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Review

A comprehensive characterisation of safflower oil for its potential applications as a bioactive food ingredient - A review

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ABSTRACT

Background: Safflower is a multiple purpose crop generally grown for oil production. The safflower oil is considered to be a better oil since it contains higher amount of oleic and linoleic acids than other oil seed crops. Safflower oil has numerous applications in food, cosmetics, pharmaceutical and feed industry. An added advantage of safflower oil is lower cost of production thus can become an alternate option for those who cannot afford to buy olive and other functional oils.

Scope and approach: This manuscript provides a comprehensive review on critical aspects of pharmacological and nutritional applications of safflower oil. A higher antioxidant activity renders better stability of safflower seed oil over extended storage period. Moreover, a higher content of omega six fatty acids makes it a healthier choice for consumption especially where olive oil being the only but costly choice. There has been a surge in developing innovative and efficient methods to extract safflower oil including super critical fluid and enzymatic extraction techniques.

Key findings and conclusions: A higher stability index makes it possible to encapsulate safflower oil or used it as a carrier in bioactive functional ingredient delivery systems. The functional properties of safflower oil can be used to treat skin infections, bone related disorders, menopause and atherosclerosis. Composition and distribution of phenolic contents of safflower oil has not been explored to its full potential. There is a need to conduct exclusive research on exploring the role of phenolic compounds in food and pharma industrial applications.

1. Introduction

Safflower (*Carthamus tinctorius* L.) is a valuable oilseed crop that is still to be exploited for its greater potential for oil and protein cake. It is cultivated in Asia, North America and South America (Mihaela, Josef, Monica, & Rudolf, 2013). It can be grown almost in every part of the world in diversified environments owing to its ability to withstand drought, strong winds, hail storms and flooding. Tap root system of this plant makes it an ideal crop for arid agricultural land or areas with seasonal rains. Safflower plants varies in length (30 cm–1.5 m) with globular flower heads of different color shades ranging from yellow to orange and red. There is a growing trend to develop new varieties of safflower with higher seed oil contents. Healthy fatty acid profile with high level of mono and polyunsaturated fatty acids is another focus of research for these varieties (Bart, Palmeri, & Cavallaro, 2010).

An increasing trend for safflower production has been observed over previous few years as evident from increasing crop land at the rate of 4.9% per annum. An average global yield of safflower seeds has varied from 805 to 872 kg ha^{-1} with an annual growth rate of

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0.97% (Fig. 1a). Inspite being grown as a minor crop, production of safflower has gone upto 867,659 tonnes commercially at global level for year 2014 with an increasing rate of 5.6% per annum (Fig. 1a). Safflower is grown in more than 60 countries, however India, Kazakhstan, Mexico, USA and Argentina (Fig. 1b) are the leading countries for its production (FAOSTAT, 2015). The major production regions for this crop are America and Asia with a share of 93% cumulative production. There is a great potential in other regions to grow this crop especially Oceania and Africa (Fig. 1c) (FAOSTAT, 2015).

Safflower oil has shown many beneficial health effect in various studies performed recently. A balanced fatty acid profile found in safflower oil has shown to decrease fat accumulation in rats when compared to beef tallow diet (Shimomãoera, Tamãoera, & Suzuki, 1990). Presence of conjugated linoleic acid in safflower oil has effectively shown to decrease body weight and adipose tissues as demonstrated in clinical trials (Norris et al., 2009). Further safflower oil has been found effective in fat-induced insulin resistance (Neschen et al., 2002). Currently major application of safflower oil is in food industry owing to higher mono and poly unsaturated fatty acids. However, it may also be used solely or in combination with other oils as a biodiesel. Some evidence to its utilization in combination with castor oil to produce a biodiesel resulted in lower viscosity biodiesel (Thomas, Birney, & Auld, 2012). Oil extraction techniques have gained focussed attention to increase the yield. Mechanical, solvent and supercritical CO_2 extraction techniques have been tried to address the issues of flammability, toxicity and corrosiveness. There are certain challenges to commercial scale extraction using high tech extraction techniques (Ayas & Yilmaz, 2014; Norris et al., 2009).

Therefore in this manuscript, safflower seed production trends, oil extraction techniques, physiochemical properties of oils, and food/nutraceutical applications with reference to its health benefits are discussed. There is a need to provide a consolidated direction in evaluating and developing the potential of safflower seed oil through a critical review of current reported literature. This review is designed to focus on the application of safflower oil fatty acid profiles that are of paramount importance to improving physiological functions of human health (Asgarpanah & Kazemivash, 2013; Choi, Kim, & Im, 2011; Zhou, Tang, Xu, Zhou, & Wang, 2014).

2. Oil extraction process and techniques

Safflower oil contents can vary depending upon the process and technique of oil extraction (Han, Cheng, Zhang, & Bi, 2009). Traditionally safflower oil has been extracted using local mills called “ghani” (mainly in Indian regions) which is a combination of pestle and mortar (Achaya, 1994; Knowles, 1967) technique. This process leaves about 10–15% oil in the residual cake. The cake or the meal obtained from ghani is partially dehulled before milling. A further extraction using expellers can reduce the residual oil to 6–8%. The use of solvent extraction mill can reduce the residual oil level up to

