Therapeutics, Phytochemistry and Pharmacology of an Important Unani Drug Qurtum (*Catharanthus tinctorius* L.) : A Review

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Abstract

Unani drug *Qurtum* is comprised of the seeds of a plant *Carthamus tinctorius* Linn. It is one of the most ancient crops cultivated in Egypt as a dye yielding herb. Now it is cultivated as an oil seed plant and regarded as substitute for sunflower.The seeds are white, somewhat flat, angular, smooth and shining like little conch shells, broad at the base and pointed towards the apex. Fixed oil is obtained from the ripe and dry seeds. The plant has shown diverse biological and pharmacological activities. It has been used in Unani Medicine (*Tibb-e-Unani*) and other Traditional Systems of Medicine from time immemorial. Keeping in view the high medicinal importance of the drug in Unani Medicine, the present review provides available information on traditional uses, phytochemistry and pharmacological properties of the unani drug Qurtum.

Keywords: *Carthamus tinctorius*, Qurtum, Unani Medicine

Introduction

Qurtum is a famous Unani drug used in a number of pathological conditions. Although the entire plant has medicinal value but its seed, oil and flowers have more important and interesting medicinal values. Its different parts are used after little processing as a single drug but mostly it is included as an ingredient in Unani formulations. Botanicalyy known as *Carthamus tinctorius* Linn. (Family: Asteraceae). Qurtum is a slender, glabrous or pubescent, much branched, annual herb (Chatterjee & Pakrashi, 1997), growing to a height of 45-60 cm (tall varieties 85-150 cm) (Anonymous, 1992) (Fig 1). The leaves are broad, lanceolate, spinosely serrate (rarely unarmed) sub erect, oblong, sessile (Kirtikar & Basu, 1987; Khory & Katrak, 1985). Flowering takes place during December to January (Chatterjee & Pakrashi, 1997). The flowers have a bitter taste and a bad odour (Kirtikar & Basu, 1987). Flower heads are orange-red, sometimes white or yellow in colour and globular in shape (Anonymous, 1992). Terminal heads of flowers are 2.5-3.3 cm long. Outer involucral bracts are large, foliaceous ovate-oblong 2.5-3.8 cm long constricted above the base, green, usually spinous, inner ovate-oblong or lanceolate acute (Kirtikar & Basu, 1987). They are orange-red achenes (often deformed) obovoid 4-angled truncate at the top with 4 bosses pappus (Hooker, 1882). Seeds (Fig 2) are white, somewhat flat, angular, smooth and shining like little conch shells, broad at the base and pointed towards the apex; apex is marked with concentric rings. Near the base is a small brownish scar; cotyledons, greyish and oily; odour slight, taste bitter (Khory & Katrak, 1985; Singh, 1974).The oil of *Carthamus tinctorius* is golden or clear straw colour used

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mainly for edible and illuminating purposes and for manufacture of soap (Anonymous, 1950; Nadkarni, 1954). It has characteristic odour and taste. It thickens and becomes rancid on exposure to air. It is slightly soluble in alcohol and freely soluble in ether, chloroform, benzene and petroleum ether (Kokate *et al*., 2004). Whole plant, seed, flower (Chatterjee & Pakrashi, 1997), root (Nadkarni, 1954) and oil are medicinally used (Khare, 2004).

Fig 1. Carthamus tinctorius Plant

Fig 2. Carthamus tinctorius Seeds

The plant is native to Europe and Asia (Anonymous, 1992). The cultivated safflower is considered to have originated either from the saffron thistle (*Carthamus lanata*) or the wild safflower (*Carthamus oxyacantha*) in the two primary centres of origin i.e. the mountainous regions of Ethiopia and Afghanistan; and also from the plains of India and Mayanmar (Burma), which are considered to be its secondary centre of origin. India is the second largest producer of safflower in the world, Mexico producing the maximum safflower (Anonymous, 1992). The plant is cultivated throughout a large part of India (Chopra *et al*., 1956; Hooker, 1882; Kirtikar & Basu, 1987) as an oil seed crop, particularly in Andhra Pradesh, Bihar, Gujarat, Karnataka, Madhya Pradesh, Maharashtra, Tamil Nadu, Uttar Pradesh and West Bengal (Chatterjee & Pakrashi, 1997).

Numerous varieties of safflower are known under cultivation. Nearly 63 types have been recorded. The plant can be broadly classified under two distinct varieties; one with very spinous leaves and the other with spineless or moderately spinous leaves. The spinous varieties are considered particularly valuable for oil production and spineless forms for dye extraction (Anonymous, 1950).

