



## HEPATOBIILIARY PROTECTIVE AND THERAPEUTIC APPLICATION OF QURTUM (*CARTHAMUS TINCTORIUS* L.): A REVIEW

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### ABSTRACT

Qurtum (*Carthamus tinctorius* L.) is a plant origin drug belongs to traditional system of medicine. Botanicals are the main component of prescriptions of Unani physicians in the treatment of disease. The Unani System of Unani (USM) is one of the traditional systems of medicine that deals with plants. Plants are the large source of medicine. Qurtum (*Carthamus tinctorius* L.) is one of the plant origin drugs, has been used for various therapeutic purposes in USM. Its active constituents are responsible for their actions described in Unani classical literature such as are mushil-e-balgham (Phlegmagogue), munaffith-e-balgham (Expectorant), mussafi-e-saut (Clear voice), muququawi-e-bah (Aphrodisiac), mudirr-e-hayz (Emmenagogue), muwallid-e-mani (Spermatogenic), antidote, mulattif (Demulcent), muhallil-e-waram (Inflammation resolvent), muhallil-e-riyah (Carminative), mudirr-i-bowl (Diuretic). It concluded, according to these properties they are effective in Hepatitis, Fatty Liver, Cirrhosis of liver, Ascites, Dyslipidemia, Hypertension Ischemic Heart Disease (IHD), Atherosclerosis, Alzheimer's disease, Cerebral ischemia, Diabetes Mellitus, Osteoporosis, Gastric Ulcer, Urolithiasis. This is a review paper which discusses morphology, pharmacological action, ethno-medicinal and therapeutic uses of this medicinal plant in perspective of Unani medicine. This review has been done through online searches of databases such as PubMed, Google Scholar, Embase, science direct and hand search for classical textbook available in different libraries.

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### INTRODUCTION

In Unani System of Medicine (USM) liver is one of the vital organs also known as *Kabid* or *Matbakh* (Kitchen) of the body, it plays an important role in metabolism. liver is origin of all *Quwaa* (Natural powers) such as *Quwwat-e-jadhba* (Power of absorption), *Quwwat-e-ghadhiya* (Power of digestion), *Quwwat Masika* (Power of retention) and *Quwwat-e-Dafi'a* (Power of excretion).<sup>1,2</sup> Liver is the organ responsible for source

of energy (*Hararat-e-ghariziyya*) in our body like sun (for other planets). Liver also responsible for production of *akhlat-e-Arba*.<sup>3,4,5</sup> Now a day's excessive use of conventional medicines such as steroids, antiviral, antibiotic, anti-inflammatory and vaccine give temporary benefits with serious risks of toxicity if we use chronically, bad habits like chronic alcoholism, viral infections, environmental pollution and chemical (paracetamol, carbon tetra chloride

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(CCL<sub>4</sub>) thioacetamide) may directly effect on it.<sup>6,7,8</sup> Because liver is first bypass of all foreign compounds that may cause hepatotoxicity and liver diseases like hepatitis, abscess, cirrhosis, hepatomegaly, and hepatocellular inflammations.<sup>6</sup> Hepatotoxicity is one of the major problems all over the world about 20,000 deaths occurs, every year 2, 50,000 new cases of hepatocellular carcinoma cases newly diagnosed.<sup>9</sup> So there is needed to search alternative treatment hence various traditional medicines are Centre of attraction. They have been uses as hepatoprotective for their primary healthcare because of their medicinal activities and highly safety effect with fewer side effects.<sup>10</sup>