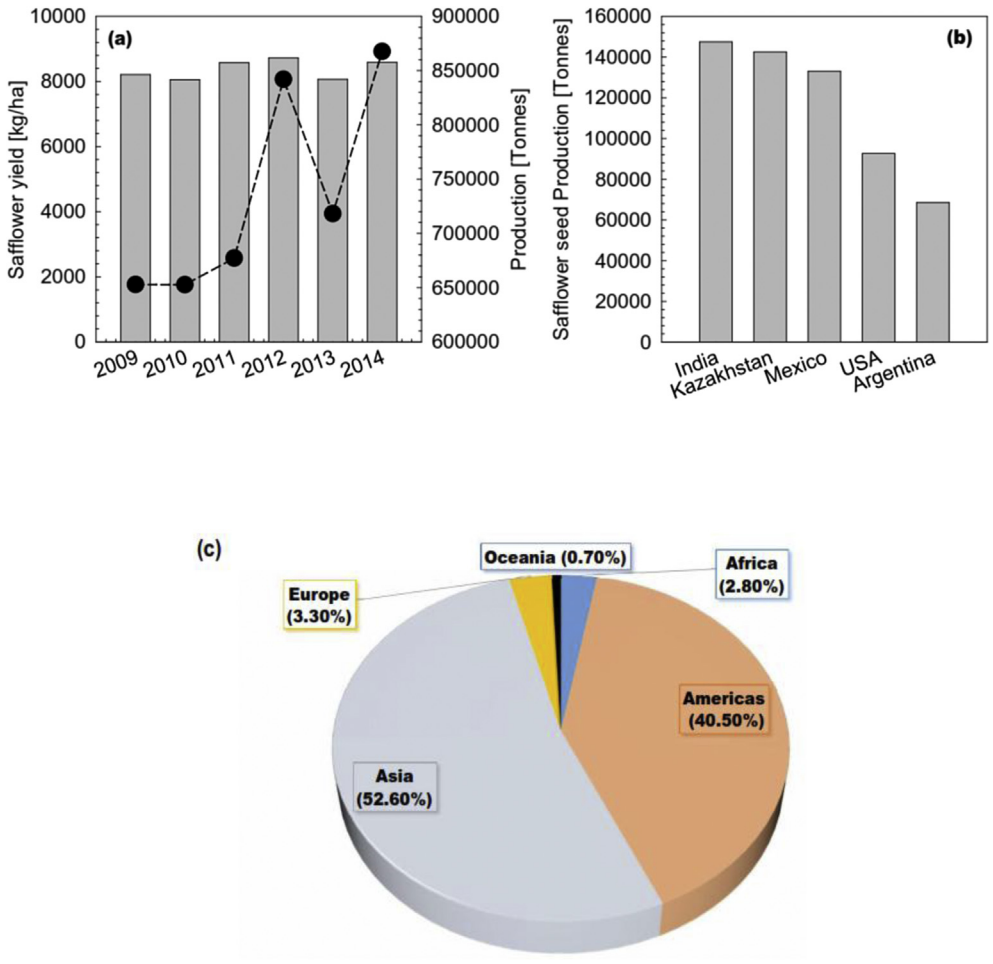

Fig. 1. Production statistics of safflower (FAOSTAT, 2015). (a) Top five safflower seed producing countries of the world. (b) Safflower production and yield during last six years. Bars indicates yield, while line shows production data. (c) Region wise (continents) distribution of safflower production.

0.5–2% (Smith, 1996). There are certain other factors that can affect the extraction process including degree of decortication (i.e. shifting, grinding or air floatation), water addition, acidulated soap stocks and spent filter clay (Smith, 1996). The typical production steps for safflower seed processing is given in Fig. 2.

In USA and Mexico, oil is extracted using expellers or extruders while subsequent extraction is completed through a solvent extraction. Often a brief decorticating process is also involved to reduce the energy cost of extraction process. There have been consistent efforts to increase the efficiency of extraction method by applying new and innovative techniques i.e., supercritical extraction techniques (Han et al., 2009), enzymatic extraction techniques (Gibbins, Aksoy, & Ustun, 2012), ultrasonic extraction (Hu et al., 2012) and combination of these methods. The brief review of various production techniques is given below.

2.1. Traditional ghani extraction

The ghani comprises of pestle and mortar and is driven by mule or donkey. The safflower seeds are placed in the mortar and movement of pestle grind the seeds to remove the oil (Achaya, 1993). Whole process takes 3–4 h to complete with yield about 4% (Achaya, 1994). Currently ~40% of the safflower seeds are crushed using ghani extraction technique around the world (Achaya, 1994).

2.2. Supercritical fluid extraction techniques

An innovative and modern extraction techniques is Supercritical Fluid Extraction (SFE) which is considered to be a green processing technique i.e., environment friendly technique (Crampon et al., 2017; Han et al., 2009). Han et al. (2009) used Supercritical CO_2 (SC-CO_2) to extract safflower oil by changing operational parameters such as flow rate, temperature, pressure and particle size on a bench size apparatus. It was found that the extraction yield as a function of time is largely affected by the flow rate, particle size and extraction pressure. Moreover, the quality of oil was far more better in SC-CO_2 extraction with a maximum oil yield of <27% at 28 MPa and 308 K temperature. In another study the optimized conditions for SC-CO_2 for safflower oil extraction includes a constant CO_2 flow rate of 3 mL/min, with 347 K and 50 MPa pressure. The total running time was 76 min (Ayas & Yilmaz, 2014). The recovery of oil was 96.3% with total oil yield of 40% (Ayas & Yilmaz, 2014).

