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Review Article

A Review on Potential Pharmacological Uses of *Carthamus tinctorius* L.

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ABSTRACT

Carthamus tinctorius L. (Safflower) of family Asteraceae is a medicinal plant with great potential. Its extract and oil has many therapeutic uses and having great pharmacological importance. Plant is mainly cultivated for its seeds, oil and flowers. It is to cure many day to day ailment, and has proved importance as purgative, analgesic, anti-inflammatory, antipyretic, menstrual problems, post-partum hemorrhage, osteoporosis, diabetes, hepatoprotection, cancer, fibrosis and antioxidant. Carthamine, hydroxyl safflower yellow-A, carthamidine, luteolin are the main phytoactive principles of this plant. This review highlights the pharmacological aspects of *Carthamus tinctorius.*

Keywords- Carthamus tinctorius, Safflower, Pharmacology, future drug.

INTRODUCTION

Carthamus tintorius L. safflower rather false saffron, belongs to family Asteraceae or compositae in the order Asterales, native of Egypt. Safflower planted and cultivated in places with dry hot climate and moderate rainfall. It is a thistle like annual, bushy, herbaceous plant with profuse branching attains height up to 1 meter. Leaves are stalk less, lanceolate, half-clasping 4 to 10.5 centimeter long, 1 to 2.8 centimeter wide narrow towards the top, toothed spiny margin and have numerous spines all around. Flowers are bright yellow orange or red in color, large and surrounded by a cluster of leafy bracts which forms involucre 3 centimeter across. The fruits are achenes, obovoid in shape 4 ribbed deformed and truncate at the top. Seeds are with and without hair having thick pericarp. This plant is also suitable for rain cropping system because its deep tap root system helps to take water and nutrient from the depth of the soil.

Cultivated in various parts of the world mainly for its seeds oil and carthamin dye from flowers. Flower dye is used as substitute for the saffron. In China young shoots eaten at the time of scarcity. In Chhattishgarh, India, its tender leaves has been used as leafy vegetable. India, United State and Mexico are the leading producer along with Ethiopia, Kazakhstan, China, Argentina and Australia as emerging countries. Vernacular names of safflower are as follows Arabic: Asfur, Asfoor, Usfur; Croatian: Bojadisarski Bodalj, Šafranika; Czech: Azafrán, Světlice Barvířská; Danish: Farvetidsel, Safflor; Dutch: Carthamusbloem, Saffloer, Saffloer-Bloem; Finnish: Värisaflori; French: Carthame Des Teinturiers, Fleur De Carthame, Graine De Carthame, Safran Bâtard; German: Färberdistel, Färbersaflor, Falscher Safran, Saflor; Greek: Knikos; Hindi: Kusum; Hungarian: Magyar Pirosító, Pórsáfrány, Sáfrányos Szeklice, Szaflór, Szeklice; Italian: Cartamo, Falso Zafferano; Japanese: BeniBana; Korean: Hong Hwa; Persian: Gulrang; Portuguese: Açafrão-Bastardo, Cártamo, Falso-Açafrão; Russian: Saflor, Saflor Krasil'nyi; Slovenian: Barvilni Rumenik, Barvilni Žafran, Žafranika; Slovakian: Požlt Farbiarska; Spanish: Alazor, Alazor Bastardo, Azafrán Bastardo, Cártamo; Swedish: Färgtistel, Safflor; Tamil: Kusumb; Turkish: Safran Yalancı, Yalancı Safran; Urdu: Gul Rang; Vietnamese: CâyRum, Hồng Hoa.