Safflower (*Carthamus tinctorius* L.) is one of the best hepatoprotective medicines in traditional system of medicine belong to plant origin of the family Asteraceae.<sup>11,12</sup> In oriental countries used traditionally for preparation of herbal medicines, coloring, cosmetic and dyeing fabrics and painting.<sup>12</sup> *Qurtum* (*Carthamus tinctorius* L.) an erect branching herb half meter high with broad lanceolate, rough and thorny leaves with orange-red buds which further develop into flowers. seeds are sanobari in their appearance with white covering and oily. Safflower (*Carthamus tinctorius* L.) has wild and domestic types. Mostly Safflower (*Carthamus tinctorius* L.) means domestic type. They are *mushil-e-balgham* (Phlegmagogue), *munaffith-e-balgham* (Expectorant), *mussafi-e-saut* (Clear voice), *muqquawi-e-bah* (Aphrodisiac), *mudirr-e-hayz* (Emmenagogue), *muwallid-e-mani* (Spermatogenic), antidote, *mulattif* (Demulcent), *muhallil-e-waram* (Inflammation resolvent), *muhallil-e-riyah* (Carminative), *mudirr-i-bowl* (Diuretic) according to this properties they are effective in *Sual-o-Surfa* (Cough/ Bronchitis), *Waram-e-reham* (Metritis), *waram-e-ahsha* (Inflammation of organ), *waram-e-kabid* (Hepatitis), cure inflammations, boils, ringworm, scabies, vitiligo, piles, bronchitis, improve complexion, worm infestation. It is used as a substitute for saffron in measles, scarlatina and exanthematous to promote the eruption.<sup>13,14,15,16,17</sup>

Many studies revealed that Safflower has powerful antioxidant and hepatoprotective effect against CCL<sub>4</sub>-induced liver injury.<sup>18,19,20</sup>

**Safflower has different name all over the world in their regional languages:**<sup>13</sup>

**Arabic:** Qirtum, Qurtum

**Persian:** Khasakdana, Kajirah, Kazirra

**Bengali:** Kajirah, Kusamphul, Kusum

**Hindi:** Barre, Karrah, Kusumba, Kusum, Kamalottara, Kamalottam, Kukkutashikha, Aginishika, Padmottare, Papaka.

**English:** Safflower

**Malayam:** Chenurakam

**Marathi:** Kudaya, Karahi, Kasdi, Kurdi, Shumba

**Punjabi:** Kar, Karar, Kurtam, Kusam, Kushumbha

**Sanskrit:** Pita, Rakta, Varsranjana, Kusumbha, Lohita

**Tamil:** Chendurakam, Sendurakam

**Telgu:** Agnisikha, Kushumba, Kusumba

**Urdu:** Karha, kusum

**Temperament:** Hot Dry 2<sup>13</sup>

**Dose:** 3-5 gm.<sup>13</sup>

**Parts use:** Flower, Seeds, Root and whole plant.<sup>13,21</sup>

**Active constituents:**

In petals active constituents are carthamin, carthamidine, isocarthamidine, safflower yellow A, safflower yellow B, safflomin C, hydroxyl safflower yellow A, isocarthamin, isocarthamidin, puerarin, 3'-methoxyl-puerarin, puerarinapioside tinctoramine, quercetin, kaempferol and phenolic acids (phenolic compound, caffeic acid). In addition to flavones, luteolin, lauric acid, myristic acid, palmitic acid.<sup>22</sup>

**Traditional uses:**

**Flowers:** Red orange in color, bitter in taste, laxative, expectorant, pneumonic, diuretic, stimulant, sedative, emmenagogue, purgative, flatulence, antihydrotic, abortifacient properties in nature can cure strangury, leprosy, inflammation, arthritis, bronchitis, ringworm, scabies, boils, leucoderma, and jaundice and chest pains. Tea made from flower is used to treat eruptive fever, soothe coughs and bronchial condition, also used as infusion with honey for asthma, hemiplegia and facial palsy.

**Seeds:** sweet, acrid, oleaginous with aphrodisiac properties can cure leprosy, constipation, powder of dry seeds half teaspoon mixed in one tablespoon of honey can cure bronchial asthma, act as expectorant and reduces spasm of airways during asthmatics attack.

