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Review

Main chemical compounds and pharmacological activities of stigmas and tepals of 'red gold'; saffron

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A R T I C L E I N F O

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A B S T R A C T

Background: *Crocus sativus* L. (saffron) belongs to Iridaceae family which is commonly cultivated in Asia, Europe and America. The commercial product and use of saffron comes from the dried stigmas which gives a yellow color, bitter taste and intense aroma. This spice has been used since ancient times because of its aromatic, flavor and coloring properties along with its functional characteristics. Saffron is applied in many food products as well as being utilized in medical treatments.

Scope and approach: Lately, scholars have focused on using herbal medicine for the healing of various diseases such as, tumor and heart-related disorders, along with functions such as antitussive, antioxidant, anti-inflammatory and antinociceptive, antidepressing, memory enhancing and treatment of Alzheimer's disease. The main purpose of this review is to highlight the recent advances of experimental *in vitro* and *in vivo* investigations focused on the stigmas and tepals of saffron, chemical composition, and application of its principal ingredients (crocin, picrocrocin and saffranal) in treatment of different diseases.

Key findings and conclusions: Despite the main usage of saffron is for culinary purposes, it also has significant applications in pharmaceutical and clinical fields. Saffron contains a number of bioactive components which are believed to be largely responsible for its health promoting properties including treating various disorders like asthma, atherosclerosis, painful menstrual periods and even depression; its role as an antioxidant with anti-cancerous and memory enhancing properties; its effectiveness at treating mild to moderate depression; and its high efficiency in lowering the levels of cholesterol and triglycerides in the blood of people suffering from cardiovascular diseases. The clinical findings suggest that saffron is a safe and effective plant. In the last decade, saffron has been studied for its unique properties to be employed within medical fields to treat many diseases.

1. Introduction

Filaments of saffron are made from the dried and dark red stigmas of *Crocus sativus* L. flowers (an autumn-flowering geophyte) belonging to the Iridaceae family. Za'afarn is the original Persian name of saffron, meaning yellow flowers (Ramadan, Soliman, Mahmoud, Nofal, & Abdel-Rahman, 2010). Also, since it is the most expensive spice in the whole world, saffron has been named 'red gold'. Another point is that harvesting and post-harvest operations are normally performed without mechanical equipment; in fact picking of saffron flowers is done daily by hand, lasting only 2–3 weeks (Molina, Valero, Navarro, Guardiola, & García-Luis, 2005).

Cultivation history of saffron returns to 2500–1500 BCE. Iran, saffron's origin, owns more than 80% of its world's production, with the planting implemented mainly in the South Khorasan province with cold winters and hot summers even without the application of mineral fertilization or pesticides) although it could be cultivated around the world e.g. in China, Spain, Italy, India, Pakistan, Turkey, France, Switzerland and Greece (Cavuolu, Erkel, & Sülüolu, 2009; Hosseinzadeh, Ziaee, & Sadeghi, 2008b; Pitsikas, 2016; Bolandi & Ghoddusi, 2006).

Annual production of saffron throughout the world exceeds 220,000 kg. About 110000 to 165000 flowers, nearly 80 kg flowers, are needed to produce 1 kg of dried saffron (Gracia, Perez-Vidal, & Gracia-López, 2009; Husaini et al., 2009).

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Quality of this merchandise is closely related to the concentration of its major constituents, in close relationship with the different parts of saffron flowers and methods of its processing including drying, extraction, separation, storage and quantification stages (Caballero-Ortega, Pereda-Miranda, & Abdullaev, 2007; D'Archivio, Giannitto, Maggi, & Ruggieri, 2016). Main biologically active constitutes of saffron are crocetin and its glycosidic form, crocin as dye materials, saffranal (spicy aroma), and picrocrocin giving bitter taste (Milajerdi, Djafarian, & Hosseini, 2016). These compounds are derivative of oxidative fractionation of a carotenoid called zeaxanthin (Husaini et al., 2009). Indeed, diverse organoleptic properties and the final value of saffron are ascribed to the relative percentage of these three main components. In following sections, we will explore chemical constituents, pharmacological effects *in vivo* and *in vitro* assays plus the applications and toxicity rate of stigma and tepals of saffron.

2. Applications of saffron in the food and pharmaceutical industry

Authenticated sources have reported that planting *crocus sativus* was commonplace in the past. In ancient times, Egyptians and Romans got used to deploy saffron as an odor in perfume, as a coloring agent in expensive clothes and as a spice for culinary purposes. Saffron, as a popular medicinal herb, is also widely used in food flavoring and coloring, cosmetics, textile dye, perfume and pharmaceutical industry (Tarantilis, Beljebbar, Manfait, & Polissiou, 1998).

These days, the usage of plant components as natural ingredients in food products is a commercial fact. In the food industry, saffron is used as an odoring, tasting and coloring agent in cream, cheese, butter, ice cream, bouillabaisse, chicken, bread, soups, sauces, puddings, rice and paella in industrial scales (Tarantilis, Polissiou, & Manfait, 1994; Nilkashi, Gadiya, & Abhyankar, 2011). Recently, there have been some efforts for the extraction of bioactive components from stigma (Sarfarazi, Jafari, & Rajabzadeh, 2015) and tepals (Mahdavi Khazaei et al., 2016) of saffron along with micro/nano encapsulation of these nutraceuticals (Mahdavee Khazaei, Jafari, Ghorbani, & Hemmati Kakhki, 2014; Rajabi, Ghorbani, Jafari, Sadeghi Mahoonak, & Rajabzadeh, 2015; Esfanjani, Jafari, Assadpoor, & Mohammadi, 2015; Mehrnia, Jafari, Makhmal-Zadeh, & Maghsoudlou, 2016; Jafari, Mahdavi-Khazaei, & Hemmati-Kakhki, 2016).

