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Safflower (*Carthamus tinctorius* L.): An underutilized crop with potential medicinal values

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Abstract

Safflower (*Carthamus tinctorius* L.), is cultivated mainly for its seed, which is used for the extraction of high quality edible oil. Traditionally, the crop is grown for its flowers, used for paint industry, textile industry, flavouring foods and making dyes. Safflower is used as cut flowers and also having pharmaceutical potential for the treatment of male and female infertility, cardiovascular diseases, reduction in the blood glucose level, treatment of cancer and reduction in the plasma cholesterol level, *etc*. Despite having such significant potency, the crop has remained minor, neglected and underutilized. Therefore, there is a need of scientific community to focus the research on this crop and make it popularize as a commercial crop with various values added products. Safflower contains numerous chemical components (secondary metabolites) that possess anticoagulant, antioxidant activities and other human health benefits with pharmacological importance such as treatment against cardiac, reproductive and gastrointestinal diseases. Research should be focused on the development of spineless varieties with high oil contents. With all these merits, safflower genetic improvement required to be taken up for enhancing overall productivity and income per unit area. This review provides a brief insight in to the safflower crop biology, related species, world production scenario, its phytomedicinal properties and applications, production constraints and future strategies for its overall improvement.

1. Introduction

Safflower (*Carthamus tinctorius* L.) is an oilseed crop, having 2n=24 chromosomes and belongs to the family *Compositae* or *Asteraceae*. *Carthamus* is the latinized synonym of the Arabic word *quartum*, or *gurtum*, which means the dye color extracted from safflower flowers (Singh and Nimbkar, 2006). An underutilized crop defined as those domesticated species whose genetic potential has been unraveled and having "larger biodiversity portfolio" or genetic diversity but underused for the commercial cultivation (Padulosi and Hoeschle-Zeledon, 2004). Such species offers viable agricultural alternatives in response to climate change and are adapted to cultivation on the marginal lands. Thus, it provides additional option for generating the income to farmers and agricultural businesses (Mayes *et al*., 2012; Thies, 2000). Safflower, a diversified crop has been extensively grown in India, mostly for its quality oil rich in polyunsaturated fatty acids (linoleic acid) and for the carthamin (orange-red dye), extracted from the brilliantly colored flowers. Safflower flowers are commercially exploited for the herbal preparations in China and having medicinal and culinary properties (Li and Mundel, 1996). The dried flower petal (*Carthamiflos*) is a valued drug in traditional Chinese medicine and has been used clinically for the prevention and treatment of cardiovascular diseases (Guo *et al*., 2017). Though, crop having tremendous genetic potential and great exploitation for various purposes, the area under safflower around the world is diminishing due to lack of information on its improved crop management practices, other competitive crops, global import export policies and value-added product development from it. The research and development on different aspects of safflower, despite its adaptability to varied growing conditions with very high yield potential and diversified uses of different plant parts, have not received due attention. This probably is the main reason for its negligence and as a minor crop around the world in terms of area and production, compared to the other oilseed crops. However, interest has been rekindled in this crop in past few years due to three main reasons; scanty rainfall leads a huge shortfall of oilseed production in the country to which safflower is most suited and withstand in limited availability of water; consumers preference for healthy oil with less amounts of saturated fats for which safflower is well known; and herbal medicinal properties and extraction of edible dyes from flowers to which safflower is mainly recognized. Each and every plant parts of the safflower have utility either as a food or a phytomedicine.

1.1 World's distribution and production

Safflower has a long history of cultivation for hundreds of years from China to the Mediterranean region and all along the Nile valley spanning up to Ethiopia (Weiss, 1971). Presently it's grown

