Afkham, K., Jamshidi, A., & Khalighi-Cigaroudi, F. (2004). Comparison of Crocus sativus L. and imipramine in the treatment of mild to moderate depression: A pilot double-blind randomized trial. BMC Complementary Alternative Medicine, 4, 12.
24. Kim, Y.K., Jung, J.S., Lee, S.H., Kim, Y.W., 1997. Effects of antioxidants and Ca2+ in cisplatin-induced cell injury in rabbit renal cortical slices. Toxicol. Appl.Pharmacol. 146, 261–269.
25. Limaye, P.V., Raghuram, N., Sivakami, S., 2003. Oxidative stress and gene expression of antioxidant enzymes in the renal cortex of streptozotocin induced diabetic rats. Mol. Cell. Biochem. 243, 147–152.
26. Kaur, G., Han, S.J., Yang, I., Crane, C., 2010. Microglia and central nervous system immunity. Neurosurg. Clin. N. Am. 21, 43–51.
27. Graeber, M.B., Streit, W.J., 2010. Microglia: biology and pathology. Acta Neuropathol. 119, 89–105.
28. Sagoo, S. K., Little, C. L., Greenwood, M., Mithani, V., Grant, K. A., McLauchlin, J., et al. (2009). Assessment of the microbiological safety of dried spices and herbs from production and retail premises in the United Kingdom. Food Microbiology, 26, 39-43.
29. Gustavsen, S., & Breen, O. (1984). Investigation of an outbreak of Salmonella oranienburg infections in Norway, caused by contaminated black pepper. American Journal of Epidemiology, 119, 806-812.

30. Cosano, I., Pintado, C., Acevedo, A., Novella, J., Carmona, M., de la Rosa, C., et al. (2009). Microbiological quality of saffron from the main producer countries. Journal of Food Protection, 72, 2217-2220.
31. Verma SK, Bordia A. Antioxidant property of saffron in man. Indian J Med Sci 1998; 52(5):205–7.
32. Abe K, Saito H. Effects of saffron extract and its constituent crocin on learning behaviour and long-term potentiation. Phytother Res 2000; 14(3):49–52.
33. Abe K, Suguira M, Yamaguchi S, Shoyama Y, Saito H. Saffron extract prevents acetaldehyde-induced inhibition of long-term potentiation in the rat dentate gyrus in vivo. Brain Res 1999;851(1–2):287–9.
34. Zhang Y, Shoyama Y, Sugiura M, Satto H. Effects of Crocus sativus L. on the ethanol-induced impairments of passive avoidance performances in mice. Biol Pharm Bull 1994;17(2):217–21.
35. Sugiura M, Shoyama Y, Saito H, Abe K, Crocin. (crocetin di-gentiobiose ester) prevents the inhibitory effect of ethanol on long-term potentiation in the dentate gyrus in vivo. JPET 1994;271(2):703–7.
36. Sugiura M, Shoyama Y, Saito H, Nishiyama N. Crocin improves the ethanol-induced impairment of learning behaviors of mice in passive avoidance tasks. Proc Jpn Acad 1995;71(ser B):319–24.
37. Sugiura M, Saito H, Abe K. Ethanol extract of Crocus sativus L. antagonizes the inhibitory action of ethanol on hippocampal long-term potentiation in vivo. Phytother Res 1995;9:100–4.
38. Hans peterW, Deuter M, Imilda E: Chemoprevention of tobacco smoke induced lung carcinogenesis in mice. Carcinogenesis 21: 977–82, 2000.
39. Anto RJ, Mukhopadyah A, Denning K, Aggarwal BB: Curcumin induces apoptosis through activation of caspase-8, BID cleavage and cytochrome *c* release: its suppression by ectopic expression of Bcl-2 and Bcl-xl. Carcinogenesis 23: 143–50, 2002.
40. Stephen S, Pramod Upadhaya, Mingyao Wang, Robin L. Bliss, Edward J. Mcintee, Patrick MJ Kenney: Inhibition of lung tumorigenesis in A/J mice by N-acetyl-S-(N-2-phenethylthiocarbamoyl)-L- cysteine and myo-inositol, individually and in combination. Carcinogenesis 29: 1455–1461, 2002.

41. Demming-Adams B, Gilmore AM, Adams WW: *In Vivo Functions Of Carotenoids In Higher Plants*, FASEB Journal 10: 403–412, 1996.

42. Jagadeswaran R, Thirunavukkarasu C, Gunasekaran P, Nalini Ramamurthy, Sakthisekaran D: *In vitro* studies on the selective cytotoxic effect of crocetin and quercetin. Fitoterapia 71: 395–399, 2000.

43. Abdullaev FI: Cancer chemopreventive and tumoricidal properties of saffron (*Crocus sativus*,L*)*. Exptl Biol Med 227: 20–5, 2002.

44. Chang VC, Lin YL, Lee MJ, Show SJ, Wang CJ: Inhibitory effect of crocetin on benzo(a)pyrece genotoxicity and neoplastic transformation in C3H1OT1/2 cells. Anticancer Res 765: 3603–3608, 1996.

45. Nair SC, Pannikar B, Pannikar KR: Antitumour activity of saffron (*Crocus sativus*). Cancer Lett 57: 109–14, 1991.

46. Salomi MJ, Nair SC, Panikkar PR: Cytotoxicity and nonmutagenicity of *Nigela sativa* and saffron (*Crocus sativus*) in vitro. Proc Ker Congr 5: 244, 1991.

47. Tarantilis PA, Tsoupras G, Polissiou M: Determination of saffron (*Crocus sativus*. L) components in crude plant extract using HPLC-UV Visible photodiode-array detection-mass spectrometry. J Chromatography 699: 107–18, 1995.

48. Daly ES: Protective effect of cystein and vitamin A, *Crocus sativus* and *Nigela sativa* extracts on cysplatin induced toxicity in rats. J Pharm Belg 53: 93–5, 1998.

49. Hosseinzadeh H and Khosravan V, *Anticonvulsant effects aqueous and ethanolic extracts of Crocus sativus stigmas in mice*, Archives of Iranian Medicine 2002; 5: 44–47.

50. . Xuan B, Zhou YH, Li N, Min ZD, Chiou GC. Effects of crocin analogs on ocular blood flow and retinal function. J Ocul Pharmacol Ther . 1999;15(2):143-152.

51. Laabich A, Vissvesvaran GP, Lieu KL, et al. Protective effect of crocin against blue light- and white light-mediated photoreceptor cell death in bovine and primate retinal primary cell culture. Invest Ophthalmol Vis Sci. 2006;47(7):3156-3163.

52. Maccarone R, Di Marco S, Bisti S. Saffron supplement maintains morphology and function after exposure to damaging light in mammalian retina. Invest Ophthalmol Vis Sci2008;49(3):1254-1261.

53. Brown AC, Hairfield M, Richards DG, McMillin DL, Mein EA, Nelson CD. Medical nutrition therapy as a potential complementary treatment for psoriasis—five case reports. AlternMedRev2004;9(3):297-307.

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