It is recorded that the grave clothes of the ancient Egyptian mummies used to be dyed with a safflower dye. Fragments of the safflower plants and seeds have been found in some of the ancient tombs (Anonymous, 1992). It is one of the most ancient crops cultivated in Egypt as a dye yielding herb. Now it is cultivated as an oil seed plant and regarded as substitute for sunflower. Fixed oil is obtained from the ripe and dry seeds. About 1000 seeds of safflower weigh 20 to 50 gm. The seeds normally contain 35-38 % of fixed oil. The oil is prepared by expression in expellers or with the help of hydraulic presses. The oil is filtered and further purified. The seed meal or round seeds are subjected to cooking by means of open steam, which ensures maximum yield of oil. The filtered and decolourized oil is packed into suitable containers (Kokate *et al*., 2004).

Vernaculars

The plant is known by different vernacular names: *Usfar*, *Qurtum*, *Bazrul Ahris*, *Habbul Asfar*, *Habbul Mu'safar*, *Hariz*, *Mu'safar*, *Turan*, *Ahris*, *Khari* (Arabic); *Kusum*, *Kajirah*, *Kusum phul* (Bengali); *Heboo*, *Hshu*, *Su*, *Suban*, *Supan* (Burma); *Hong Hoa*, *Hong lang Hoa* (Chinese); *Safflower*, *Parrot Seed*, *Bastard Saffron*, *Wild Saffron*, *African Saffron*, *American saffron*, *Dyer's Saffron* (English); *Carthame*, *Faux safran*, *Safranon* (French); *Farber safflor*, *Safflor*, *Gartensafran*, *Falschesafran* (German); *Kusumbi*, *Karada*, *Kabri*, *Kusumbo* (Gujrati); *Kur*, *Kasumba*, *Kusumbar*, *Kusum*, *Barre*, *Karrah* (Hindi); *Carthamus tinctorius*, Linn (Latin); *Chendurakam* (Malyalam); *Galapmachu* (Manipur); *Kadaya*, *Kararhi*, *Kardai*, *Kardi*, *Sadhi* (Marathi); *Khasakdana*, *Kazirah*, *Gule ma'sfar*, *Mua'sfir*,

Bahram, *Bahraman*, *Kafisha*, *Gule Kafisha*, *Tukhme Kafisha*, *Tukhme Kajira* (Persian); *Karkarar*, *Kurtam*, *Kusam*, *Kushumbha*, *Kusumba*, *Ma'safir* (Punjabi); *Saflor* (Russian); *Kamalottara*, *Kusumba*, *Agnishikha*, *Gramyakunkuma*, *Rakta*, *Kamalottama*, *Kukkutashikha*, *Kusumbha*, *Lohita*, *Maharajana*, *Padmottara*, *Papaka*, *Pawadi*, *Pita*, *Vanishikha*, *Vasraranjana* (Sanskirit); *Sendurkam*, *Sendurukkai*, *Kusumbavirai*, *Chendurukam*, *Kusumba*, *Sendurgam*, *Sendurakam*, *Sethurangam* (Tamil); *Agnisikha*, *Kusumbha*, *Kushumba*, *Kusumbalu* (Telgu); *Atarqatoos*, *Faiqas* (Unani); *Karha*, *Qurtum*, *Kusum* (Urdu) (Aawan, 1984; Ibn Nafees, 1891; Anonymous, 1992; Chatterjee & Pakrashi, 1997; Chopra *et al*., 1956; Farooq, 2005; Ghani, 1920; Hakim 1999; Ibn Baitar, 2003; Ibn Sina, 1992; Karim, 1888; Khan, 1313H; Khare, 2004; Khory & Katrak 1985; Kirtikar and Basu, 1987; Nabi, 1893; Singh, 1974).

Mizaj (Temperament)

The Unani physicians described the temperament of *Qurtum* as Hot in second degree and Dry in first degree (Ghani, 1920; Hakim, 1999; Karim, 1888; Khan, 1313H; Nabi, 1893).

Afa'al (Action)

In classical Unani literature, various actions of the plant *Carthamus tinctorius* have been described such as *Mudirr-e-Baul wa Haiz* (Aawan, 1984), *Mohallil* (Husain, 1872; Ibn Nafees, 1891), *Kasir-e-Riyah* (Ibn Baitar, 2003), *Mohallil-e-Riyah*, *Munzij* (Ghani, 1920; Hakim, 1999; Karim, 1888; Nabi, 1893), *Mukhrij-e-Balgham Ghaleez*, *Mukhrij Khilt-e-Sauda*, *Mulaiyan* (Ghani, 1920), *Mushil* (Ghani, 1920; Hakim, 1999; Husain, 1872; Ibn Baitar, 2003; Khan, 1313H), *Mushil-e-Balgham* (Aawan, 1984; Ibn Baitar, 2003; Khan, 1313H; Nabi, 1893), *Mushil-e-Balgham Sokhta* (Ibn Baitar, 2003; Ibn Sina, 1992), *Mushil-e-Kaimus Sokhta Ghaleez* (Ibn Baitar, 2003), *Mushil wa Mukhrij-e-Balgham Raqeeq wa Akhlat-e-Muharriqa* (Karim, 1888), *Mushil wa Mukhrij-e-Balgham Ghaleez wa Akhlat-e-Muharriqa* (Hakim, 1999), *Muqawwi-e-Basr* (Nabi, 1893), *Munaqqi-e-Sadr*, *Musffi-e-Saut* (Aawan, 1984; Ghani, 1920; Hakim, 1999; Ibn Sina, 1992; Karim, 1888; Khan, 1313H; Nabi, 1893), *Muqawwi-e-Bah* (Hakim, 1999; Ibn Sina, 1992; Karim, 1888; Nabi, 1893) along with milk or honey or *anjeer* (Ibn Baitar, 2003), *Muwallid-e-Mani* (Aawan, 1984; Hakim, 1999; Ibn Baitar, 2003; Karim, 1888; Nabi, 1893).