Phytochemistry of *Carthamus tinctorius*

Meselhy et al. 1993, reported quinochalcone C-glycosides, tinctormine yellow pigments from *Carthamus tictorius* and studied calcium antagonistic activity of tictormine [1]

Triterpene alcohol constituents, Heliaol, α-amyrin, β-amyrin, lupeol, cycloartenol, 24-methylenecycloartanol, tirucalla-7,24-dienol and dammaradienol isolated from the Carthamus

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flowers act as anti-inflammatory agents reported by Akishia et al, 1996[2]. Akisia et al. 1997, recorded 11 novel secondary alkane-1,3-diols from the dried flower petals of C. tinctorius[3]. Zhang et al. 1997 isolated Seven antioxidative compounds from safflower oil cake most of which were serotonin derivatives, N-[2-(5-hydroxy-1H-indol-3-yl)ethyl]-ferulamide, N-[2-(5-ydroxy-1H-indol-3-yl)ethyl]-p-coumaramide,N-,N-[2,2'-(5,5-dihydroxy-4,4'-bi-1H-indol-3,3'-yl) diethyl]-di-pcomaramide, N-[[3'[2-(p-comaramido) ethyl]-5, 5'-dihydroxy-4,4'-bi-1H-indol-3-yl]ethyl] ferulamide, N,N'-[2,2'-(5,5'-dihydroxy-4,4'-1H-indol-3,3'yl)diferulamide, N-[2[5-(beta-D-glucosyloxy)-1H-indol-3-ylethyl]-p-comatamide and N-[2-[5-(beta-D-lucosyloxy)-1H-indol-3-yl]-ethyl] ferumaramide[4].

Kim et al. 2000 studied the properties of chemical composition of *Carthamus tinctorius* seeds and reported that crude protein ranged from 14.9% to 17%, total sugar from 3.2% to 9.2% and extractable lipids from 25% to 40%. Oil content of the seeds is similar to that of olive and includes linoleic acid (63%–72%), oleic acid (16%–25%) and linolenic acid (1%–6%).[5] Serotomide (trans-N-caffeoylserotonin) and safflomide (trans-N-caffeoyltryptamine) belonging to serotonin-derived phenyl propenoid amides modulate forskolin stimulated cAMP formation via 5-HT1receptor have been reported by Park, [6]2008 in *C. tinctorius.*Lee et al. 2002, while studying anti oxidative flavonoids of *Carthamus* leaves isolated Luteolin and its glucopyranosides[7].The essential oils from flowers of safflower contains chalcones including hydroxysafflor yellow A, safflor yellow A, safflamin C and safflamin A, and safflomin-A has been reported by Jiang and Wang, 2005[8]Huang et al. 2007 reported Nicotiflorin, a natural flavonoid extracted from coronal of *C. tinctorius* and its protectivesffects on reducing memory dysfuntion, energy metabolism failure and oxidative stress in rats [9]. Systematic screening and characterization of flavonoid glycosides in *Carthamus tinctorius* was carried out by Jin et al. 2008 [10]. Zhau and Zhao, 2009 reported some 200 compounds from *C. tinctorius* and the commonly known ones are flavonoids, phenylethanoid glycosides, coumarins, fatty acids, steroids and polysaccharides[11].A new coumaroyl spermidine elucidated as N(1),N(5)-(Z)-N(10)-(E)-tri-p-coumaroyl spermidine with serotonin transporter inhibition from safflower was identified by Zhao et al., 2010[12]. Shao et al. 2011, studied daily variations in essential oil composition of flower of different accessions from *Carthamus* flower and identified Caryophyllene, p-allyl toluene, 1-acetoxytetralin and heneicosane as the major constituents [13].

Phytochemistry, pharmacology and medicinal properties of Carthmus tinctorius was reviewed by Asgarpanah and Kazemivash, 2013[14].

Pharmacological Properties of C*arthamus tinctorius*

Anti-inflammatory activity: A substance with its property to reduce the swelling is known as anti-inflammatory substance.Ho-1 is a potent anti-inflammatory agents. Methanolic extract of *Carthamus tinctorius* is proved to induce the expression of ho-1 via translocation of Nrf -2. Methanolic extract of *Carthamus* triggers the inhibition of nf-kB activity, nf-κB is a transcription factor for the inflammation [15].Vascular adhesion molecule is unable to express by the inhibition of TNF–α in the presence of ethanolic extract of *Carthamus tinctorius* whose expression causes chronic inflammatory disorders.

