# Chemistry, Pharmacology and Medicinal Property of Saffron as A Viable Agent in the Treatment of Prostate, Pancreatic or Other Types of Cancer

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## Abstract

Sage (Salvia) species is known as the Functional Novel Natural Medicine, Salvia Extract are considered important for drug development, because they are reported to have Pharmacological activity in the Asia, Middle East especially China and India. For a long time Salvia has been used in traditional medicine for the relief of pain, protecting the body against oxidative stress, free radical damages, angiogenesis, inflammation, bacterial and virus infection, etc. Several studies suggest that sage might potentially provide novel natural treatments for the relief or cure of many serious and life threatening diseases in addition to treating minor common illnesses such as depression, dementia, obesity, diabetes, lupus, heart disease and cancer. This plant is used as Medicine in Asia, Africa, Middle East, South America, and some Countries in Europe. This article presents comprehensive analysis information on botanical, chemical and Pharmacological aspect of Sage (Saliva).

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***Index terms***— sage (salvia species), traditional remedies, pharmacological property.

## 1 Introduction

affron is one of the most expensive spices in the world, derived from the dry stigmata of Crocus sativus L., a member of the Iridaceae (Iris) family (Peter, 2000). Saffron is hand-harvested during the flowering season. This process is very time consuming which involves picking the stigmata by hand and then carefully drying the stigmata to produce a quality product (Peter, 2000). One stigma of saffron weighs about 2 mg and each flower has three stigmata. In order to obtain 1 kg of spice, 150,000 flowers must be carefully picked (Peter, 2000). Saffron (Crocus sativus L.) is mostly cultivated in Spain, Iran, India, Greece, Authors ? ? ? ?: President, Pars Bioscience, Leawood, Kansas, United States. e-mails: rafie@parsbioscience.com, soheila@parsbioscience.com, Mohsen @parsbioscience.com mina @parsbioscience.com China and some other European and Asian countries (Peter, 2000). The quality and chemical composition of saffron are affected by the region in which saffron is grown (Peter, 2000), the drying process, the conditions of packaging, storage of saffron, and the analytical extraction methods which have been used (Caballero-Ortega et al., 2007).

The nutritional supplement value of Saffron (Crocus sativus L.) which was provided by Pars Bioscience LLC in powder form, to Covance, Madison. WI laboratory was analyzed and shown to include the following contents: NL-Proximate (moisture, ash, protein, fat, total carbohydrates, calories, and calories from fat), results of these analyses are detailed (Table 1). Vitamins (vitamin A, C, and folic acid), and minerals (calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium, and zinc), are detailed in (Table 2). The results of analysis of saffron fatty acid profile are detailed in (Table 3). Also to identify the major components of Saffron, the analysis of the saffron was conducted by grinding and extracting saffron, and analyzing the extract using HPLC/UV-MS analysis by Pars Bioscience which is shown in (Figure 1).

To date, the following components have been identified in saffron: safranal which is the principal substance responsible for the aroma of saffron, dimethylcrocetin, crocetin esters (cis-crocetin, and trans crocetin), picrocrocin is the substance responsible for bitter taste of saffron (Peter, 2000), crocin which are the major components responsible for the color of saffron, trans-crocin-2, trans-crocin-2', trans-crocin-3, trans crocin-4, cis-crocin-1, cis-crocin-2, cis-crocin-3, ciscrocin-4, cis-crocin-5, anthocyanin, carotene, and lycopene (Peter, 2000 The main uses of saffron are in cooking, food coloring, in perfume and Cosmetics (Peter, 2000;Abdullaev, 2002). Saffron has also traditionally been regarded as a highly valued medicinal plant to treat wide variety of ailments such as depression, respiratory problems, colds, asthma, and heart diseases. (Abdullaev and Espinosa-Aguirre, 2004). More recently, as the current culture has been changing, more researches have been done analyzing the effects of traditional herbs and spices as treatment for the severe diseases (Abdullaev, 2002).

Several studies have been performed on the use of saffron or it's constituents in the treatment of a variety of cancers including colorectal cancer cells (HCT-116, SW-480, and HT-29) , non-small cell lung cancer (NSCLC) cells (Aung et al., 2007) The commonly known Saffron contains more than 150 volatile and aroma-yielding compounds. It also has many nonvolatile active components (Surh et al., 2005), many of which are carotenoids, including zeaxanthin, lycopene, and various ?-and ?-carotenes. However, saffron's golden yellow-orange color is primarily the result of ?-crocin. This crocin is transcrocetin di-(?-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 (Schmidt et al., 2007). Crocins themselves are a series of hydrophilic carotenoids that are either monoglycosyl or diglycosyl polyene esters of crocetin (Escribano et al., 1996). Crocetin is a conjugated polyene dicarboxylic acid that is hydrophobic, and thus oil-soluble. When crocetin is esterifies with two water-soluble gentiobioses, which are sugars, a product results that is it water-soluble. The resultant ?-crocin is a carotenoid pigment that may comprise more than 10% of dry saffron's mass. The two esterifies gentiobioses make ?crocin ideal for coloring water-based and non-fatty foods such as rice dishes (Schmidt et al., 2007).