Istemal (Uses)

Qurtum Has been described to be useful in various ailments such as *Istisqa* (Ghani, 1920; Hakim, 1999), *Malikholiya* (given with *Aftimoon*) (Ghani, 1920; Hakim, 1999; Nabi, 1893), *Wiswas*, *Kharish* (Ghani, 1920; Nabi, 1893), all types of *Jarb* (Ibn Baitar, 2003), *Khadr*, *Wajaul Mafasil* (oil is locally applied), *Surfa*,

Zeequn Nafas (Aawan, 1984), *Khafqan*, *Amraz-e-Saudawi* (Hakim, 1999), *Juzam* (Ghani, 1920; Hakim, 1999; Ibn Baitar, 2003), *Qaulanj* (Aawan, 1984;Ghani, 1920; Hakim, 1999; Ibn Baitar, 2003; Ibn Sina, 1992;Nabi, 1893); useful in almost all respiratory diseases (Hakim, 1999; Karim, 1888). Powder of the seed improves the complexion (Ghani, 1920; Karim, 1888) and the whole plant is good for old people (Hakim, 1999).

Pharmacological Actions (As described in Ethnobatanical and Traditional literature)

The drug *Carthamus tinctorius* is described in detail in ethnobotanical and scientific literature. Some pharmacological actions and therapeutic uses are as follows:

The flowers of the plant act as analgesic, circulatory stimulant and mensturation regulator (Evans, 2002). They are also used as emmenogogue, sedative, stimulant (Kirtikar and Basu, 1987), diaphoretic and laxative (Chatterjee & Pakrashi, 1997; Chopra *et al*., 1956). The flowers have also been described to be diuretic, hypnotic, expectorant and tonic to liver (Kirtikar and Basu, 1987); and cure the jaundice (Nadkarni, 1954; Chopra *et al*., 1956).

In Chinese medicine, the flowers are given to stimulate menstruation and to relieve abdominal pain. The flowers are also used to cleanse and heal the wound and sores. Chinese researchers indicate that the flowers and oil can reduce coronary artery disease and lowers the cholesterol levels (Khare, 2004). The seeds are purgative (Nadkarni, 1954), diuretic, tonic (Chopra *et al*., 1956) and antirheumatic (Chatterjee & Pakrashi, 1997). They are antihypertensive (Farooq, 2005); laxative (Dymock, 1891) and nephroprotective (Huang, 1999). Oil from seed is sweetish; good in all disease; tonic, purgative, carminative, aphrodisiac, bechic and cures pain in liver and joints (Kirtikar & Basu, 1987). Patients with hypertension and heart ailments use the refined oil in cooking, as it is rich in polyunsaturated fatty acids (Khare, 2004). The root is diuretic (Anonymous, 1950; Farooq, 2005).

Therapeutic Uses

The whole plant is valuable remedy for itch, paralytic limbs, rheumatism and intractable ulcers (Chatterjee & Pakrashi, 1997). Plant boiled in sesamum oil is a valuable remedy for itch. This medicated oil is locally applied to rheumatic and painful joints, paralytic limbs and intractable ulcers. Hot infusion of dried flowers is given as a diaphoretic in jaundice, nasal catarrh and muscular rheumatism (Nadkarni, 1954). An infusion of flowers is given to children and infants in measles, fevers and eruptive skin affections (Khare, 2004). Flowers cure