The methanolic extract of *Carthamus tinctorius* is also induces the expression of HO-1 which is an anti – inflammatory agent via Nrf2 translocation pathway [16]. Flavones luteolin and its glucopyranoside luteolin 7-O-beta-D-glucopyranoside and luteolin-7-O-(6”-O-acetyl)-beta-D-glucopyranosideare the reported anti-inflammatory substances from *Carthamus tinctorius* [16]. Helianol sterols and alkane-6,8 diols, ψ-taraxasterol and taraxasterol are the anti-inflammatory substances isolated from the flower having anti-inflammatory response against 12-O-Tetradecanoylphorbol-13-acetate- induced inflammation.

Analgesic properties: Analgesics are commercially available drugs or group of drug used to achieve relief from pain, which acts in various ways on central and peripheral nervous system. *Carthamu*s flower is reported to be a potent of analgesic isolated from the seeds of *Carthamus tinctorius*. In one such study a dose of 100ul causes a marked reduction in nociceptive and proprioceptive activity. Anti-oxidative activity of flower also has analgesic effect. Serotonin conjugates are also reported from the flower inhibits the tyrosinase action and this inhibition in tyrosinase causes increase in serotonin content and ultimately serotonin is a common agent use to provide relief against sciatic pain. *Carthamus* oil is a rich source of unsaturated linoleic acid, unsaturated linoleic acid triggers the inhibition of tyrosinase enzyme. Proteolytic degradation of tyrosinase is responsible for the inhibition of monoaminergic neurotransmitter (a pain signal transmitter). *Carthamus* flower can be used in Korean pharmacopuncture. In another study it was found

that 50-100 mg/kg dose of carthamus flower sustained analgesic activity [17].

Antioxidant Activity: Energy is a first requirement for the survival of all living organism which is obtained from the food Oxygen is a prerequisite for the metabolism and for the use of dietary nutrient. Oxygen mediates many reactions and metabolize fat, protein, carbohydrates .Oxygen is also a part of life damaging molecule called free radical. Free radicals neutralize themselves by capturing other substances their formation is controlled by antioxidants. Flavonoids are the phenolic compounds found in many plants as a major phytochemical work as an antioxidant.

Antioxidants help in the prevention of diseases like atherosclerosis, heart disease, Parkinson's, ischemic Alzheimer's, and aging [18,19]. Ethanol ethyl acetate extract of safflower defatted seeds reported to have phenolic compounds and serotonin derivatives which are effective against atherosclerosis [20]. The serotonin are the unique phenolic constituent of safflower defatted seeds [21]. 0.4 % of serotonin derivatives dose results in a lesion reduction with the inhibition of V 70 and Cu 2+ induced oxidation this marked inhibition is due to the presence of derivative N-pcoumaryl serotonin and N-feruloylserotonine [21]. DPPH scavenging assay is widely used to determine antioxidant activity .*Carthamus tinctorius* shows scavenging effect on the DPPH and reduction of ferric [22]. *Carthamus tinctorius* flowers aqueous extract shows 99.65% DPPH scavenging activity. Ferric reduction determined was 1,140umol/g at 50% concentration value [22]. Methanolic and aqueous extract reported to have phenolic content 2.12 and 1.32g/100g respectively [23]. Phenolic compound in a plant is associated with its anti-oxidative activity [24].