# 2 Esterification reaction between crocetin and gentiobiose. Components of ?-crocin:

The bitter glucoside picrocrocin is responsible for saffron's flavor. Picrocrocin (chemical formula: C16H26O7; systematic name: 4-(?-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 pesticide 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 terrene aldehyde safranal. The reddish-colored zeaxanthin is, incidentally, one of the carotenoids naturally present within the retina of the human eye (Schmidt et al., 2007).

When saffron is dried after its harvest, the heat, combined with enzymatic action, splits picrocrocin to yield D-glucose and a free safranal molecule (Surh et al., 2005). Safranal, a volatile oil, gives saffron much of its distinctive aroma (Escribano et al., 1996;Schmidt et al., 2007). Safranal is less bitter than picrocrocin and may comprise up to 70% of dry saffron's volatile fraction in some samples (Escribano et al.,1996). A second element underlying saffron's aroma is 2-hydroxy-4, 4, 6-trimethyl-2, 5-cyclohexadien-1-one, the scent of which has been described as "saffron, dried hay like". Chemists found this to be the most powerful contributor to saffron's fragrance despite its being present in a lesser quantity than safranal (Escribano et al., 1996). 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 in order to minimize contact with atmospheric oxygen. Saffron is somewhat more resistant to heat.

# 3 II.

# 4 Discussion

Saffron is a very valuable spice with many traditional medicinal usages. The high amount of carotenoids in saffron including crocin, crocetin and dimethylcrocetin are responsible for some biological functions of saffron. Most of the studies on the effect of saffron, indicates the significant inhibitory effects of the Crocus sativus components on the synthesis of nucleic acids in different human cancer cell lines (Afshari et al., 2005).

As the studies have shown, diets rich in antioxidants will lower the risk of several chronic diseases and protect the body against the development and growth of tumor cells. Therefore, Saffron and it's constituents with their antioxidant properties can act as a protecting agent for the prevention of some serious diseases like cancer (Premkumar et al., 2006).

Crocus sativus L. extract (CSE) used in several studies were prepared from stigmas of Crocus sativus. Crocus sativus L. contains several pharmacologically active constituents. Saffron has antioxidant properties; these have been showed in humans, where saffron (50 mg, twice a day) decreases the lipoprotein oxidation susceptibility (Verma and Bordia, 1998). Also crude methanol extract of saffron and its compound crocin have been exhibited high antioxidant and scavenging properties (Assimopoulou et al., 2005).

The oral administration of the saffron ethanolic extract (200 mg/kg body wt) increased the life span of Swiss albino mice intraperitoneally transplanted with sarcoma-180 (S-180) cells, Ehrlich ascites carcinoma (EAC) or Dalton's lymphoma ascites (DLA) tumors (Nair et al., 1991), and it has an inhibitory effect on chemical carcinogenesis in mice using two stage assay system (Salomi et al., 1991).

Crocetin protects body against free radicals and the studies have shown its role as an antitumor agent (Magesh et al., 2006).

The effect of crocetin on two different types of animal tumors, Skin papillomas and Rous sarcoma have been studied and shown that crocetin decreased the number of tumor cells and delayed the onset of the tumors as well (Grainer et al.,1976). A recent study showed that crocetin (20 mg/kg) reverted the level of lipid peroxidation induced by Benzo (a) pyrene B (a) b, also increased the activities of the enzymic antioxidants and glutathione metabolizing enzymes. Showing that crocetin is a scavenger of free radicals and a potent antitumor agent (Magesh et al., 2006).

Crocin inhibits the growth of HeLa cells and suggested apoptosis induction and showed important inhibitory effects on skin-tumor initiation and promotion induced by 7, 12-dimethylbenz[a] anthracene (DMBA) and 12-0-tetradecanoylphorbol-13-acetate (TPA), respectively (Escribano et al., 1996).

Many studies during the last decade, demonstrated the inhibitory effect of saffron and its components in vitro, on several cancer types like carcinoma, leukemia, prostate, pancreatic, and several other tumor cells **??**Jafarova et al., 2006).