inflammation, boils, ring worm, scabies, leucoderma, piles, and bronchitis, and improve the complexion (Kirtikar & Basu, 1987). They are also used in abdominal pain (Anonymous, 1996); dysmenorrhoea (Caius, 2003) and fever (Bhattacharjee, 2004; Bhattacharjee and De, 2005; Caius, 2003; Anonymous, 1996). Tender leaves and stems, from the 4^{th} to the 6^{th} week of sowing, are eaten boiled as a vegetable (Nadkarni, 1954). The seeds are used to cure the pain in chest and throat, catarrh, leucoderma and scabies (Kirtikar & Basu, 1987). They are also used in rheumatism (Chopra *et al*., 1956; Nadkarni, 1954); hypercholesteremia (Farooq, 2005) and lupus erythematosus (Huang, 1999). The oil from the seed is used for healing sore and in rheumatism (Chopra *et al*., 1956). It is most valuable edible oil used in cookery. It is also used in the manufacture of soap and oil paints (Nadkarni, 1954).The edible oil is used in the manufacture of oleomargarine, as a dietary supplement in hypercholesteremia and also in the treatment of atherosclerosis. Due to its high linoleic acid content, it is consumed for preparation of vegetable ghee. Industrially, it is used for preparation of soft-soap varnishes, linoleum and water proofing material (Kokate *et al*., 2004).

Phyto-chemistry

The flowers contain red colouring principle carthamin or carthamite($C_{14}H_{16}O_7$) insoluble in water 0.3-0.6%, a yellow colouring matter soluble in water26.1-36.01%, extractive matter 3.6-5.6%, albumin 1.5-8.0%, wax 0.6-1.5%, cellulose 38.4-56.0%, silica 1.0-8.4%, alumina and oxide of iron 0.4-1.6%, manganese 0.1- 0.5% (Dymock 1891).Carthamin and neocarthamin from yellow and ivory white varieties of plant, kaempferol-3-rhamnoglucoside and kaempferol glycoside from ivory white flowershave been isolated (Rastogi & Mehrotra, 1990). Three acyl-serotonins isolated from oil-free safflower and identified as N-feruloyl-serotonin, N-p-coumaroyl-serotonin and N-p-coumaroyl-serotonin-*â*-D-glucopyranoside. A steroid cellobiosidehas been isolated from flowers (Rastogi & Mehrotra, 1991).Safflor yellow B isolated from petals. Nonacosane, *â*-sitosterol, palmitic, myristic and lauric acids isolated from flowers (Rastogi & Mehrotra, 1993). Luteolin and its 7-O-glucoside, and glucoside of*â*-sitosterol were isolated from flowers (Rastogi & Mehrotra, 1995).Safflor yellow A and B, safflomin A and C, isocarthamin, isocarthamidin, hydroxysafflor yellow A, and tinctormine have been reported from the flower petals of *Carthamus tinctorius*, as well as several new flavonoids and phenolic compounds. Four compounds including a new flavonoid glucoside were also isolated from 95% ethanol extract of dried petals. They are 6-hydroxykaempferol 3-O-glucoside, 6-hydroxykaempferol 7-O-glucoside, kaempferol 3-O-rutinoside and quercetin 3-O-glucoside (Li & Che, 1998).The flower petals reported to contain C-glycosylquinocholcone. They also contain the flavonoids, 6-hydroxykaempherol, and its 3 glucoside 3,6 diglucoside,

3,6,7-triglucoside and 3-rutinoside-6-glucoside (Anonymous 2000).The flowercontains 1-O-hexadecanolenin, trans-3-tridecene-5,7,9,11-tetrayne-1,2-diol, trans-trans-3,11-tridecadiene-5,7,9-triyne-1,2-diol, coumaric acid, daucosterol and apigenin(Liu *et al*., 2005). Two new acetylenic glucoside, 4', 6'-acetonide-8Z-decaene-4,6-diyne-1-O-beta-D-glucopyranoside named carthamoside A1 and 4,6-decadiyne-1-O-beta-D-glucopyranoside named carthamoside A2, along with one known acetylenic glucoside, 8Z-decaene-4,6-diyne-1-O-beta-D-glucopyranoside, were isolated from the air dried flower (Zhou *et al*., 2006). Two new spermidine compounds, namely safflospermidine A (1) and safflospermidine B (2), together with two known compounds, N(1),N(5),N(10)-(Z)-tri-p-coumaroylspermidine (3) and N(1),N(5),N(10)-(E)-tri-p-coumaroylspermidine (4), were isolated from the florets of *Carthamus tinctorius* (Jiang *et al*., 2008). From the dried petalsof *Carthamus tinctorius*, a new flavonoid, (2R)-4',5-dihydroxyl-6,7-di-O-beta-D-glucopyranosyl flavanone and a new aromatic glucoside, methyl-3-(4-O-beta-D-glucopyranosylphenyl) propionate were isolated along with four known compounds (25)-4', 5-dihydroxyl-6, 7-di-O-beta-D-glucopyranosyl flavanone (1), 6-hydroxykaempferol-3, 6-di-O-beta-D-glucopyranoside (2), 4-O-beta-D-glucosyl-trans-p-coumaric acid (3), and 4-O-beta-D-glucosyl-cis-p-coumaric acid (4) (Zhou *et al*., 2008).A study reveals that ten chemical constituents from the flowers were isolated and identified as 7,8-dimethylpyrazino [2,3-g] quinazolin-2, 4-(1H, 3H) -dione (1), adenosine (2), adenine (3), uridine (4), thymine (5), uracil (6), roseoside (7), 4'-O-dihydrophaseic acid-beta-D-glucopyranoside methylester (8), 4-O-beta-D-glucopyranosyloxy-benzoic acid (9) and p-hydroxybenzoic acid (10) (Jiang *et al*., 2008).Three new aromatic glucosides, 2,3-dimethoxy-5-methylphenyl-1-O-beta-d-glucopyranoside (1), 2,6-dimethoxy-4-methylphenyl-1-O-beta-d-glucopyranoside (2), and ethyl-3-(4-O-beta-d-glucopyranosyl-3-methoxyphenyl)propionate (3), named as carthamosides B1, B2, and B3, respectively, along with three known aromatic glucosides, methyl-3-(4-O-beta-D-glucopyranosyl-3-methoxyphenyl)propionate (4), ethylsyringin (5), and methylsyringin (6), have been isolated from the air-dried flower of *Carthamus tinctorius* (Zhou *et al*., 2008).