**Oil** of seeds is indigestible. Bitter in taste, purgative, carminative, aphrodisiac can cure scabies, leucoderma, catarrh, pain in chest and throat. Oil of

seeds is sweetish purgative, carminative, aphrodisiac in nature cure pain in the liver and joint. Oil used as a dressing of bad ulcer, itching, rheumatism, dysmenorrhea, paralysis, decoction of dry seeds used to cure dysmenorrhea, flatulent, colic, constipation, strangury, endometritis, powder of dry seeds mixed with equal quantity of madder used for treatment of urolithiasis medicine. Powder of dry seeds with pistachio nuts, honey and almond is used with milk at bed time very effective as aphrodisiac.

**Leaves** are sweet, hot with pungent smell. Laxative, diuretic, appetizer can cure urinary discharges. *Qurtum* (*Carthamus tinctorius L.*) soaked within the milk then used it, act as *mushil* (Purgative) and evacuate *ikhlat-e-muhareka* from the body, laxative, stimulates menstrual flow and induces perspiration. When it is uses with *Aftimoon* (*Cuscuta reflexa roxb.*) cure melancholia and leprosy. *Qurtum* (*Carthamus tinctorius L.*) use in *habb* form acts as carminative and aphrodisiac. *Qurtum* (*Carthamus tinctorius L.*) used as gargle improve voice clearance. *Qurtum* (*Carthamus tinctorius L.*) mixed with honey and *Anjeer* (*Ficus carica*) evacuate *balgham* (phlegm) and *muquaw-i-bah* (Aphrodisiac), it is used 17.5 gm with salt act as *mushily-i-balgham* (phlegm) 5.25gm *qurtum* and 16gm sugar cure jaundice. *Qurtum* (*Carthamus tinctorius L.*) pummel and rap within the cloth and soaked in maul jubn, filter and use can cure melancholia, palpitation, scabies, pruritis, leprosy and all the melanic diseases. This compound within honey can improve voice, expectorant, clear airway tract, carminative, aphrodisiac, and improve fairness. Patient with cardiovascular disorders advised to use safflowers oil. The plant boiled in oil used as liniment in rheumatism, scabies, ulcer, paralysis of the limbs.<sup>13,</sup>

<sup>14, 15, 16, 17, 21, 23, 24</sup>

#### Conventional uses:

There is various disease of hepatobiliary system in which Unani System of Medicine (USM) play an important role in treatment.

#### Hepatitis:

In USM hepatitis is also known as *Warm-e-Kabid*, Hepatitis is Greek word formed by two worlds, heper means liver and itis means inflammation refers as inflammation of liver tissue.<sup>25-28</sup> Sometimes inflammation associated with muscles related to the liver and mesentery, liver peritoneum or in the liver blood vessels. It is due to conventional medicines such as steroids, antiviral, anti-tubercular drug (isoniazid and rifampicin) and vaccine give temporary

benefits with serious risks of toxicity if we use chronically, bad habits like chronic alcoholism, viral infections, environmental pollution and chemical (paracetamol, carbon tetra chloride ((CCL<sub>4</sub>), thioacetamide)<sup>6, 7, 8</sup> may directly affect on it and cause inflammation of liver tissue, tumor necrosis. Factor-alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) are increased due to intercellular damage. Then serum hepatic enzyme that is aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels increased. The leaves of safflower having active constituent dehydroabietylamine significantly reduced the toxic effect of ccl<sub>4</sub> also decrease AST, ALT and ALP, total bilirubin and increased protein synthesis. Flowers has polyphenolic compounds showed antioxidant and anti-inflammatory effects by inhibition of NF-KB transactivation; inhibiting prostaglandin synthesis, IL-6 production, and iNOS protein synthesis and decrease the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP), total bilirubin.<sup>29-35, 11</sup>

#### Fatty Liver:

Fatty liver also known as fatty liver diseases (FLD) and in USM called as "*Tashahhum Kabid*" in which abnormal collection of fat on liver more than 5-10% of liver weight, by the process of steatosis large vacuoles of triglyceride accumulate in the liver.<sup>36</sup> Fatty liver is always associated with metabolic syndrome like diabetes, obesity, and dyslipidemia if untreated caused cirrhosis of liver in 20% of cases, and death in 11%. In India prevalence of FLD is 35%.<sup>37, 38</sup> Powder of seeds and ethanol or aqueous extract of seeds of Safflower (*Carthamus tinctorius L.*) was significantly reduced total cholesterol as well as hepatic triglyceride also plays an important role in reduction of plasma cholesterol and triglyceride hence significantly treats the associated conditions such as diabetes, obesity, and dyslipidemia.<sup>39</sup>