The total unsaturated fatty acids and linoleic acid contents in oil

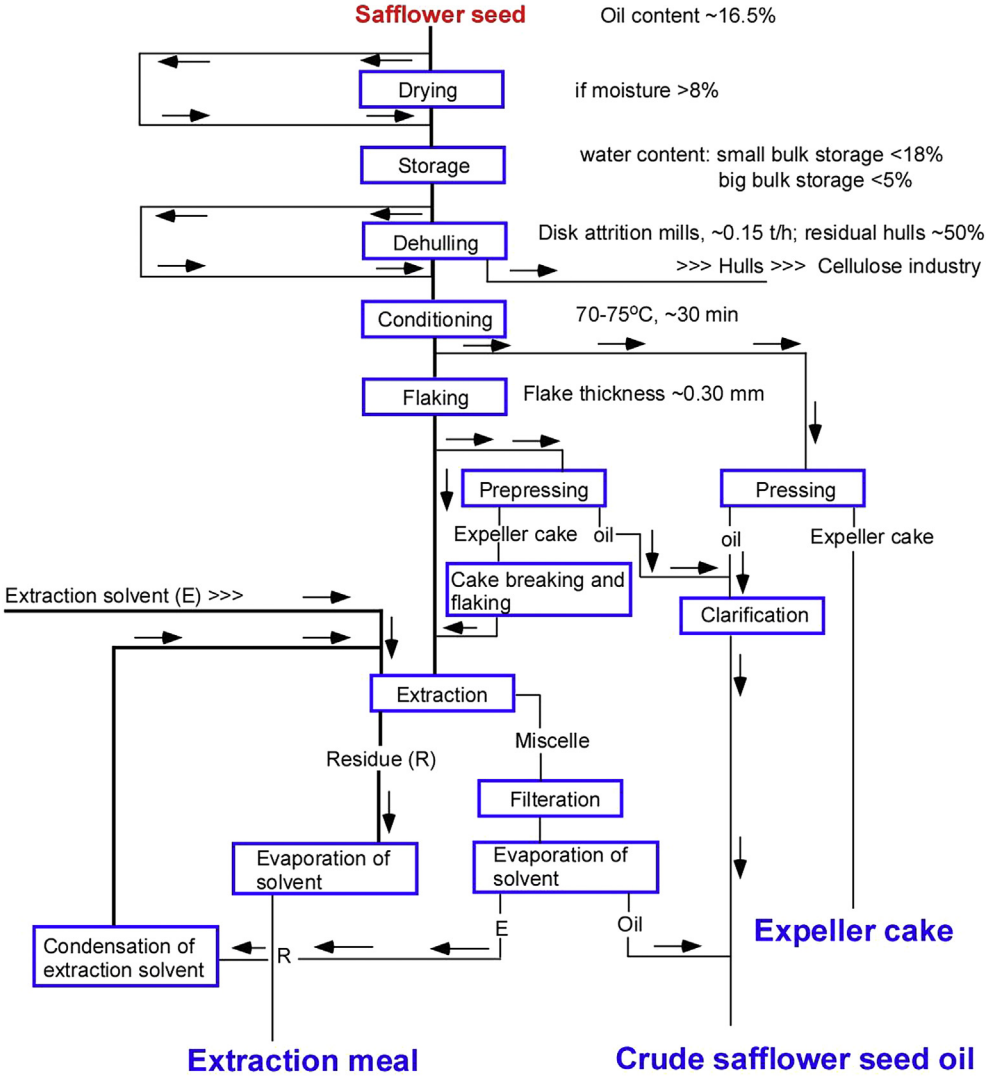

Fig. 2. Typical safflower oil production step in processing industry. The important fractions include safflower seed oil, meal and cake. The extraction efficiency depend upon type of solvent used and initial moisture content in safflower seed. Modified from Bockisch (1998).

extracted through SC-CO_2 were higher than those obtained from traditional methods. SC-CO_2 under pressure has a higher density resulting in higher dissolvability of oils (Han et al., 2009). Moreover, lower temperature and smaller particle size favours the extraction efficiency. This has an added advantage of producing lesser free fatty acids (FFAs) as compared to traditional oil extraction methods (Crampon et al., 2017; Han et al., 2009).

2.3. Enzymatic oil extraction method

Aqueous enzymatic extraction is also a safe and environmental friendly technique (Mat Yusoff, 2017). The basic principle in this technique is to break the cell wall of plant materials with the help of enzymes. In this technique low temperature and low pH conditions are used to extract the oil (Konopka, Roszkowska, Czaplicki, & Tańska, 2016). Various type of enzymes are used like pectinase, hemicellulase, α-amylase and many others. Gibbins et al. (2012) used alcalase and celluclast to extract safflower oil. Various parameters such as temperature, churning rate, dilution rates, enzyme type, amount, particle size and pH have been found to affect the extraction rate. Further, Response Surface Methodology (RSM) has predicted optimized conditions at pH 4.84, 48.3 °C and 0.25 mL enzyme/g substance for optimum oil extraction yield. Under these optimized conditions, ~28.2% oil was extracted with an oil yield of 65%. Moreover, particle size have been fund to affect the extraction rate as more extraction rate was achieved at particle size <0.6 mm (Gibbins et al., 2012). Commercial lipases from *Thermomyces lanuginosus, Candida rugosa* and porcine pancreas have been used to hydrolyze safflower oil for separating linoleic acid. *Candida rugosa* hydrolyze safflower oil with efficiency of 84.1% in comparison to other lipases (Aziz, Husson, & Kermasha, 2015).

2.4. Ultrasonic oil extraction method

The ultrasonic extraction has several advantages over tradition methods such as lower extraction temperatures, shorter processing time, decreased solvent quantities and improved oil yield (Chen, Zhang, Liu, Gu, & Yang, 2017; Zhang et al., 2017). Few studies were conducted to extract the safflower oil using ultrasonic treatments. Hu et al. (2012) showed optimized conditions of ultrasonic power, extraction time, liquid-solid ratio and solvent for safflower oil extraction. The optimized condition includes ultrasonic power of 300 W, with hexane as solvent. The extraction yield increased to >27% at liquid-solid ratio of 6 with extraction time of 60 min at 35 °C (Hu et al., 2012). In another study, the extraction rate of 27.8% was achieved with petroleum ether, when ultrasonic waves were applied for 20 min at 35 °C. The solid to liquid ratio was set at 1:9 (g/mL) (Kai-bo, Jing, & Xiang-xiang, 2015).

3. Chemical characterization of safflower oil

Safflower contains medium to high oil contents (23–36%) depending upon variety used. The functionality of oil seeds in industrial, pharmaceutical and food products depends upon its fatty acid composition. The fatty acid composition of oils varies with plant species, cultivar and growing conditions (Kostik, Memeti, & Bauer, 2013; Sabzalian, Saeidi, & Mirlohi, 2008). The fatty acid composition and physicochemical parameters of safflower oil varies (Table 1) slightly in different species (Sabzalian et al., 2008). Moreover, stress factor such as salinity and drought significantly affect the fatty acid profile. Effect of physiologial stress on safflower oil yield and its quality has already been reviewed by Hussain, Lyra, Farooq, Nikoloudakis, and Khalid (2016). Therefore this section is aimed at critically evaluating the physicochemical parameters of safflower oil.

Table 1
Physicochemical parameters of different cultivars of safflower seed oil (Al Surmi et al., 2015).