A total of eight flavonoids (1-8), including a novel quercetin-7-O-(6''-O-acetyl)-beta-D-glucopyranoside (6) and seven known flavonoids, luteolin (1), quercetin (2), luteolin 7-O-beta-D-glucopyranoside (3), luteolin-7-O-(6''-O-acetyl)-beta-D-glucopyranoside (4) quercetin 7-O-beta-D-glucopyranoside (5), acacetin 7-O-beta-D-glucuronide (7) and apigenin-6-C-beta-D-glucopyrano syl-8-C-beta-D-glucopyranoside (8), have been isolated from the leaves of the *Carthamus tinctorius* (Lee *et al*., 2002).A new triterpenoid saponin was obtained from the ethanolic fraction of the leaves (Yadav & Navneeta, 2007).

Seeds contain a clear straw coloured fixed oil (Nadkarni, 1954).A glucopyranoside

of tracheloside, *â*-sitosterol, campesterol, glucose, maltose and raffinose isolated from seeds; seed cake contained protein (37.53%) and carbohydrates (57.98%). Three new serotonins – N-feruloylserotonin, N – (p-coumaroyl) serotonin and N – (p-coumaroyl) serotonin-mono-*â*-D-glucopyranoside isolated from seeds along with 2-hydroxyarctin, matairesinol mono- *â*-D-glucopyranoside and acacetin (Rastogi & Mehrotra, 1993).New indole alkaloid serotobenine – isolated from seeds along with N-feruloyltryptamine and N- (p-coumaroyl) tryptamine (Rastogi & Mehrotra, 1995).Seven antioxidative serotonin derivatives were isolated from safflower oil cake. Their structures were established as N-[2-(5-hydroxy-1H-indol-3-yl)ethyl]ferulamide (1), N-[2-(5-hydroxy-1H-indol-3-yl)ethyl]-p-coumaramide (2), N,N'-[2,2'-(5,5'-dihydroxy-4,4'-bi-1H-indol-3,3'-yl)diethyl]- di-p-coumaramide (3), N-[2-[3'-[2-(p-coumaramido)ethyl]-5,5'-dihydroxy- 4,4'-bi-1H-indol-3-yl]ethyl]ferulamide (4), and N,N'-[2,2'-(5,5'-dihydroxy-4,4'-bi-1H-indol-3,3'-yl)diethyl]- diferulamide (5), N-[2-[5-(beta-D-glucosyloxy)-1H-indol-3-yl)ethyl]- p-coumaramide (6), and N-[2-[5-(beta-D-glucosyloxy)-1H-indol-3-yl)ethyl]ferulamide (7) (Zhang *et al*., 1997). From the aqueous ethanol extract of seeds of *Carthamus tinctorius*, a new acacetin diglycoside has been isolated and identified as acacetin 7-O-beta-D-apiofuranosyl-(1"'—>6" instead of 6')-O-beta-D-glucopyranoside together with previously isolated kaempferol 7-O-beta-D-glucopyranoside, acacetin 7-O-alpha-L-rhamnopyranoside and acacetin (Ahmed *et al*., 2000). Safflower oil contains glycerides of palmitic (6.5%), stearic (3%), arachidic (0.296), oleic (13%), linoleic (76-79%) and linolenic acids (90.15%). The polyunsaturated fatty acid content of the oil is highest (75%) and is said to be responsible to control cholesterol level in the blood, and thereby, reduces incidence of heart attacks (Kokate *et al*., 2004).

