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Review Paper

Both sides of the saffron's coin

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Abstract

Saffron (*Crocus sativus* L.), a popular traditionally-used compound is known for its promising beneficial health effects. However, it has been reported to have a number of toxic effects in human and other animals. This paper aims to summarize saffron's beneficial and toxic effects. The findings suggest that sufficient precautions are needed in using saffron and its constituents as they have both beneficial and toxicological impacts on human.

Keywords: *Crocus sativus; saffron; traditionally-used compound; beneficial effects; toxicity.*

1. Introduction

Saffron (*Crocus sativus* L.) has been used as a food additive for its color, taste and odor since ancient times (more than 3000 years ago) (Thorndike 1929) To date, both saffron and a number of its derivatives have been reported for some important biological activities (Aung et al. 2007; Mousavi et al. 2009; Samarghandian et al. 2010; Milajerdi et al. 2016). In parallel, saffron and its derivatives also reported to have some toxicological effects (HosseinZadeh et al. 2013; Taheri et al. 2014; Riahi-Zanjani et al. 2015). Therefore, this review aims to report both types of effects of saffron and its derivatives.

2. Beneficial effects of saffron

It is used as an amulet, cardiac medicament (cardiotonic), sedative (Thorndike 1929; Encyc. Brit. 1974), carminative, diaphoretic, emmenagogue (Grisolia 1974), abortifacient (Martindale 1941), anticoagulant (Ferrence and Bendersky 2004), styptic, soothing agent (Ferrence and Bendersky 2004; Giaccio 2004; Tolner 2005), hypnotic, diuretic, aphrodisiac, immunostimulator, antipoisonous, tonic (cardiac, livo and nervine), carminative, diaphoretic, emmenagogue, lactogogue, febrifuge, stimulant, relaxant, anti-stress, anti-anxiety, (Rios et al. 1996), anti-bacterial, anti-fungal, analgesic, anti-spasmodic, emmenagogue, diaphoretic.; and used in kidney and liver (enlargement) problems (Baumann 1960), appetite, catarrhal infections, for melancholia, (Encyc. Brit. 1974), atherosclerosis (Gainer and Chisolm 1974), dyspnea, problems of eye (inflammation, painful eye, blue discoloration, morbid matters, corneal disease and cataract, purulent eye infection) and head, menstruation, delivery and painful urination (Blois and Spek 2005; Tolner 2005), earache, tooth-ache, ulcers (skin, mouth, genitalia), erysipelas (Ferrence and Bendersky 2004; Giaccio 2004; Tolner 2005), refreshing and strengthening drugs (Abrishami 1997; Abrishami 2004), invigorate the body, strengthen senses, mood disorders, intoxication and preventing hangovers, major external bleedings, obstructions inside brain, severe headaches, insomnia, conjunctivitis, respiratory diseases, gout and joints, uterus pain, ulcers, pleurisy, refresh facial skin, coughs, diaphragmitis (Abrishami 1997), general debility, alcoholism, inflammation, diabetes, children's disorders (unknown etiology), insect bites, stings, edema, acne, skin diseases, wounds, depression, mental disorders, weak eyesight, asthma, sore throat and cold, vomiting, dyspepsia, prolapse of anus, dysmennhorea, impotency (both male and female), arthritis, apoplexy, and neurasthenia. saffaran and its derived components (e.g. – safranal, crocin) is evident to exert anticancer effects in a numner of cancer cell lines (Salomi et al. 1991; Garc-Olmo et al. 1999; Abdullaev 2002; Trujillo-Jiménez et al. 2004; Aung et al. 2007; Mousavi et al. 2009; Samarghandian et al. 2010; Milajerdi et al. 2016).

It can the regulate menstrual cycle as well. It is used in anal pain, stomach and spleen problems. It is useful in day blindness, lacrimation and keratitis. As an anti-inflammatory agent it can be used for swellings, otitis and wounds. It can reduce the resistance of coronary arteries and can improve blood circulation. It can be used in case of broken bones, dislocated joints, sprains, painful joints, purpura, eczema, rheumatoid arthritis, and measles.