#### Cirrhosis of liver:

In USM known as "*Taleef-ul-Kabid*" due to chronic liver injuries development of regenerative nodules, which are surrounded by fibrous bands called as cirrhosis of liver.<sup>40</sup> Cirrhosis of liver was 23<sup>rd</sup> leading cause of the death worldwide in 2010. It has multifactorial causes such as hepatitis (type B and type C), alcohol consumption, obesity, DMT2, HTN, dyslipidemia, fatty liver causes increase of serum hepatic enzyme that is AST, ALT, and ALP levels also lead to liver failure, portal hypertension, coagulation

disorders (due to impaired production of coagulation factors), ascites and other complications, including hepatic encephalopathy and the hepatorenal syndrom.<sup>39,40,41,11</sup> The leaves having active constituent dehydroabietylamine significantly reduced AST, ALT and ALP, total bilirubin and increase in the protein synthesis also the flowers has polyphenolic compounds decrease the levels of AST, ALT, ALP and total bilirubin.<sup>11,29-35, 41.</sup>

#### **Ascites:**

Ascites is defining as collection of fluid in peritoneal cavity more than 25ml. mostly superimpose with cirrhosis of liver and other causes are peritoneal carcinomatosis, hepatocellular carcinoma, Budd-Chiari syndrome, congestive heart failure, pancreatitis, Chronic alcohol, Obesity, Hypercholesterolemia, Type 2 diabetes, Nephrotic syndrome, Severe malnutrition, and tuberculosis. Ascites is the complications of cirrhosis then increase of serum hepatic enzyme that is AST, ALT, and ALP levels due to liver cell damage.<sup>42</sup> The leaves having active constituent dehydroabietylamine significantly reduced AST, ALT, ALP and total bilirubin and increase in the protein synthesis also the flowers have polyphenolic compounds which can decrease the levels of AST, ALT, ALP and total bilirubin.<sup>11,29-35</sup>

#### **Atherosclerosis:**

Atherosclerosis is one of the major problems having high morbidities and mortalities rate worldwide. It has major risk factors are hypertension, tobacco smoke, diabetes mellitus, obesity, inactive lifestyle, cholesterolemia. In Unani system known as Tasaddud Shahmi Kils. Atherosclerosis is a Greek word depends on two parts; atheros and sclerosis meaning thickening of the intimal layer of arteries due to accumulation of fat always associated with hyperlipidemia and hyperglycemia, in which plaque grows gradually due to proliferation of fibrous tissues and the surrounding smooth muscle and surge hence reduces blood flow inside the arteries also calcium deposition on lesion can cause hardening of arteries.<sup>43.</sup>

<sup>44</sup> Powder of seeds or ethanol and aqueous extract of seeds of Safflower (*Carthamus tinctorius* L.) was significantly reduced plasma total cholesterol as well as triglyceride level by increasing 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCoA) activity and decrease hepatic acyl-coenzyme A cholesterol acyltransferase activity hence seeds are play an important role to reduce atherosclerosis due to cholesterolemia.<sup>22,39</sup>

#### **Ischemic heart disease (IHD):**

Ischemic heart disease (IHD) is one of the serious and

life-threatening illness all over the world. It directly effects on economic condition of country. Ischemic Heart Disease can cause 8.92 million deaths per year all over the world, because in which imbalance occurs between myocardial blood supply and demand of body tissue. Risk factors are individual's age, gender, and genetics, Hypertension, hyperlipidemia, insulin resistance, obesity, and diabetes.<sup>45, 46</sup> In vitro and vivo study showed that of *Carthamus tinctorius* has cardioprotective effect in which *Carthamus tinctorius* injection inhibits S-T segment elevation and reduced serum IL-6 and TNF- $\alpha$  enzymes as well as suppressed overexpression of BAX protein and increase BCL-2 expression their ratio also decreases. Safflower injection (SI) improved the functions of cardiac contraction and dilation, increasing coronary blood flow, and strengthening the bcl-2 protein expression. On the basis of these finding *Carthamus tinctorius* has cardioprotective properties.<sup>22,39</sup>