Physico-chemical parameters	Malawi	Giza1	Ethiopian
Acid Value (% oleic acid)	0.921	0.92	0.919
Iodine Value (g/100 g Oil)	147	144	143
Peroxide Value (meq/K)	3.78	4.50	4.10
Saponification value (mg KOH/g)	211.5	215.7	218.4
Unsaponifable matter (%)	1.2	1.45	1.25
Thiobarbituric acid (TBA) (mg/kg)	1.30	0.96	1.24
Specific gravity (25 °C)	0.921	0.920	0.919
Refractive Index (25 °C)	1.471	1.469	1.468
Lipid fraction			
Polar lipids	1.43	1.53	1.84
Monoglycerides	1.86	2.18 2.13	
Diglycerides	5.58	6.69	2.70
Triglycerides	85.34	81.70	84.63
Free sterols	1.1	1.59	1.24
Free fatty acids	0.38	1.01	0.43
Sterol esters and hydrocarbons	4.31	5.30	4.67

3.1. Fatty acid composition and free fatty acids (FFAs)

Safflower oil contains high proportion of polyunsaturated fatty acids such as linoleic acid and tocopherol that are used for medicinal as well as dietetic purposes (Han et al., 2009). Major unsaturated fatty acids are linoleic and oleic acid comprising 77.9–79.5% and 9.5–11.3% of total fatty acids respectively (Mihaela et al., 2013). While, saturated fatty acids are present in lower proportion ranging from 9.7% to 10.8% of total fatty acids. Major saturated fatty acids are palmitic and stearic acids consisted of 7.2–8.6% and 2.0–2.4% content respectively (Ben Moumen et al., 2013). Sabzalian et al. (2008) analyzed three different species of safflower and reported that oleic, linoleic, stearic and palmitic acids are the major fatty acids constituting 96–99% of the total fatty acids. Table 2 indicates fatty acid composition of safflower oil reported in different studies. Small variations in fatty acid profile of 12 different safflower cultivars from different countries were observed by Mailer, Potter, Redden, and Ayton (2008). They reported higher linoleic acid contents (75–84%) in all different cultivars. Moreover, small quantity of behenic, ecosenoic and lignoceric acid was also observed in different cultivars (Al Surmi, El Dengawi, Khalefa, & Yahia, 2015; Mailer et al., 2008). Four different genotypes of safflower i.e., Sharda monovarietal, Cartamar, Rancho and Cartafri, were evaluated using ten main triacylglycerols (SOO (stearate), OOO (oleate), POO, PPL, POP, PLO-palmitate, LLS, LLL, LPL, LLO-linoleate moiety). It was found that LLL, LLO and LLP species of triglycerides contain more than 80% of total triglycerides in oils (Ben Moumen et al., 2013; Ben Moumen et al., 2015).

FFA contents also termed as acid value is critical to evaluate the quality of an oil. The FFA value indicates the extent of triglyceride hydrolysis to give monoglycerides and diglycerides. An acceptable level FFA in oils should not exceed 1% (Freedman, Pryde, & Mounts, 1984; Liu, 1994; Mittelbach, Pokits, & Silberholz, 1992). Safflower varieties rancho and sharda found to contain 0.7% FFAs whereas cartafri and cartamar oil contain 0.67% and 0.63% FFAs (Ben Moumen et al., 2013). These results reflect the stability of safflower oil and hence can have huge implications for industrial and domestic uses.

Irrespective of the extraction methods, safflower seed oil is rich in natural antioxidants i.e., α-tocopherol (46.05–70.93 mg/100 g), β-tocopherol (0.85–2.16 mg/100 g) and γ-tocopherol (from trace amount to 0.45 mg/100 g oils). Significant variation exist in antioxidants content of various varieties of safflower oil (Matthaus, Özcan, & Al Juhaimi, 2015).

Table 2
Fatty acid composition of safflower oil determined by different research groups.

Fatty acid	Contents (%)					
Myristic C14:0	0.50	–	–	–	0.12–0.16	0.11–0.13
Palmitic C16:0	4.00	6.48	6.03–6.66	4.90–8.10	7.20–8.60	6.07–6.32
Stearic C18:0	2.50	2.30	2.01–2.61	1.70–2.80	2.00–2.39	2.06–2.24
Oleic C18:1	16.60	14.17	11.22–14.19	8.10–13.10	9.50–11.29	7.51–18.38
Linoleic C18:2	76.00	73.87	74.60–78.24	75.20–83.70	77.49–79.98	71.56–73.32
Linolenic C18:3	–	0.37	0.07–0.08	0–0.1	0.09	0.07–0.09
Arachidonic C20:4	–	–	–	0–0.4	–	–
Eicosaenoic C20:1	–	–	0.17–0.19	0.2	Not detected	0.13–0.15
References	Kostik et al. (2013)	Sabzalian et al. (2008)	Al Surmi et al. (2015)	Mailer et al. (2008)	Ben Moumen et al. (2013)	Coşge, Gürbüz, and Kiralan (2007)

3.2. Phospholipids

Phospholipids are used as additives in foods and non-food applications. These lipids are also effective as hypocholesterolemic agents (Van Nieuwenhuyzen, 1981). Crude safflower contains 50% neutral lipids. Iwata et al. (1992) reported that consumption of safflower phospholipids exhibited desirable effect on human health i.e., plasma membrane reduction, lipids level reduction in liver and an increase in high density lipoprotein (Iwata, Hoshi, Tsutsumi, Furukawa, & Kimura, 1991; Iwata et al., 1992). Y. Lee, Kim, et al. (2004) and Lee, Oh, et al. (2004) evaluated the phospholipid profile of safflower oil using roasting and expelling techniques. It was observed that the phospholipid contents increased with an increase in roasting temperatures. Further phosphatidic acid, phosphatidylcholine, phosphatidylethanolamine and phosphatidylinositol were the major phospholipids identified in safflower oil (Lee, Kim et al., 2004).