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commercially in India, United States of America, Mexico, Ethiopia, Kazakhstan, Australia, Argentina, Uzbekistan, China, and Russian Federation. Pakistan, Spain, Turkey, Canada, Iran, and Israel also grow safflower to a limited extent. Historically, safflower acreage and production around the world have witnessed wide fluctuations in the past. Safflower seed production in the world rose from 487,000 tonnes in the year 1965 to 1,007,000 tonnes in 1975, and subsequently, it decreased to 921,000 tonnes in 1985 (Anonymous, 2002). Mexico was the most important producer of safflower in the world until 1980, when it occupied an area of 528,000 ha with a production of above 600,000 tonnes during the year 1979-1980. However, the production of safflower in Mexico decreased significantly in later years, becoming only 10% of the worlds production recorded for the year 1979-1980 (Cervantes-Martinez, 2001). Commercial production of safflower in the United States of America was started during 1950s, and therefore, the area rapidly increased to 175,000 ha mainly in the states of California, Nebraska, Arizona, and Montana. Safflower in China occupied an area from 35,000 to 55,000 ha, producing 50 MT to 80 MT seeds annually. Xinjiang was the largest safflower producer state, which accounted for 80% of total safflower production in China (Zhaomu and Lijie, 2001).World's safflower seed production was about 627,653 tonnes in the year 2018. This was decreased by about 17.7 % compared to the previous year and if it is compared to production 10 years ago, it was decreased by 1.72% (Anonymous, 2020a). In the year 2019, Kazakhstan was the top country by safflower seed production among 13 countries. Safflower seed production in Kazakhstan was 199,789 tonnes that accounts for 34.87% of total safflower seed production in the World. The top five countries (Kazakhstan, United States of America, Russian Federation, Mexico, and China) accounted for 79.23% of it. The total safflower seed production was estimated at 572,879 tonnes in 2019 (Anonymous, 2020b). The world's top safflower-producing countries in 2019 are depicted in Figure 1. The safflower area in India in the year 2004-2005 was 387,000 ha, with a production of 154,000 tonnes of seed (Anonymous, 2004). Presently, it has come down to 24,640 tonnes. In India, Maharashtra and Karnataka states occupied about 72% area and have produced about 24% safflower seeds. Along with these two states, other safflower producing states in India are Andhra Pradesh, Odisha, Madhya Pradesh, Chhattisgarh, and Bihar. Safflower production in India is usually confined to rain-fed farming during post rainy season.