#### **Hypertension:**

Hypertension is a common lifestyle disorder with a very strong risk factor predilection for cardiovascular diseases. Several surveys in the last two decades have reported a prevalence of 6.1% to 36.35% in men and 2%-39.4% in women in urban areas, and from 3%-36% in men and 5.8%-37.2% in women in rural areas respectively. The prevalence of hypertension increases with age and it is estimated that starting from around 15% -20% in early age, it increases to 75% -80% in individuals above 70 years of age.<sup>47</sup> Hypertension is the leading cause of mortality worldwide for ischemic heart disease and cerebrovascular stroke. Suboptimal blood pressure control has been identified as the third ranked factor for disability-adjusted life year.<sup>48</sup> In animal study safflower manifested to reduced blood pressure of spontaneously hypertensive rats at dose of 1-2 g/ kg / day for 5 weeks by inactivation or diminishing of renin-angiotensin system.<sup>22</sup> In this study, safflower yellow decreased patients' HR and blood pressure. Safflower yellow blocks myocardial potassium channels, resulting in decreased calcium influx, which leads to reductions in left ventricular systolic pressure, left ventricular end-diastolic pressure, blood pressure, and HR.<sup>22,49</sup>

#### **Diabetic Mellitus:**

Diabetic Mellitus is metabolic disorder characterized by excessive thirst, excessive urination, increased blood glucose level (hyperglycemia), increased appetite, insulin resistance, excessive loss of body



weight etc. In USM known as *Ziabetus Sukkari*. In India prevalence DM was 40.9 million and may increase up to 69.6 million by 2025. In India in 2011 caused 4.6 million deaths. In T2DM insulin resistance developed by peripheral tissue (muscle, fat and liver) with  $\beta$  cell failure then insufficient production of insulin for glucose produced by liver. DM has multifactorial causes are physical inactivity, sedentary lifestyle, cigarette smoking, and generous consumption of alcohol.<sup>50,51,52</sup> Flowers of Safflower (*Carthamus tinctorius* L.) initiate regeneration of islets of langerhans hence formation or secretion of insulin increased from  $\beta$  cells of islets of Langerhans. Then insulin level will be increased also they enhance glycogenesis in the liver also extract of seeds act as  $\alpha$ -glucosidase inhibitors hence *Carthamus tinctorius* L. play an important role in the treatment of DM.<sup>22,39</sup>

#### **Osteoporosis:**

According to the WHO criteria, osteoporosis is defined as low bone mass with declining of bone tissue. One of the major problems in old age humans, osteoporosis act as silent killer till the fracture appear will be the major cause of death in India. Mostly in old age humans.<sup>53</sup> In India about 50 million had osteoporosis in 2013.<sup>54</sup> Risk factors are age, sex, glucocorticoid use, race, family history, hormonal imbalance, prior fragility fracture, low BMI, smoking, excessive alcohol consumption and calcium deficiency.<sup>55</sup> Pathophysiology in which bone tissue is continuously lost by resorption, rebuilt by formation; bone loss occurs when the resorption rate is more than the formation rate.<sup>56</sup> Seeds of *carthamus tinctorius* having active mineral constituents (calcium, magnesium and potassium) preventing osteoporotic process in rats. Also having linoleic acid (having anti-inflammatory properties) increase intestinal calcium absorption and correcting bone loss due to estrogen deficiency in rats due to Oophorectomy. Safflower seed oil given oral administration at a dose 1ml/kg improves the osteoporosis in rats due to Oophorectomy. The aqueous extract of safflower seeds significantly accelerates rate of osteoblast formation in the experimental group. Osteoporosis due to estrogen deficiency reduced by seeds of *carthamus tinctorius* rich in Phytoestrogen and polyphenolic compound stimulate osteoblast proliferation. On processing bone metabolism, PGE2 accelerated production of IL-1b in fetal mouse osteoblast as well as prostaglandin E (PGE2) production induced by IL-1b, TNF- $\alpha$  and IL-6. IL-1b and partly prevented bone loss and

microarchitectural changes in young ovariectomized rats, showing that the protective effect on bone was exerted via the inhibition of bone resorption.<sup>22,39</sup>