3.3. Sterols and triterpenic alcohols

Sterols and phytostanols are important food constitutents improving cardiovascular health in human beings. These compounds are structurally similar to cholesterol and thus have beneficial biological functions when incorporated in diet (Nestola & Schmidt, 2016). Safflower have been reported to contain 1248–2976 mg/kg sterols, however these values may change with the varieties, growing conditions and genetic potential of the safflower specie (Mahboobeh Vosoughkia, Ghavamib, Gharachorloo, Sharrifmoghaddasi, & Omidi, 2011). Further the stage of ripening has been found to affect the composition of sterols. Hamrouni-Sellami, Salah, Kchouk, and Marzouk (2007) found β-sitosterol as dominant sterol during different ripening stages of safflower seeds (Table 3). While free and esterified sterols were found during early development of seeds. Similarly, effect of varieties on sterol, Mahboobeh Vosoughkia et al. (2011) analysed sterol composition from four different varieties of safflower and found β-sitosterol as dominant (49.16–53.51%) phytosterol followed by campesterol (6.45–14.17%), stigmasterol (4.78–6.44%) and Δ7-stigmasterol (17.65–20.19%). Moreover, Japanese safflower oil contains higher contents of β-sitosterol (52–57%) when compared to safflower oils from other countries (Itoh, Tamura, & Matsumoto, 1973).

3.4. Phenolic compounds and tocopherols

Tocopherols, usually known as vitamin E, are a set of lipid soluble structures which naturally existing in oilseeds in four different forms (α-, β-, γ-and δ-tocopherols). Tocopherols are valued for their antioxidant property to protect polyunsaturated fatty acids against oxidation (Vosoughkia, Hossainchi Ghareaghag, Ghavami, Gharachorloo, & Delkhosh, 2012). Tocopherol has broadly been used for feed, food, resins and pharmaceutical cosmetics. As an antioxidant in food, tocopherol is used for frying oil, fried snakes and margarine. Mailer et al. (2008) conducted an experiment to evaluate tocopherols and polyphenols contents of different safflower cultivars i.e. A384 (France), A446 (Japan), A539 (China), A552 (Pakistan), CP177333 (India), CP189352 (Sudan), CP189345 (Turkey), CP189367 (Afghanistan), Sirothora (Australia) and Sironaria (Australia). In these cultivars, tocopherols content ranged from 319 (Sironaria Australia) to 648 (A552 Pakistan) mg/kg oil and polyphenols ranged from 74 (CP189344 Iran) to 212 (Sirothora Australia). Matthaus et al. (2015) reported tocopherols contents from the experiment through growing the safflower species in different region of world *viz.* Alakova (Cumra Seker), Remzi Bey (Konya), Iran, India$_a$, India$_b$, Egypt, USAa, USA$_b$, USAc. The average the tocopherols are shown in Table 4. Mahboobeh Vosoughkia et al. (2011) evaluated four different Iranian safflower varieties and reported α-tocopherol as the abundant tocopherol that account approximately 94–96% of the total tocopherols. Recently, Aydeniz, Güneşer, and Yılmaz (2014) evaluated the α-tocopherol content in safflower oil using different cold press techniques, they found highest contents of α -tocopherol (502.12 mg/kg) in roasted safflower oil, whereas microwave extraction technique resulted in decreased contents up to 366.24 mg/kg. Y.-C. Lee, Oh, et al. (2004) evaluated the effect of different roasting temperatures

Table 3
Sterol composition of safflower oil from different countries. β-sitosterol is the dominant sterol present in different safflower oil types.

Sterol	Safflower (linoleic rich) (%)	Safflower (Oleic rich) (%)	Safflower (Zendehrood, Iran) (%)	Safflower (Tunisia) (%)
Cholesterol	0	0	0.63	–
Brassicasterol	<0.5	0	–	–
Campesterol	13	15	10.98	0.12
Stigmasterol	9	10	4.78	0.05
β-sitosterol	52	52	49.90	0.46
Avenasterol	1	1	3.24	0.18
Stigmastenol	20	15	–	–
Avenasterol	3	5	5.25	–
Reference	Itoh et al. (1973)	Itoh et al. (1973)	Mahboobeh Vosoughkia et al. (2011)	Hamrouni-Sellami et al. (2007)

Table 4
Tocopherol contents in various varieties of safflower oil. The tocopherol contents various according to the extraction techniques. Cold press technique favour an increase in tocopherol contents in comparison to other processing techniques.

	Compound	Contents	References
Tocopherols (%)	α-tocopherol	0.0554	Matthaus et al. (2015)
	β-tocopherol	0.001	Matthaus et al. (2015)
	γ-tocopherol	0.0002	Matthaus et al. (2015)
Tocopherols (Iran; mg/kg)	α-tocopherol	192.05–439.64	Mahboobeh Vosoughkia et al. (2011)
	β-tocopherol	Not detected	Mahboobeh Vosoughkia et al. (2011)
	γ-tocopherol	5.59–14.68	Mahboobeh Vosoughkia et al. (2011)
	δ-tocopherol	3.06–11.50	Mahboobeh Vosoughkia et al. (2011)
Tocopherols (Cold press; mg/kg)	α-tocopherol	366.24–502.12	Aydeniz et al. (2014)
Tocopherols (mg/kg)	α-tocopherol	386–520	Y.-C. Lee, Kim, et al. (2004) and Lee, Oh, et al. (2004)
	β-tocopherol	8.9–12.4	Y.-C. Lee, Kim, et al. (2004) and Lee, Oh, et al. (2004)
	γ-tocopherol	2.4–7.7	Y.-C. Lee, Kim, et al. (2004) and Lee, Oh, et al. (2004)

(140–180 °C) on tocopherol contents of safflower oil and found an increase in α–tocopherol content (441–520 mg/kg) when roasting temperature was increased from 140 to 180 °C. The same authors reported the decreasing trend in tocopherol content when roasting was coupled with expelling temperatures (110–150 °C). The level of α-tocopherol content decreased from 555.9 to 488.9 mg/kg when expelling temperature increased from 110 to 150 °C (Lee, Kim et al., 2004).