Saffron has traditionally been used as a known cure against many diseases, for instance as an aphrodisiac agent, anticatarrhal, laxative, eupeptic, timulant, antispasmodic, antidepressant, a respiratory decongestant, nerve sedative, stomachic, expectorant, emmenagogue, carminative, diaphoretic, anodyne, gingival sedative, galactogogue, amenor-rhea, dysmenorrhea and in treatment of bladder, liver, kidney, eye, acne, and several skin diseases (Hosseinzadeh et al., 2008b; Pitsikas et al., 2007; Pitsikas, Boultadakis, Georgiadou, Tarantilis, & Sakellaridis, 2008). Other penetration fields of this panacea are ascites, naevus, freckles, ulcer, headache, cold, smallpox, scarlet fever, bronchitis, pharyngopathy, vomiting, asthma, myopia, discomfort of teething infants, cholera, inflammation, melancholia, epilepsy, menstruation disorder, painful labor, strengthening the heart and memory enhancer (Nilkashi et al., 2011).

In traditional medicine, extract of *C. sativus* has been found useful in the treatment of cough. In details, it was reported that the ethanol extract of saffron stigma (100–800 mg/kg) and saffranal (0.25–0.75 ml/kg) in male and female guinea pigs significantly reduced cough numbers in 10-min spans (Hosseinzadeh & Ghenaati, 2006).

3. Chemical composition and structure of saffron

Chemical composition of saffron is moisture (10%w/w), protein (12%w/w), fat (5%w/w), minerals (5%w/w), mainly calcium, phosphorous, potassium, sodium, zinc and manganese in small quantities, crude fibre (5%w/w), and carbohydrates (63%w/w) including starch, reducing sugars (glucose, fructose, gentiobiose and a small quantity of xylose and ramnose), pentosans, gums, pectin, and dextrins (Habibi & Bagheri, 1989; Melnyk, Wang, & Marcone, 2010).

The saffron plant is made up basically from tepal and stigma, with the latter being the main component (Fig. 1). Saffron flowers are mostly made up of 2–3 cm triple stigmas in length, three anthers and six light purple tepals. The female sexual part of saffron flower consists of stigma, style, ovary, peduncle and its male part, stamens are yellow in color (Aytekin & Acikgoz, 2008).

4. Chemical composition of stigma

Commercial saffron is the dried red stigma and attached yellowish style. The weight of saffron stigma is approximately 2 mg, furthermore each normal flower of *Crocus sativus* L. has three stigmata separated from each other by hand after harvesting (Modaghegh, Shahabian, Esmaeili, Rajbai, & Hosseinzadeh, 2008; Tarantilis et al., 1998).

Chemical analysis has shown the presence of more than 150 components in saffron stigmas, which contain lipophilic and hydrophilic carbohydrates, proteins, amino acids, minerals, mucilage, starch, gums, vitamins (especially riboflavin and thiamine), pigments (crocin, alfa and beta carotenes, mangicrocin, xanthone-carotenoid glycosidic conjugate, anthocyanin, lycopene, flavonoids and zeaxanthin), alkaloids, saponins, saffranal (aromatic essence terpene) and picrocrocin (bitter flavor) together with other chemical compounds (Carmona, Zalacain, Sanchez, Novel la, & Alonso, 2006; Samarghandian and Borji, 2014; Singla & Bhat, 2011; Zarinkamar, Tajik, & Soleimanpour, 2011). The main components of stigma are crocetin, its glucosidic derivatives, crocins, picrocrocin, safranal (Rubio-Moraga, Trapero, Ahrazem, & Gómez-Gómez, 2010) and flavonoids including quercetin and kaempferol (Pitsikas et al., 2007).

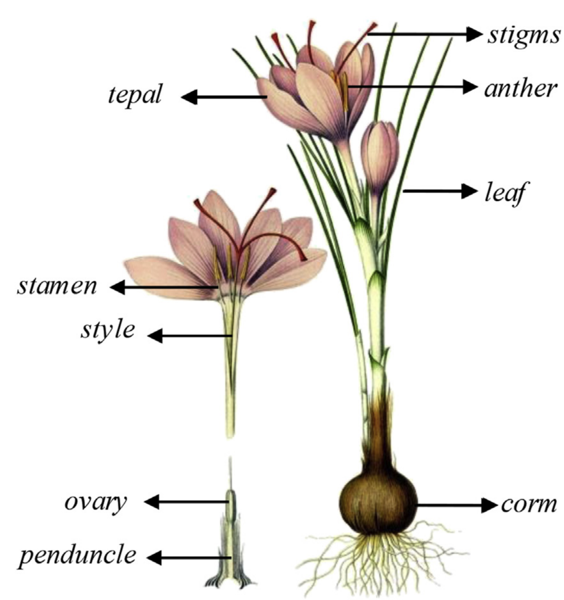

Fig. 1. Structure of different parts of saffron plant (Adapted from Rubio-Moraga et al., 2010; Ozdemir & Kilinc, 2008).