#### **Dyslipidemia:**

Dyslipidemia also known as Hyperlipidemia or Hyperlipoproteinemia, in unani system of medicine co-relate with *Siman-e-Mufri* defined as disorder of lipoprotein metabolism with overproduction of lipoprotein manifested by elevation of the total cholesterol, the low-density lipoprotein (LDL), triglyceride concentrations and decrease in high-density lipoprotein (HDL) concentration in the blood.<sup>57</sup> Nearly 2.8 million individuals die each year due to obesity.<sup>58</sup> Hyperlipidemia may complicated to Atherosclerosis, IHD, HTN, Stroke, Nephropathy, Retinopathy, Diabetes, Obesity, Fatty liver.<sup>59</sup> The dichloromethane extract of *carthamus tinctorius* reduced total cholesterol, the low-density lipoprotein (LDL) and the triglyceride concentrations, and increase in high-density lipoprotein (HDL) concentration in the blood.<sup>22,39</sup>

#### **Alzheimer's disease:**

It is one of the degenerative diseases of the cerebral cortex.<sup>60</sup> All over the world 24.3 million people are suffering from Alzheimer's disease. It will become 7<sup>th</sup> leading cause of death. Gradually worsening ability to remember new information, risk factors are age, genetic factors, diabetes mellitus, hypertension, and cardiovascular disease.<sup>61, 62</sup> *Carthamus tinctorius* administered 1-10g/kg body weight subcutaneously or methanol extract of the flowers are inhibited pentylenetetrazole and delay convulsion, act as central nervous system depressant. *Carthamus tinctorius* act as neuroprotective substant on mitigating brain infarction and global ischemia and also prevent neurodegeneration by improving cerebral blood circulation and reduce the symptoms of degenerative diseases Alzheimer's and Parkinson. In *Carthamus tinctorius* having hydroxysafflor yellow A (HSYA) having neuroprotective effect in cerebral ischemic injury in both vitro and vivo studies. Extract of petals leaf, stem, root and seeds showed scavenging activity of free radicals and neuroprotective effect due to presence of active constituents such as carthamin and polyphenols examined on mice brain.<sup>22,39</sup>

#### **Cerebral ischemia:**

Ischemic stroke is the second most common cause of death in humans mortality rate 5.5 million annually, it create economic, social burden on patient family, this is state of hypercoagulability and hyper viscosity in