A new bioactive triterpenoid saponin 3beta-O-[beta-D-xylopyranosyl(1 -> 3)-O-beta-D-galactopyranosyl]-lup-12-ene-28 oic acid-28-O-alpha-L-rhamnopyranosyl ester compound (A), was isolated from the methanolic fraction of the roots of *Carthamus tinctorius* (Yadava & Chakravarti, 2008).

Pharmacological Studies

A number of studies have been carried out on*Carthamus tinctorius* in recent years showing that it possesses diverse pharmacological effects. Some of the important pharmacological effects are as follows:

Anticoagulant

Thrombolytic and anticoagulant activity of *Carthamus tinctorius* in carrageenan induced mice model has been reported. The fermented extracts demonstrated significant thrombolytic and anticoagulant effect (He *et al*., 2005).

Anti-estrogenic

Anti-estrogenic activity of the lignan glycoside, tracheloside, isolated from seeds of *Carthamus tinctorius* was investigated against cultured Ishikawa cells by employing a bioassay-linked HPLC-ELSD method. Tracheloside significantly decreased the activity of alkaline phosphatase (AP), an estrogen-inducible marker enzyme, a level of inhibition comparable to that of tamoxifen (Yoo *et al*., 2006).

Antihypertensive

A study reported that safflower yellow, a mixture of chalconoid compounds extracted from *Carthamus tinctorius* increased blood pressure, plasma rennin and angiotensin II level in experimental group (Liu *et al*., 1992).

Antiinflammatory

The effects of dried safflower petals aqueous extracts and Carthamus yellow, the main constituent of safflower, on lipopolysaccharide-induced inflammation were investigated. The results suggest that they provide anti-inflammatory response (Wang *et al*., 2011). In an experimental study the possible molecular mechanism by which methanol extracts of *Carthamus tinctorius* produced anti-inflammatory action has been explored. The extract induces heme oxygenase-1 expression so that it reduces inflammation by suppression of inducible nitric oxide synthase and cyclooxygenase-2 expression in cells activated with lipopolysaccharide (Jun *et al*., 2011).

A new bioactive triterpenoid saponin, isolated from the methanolic fraction of the root of *Carthamus tinctorius*, showed anti-inflammatory activity (Yadava & Chakravarti, 2008). It has also been reported that N-(p-coumaroyl) serotonin isolated from safflower oil cake inhibits the production of pro inflammatory cytokines by endotoxin (LPS)- stimulated human monocytes. The results indicate that serotonin and its derivatives inhibit the production of pro inflammatory cytokines through multiple mechanisms (Takii *et al*., 2003).

Antimicrobial

Methanolic extract from the leaves of *Carthamus tinctorius* subjected to screen anthelmintic, antibacterial and antiviral activities, was found to possess significan effect. The anthelmintic activity of extract was performed on Indian earthworm. It exhibited significant reduction in time of paralysis and death of worms. The antibacterial activity was carried out on different pathogens however *Pseudomonas auerogenosa* was found to be more sensitive. The antiviral activity of the extract was studied successfully against tobacco viruses (Paramesh *et al*., 2009).

Antioxidant

It has been reported that the flavonoids isolated from the leaves of the *Carthamus tinctorius* have significant anti-oxidant activities against 2-deoxyribose degradation and lipid per-oxidation in rat liver microsomes (Lee *et al*., 2002). Safflower yellow from *Carthamus tinctorius* has also been reported to possess anti-oxidant property. It has hydroxyl radical scavenging effect and decreases the rate of lipid peroxidation in mouse liver suspension (Jin *et al*., 2004). *In vitro* antioxidant activity of the extract of *Carthamus tinctorius* was also evaluated and it has been reported that flavonoids were the main components of extract and were active in scavenging all three radicals in a dose-dependent manner (Han *et al*., 2010). The antioxidant effect of its aqueous extract was found effective in ox-LDL induced injury in rat cardiac microvascular endothelial cell as it decrease the oxygen derived free radicals. The mechanism has been related with scavenging of free radicals, enhancing its clearance and enhancing endogenous antioxidant activity (Ye *et al*., 2008). The serotonin derivatives isolated from safflower oil cake been found to have relatively strong antioxidative activity (Zhang *et al*., 1997). The potential protective effects of *Carthamus tinctorius* flower extract against reactive oxygen species induced osteoblast dysfunction were investigated. The results demonstrate that it can act as a biological antioxidant in a cell culture experimental model and protect osteoblasts from oxidative stress-induced toxicity (Choi *et al*., 2010). Hiramatsu *et al*. (2009) have reported that petal extract of *Carthamus tinctorius* has free radical scavenging activity and neuroprotective effect and carthamin is one of the major active components. Kinobeon A, isolated from cultured cells of safflower has been shown to be a useful cytoprotective agent as it has demonstrated to prevent oxidative stresses (Kanehira *et al*., 2003).