The polyphenolic contents in safflower oil ranged between 2616.10 and 4079.30 μg/100 g gallic acid equivalent (Aydeniz et al., 2014). The contents varying according to extraction procedure, microwave extraction increased the polyphenolic contents up to 4079.30 μg/100 g in comparison to solvent extracted oil (Aydeniz et al., 2014). Recently, Abdessamad Ben Moumen et al. (2015) identified 13 phenolic compounds from four different varieties of Moroccan safflower oil. These includes two two hydroxybenzoic acids (syringic acids and vanillic acid), naringin, tyrosol, rutin, vanillin, pinoresinol, trans-chalcone and four hydroxycinnamic acids including ferulic acid, sinapic acid, cinnamic acid and *p*-coumaric acid. The polyphenol content in these varieties vary between 79.50 and 143.70 mg/kg (Ben Moumen et al., 2015). There was hardly any study indicating different phenolic compounds from safflower oil from different areas of world. The distribution of phenolic compounds in safflower oils might be the interesting area for future research. Four different types of carotenoids were also reported in safflower oil, these includes α, β and γ carotenoids and β-cryptoxanthin (Ben Moumen et al., 2015). The total carotenoid contents in different varieties of safflower oil ranged between 1.14 and 1.34 mg/kg with β-carotene and β-cryptoxanthin as the dominant carotenoid (Ben Moumen et al., 2015).

3.5. Comparative physicochemical profile analysis

Safflower has three distinctive attributes that makes it a suitable choice for consumption i.e., unsaturated fat, little taste and high stability at elevated temperature. Safflower oil is similar to sunflower oil in terms of its color and flavor (Han et al., 2009). Moreover safflower oil has higher contetns of vitamin E when compare to olive oil. These attribute have developed an immense concentration from the consumer society to use it as an alternative to costly edible oils in the market. It has been lined to improve various physiological systems such as treatment and prevention of arteriosclerosis, hyperlipidemia and coronary heart disease (Abidi, 2001). Further safflower oil is stable at lower temperature as well, making it suitable for chilled food products development. It has been found that the salad dressing of safflower oil has persisted its stability adequately to −12 °C (Weiss, 1971). Further on heating, higher oleic safflower oil contetns are very stable and do not give produce smoke smell (Gyulai, 1996).

Safflower oils are also found to be more suitable for hydrogenations of margarine compared to canola or soy oil. It has been applied on different edible product to restrict the migration of moisture and thus ensuring better shelf-life (Kleingarten, 1993). Due to its reported non-allergic nature, it being used extensively in cosmetics (Weiss, 1971). Moreover, safflower oils being rich in linoleic (premium grade high polyunsaturated essential fatty acids) makes it therapeutically and nutritionally valuable commodity for human consumption (Vosoughkia et al., 2012; Vosoughkia et al., 2011).

4. Nutritional and health benefits of safflower oil

Degenerative disease mainly affect the bone and joints health. Safflower seeds and oil have been reported to curtail these degenerative diseases. Recently, few studies have been designed to develop functional foods using safflower seeds and oil (Choi et al., 2011; Zhou et al., 2014). There has been a concentrated effort to design dietray supplements containing higher amount of polyunsaturated fatty acids from various vegetable sources. Further traditional and oriental medicines have been found to contain safflower seeds to treat neuropathy, chicken pox sores and numbness and tingling (Choi et al., 2011). India, USA and Japan have been reported to use safflower oil in controlling blood parameters such as cholesterol and high density lipoprotein (HDL) levels (Choi et al., 2011). There has been evidences of boosting skin health, control muscle contractions, aid in weight loss, improve hair growth, managing the onsets of premenstrual syndrome (PMS) and boasting immune system (Table 5) by the application of safflower seeds and oil (Asgarpanah & Kazemivash, 2013; Zhou et al., 2014).

4.1. Osteological modifying properties

Safflower seeds have been used in Korea and Japan to promote bone formation and to prevent the onset of osteoporosis (Cho et al., 2011). Experiments, where rat based models have been used, suggested that safflower seeds and extracts stimulate the differentiation of osteoblasts and promote speedy recovery in bone fracture incidents (Chung et al., 1999; Kim et al., 1998; Lee, Chang, Kim, Park, & Choi, 2002; Seo et al., 2000). It was found that the water extract of germinated safflower seeds have proliferative effect on calvarial bone cells in mouse whereas the major component that promotes differentiation and proliferation is safflower trachelogenin (Kim, Kim, Lee, & Choi, 2009). Similarly, mixed polyphenolic compounds in safflower stimulates proliferation of ROS 17/2.8 osteoblast-like cells (Cho et al., 2007; Kim et al., 2002). Further it was observed that the defatted ethanol extracts and seed powders

Table 5
The biological and functional activities of safflower oil.

Biological activities	References
Cholesterol modifying properties; prevention of atherosclerosis	Koyama et al. (2006); Hotta et al. (2002)
Cure of pimples and acne; other skin diseases	Roh et al. (2004); Harbige et al. (1995)
Rhumatological problems; joint movement and arthritis; osteoporosis	Cho et al. (2011); Kim et al. (2009)
Hepatoprotective properties	Rahimi et al. (2014); Paramesha et al. (2011)
Controlling breast cancer; skin cancer; other melanoma based cancers	Loo et al. (2004); Roh et al. (2004); Yasukawa et al. (1996)
Antidiabitic activities	Higa et al. (2010); Rahimi et al. (2014)
Anabolic effects; antiestrogenic activities	Kim et al. (2009); Jang et al. (2007); Yoo, Park, and Kwon (2006); Hong et al. (2002)
Activation of prostaglandin F2α metabolites	Grant et al. (2005)
Immunomodulatory activities; anti-inflammatory activities	Takii et al. (1999)
Post-menstruation syndrome	Zhou et al. (2014)
Antioxidant effects; prevention of atherosclerosis; ostischemic myocardial dysfunction	Koyama et al. (2006); Hotta et al. (2002)

decreased the bone loss in ovariectomized rats (Cho et al., 2007; Kim et al., 2002).

4.2. Cardio-protective properties

Safflower oil fatty acid composition is quite similar to that of olive oil especially in oleic and linoleic acid contents with a much lower price for consumers. The polyunsaturated fatty acids in safflower oil suppress the level of low density lipoproteins (LDL, bad cholesterol). Therefore, in North America, Germany and Japan a large quantity of safflower oil is consumed. An added advantage of safflower oil is minimum allergic responses compared to other functional oils making it suitable in many cosmetic products. Defatted safflower seed powder increased the level of plasma HDL-cholesterol (high density lipoproteins, good cholesterol) in ovariectomized rats (Cho, Choi, Choi, & Lee, 2000). Water and ethanol extracts of safflower seeds contains phenolic compounds had an effect on triglyceride levels in male rats, resulting in increased HDL/total cholesterol ratios (Moon et al., 2001). The cholesterol modifying and lowering effects are mainly due to serotonin derivatives, flavones and lignans that are present in safflower seeds. These polyphenolics also improves the overall body lipid status that may have weakened due to estrogen deficiency. The serotonin in safflower seed extract prevents LDL oxidation and atherosclerosis in apolipoprotein E-deficient mice both *in vitro* and *ex vivo*, respectively (Koyama et al., 2006).