circulation. Various risk factor that are responsible for CI but some important are hypertension, diabetes mellitus, high blood cholesterol, cardiovascular diseases, sedentary lifestyle, atrial fibrillation, smoking, and alcohol consumption, age and gender.<sup>63</sup> Hydroxysafflor yellow A (HSYA) showed neuroprotective effect in vitro and vivo experiment on Wistar-Kyoto (WKY) rats with middle cerebral artery occlusion manifest neurological deficit scores also effect on infarction area of brain. sublingual vein injection of HSYA showed neuroprotective effect on cerebral ischemic injury by reducing neurological deficit scores and infarct area at doses of 3.0 mg/kg and 6.0 mg/kg in vivo. Extract of petals (bud, early stage, full blooming and ending stage), leaf, stem, root and seeds of *Carthamus tinctorius* having active constituent carthamin and polyphenols showed neuroprotective effect in brain of mice as well as rats. The brain injury induced bay lymphostatic encephalopathy HSYA (5 mg/kg, ip) might provide neuroprotection investigated in rats by measurement Heart rate variability, recording the ECG signals by reduced neurological deficits also on Histological examination manifest that HSYA diminished LE-induced cell apoptosis in the rostral ventrolateral medulla (RVLM). Studies have demonstrated that Hydroxysafflor yellow A (HSYA) contained in *C. tinctorius* flowers markedly extended coagulation time in mice, which raises the possibility that it might exert therapeutic actives on cerebral ischemia induced by thrombosis. Followed researches have shown that HSYA dose dependently improved the neurological deficit scores and reduced the cerebral infarct area and it bore a similarity in potency of the therapeutic effects on focal cerebral ischemia to nimodipine as the standard drug. The inhibition rates of thrombosis formation by HSYA at the doses of 1.5, 3.0 and 6.0 mg/kg, at 30 min after the onset of ischemia were 20.3%, 43.6% and 54.2%, respectively. Inhibitory activities of HSYA were observed on adenosine diphosphate (ADP)-induced platelets aggregation in a dose-dependent manner, and the maximum inhibitory aggregation rate of HSYA was 41.8%. Blood rheological parameters were markedly improved by HSYA, such as whole blood viscosity, plasma viscosity, deformability and aggregation of erythrocyte, but no significant effect of HSYA on hematocrit was found. The underlying mechanisms exerted by HSYA might be involved in its inhibitory effects on thrombosis formation and platelet aggregation as well as its beneficial action on regulation of prostacyclin/thromboxane (PGI<sub>2</sub>/TXA<sub>2</sub>)

and blood rheological changes in rats. *C. tinctorius* is commonly used in Chinese medicine to promote blood circulation and remove blood stasis. Blood stasis, i.e. the decrease of blood flow velocity, indicates hemorheological abnormalities. Studies have been shown the effects of carthamins yellow contained in safflower flowers on blood stasis. Results have demonstrated that this compound significantly decreased the whole blood viscosity, plasma viscosity and erythrocyte aggregation index which were increased in blood stasis. Hematocrit and platelet aggregation were reduced while the prothrombin time was delayed. So this natural food coloring agent could be a great value in the prevention of hemorheological disorders-associated diseases in at risk patients.<sup>22, 39</sup>

#### **Gastric ulceration:**

Gastric ulcer in USM known as Qara-e-Mida in which ulceration of gastric mucosa that penetrates up to muscularis mucosa. Most common disorder of gastrointestinal tract, risk factors is *Helicobacter pylori* bacteria, excessive use of Non-Steroidal Anti-Inflammatory Drugs (NSAID) such as aspirin, ibuprofen, indomethacin and diclofenac sodium, cigarette smoking etc. The incidence of ulcer disease increases with age, due to excessive use of NSAIDs and the reduction in tissue prostaglandins and certain lifestyle factors like excessive consumption of tobacco, alcohol, tea, coffee, betel nut and spicy foods are believed to stimulate gastric acid secretion.<sup>64, 65</sup> Methanol extract of *Carthamus tinctorius* with carbachol showed protective effect against gastric ulcer after pylorus ligation also reduced the volume of gastric secretion and increase PH of gastric juice at dose of 200-400mg/kg.<sup>22, 66</sup>

#### **Urolithiasis:**

Urolithiasis is a multifactorial disease in which stones are formed at any location within the urinary tract. Prevalence of urolithiasis in men is about 15% and in women 6%. The ratio increases due to changes in eating, habits, lifestyle, and obesity. Renal failure is one of the major complications of urolithiasis.<sup>67</sup> Active constituents such as Flos carthami of *carthamus tinctorius* showed anti urolithiasis properties at dose of 600-1200 mg/day. Standard group on histopathological examination of kidney tissue showed low crystal deposition was evaluated by a semi-quantitative scoring method by using polarized light microscope.<sup>68</sup>