Atherosclerosis

The effect of defatted safflower seed extract and its phenolic constituents, serotonin derivatives, were studied on atherosclerosis. The findings demonstrate that serotonin derivatives of ethanol-ethyl acetate extract of safflower seeds are absorbed into circulation and attenuate atherosclerotic lesion development possibly because of the inhibition of oxidized low-density lipoprotein (LDL) formation through their strong antioxidative activity (Koyama *et al*., 2006).

Blood

The carthamin yellow has been reported to significantly decrease the whole blood viscosity, plasma viscosity, and erythrocyte aggregation index, which were found increased in blood stasis model. Hematocrit and platelet aggregation were reduced, while prothrombin time delayed with the increasing dose (Li *et al*., 2009).

In a rat model of left heart failure after myocardial infarction injection of *Carthamus tinctorius* was given for activating blood circulation. It showed certain inhibitory effect of left ventricular remodeling (Wang *et al*., 2002).

Bone

Kim *et al.* (2002) reported that safflower seeds have a protective effect on bone loss caused by estrogen deficiency, without substantial effect on the uterus. E2 (17b-estradiol) treatment almost completely prevented bone loss as well as marrow adiposity. However, safflower seeds partially prevented ovariectomy-induced bone loss and slightly reduced marrow adiposity. Monfared and Salati (2013) on the other hand have reported detrimental effects on the ovarian histomorphology and female reproductive hormones. The effect of methanolic extract of safflower seeds, containing high mineral content, such as calcium, potassium and phosphorous, were evaluated on bone formation and is likely appears to be mediated by insulin-like growth factor I at the early stage of treatment (Lee *et al*., 2009). It has also been reported to be useful for the treatment of diseases associated with elevated bone loss (Yuk *et al*., 2002).

Diuretic and Nephroprotective

Hydroalcoholic extract of seeds of *Carthamus tinctorius* have been reported to possess protective and curative effects against gentamicin induced acute renal injury along with diuretic effect, in albino rats (Wasim *et al*., 2011).

Enzyme Inhibiting

Hung *et al* (2007) has demonstrated inhibiting activity of the enzymes of alpha-amylase and protein tyrosine phosphatase IB by using the ethyl acetate extract of *Carthamus tinctorius*. It supports the ethnomedicinal use of the drug in diabetes.

Food Additive

Nobakht *et al*., (2000) have studied its flowers for teratogenic and cytotoxic effect of flowers of *Carthamus tinctorius*, which is used as a coloring and flavoring agent in food items. They have concluded that the use of flowers as a food additive should be reconsidered.

Hepatoprotective

Hydroxyl safflor yellow A has been shown to possess hepatoprotective effect aginst carbon tetrachloride induced liver fibrosis. Its promising role as an

antifibrotic agent in chronic liver disease has also been predicted (Zhang *et al*., 2011).

Immune Function

Suppressive effect of safflower yellow on immune functionwas was carried out and it has been reported that it decreases both nonspecific and specific immune functions (Lu *et al*., 1991).

Melanin

Roh *et al*., (2004) reported the inhibitory effect of active compounds isolated from safflower seeds for melanogenesis. It was found that N-feruloylserotonin and N-(p-coumaroyl) serotoninstrongly inhibited the melanin production in comparison with a known melanogenesis inhibitor, arbutin.

Memory

Protective effect of Nicotiflorin, a natural flavonoid extracted from coronal of *Carthamus tinctorius*, was evaluated on cerebral multi-infarct dementia in rats. The result suggested that it has protective effects on reducing memory dysfunction, energy metabolism failure and oxidative stress in multi-infarct dementia rat model (Huang *et al*., 2007).

Myocardial ischemia

In a study, effect of a purified extract of *Carthamus tinctorius* on myocardial ischemia was investigated using both *in vivo* and *in vitro* models. The result revealed that pretreatment with the extract could protect the heart from ischemia injury by limiting infarct size and improving cardiac function (Han *et al*., 2009).

The protective effects of N-(p-Coumaroyl) serotonin (C) and N-feruroylserotonin (F), present in safflower oil,were investigated in perfused guinea-pig Langendorff hearts subjected to ischemia and reperfusion.The findings suggest that the antioxidant effects of both derivatives isolated from safflower play an important role in ischemia-reperfusion hearts in close relation with nitric oxide (Hotta *et al*., 2002). The protective effects of *Carthamus tinctorius* injection on isoprenaline-induced acute myocardial ischemia in rats has been reported by Wan *et al*., (2011). Further it has also been reported that aqueous extracts of *Carthamus tinctorius* reduce myocardial infarct size and leakage of myocardial enzyme, and increase the level of 6-keto-PGF1alpha, so as to inhibit platelet aggregation and prevent thrombosis, the result of which is to reduce myocardial ischemic reperfusion injury (Liu *et al*., 2011).