Antidiabetic effect: High blood sugar levels over a prolonged period result in a metabolic disorder called Diabetes mellitus in this major endocrine disorder pancreas do not produce sufficient insulin. Associated common symptoms are frequent urination, increased thrust, and increased urination. The process like glycogenolysis, glycogenesis and gluconeogenesis takes place in a vital organ liver [25]. It has been reported, after alloxan injection increase in alanine and aspartate transferase occurs [26]. The oil obtained from the seeds of *Carthamus tinctorius* is rich source of mono and polyunsaturated fatty acid regulate insulin secretion response and glucose homeostasis. The higher activity of enzymes like glutamic pyruvic transaminase, serum glutamic transaminase and ALP shows that diabetes associated with the liver dysfunction. It has been observed that 28 days doses of Carthamus tinctorius oil recovers the activities of the above enzymes in the alloxan induced diabetic rats [26]. Protein breakdown and glycogenesis process restores after Carthamus tinctorius flower extract administration. N-P-coumaryl and N-feruloyl are the active alpha glucosidase inhibitors isolated from the seeds of C. *tinctorius* their IC 50 value were calculated as 47.2 umol/L and 99.8 u mol/L while that of the reference drug as 907.5 umol/L and 278.0 umol/L for the drugs ascarbose and 1- deoxy-nojirimycin respectively [27] With the *Carthamus tinctorius* supplementation renal abnormalities like glycosylated protein tissue levels, heamodynamics changes within the kidney tissue and increased oxidative stress, high plasma urea, uric acid and creatinine level glucose simultaneously glucose level are also regulated in streptocin induced diabetic rats.

Increase in the insulin level simultaneously lowering in the level of cholesterol, LDL-C, VLDL-C observed in a male wistar rats treated with Carthamus tinctorius hydroalcoholic extract [28]. The increase in the size of islets of Langerhan cell with the *Carthamus tintorius* administration also reported [28].

As anticoagulant: Coagulation or clotting is a process in which blood changes from a liquid to a gel. It results into hemostasis. Anticoagulants are the class of drugs that work to prevent the coagulation of blood. Ischemia –induced damages occurs in brain followed by thrombotic block. cerebral ischemia is result of hypercoagulation and hyper viscosity in blood circulation more prone to thrombosis [29]. Studies demonstrated the therapeutic effect of hydroxyl safflor yellow A on focal cerebral ischemia injury in rats, HYSA dose dependently improve the neurological defect and reduced the cerebral infract area HYSA shows its inhibitory action on ADP-induced platelets aggregation in a dose dependent manner. With the maximum inhibitory aggregation rate 41.8%.HYSA suppress the production of TXA2 without significant effect on plasma PGI2. Blood rheological parameter were improved after HYSA dose such as whole blood viscosity ,plasma viscosity, deformability and aggregation of erythrocyte but no effect on hematocrit was found. HYSA has a potential to treat cerebral ischemia and underlying mechanisms might be involved the inhibitory effects on thrombosis formation and platelet aggregation [29].

Carthamine yellow (CY) obtained from the Carthamus tinctorius used for coloring food is also proved to be effective in hemorological disorders of blood stasis in rats. CY administration decreases the whole blood viscosity, plasma viscosity and

erythrocyte aggregation index in a stasis rat. Hematocrit and platelet aggregation were reduced while prothrombin time was delayed after the administration of CY dose. BY increasing blood fluidity CY decreases the plasma visosity [31].

***Effect on Osteoporosis*:** Osteoporosis is a progressive bone disease characterized by a decrease in bone mass and density which can lead to the increased risk of fracture. The disease classified as primary type -1, primary type 2 or secondary. Women are commonly suffered from primary type- 2 disease. Aging, post menopause calcium loss, general calcium deficiency, immobilization, lack of nutrition, and endocrinology changes are the causes of osteoporosis. Osteoporosis associated with the estrogen deficiency occurs after the menopause in women. Estrogen deficiency and calcium deficiency are the reason behind the genesis of this diseases [31].

High mineral content such as Ca, K, P are reported from the methanolic extract of Safflor extract used in Korea as a folk medicine and these osteoblast markers increases. In Sprague –Dowley rat after the administration of methanolic extract of safflower seed Osteoblast content, bone specific alkaline phosphatase, insulin like growth factor-I are reported to increases . Simultaneous enhancement in the growth parameter like length of tibia and femur are also observed as well as MESS cytotoxicity are absent under the experimental conditions .