It has been reported that the supplementation of safflower seed extract in diet also reduces oxidative stress, inflammation and/or arterial stiffness in healthy volunteers (Koyama et al., 2009). Safflower seed polyphenols (N- (*p*-coumaroyl) serotonin and the N-feruloylserotonin) improve the elasticity of the aorta wall in the Kurosawa and Kusanagi-hypercholesterolemic (KHC) rabbits and improved atherosclerosis (Katsuda et al., 2009).

4.3. Hepatoprotective properties

Safflower seeds and oils have been found to contain the damage/toxicity to liver by reducing plasma and hepatic total-cholesterol, plasma triglycerides, and atherogenic index in high-cholesterol fed rats. The supplementation also increased the activity of hepatic HMG-CoA reductase activity (Moon et al., 2001). Another study by Rahimi, Asgary, and Kabiri (2014) has shown that the levels of blood glucose, total cholesterol, triglycerides LDL, alanine aminotransferase (ALT), alkaline phosphatase (ALP) and aspartate aminotransferase (AST), have decreased in alloxan induced diabetic rats after treatment with 200 mg/kg safflower seed oil in diet. Further methanolic extracts of safflower seeds showed significant liver protection against carbon tetrachloride (CCl_4) induced hepatotoxicity in rats (Paramesha, Ramesh, Krishna, Kumar, & Parvathi, 2011). Similarly, dehydroabietylamine (antioxidant compound) extracted from safflower seed and leaves showed strong hepatoprotective effects in CCl_4 induced hepatotoxicity in rats (Paramesha et al., 2011).

4.4. Phytoestrogens related properties

Safflower seed lignans and flavonoids represent the physiological effects similar to that of estrogen hence called as phytoestrogens. These phytoestrogens have anticarcenogic properties, bone health improvement, antioxidant activities and regulation of serum cholesterol (Draper et al., 1997; JB & Garner, 1997). The oophorectomized rat model suggested that administration of phytoestrogens decreased the calcium excretion via urine and had great effect on decreasing bone resorption (Draper et al., 1997). The presence of lignans, flavones and serotonin extracts in safflower work as phytoestrogens along with regulating the metabolism of bone formation and protection (Kang, Chang, & Park, 1999). Similarly, these phytoestrogens extracted from defatted safflower oil has shown to improve blood lipid status and cholesterol excretion without significant uterotropic action in estrogen-deficient animal models (Cho et al., 2004). Further these phytoestrogens also possess anti-androgenic activity as found in castrated rats where reduction in prostate weight and in testosterone levels after administration of 300 mg per kg body weight safflower seed extracts (Rashed, Shallan, Mohamed, Fouda, & Hanna, 2014).

4.5. Antioxidant properties

Safflower seeds have been reported to contain sufficient amount of antioxidants. Kang et al. (1999) and E.-O. Kim, Oh, Lee, Lee, and Choi (2007) isolated matairesinol and 8-hydroxyarctigenin (lignans), acacetin and acacetin 7-*O*-glucoside (flavones) and N-feruloylserotonin and N-*p*-coumaroyl (serotonin derivatives) from roasted safflower seeds that showed strong antioxidant activity *in vitro* (Kang et al., 1999; Kim et al., 2007). Further the serotonin derivatives showed strong radical scavenging activity and lipid peroxidation than that of α-tocopherol, acacetin and matairesinol (Kang et al., 1999). H. L. Zhang, Nagatsu, Watanabe, and Okuyama (1997) isolated seven antioxidant serotonin derivatives from safflower seed cake, most of these had comparatively strong antioxidant effect in the ferric thiocyanate and α, α-diphenyl-β-picrylhydrazyl (DPPH) assays. Similarly, N-*p*-coumaroyl serotonin has antioxidant and anti-inflammatory action for fibroblasts and helps in fibroblast cell proliferation (Takemasa Takii et al., 1999).

4.6. Anti-diabetic and anti-obesity properties

Safflower oil is a rich source of polyunsaturated fatty acids. The

Sprague-Dawley rat's model shows increased concentration of arachidonic acid after safflower oil supplementation. The increased arachidonic acid results in the reduced incidence of diabetic embryopathy (Reece et al., 1996). Recently, Higa et al. (2010) showed that safflower supplementation reduced the malformation rates in maternal diabetes. The reduction was resorption was due to regulation of nitric oxide homeostasis and arachidonic acid in embryos, which prevent developmental damage during organogenesis. Safflower oil exhibited significant hypoglycemic and hypolipidemic effect in hyperglycemic rats when supplemented at a rate of 200 mg per kg body weight for a period of 30 days (Rahimi et al., 2014). Asp et al. (2011) carried randomized, double-masked crossover study with 55 post-menopausal, obese women with type 2 diabetes and concluded that addition of 8 g safflower oil in diet improves glycemia, inflammation, and blood lipids over period of 16 weeks.

A high oleic acid-rich safflower oil diet was shown to be as effective in lowering body fat accumulation in meal-fed Sprague–Dawley rats (Takeuchi, Matsuo, Tokuyama, Shimomura, & Suzuki, 1995). Z. Zhang, Li, Liu, Sun, and Zhang (2010) showed that safflower oil supplemented diet can potently alter adipocytic adiposity-related gene expression and result in effective amelioration of diet-induced obesity. Shimomãoera et al. (1990) showed that consumption of the safflower oil diet increased lipoprotein lipase activity in heart and skeletal muscle that results in the elevation of fat oxidation rate and the depression of serum triacylglycerol level. Fat induced insulin resistance is a common problem, safflower oil protect these individuals against these problems through increasing the peroxisomal acyl-CoA oxidase and 3-ketoacyl-CoA thiolase in liver but reduce these enzyme systems in muscle.