# 5 III.

# 6 Toxicity of Saffron

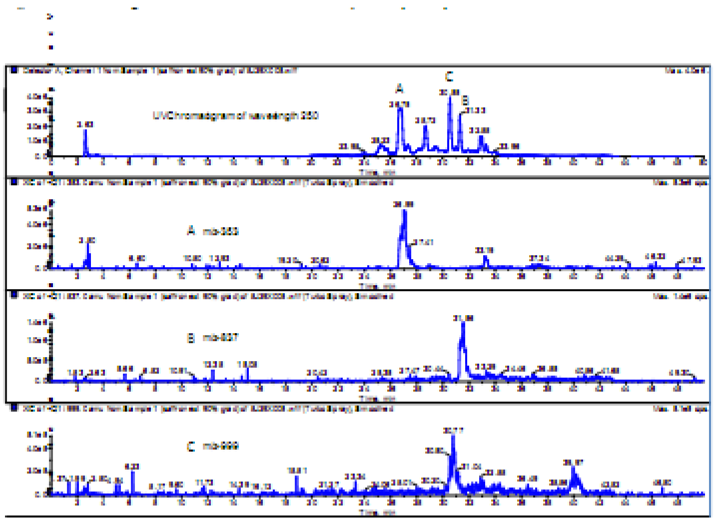
There are no reports of negative side effects as far we know associated with Saffron despite of their usages for many centuries. The toxicity of saffron has been studied by many researchers and the levels of toxicity found to be very low. The studies showed that the concentration of 0 to 5gr/kg was non-toxic to mice (Chryssanthi et al., 2007). Also hematological and biochemical studies on the toxicity of saffron extract indicates that there are no severe toxicological sign found in kidney, liver or bladder within the normal range of use (Nair et al., 1991).

IV.

# 7 Conclusion

The objective of this paper has been the recent advance in the exploration of saffron as phytotherapy and to illustrate its potential as a therapeutic agent. Saffron may represent natural, safe and effective treatments for many diseases and their symptoms. In recent decades, with the increase of pharmacological knowledge about the beneficial effects of saffron especially three major component that we analysis and identify in Figure 1, these herbal medicines with antibacterial, anti-oxidant, anti-inflammatory, free radical scavenging and anti-tumor activities, have found to be very effective in the development of novel natural drugs to prevent, control and treat many minor health problems as well as more serious and complicated diseases such as diabetes, Alzheimer's and cancer. It must be kept in mind that clinicians should remain cautious until more definite studies demonstrate the safety, quality and efficacy of saffron and saffron component. For these reasons, extensive pharmacological and chemical experiments, together with human metabolism should be focus of our next studies and further potential of saffron to be employed in new therapeutic drugs and provide a basis for future research on the application of medicinal plants. [1] [2]

Figure 1:



**1**

Figure 2: Figure 1 :

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Figure 3: Figure 2 :

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Figure 4: Figure 3 :

4

Figure 5: Figure 4 :

**1**

Figure 6: Table 1 :

**2**

| Analysis | Results (per 100 g serving size) |
|---|---|
| Moisture | 7.7 g |
| Ash | 4.6 g |
| Protein | 15.6 g |
| Fat | 5.5 g |
| Total Carbohydrates | 69.6 g |
| Calories | 363 Cal |
| Calories from Fat | 22.1 Cal |
| Vitamins | D D D D ) B |
| Vitamin A Vitamin C Folic Acid Minerals Calcium Copper Iron Magnesium Manganese Phosphorus Potassi | |

Figure 7: Table 2 :

**3**

| Analysis | Results (per 100 g serving size) |
|---|---|
| 8:0 Caprylic | < 0.003 g |
| 10:0 Capric | < 0.003 g |
| 12:0 Lauric | 0.011 g |
| 14:0 Myristic | 0.012 g |
| 14:1 Myristoleic | < 0.003 g |
| 15:0 Pentadecanoic | 0.003 g |
| 15:1 Pentadecenoic | < 0.003 g |
| 16:0 Palmitic | 0.425 g |
| 16:1 Palmitoleic | 0.008 g |
| 17:0 Heptadecanoic | 0.006 g |
| 17:1 Heptadecenoic | < 0.003 g |
| 18:0 Stearic | 0.030 g |
| 18:1 Oleic | 0.314 g |
| 18:2 Linoleic | 1.20 g |
| 18:3 Gamma Linolenic | < 0.003 g |
| 18:3 Linolenic | 0.394 g |
| 20:0 Arachidic | < 0.003 g |
| 20:1 Eicosenoic | 0.012 g |
| 20:2 Eicosadienoic | 0.036 g |
| 20:3 Eicosatrienoic | < 0.003 g |
| 20:4 Arachidonic | < 0.003 g |
| 22:0 Behenic | 0.008 g |
| Saturated Fat | 0.471 g |
| Monounsaturated Fat | 0.321 g |
| Polyunsaturated Fat | 1.56 g |
| Sum of Fatty Acids | 2.46 g |

*[Note: Chemistry and Chemical Composition Structure of picrocrocin (Surh et al., 2005) : ?-D-glucopyranose derivative]*

Figure 8: Table 3 :

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