#### **Anti-inflammatory antipyretic and analgesic effects:**

When 50% methanol extracts of *Carthamus tinctorius*

(flowers) administrated Intragastric showed anti-inflammatory effect at dose of 30 mg/kg body weight, inflammation induced in mice by carrageenan, serotonin, bradykinin, histamine or prostaglandin and measured by footpad oedema also effective on writhing induced by acetic acid, CT showed same effect on subcutaneous administration at 10 g/kg bw dose, in the hot-plate test does not manifest pain killer or analgesic effect. Lipopolysaccharide (LPS)-induced inflammation by stimulating nitric oxide (NO), prostaglandin E2 (PGE2), and interleukin 1 $\beta$  (IL-1 $\beta$ ) release. In vitro aqueous extract of dried safflower and Carthamus yellow suppressed the LPS-induced phosphorylation of nuclear factor- $\beta$ B, which was associated with the inhibition of I $\beta$ B- $\beta$  degradation. N-(p-Coumaroyl) serotonin (CS) inhibited proinflammatory cytokine generation from human monocytes. The result showed that intravenous injection of HSYA (10 mg/kg) to rats after cerebral occlusion, the p65 translocation activity and the phosphorylation of I $\kappa$ B- $\alpha$  were significantly inhibited. At the same time, HSYA suppressed p65 binding activity and the transcriptional level of proinflammatory cytokines including TNF- $\alpha$ , IL-1 $\beta$  and IL-6, and promoted the mRNA expression of anti-inflammatory cytokine IL-10. The authors suggested that the anti-cerebral ischemic mechanism of HSYA may be due to its inhibition of NF- $\kappa$ B activity and the mRNA expression of cytokines in the inflammatory transduction pathway. The effects of Hydroxysafflor yellow A (HSYA) suppressed the expression of TLR-4, Myd88, ICAM-1, TNF $\alpha$ , IL-1 $\alpha$  and IL-6 at the mRNA and protein level, and inhibited the adhesion of leukocytes to A549 cells. HSYA treatment also decreased NF- $\beta$ B p65 nuclear translocation and inhibited the phosphorylation of p38 mitogen-activated protein kinase (p38 MAPK). Methanolic extract of root of Carthamus tinctorius having bioactive constituents are triterpenoid saponin 3 $\beta$ O-[ $\beta$ -D-xylopyranosyl(1 $\beta$ 3)-O- $\beta$ -D-galacto pyranosyl] -lup-12-ene-28oic acid-28-O-alpha-L-rhamno pyranosyl ester showed anti-inflammatory activity. Florets of Carthamus tinctorius having polyacetylene glucosides compounds 11 in number showed anti-inflammatory activity. Methanol extracts of Carthamus tinctorius (MEC) increased expression of HO-1 protein in macrophages also inhibit regulation of both iNOS and COX-2 and ntly reduced production of NO and PGE2. In addition, the binding of NF- $\kappa$ B as well as NF- $\kappa$ B luciferase activity was also significantly diminished by MEC also tumor

necrosis factor (TNF)- $\beta$ -mediated VCAM-1 expression in endothelial cell was significantly inhibited by MEC. Intragastric administration of 500 mg/kg body weight (bw) of a 95% ethanol extract of Flos Carthami reduced the responsiveness of mice as measured in the hot-plate test, indicating an analgesic effect, and also decreased yeast-induced fevers. Flowers of *C. tinctorius* possess central analgesic activity (500 mg/kg) and potentially may lead to the development of morphine-like substances devoid of the side effects of morphine and related drugs.<sup>22,39</sup>

#### Antimicrobial effect:

Methanol extract of Carthamus tinctorius showed antibacterial activity against *H. pylori* at concentration 2 mg/disc and at 0.5 mg/plate concentration of ethanol extract of flower of Carthamus tinctorius showed bactericidal effect against *Staphylococcus aureus*. In vitro at a concentration of 100  $\mu$ g/plate of ethanol extract of the flowers showed bactericidal activity against *Bacillus subtilis*, *Candida albicans*, *Salmonella typhosa* and *Staphylococcus aureus*. Carthamus tinctorius L. also proved antiviral activity against herpes virus infection also disrupted two stages of KSHV life cycle in host cell by abnormally inducing KSHV lytic reactivation and preventing KSHV virion release, in vitro study aqueous extract of the flowers inhibited replication of poliomyelitis virus type 1.<sup>22</sup>

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