3. Toxicological effects of saffron and its derivatives

The lethal dose 50% (LD_{50}) values of saffron in mice are 4120 ± 556 mg/kg and 1.6 g/kg in oral (p.o.) intraperitoneal (i.p.), respectively (HosseinZadeh et al. 2013). For crocin (a component of saffron) the LD_{50} values found as 6 g/kg (i.p.) (HosseinZadeh et al. 2013), while more than 3 g/kg for oral (HosseinZadeh et al., 2010). For safranal (other components of saffron) the LD_{50}s was 5.53 to 21.42 ml/kg (p.o.) and 1.48 to 1.88 ml/kg (i.p.) in rats and mice (HosseinZadeh et al. 2013).

Repeated administration of saffron (i.p.: 350 to 3600 mg/kg; p.o.: 200 to 5000 mg/kg for 2-4 weeks) and its major constituents (stigma: (i.p.: 160 to 480 g/kg for 2 weeks); crocin: (i.p.: 15 to 180 mg/kg up to 4 weeks); safranal: (p.o.: 100 to 500 ml/kg for 3 weeks)) are also evident to alter hematological (e.g. – hemoglobin (Hb), hematocrit (HCT), red blood corpuscles (RBC), white blood corpuscles (WBC), and platelets) and biochemical (e.g. - alanine aminotransferase (ALT), aspartate amino-

transferase (AST), urea, uric acid, blood urea nitrogen (BUN), creatinine, cholesterol, triglycerides (TGs), lon-density lipoprotein (LDL), alkaline phosphatase (ALP), malondialdehyde (MDA), fasting blood sugar, amylase, Na^+, and gluthatione (GSH)) parameters, food intake, body weight, spermatogenesis index (e.g. - repopula-tion index (RI), spermatogenesis index (SI) and tubular differentiation index (TDI)), alteration in the kidney and alveolar size in rodents (Karimi et al. 2004; Mohajeri et al. 2007; Modaghegh et al. 2008; Hosseinzadeh et al. 2010; Khayatnouri et al. 2011; Mohamadpour et al. 2013; Rezaee and HosseinZadeh 2013; Fadai et al. 2014; Taheri et al. 2014; Eaton et al. 2015; Muosa et al. 2015; Riahi-Zanjani et al. 2015).

The aqueous extract of saffron (0.2 - 0.8 %) was evident to reduce the tail length, biparietal diameter, placental diameter and weight of fetal during gestational period in BALB/*c* mice in a dose dependent manner (Zeynali et al. 2009). On the other hand, crocin (i.p.: 200 and 600 mg/kg) and safranal (i.p.: 0.075 and 0.225 ml/kg) disrupted skeleton formation as well as adversely affected in the weight, length, growth, mandible and calvaria of fetuses in mice (Moallem et al. 2013). Crocetin (10 - 200 μM) was found to exert a teratogenic effect in frog (Xenopus) embryos, where a decreased in head-to-tail length and eye diameters was observed (Martin et al. 2002). Saffron is also evident to exert co-mutagenicity with BP (benzo[a]-pyrene) and 2AA (2-amino-antracene) in *Salmonella typhimurium* (Abdullaev et al. 2003).

Moreover, 400 mg saffron tablets are evident to de-crease in blood pressure (Modaghegh et al. 2008). Saffron is also found to increase the abortion rate in pregnant females (Ajam et al. 2014). Common adverse effects of saffron and its component products are: anxiety, appetite (decreased and increased), sedation, nausea, vomiting, headache, hypomania, dizziness, dry mouth, fatigue, restlessness, tachycardia, constipation, reflux, abdominal pain, drowsiness (daily and morning), nervousness, sexual dys-function, tremor, sweating, heart pounding, insomnia, and urinary retention (Akhondzadeh et al. 2004; Akhondzadeh et al. 2005; Basti et al. 2007; Akhondzadeh et al. 2010; Mansoori et al. 2011; Shahmansouri et al. 2014).

Thus, adequate precautions should be taken in using saffron and its constituents as it has both benefits and toxicological impacts on human and other animals.

Conflicts of interest

None declared.

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