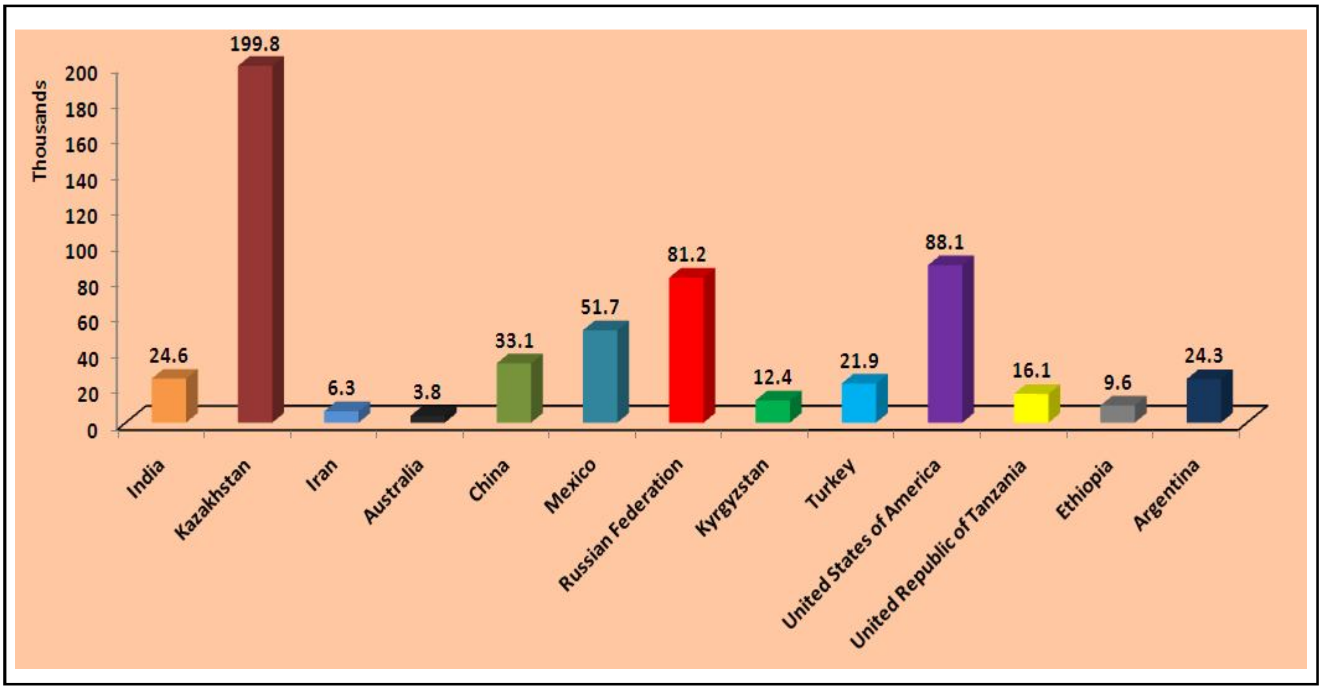

Figure 1: World's top safflower-producing (in thousand tonnes) countries in 2019.

1.2 Cultivated safflower and its relatives

Cytogenetic studies led by Imrie and Knowles (1970) and Khidir and Knowles (1970) suggest that *Carthamus palaestinus*, a self-compatible wild species restricted to the deserts of southern Israel and western Iraq (Zeven and Zhukovsky, 1975), with white and yellow flowered forms, is the progenitor from which derived the weedy species *C. oxyacanthus*, a mix of self-compatible and self-incompatible types, and *C. persicus* Wild., a self-incompatible species. These successively are considered the parental species of the cultivated species *C. tinctorius* L. (Ashri and Knowles, 1960). These four reported safflower species represent the genome denoted as "BB" with chromosome number 2n = 24. These can be intercrossed in all combinations to produce fertile hybrids (Knowles, 1959). Due to similarity in chromosome number in these species, there is a complete chromosome pairing in hybrids which is not often noticed where parental species differ in chromosome numbers (Ashri and Knowles, 1960). Introgression of the weedy and cultivated species should be taken up to improve the cultivated safflower (Zeven and Zhukovsky 1975). The weedy progenitors of cultivated safflower are cosmopolitan within the areas where safflower is grown.

Carthamus oxyacanthus, a branchy, very spiny and annual weed is a very serious common weed of Pakistan and Northwest India (Ashri and Knowles, 1960). Seeds contain approximately 28% oil and can be used for culinary purposes and as lighting fuel (Weiss, 1983).

Seeds are mostly small and black with no pappus. *Carthamu spersicus* is additionally a really serious weed, in Syria, Lebanon and Turkey (Knowles, 1959) with light yellow to orange flowers. Outer involucral bracts are narrow and extend beyond the top (Ashri and Knowles,1960).

1.3 Production issues

Safflower is a day length-neutral, long-day plant. During the emergence, first few leaves after a frost show little bit injury but plant compensate over it and grow quite normally. But, frost can cause substantial damage to crop during the elongation phase. As plant develop and bears flowers, this frost at the other end of the plant's development, lower oil content and yield level and sometime lead seed death (Mündel *et al*., 1992). Safflower is a poor competitor with weeds, most of the weeds become taller than the safflower crop and competes for the nutrition, sunlight and soil moisture, which effectively shed the crop and lower the yield. Weeds can cut safflower yields greatly and can cause complete crop losses (Dajue and Mundel, 1996). Very few chemical herbicides are registered in safflower for pre-plant incorporation to control a variety of grass and weeds. Seeding safflower into a firm moist seedbed not only enhances its emergence and stand, but also improves vigor and allows the crop to compete more effectively with weeds (Dajue and Mundel, 1996). Safflower owing to its good tolerance level to drought and heat because of deep taproot and xerophytic attribute of spines; does not survive in case of standing water conditions for a few hours in warm weather when the temperature goes above 20ºC and led a rapid spread of soil borne pathogens such as *Pythium* and *Phytophthora* (Rubis, 1981). This ultimately leads to the plant death (Mündel *et al*., 1995). Safflower attains maximum yield in deep fertile, well drained and sandy loamy soil and reduce the germination and seedling emergence in heavy clay soils. Prolonged and heavy rainfall during the flowering interferes the seed setting and pollination in the safflower. Also, lead to pollen shedding as the temperature moves above 32ºC (Mündel *et al*., 1992).