Neuroprotective

The hydroxyl safflor yellow A, a soluble constituent extracted from *Carthamus tinctorius*, was administered to rats after the onset of cerebral ischaemia. It exerted significant neuroprotective effects on rats with focal cerebral ischaemic injury as expressed by neurological deficit scores and reduced the infarct area as compared with saline group (Zhu *et al*., 2005).

The protective effect of hydroxyl safflor yellow A was investigated on focal cerebral ischemia in rats. In *in vitro* studies, it significantly inhibited neuron damage induced by exposure to glutamate and NaCN in cultured fetal cortical cells (Zhu *et al*., 2005).

The therapeutic effects of hydroxylsafflor yellow A on focal cerebral ischemic injury in rats and its related mechanisms have been investigated. It appears to be a good potential agent to treat focal cerebral ischemia, and the underlying mechanisms exerted by HSYA might be involved in its inhibitory effects on thrombosis formation and platelet aggregation (Zhu *et al*., 2005). Zhu *et al*. (2003) have further reported neuroprotective effect of hydroxysafflor yellow A on cerebral ischemic injury in both *in vivo* and *in vitro* studies suggesting that it might act as a potential neuroprotective agent useful in the treatment in focal cerebral ischemia In another study hydroxysafflor yellow A (5 mg/kg, i.p.) was shown to improve the brain injury induced by lymphostatic encephalopathy and significantly alleviated the neurological deficits (Pan *et al*., 2012). It has also been reported to it protect the cortical neurons, at least partially, from inhibiting the expression NR2B-containing NMDA receptors and by regulating Bcl-2 family (Yang *et al*., 2010).

Osteoporosis

The effects of safflower seed oil on osteoporosis induced-ovariectomized rats were investigated. The result suggested that the safflower seeds have possible roles in the improvement of osteoporosis induced-ovariectomized rats (Alam *et al*., 2006).

Pharmacokinetic

Studies were conducted to characterize the pharmacokinetics and excretions of hydroxysafflor yellow A in rats and dogs after administration by intravenous injection or infusion. Plasma, urine, feces and bile concentrations of HSYA were measured. The results indicated that HSYA was rapidly excreted as unchanged drug in the urine (Chu *et al*., 2006).

The pharmacokinetic characteristics of Hydroxysafflor yellow A in healthy Chinese female volunteers was investigated. The findings suggested that its

pharmacokinetic properties are based on first-order kinetics over the dose range tested (Yang *et al*., 2009).

The distributive character of safflor yellow A in mice was investigated. After IV injection of safflor yellow A in mice, the AUC of safflor yellow A was highest in plasma, followed by kidney, liver, lung, heart, spleen. But it was not found in the brain (Liu *et al*., 2004).

Spermatogenesis

The effect of aqueous extract of *Carthamus tinctorius* on mouse spermatogenesis was evaluated and testicular histopathology, morphometric analysis and spermatogenesis assessments were performed. The findings suggested that it has toxic effects on mouse testicular tissue (Mirhoseini *et al*., 2012).

Spinal Cord

The potential protective effect of Hydroxysafflor yellow A in spinal cord ischemia/ reperfusion injury was investigated. The findings suggested that it may protect spinal cords from ischemia / reperfusion injury by alleviating oxidative stress and reducing neuronal apoptosis in rabbits (Shan *et al*., 2010).

Stone

The effect of *Carthamus tinctorius* on calcium oxalate formation in ethylene glycol fed rats was investigated. Safflower administration appeared to inhibit the deposition of CaOx crystal in ethylene glycol fed rats therefore it may be effective in preventing the stone disease (Lin *et al*., 2012).

Uterus

The experimental results indicate that the decoction of *Carthamus tinctorius* has stimulating action on the uterus of mouse (*in vitro*). The stimulating action has been found related to stimulating H_1-receptor and alpha-adrenergic receptor of uterus (Shi *et al*., 1995).

α-glucosidase inhibitor

In a study α-glucosidase inhibitor activity of serotonin derivatives (e.g. N-p-coumaroyl serotonin and N-feruloyl serotonin), isolated from safflower seed (*Carthamus tinctorius*), has been evaluated (Takahashi & Miyazawa, 2012).

Conclusion

Qurtum (*Carthamus tinctorius*) has been in use since times immemorial to treat wide range of indications. It has been subjected to quite extensive phytochemical,

experimental and clinical investigations. Experimental studies have demonstrated its anticoagulant, antistress, antihypertensive, anti-inflammatory, antimicrobial, antioxidant, antiatherosclerotic, diuretic, nephroprotective, enzyme inhibiting, food additive, hepatoprotective, immune function, melanogenesis, cardioprotective, neuroprotective, antiosteoporotic, spermatogenesis and α-glucosidase inhibitor effects. The scientific studies have proved most of the claims of traditional medicines. However, further, detailed clinical research appears worthwhile to explore the full therapeutic potential of this plant in order to establish it as a standard drug.

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