Bone resorption is an osteoclast mediated breakdown of bones. In bone resorption calcium transfers from bone fluid to the blood due to the released of minerals mediated by Tyrosine kinase, cyclooxygenase and prostaglandin. *Carthamus tinctorius* called Honghwain (HHI) in Korean medicine. Synergy between IL-B, TNF-a, IL-6 on PGE2 production is due to enhanced COX 2 expression HHI is a possible Src family kinase inhibitor may be useful for the treatment of diseases associated with bone loss [32]. Safflower seed contains high linoleic acid helps in its anti-inflammatory activity by decreasing prostanoid formation and recover bone loss due to over recto-my and increasing calcium uptake [31]. Estrogen deficiency causes bone loss, safflower seeds are the rich source phytoestrogens shows the protective effect against the bone loss by estrogen deficiency without substantial effect on uterus [33].

Hepatoprotective Activity: Many major functions of human body are associated with liver, hepatocytes are the specialized tissues regulate many biochemical functions including regulation of glycogen storage, decomposition of red blood cells, plasma protein synthesis, hormone production and detoxification produces bile a compound aids in digestion via emulsification of lipids. Carthamus red is a reported hepatoprotective compound from the Carthamus tinctorius effective against liver damages induced by CCl_4 [34]. Trichloromethylene radical, oxidized macromolecules and lipids oxidative stress inducer. Carthamus red treatment lowered serum levels of ALT, AST, ALP and total protein liver damage in a rat model. It was also reported to induce the Nrf2, GsTα and NQO1 expression [34]. Safflower seed ethanolic extract and aqueous extract lowered the plasma cholesterol and triglycerides contents which are injurious to hepatocytes. The hepatic 3-hydroxy-3-methyl glutaryl-coenzyme A reductase activity were high and hepatic acyclo-enzyme A cholesterol acetyl transferase activity were low by the administration of safflor seeds extract as well as atherogenic risk factor are also reduces in high cholesterolemic rats. Dehyroabietylamine is an hepatoprotective compound isolated from the leaves of *Carthamus tinctorius* Carthamus tinctorius induces the P 450 activation, cytochrome free radicles responsible for the hepatic injuries are hidden in the presence of P 450 [35]. Dichloromethane extract of Carthamus seeds administration for a week causes decreased body weight decrease as well as reduction in total cholesterol/high density lipoprotein cholesterol observed after the dichloromethane extract doss in a hypercholestromic rats.

Antifibrosis activity: Fibrosis is a state of excess deposition of fibrous tissues as well as the connective tissues deposition in a healing process. Hydroxy safflor yellow A isolated from safflor is an antioxidative compound reported to have preventive effect against oxidative stress mediated injury. Hepatic stress is a result of oxidative stress. Carthamus tinctorius shows anti-fibrosis activity by the activation of anti-oxidative enzymes, up regulation of the expression of PPARy and MMP-2 and by down regulating the activity of TGF-B1 and TIMP-1and reducing a- SMA level [36].

Anticancer Activity: Increase in a number and growth of cells is a root of cancer, which is also invade to other parts of the body. Apoptosis in the SW 620 cell lines is reported to induced by the Dichloromethane extract of *Carthamus* due to its administration m RNA level of caspases 3, 7,9increases but do not showing its effect against the proliferation of 3 sub sets of T lymphocytes [37]. It was reported that TNFα and IL-1β were increases by the CT extract pulsed with DC vaccine. Reduced tumor weight were observed also observed after the administration of DC vaccine treated with CT Which is 15.3 % more

than the tumor lysate without CT .ex vivo CT induced population increment of cytotoxic lymphocytes were also reported[38]Zhu-Xiang a compound isolated from the herbal extract of ginseng and Carthamus tinctorius is proved to be a potent against the MAD-MB-231 breast cancer cell and in normal memory gland cell lines of human it induces the apoptosis of cell due to which cell proliferation is stopped [39]. Two polysaccharides obtained from the safflower petals stimulated the synthesis of various cytokines by peritoneal macrophages. Safflower polysaccharides proved to be activate the NF-Kβ signaling via toll like receptor 4[40].