2. Safflower importance and potential

2.1 Whole plants

Safflower use for the herbal preparation (from safflower blossom) and tea to overcome the infertility/sterility and abortion issues in women and are mostly consumed in India and Afghanistan (Weiss1983; DajueLi and Han Yuanzhou, 1993). The products from all safflower plant are sold in India and Pakistan as '*pansari*' to treat various ailments. Safflower young leaves used as curry or dishes, and as a salad in India, Burma and Pakistan.Spineless varieties have been used as cut flowers in Latin America, Japan and Western Europe.

2.2 Flowers

2.2.1 Food colour and cosmetics

For saffron, the most popular and costly spice in the world safflower dried florets are used as a common adulterant. In restaurants, sauces, pickles, bread and rice soups take on a yellow to orange colour from the florets. Kunming in Yunnan Province in China is having large factory for the production of dyes from carthamin. It is mixed with French chalk, and in Japanese cosmetics, it is used in the preparation of lipstick (Smith, 1996).

2.2.2 Dyes

Safflower florets are mostly extracted for the preparation of carthamidin (water soluble yellow coloured dye) and carthamin (water-insoluble red dye), having solubility in alkali. Florets contain 0.3-0.6% carthamin (Weiss, 1971; 1983).

2.2.3 Pharmacological application

In China, the consumption of safflower is more to prevent most of the serious illness and health related issues. Usually, safflower has bitter taste. The Institute of Botany of the Chinese Academy of Sciences in Beijing has successfully developed a non-bitter tea having sweet smell and which also contains amino acids, minerals and vitamins B_1, B_2, B_{12}, C and E (Weiss, 1971). The active and main ingredient in the safflower is water soluble yellow coloured pigment "carthamidin" having medicinal values to treat the cardiovascular disease, menstrual problems, and swelling associated with trauma. Recently, carthamin and carthamidin pigments have been used for cosmetic coloring, such as face andhair cream, and shampoo and body lotion (Mani *et al*., 2020).

Safflower remarkably shows purgative, analgesic and antipyretic characteristics, and is useful in patients with poisoning (Delshad *et al*., 2018). Safflower extracts from flowers and seeds having different pharmacological importance and use for the development of the drugs. Safflower also contains anti nutritional factors (ANFs)/ compounds in the form of tannins, acacetin, serotonin and luteolin and which have anticoagulant, antioxidant, antibacterial and anti-inflammatory activities and are associated with reduction in the blood glucose level, treatment of cancer and reduction in the level of plasma cholesterol (Singhal *et al*., 2018; Huang *et al*., 1999; Duarte *et al*., 2001; Dajas *et al*., 2003; Benavente-García andCastillo, 2008; Lin *et al*., 2008). Safflower decoctions have been used successfully for treatment of male sterility (Qin Yuehao, 1990) and dead sperm excess disease (Qu Chun, 1990). Safflower reduces hypertension, dilates arteries and increases blood flow and, hence oxygenation of tissues (Deng, 1988; Wang Guimiaoand Yili, 1985). Safflower, along with other herbs, has been used to treat respiratory diseases (whooping cough) and chronic bronchitis (Wang Guimiao and Li Yili, 1985). Hydroxysafflor yellow A and B (HSYA and HSYB) extracted from flowers elicit varied inflammatory response, including proliferation and inflammatory responses of human fetal lung fibroblasts (Liu *et al*., 2019), and an asthma-related inflammatory response in human bronchial smooth muscle cells (HBSMCs) (Guo *et al*., 2019). Safflower eye drops reduce myopia, especially in children (Wang Guimiao and Li Yili, 1985). Safflower seeds and extracts have been used to stimulate bone formation and preclude the osteoporosis occurrence (Alkhafaji *et al*., 2020). The pharmaceutical importance of safflower metabolites/extracts enlisted in Table 1.