4.7. Skin health properties

The high content of linoleic acid in safflower oil boast the quality and appearance of skin. The N-feruloylserotonin and N-*p*-coumaroyl serotonin derivatives and acacetin from ethyl acetate extracted safflower seed inhibits the formation of melanin in the skin and promotes skin whitening effect in *Streptomyces bikiniensis* and B16 melanoma cell lines (Roh, Han, Kim, & Hwang, 2004). Similarly, safflower oil have potential to improve the symptoms of meningitis (encephalomyelitis) (Harbige, Yeatman, Amor, & Crawford, 1995). Safflower oil is frequently used in formulations of skin conditioners and other cosmetics for treating acne vulgaris (Anderson, 2005; Toombs, 2005). Safflower oil also promotes hair and scalp health, numerous patents describe the usage of safflower oil in combination with other oils or as a separate ingredient in formulation of many cosmetics and herbal products (Maru, 2014; Verdun & Verdun, 2001). The growth promoting effect of safflower oil on hairs and healthy skin is due to vitamin E and its light texture, that allows its easily absorption into the scalp (Maru, 2014).

4.8. Antitumor properties

The oil extracted from the seeds contain alkane-6,8-diols, that inhibits the activity of 12-*O*-tetradecanoylphorbol-13-acetate-induced tumor promotion in mouse skin (Loo, Cheung, & Chow, 2004). N-feruloylserotonin and N-(p-coumaroyl) serotonin from seeds strongly inhibit melanin production in *Streptomyces bikiniensis* and B16 melanoma cell lines (Roh et al., 2004; Yasukawa et al., 1996). N-(*p*-coumaroyl) tryptamine and N-(*p*-coumaroyl) serotonin from seed extracts inhibit the production of proinflammatory cytokines (IL-1α, IL-1β, IL-6, IL-8 and TNF-α) from lipopolysaccharide-stimulated human monocytes (Takii et al., 2003). Safflower seed extracts together with dendritic cell (DC)-based vaccine increased the levels of TNF-α and IL-1β in mouse $CD117^+$ (c-kit)-derived DCs and shows strong antitumor activity (Chang, Hung, Chyan, Cheng, & Wu, 2011). The safflower seed extracts in methanol that was further partitioned with ethyl acetate, *n*-hexane and *n*-butanol possess moderate to strong cytotoxicity against three cancer cell lines (HepG2, MCF-7 and HeLa) in a dose dependent manner (Bae, Sun-Mi Shim, Lee, Chang, & Choi, 2002). Luteolin and acacetin were the prominent compounds in safflower seed that showed strong cytotoxicity against HepG2, MCF-7 and HeLa cell lines (Bae et al., 2002).

5. Potential applications of safflower oil in agro-food industries

Safflower oil being a potential bioactive food ingredient can be incorporated into various health supplements, cosmetics, pharmaceuticals, beverages, food products and as fortificant for feed. Safflower oil has a high nutritional value and many biological activities. The incorporation of safflower oil will increase the biological activities of diet thereby helping to reduce animal and human alimentations.

Currently, safflower seeds are used as ruminant's diet in over 60 countries (Alizadeh et al., 2012) with reported incidents of increase in ruminant body mass and milk yield (Chilliard, Ferlay, Mansbridge, & Doreau, 2000; Griinari & Bauman, 1999). Moreover, feeding safflower oil in lambs increased the content of unsaturated fatty acids in muscle tissues (Kott et al., 2003). Supplementation of 10–30 g safflower oil in goat diet has shown to improve the milk fat composition (Shi, Luo, Zhang, & Sheng, 2015). Further the combination of safflower oil and monensin increased the concentration of conjugated linoleic acid in bovine milk fat (Bell, Griinari, & Kennelly, 2006).

Safflower oil has capacity to serve as natural vehicle for stabilizing and storing biological lipophilic compounds for developing functional foods or for used as a vehicle for drug delivery. The cod liver oil can be encapsulated in safflower oil to increase the oxidative stability of polyunsaturated fatty acids in the cod liver oil (Fischer et al., 2014). Due to diverse nature of safflower oil along with good oxidative stability, it can be textured into different products like organogels (semisolids systems with self-assembled gelation capacities). The safflower oil containing organogels are non-cytotoxic and are capable for holding lipophilic compounds for longer period of time with good target deliveries at malignant site (Bastiat & Leroux, 2009; Khuphe, Mukonoweshuro, Kazlauciunas, & Thornton, 2015; Morales-Rueda, Dibildox-Alvarado, Charó-Alonso, Weiss, & Toro-Vazquez, 2009).

Safflower oil emulsions can be a good source of dietary supplements. These supplements have the ability to increase metabolism rate and supports the healthy weight program containing linoleic fatty acid diets (Maru, 2014). Vitamin D can also be encapsulated in safflower oil using microchannel emulsification. These oil-in-water (O/W) emulsions can remain stable for more than 30 days without any significant increase in droplet size (Khalid et al., 2015). Safflower oil can also be used in O/W paternal emulsions that have clinically applications for nutritional and medical purposes (Floyd, 1999; Yeh, Chao, Lin, & Chen, 2000).

6. Conclusion and future research implications

Safflower oil composition and nutritional profile changes with growing conditions, soil type and varieties. The future use of safflower oil in different food products depends upon the availability and screening of the high yielding varieties. These days safflower oil is blended with different hydrogenated vegetable oils for production of margarine oil, all-purpose shortenings in bakery products

and emulsified cake shortenings. High levels of oleic and linoleic acid and antioxidants in the safflower oil makes it as an excellent substitute in infant formulas. Due to natural flavour and mildness, safflower oil is used in many seasonings, flavour dispersants and dried fruits.

Safflower oil having a broad spectrum of biological and functional activities as shown in various reported literature, however all these studies are conducted in animal models. There is a need to assess the bioavailability and functionality of safflower seed oils in human matrices. Moreover, further studies on toxicological effects, mechanism of action in the human body, and nutritional intake data are necessary to set recommendations for regulatory bodies.

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