Table 1: List of safflower metabolites/extracts and their uses in the pharmacology

Biological activity	Safflower plant parts	Active compound	Biological/ lab model for testing	Observed activity	References
Anti-inflammatory effect	Flower	Hydroxysafflor yellow A	Human	It leads the activation of human bronchial smooth muscle cells and also inhibits platelet-activating factor (PAF) which leads the pro-inflammation	Guo *et al.*, 2019
	Flower	Carthamin yellow	Rat	It leads complete reduction of ischemia-reperfusion injury	Lu *et al.*, 2019
	Flower	Hydroxysafflor yellow B	Rat	Brain protection against cerebral ischemia reperfusion injury	Du *et al.*, 2019
Anticancer effect	Flower	Safflower polysaccharide	Human	It inhibits metastasis and the proliferation of breast cancer cell	Luo *et al.*, 2015
	Flower	Hydroxysafflor yellow B	Human	Reduces the growth of cancerous cells	Qu *et al.*, 2019
	Seed	Fatty acid and phytic acid	Rat	Anticancer activity against HEPG2 cancer cell line	Doha *et al.*, 2019
	Seed	Seed extract	*In vitro*	Inhibitory effect of the safflower seed (SS) on the proliferation of human colorectal cancer cells	Jeong *et al., 2016*
Antioxidant effect	Seed	Seed granular tea	Human	Antioxidant activity and potential effects in postmenopausal women	Cho *et al.*, 2011
	Flower	*Carthamus* red	Rat	Antioxidant and protection against hepatitis to lowered the induction of liver damage	Wu *et al*., 2013
	Seed	*Serotonin derivatives*	*In vitro*	Strong radical scavenging activity and lipid peroxidation	Khalid *et al.*, 2017
Osteoporosis effect	Seed	Seed oil	Rat	Improves osteoporosis	Alam *et al*., 2006
	Seed	Seed oil	Rat	Safflower seeds and extracts stimulate the differentiation of osteoblasts and promote speedy recovery in bone fracture incidents	Khalid *et al.*, 2017
Brain and liver disease effect	Flower	Hydroxysafflor yellow A	Rat	Potential treatment for hepatic fibro genesis	Dong *et al*., 2013
	Seed	Seed powder	Rat	Safflower seeds powder possessed cytotoxicity against hepatocarcinoma cell line HEPG2 and afford hepato-protection against non-alcoholic fatty liver disease (NAFLD)	Doha *et al.*, 2019
	Seed	Oil	Rat	Reduction in plasma and hepatic total-cholesterol, plasma triglycerides, and atherogenic index	Moon *et al.*, 2001
Cell proliferation and inhibition effect	Seed	N-(*p*-Coumaroyl) serotonin	Human	Grows the proliferation of normal human andmouse fibroblasts	Takii *et al*., 1999
	Flower	Flower extract	Rat	Effective against diabetes	Asgary *et al.*, 2012

2.3 Safflower seed utilization in food industries

Over the years there have been many studies conducted to increase the utilization of safflower seed as food and value added products. The safflower finely ground seed paste is use to enhance the cheese and curd formation in Iran (Knowles, 1965).By using safflower seed enzymes as an experimental substitution for rennin, a white cheese having pleasant smell and good softness was produced (Smith, 1996).Roasted seeds, generally mixed with chickpeas, barley or wheat, are eaten as a snack food in Ethiopia and Sudan (Belayneh and Wolde-Mariam, 1991).

2.4 Safflower oil composition and its uses

Safflower in the whole world is primarily grown for its edible oil, margarine and salad oil. Oilseeds are some of the major sources of vegetable oils used primarily for nutritional, industrial and pharmaceutical applications, as determined by their fatty acid composition and these composition varied as per plant speciesand the environmental effects (Anjani and Yadav, 2017). It has been observed that Indian safflower cultivars (ISF1, ISF2, and ISF3) have high oleic acid content under irrigated conditions compared to rainfed crop (Anjani and Yadav, 2017). Safflower oil contains two main unsaturated fatty acids: oleic (18:1) and linoleic acid (18:2), which compose 90% of the total fatty acids. The remaining 10% includes saturated fatty acids like palmitic (16:0) and stearic acid (18:0). Standard safflower oil contains about 6-8% palmitic acid, 2-3% stearicacid, 16-20% oleic acid, and 71-75% linoleic acid (Liu *et al.*, 2016). The potential uses of different parts of safflower are depicted in Figure 2.

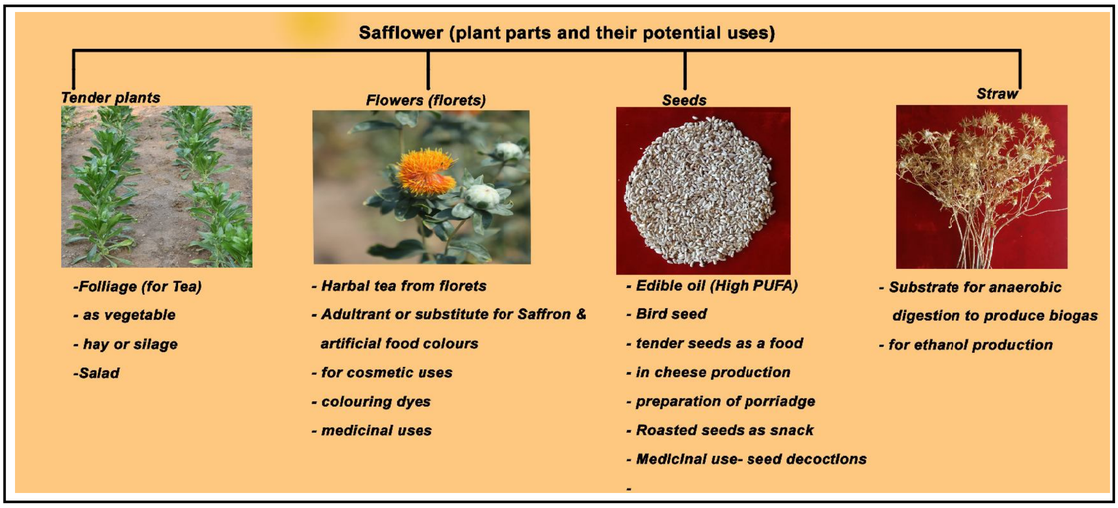

Figure 2: Safflower plant parts and their potential uses.

3. Constraints in safflower production

The major constraints such as, low per-hectare yields associated with low harvest index, and low seed-oil contents, presence of spines, research should be focused on the development of spineless high yielding varieties with high oil content. Also, lack of assured market and price support; absence of demand for safflower seed and oil in non-traditional areas, lack of awareness about region-specific agro-production technologies which do not led the full exploitation of yield potential of safflower. Also, the susceptibility of crops to pests, major fungal and bacterial diseases and abiotic stresses (mostly drought and salinity concerns) contributed to less safflower production. The processing facilities should be there at the production centers within reasonable distances (Dajue and Mundel, 1996).

4. Future directions

Flower yield and pigment content of the flowers are the other traits that have gained economic importance recently, due to an increasing demand for safflower flowers as a source of natural food color in European and other Western countries and their use in medicines for curing several chronic diseases. No attention has been paid to improvement of these traits in safflower. The improvement in yield of flowers and pigments in flowers would certainly help in increasing total remuneration from the crop to the farmer. Also, exploiting genetic diversity for the improvement of safflower through marker assisted breeding of QTLs/genes associated with agronomical traits. Therefore, genetic modification of safflower would be of enormous importance in improving productivity, production, and remuneration per unit area from the crop, which in turn would certainly help in increasing safflower area in the world.

5. Conclusion

Safflower has significant uses and having pharmacological, industrial and culinary properties. Despite this, the crop has remained minor. Therefore, a need to create awareness about the usefulness of this economically important underutilized and neglected crop is of paramount importance. The scientists should focused this crop and develop multidisciplinary research projects to address issues related to pest and disease, morphological ideotypes, agronomical traits, developmental pattern, *etc*., through genetic manipulation, product-related research to elucidate the importance of effectiveness of safflower cropfor a pharmacological uses.

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Conflicts of interest

The authors declare that there are no conflicts of interest relevant to this article.

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