CONCLUSION

Present review reveals that Carthamus tinctorius seeds and flowers has great pharmacological importance as antioxidant, anti-inflammatory, analgesic, antidiabetic, hepatoprotective, antihyperlipedemic agent. The phytochemical active principles and their derivatives has a remarkable pharmacological importance and prove to be useful in curing many diseases. The tender leaves of Carthamus tinctorius were consumed as very popular, nutritive, curative, restorative, vigor full leafy vegetable in Chhattishgarh, India, Its leaves were neglected in research which will prove to have great potential as medicine and alternate to mal nutrition. Flavonoid derivatives and Furanocoumarins is a target for inflammatory, antimicrobial, anticancer, antidiarrheal drugs. Much research is required to employ this plant as a new wonderful multipurpose broad spectrum drug.

REFERENCES

1. Meselhy MR et al. Two new quinochalcone yellow pigments from Carthamus tictorius and calcium antagonistic activity of tictormine. Chem Pharm Bull 1993;41:1796-1802.
2. Akihisa T et al. Triterpine alcohols from the flower of compositae and their anti inflammatory effects. Phytochemistry 1996; 6: 1255-1260.
3. Akihisa T et al. Alkane diols from flower petals of Carthamus tinctorius. Phytochem 1997; 45:725-728.
4. Zhang HL et al. Antioxidative compounds isolated from safflower (Carthamustinctorius L.) oil cake. Chem Pharm Bull 1997;45:1910-1914.
5. Kim SK et al. Properties of the chemical composition of safflower (Carthamus tinctorius L.) sprout. Korean J Life Sci 2000;10:68-73.
6. Park JB. Serotomide and safflomide modulate forskolin stimulated cAMP formation via 5-HT1receptor. Phytomed2008;15:1093-1098.
7 Lee JY et al. Antioxidative flavonoids from leaves of Carthamus tinctorius. Arch Pharm Res 2002; 25: 313-319.
8 Jiang T F et al. Separation and determination of chalcones from carthamus tinctorius L. and its medicinal preparation by capillary zone electrophoresis. Sep Sci 2005;28:1244-1247.
9 Huang JL et al. Protective effects of Nicotiflorin on reducing memory dysfunction, energy metabolism failure and oxidative stress in multi-infarctdementia model rats. Pharm Biochem Behav 2007; 86:741-748.
10 Jin et al. Systematic screening and characterization of flavonoid glycosides in Carthamus tinctorius L.by liquid c hromatography /UV diode- array detection/electro spray ionization tandem mass spectrometry. J Pharm Biomed Anal2008; 46: 418-430.
11 Zhou FR et al. Simultaneous determination of four nucleosides in Carthamus tinctorius L. and safflower injection using high performance liquid chromatography. J Chin Pharmaceut Sci 2009;18:326-330.
12. Zhao G et al. Structural identification of new tri- terpine p coumaroyl spermidine with serotonin transporter inhibition from safflower. Chem Pharm Bull 2010; 58: 950-952.
13 Shao JF et al. A daily variation in essential oil composition of flower of different accessions from Carthamus tinctorius L. in Sichuan province of China. J Med Plant Res 2011;5:3042-3051.
14 Asgarpanah J, Kazemivash N, Phytochemistry, Pharmacology and Medicinal Properties of Carthamus tinctorius L..Chin J Integr Med 2013;19(2):153-159
15 Jun MS et al. Anti-inflammatory action of methanol extract of Carthamus tinctorius involves in heme –oxygenase -1 induction. Ethnopharmacol 2011;133:524-530.
16 Chen CY et al. Luteolin suppresses inflammation associated gene expression by blocking NF-κ B and AP-1 activation pathway in mouse alveolar macrophages. Life Sci 2007;81:1602-1614.
17 Popilov Li et al. Analgesic properties of CF extracted from the Safflor (Carthamus tinctorius) seeds and its potential uses.Pharmaceutical chemistry 2009;43(1): 4.
18 Mates JM et al. 1999.Antioxidant enzymes and human diseases.Clin Biochem 1999;32: 595-603.
19 Aruoma OL. Methological consideration for characterizing potential antioxidant action of bioactive components in plant foods .Mutat Res 2003;523-524.
20 Naoto K et al.,Serotonin derivatives major safflower seed antioxidants, inhibit low density lipoprotein oxidantion and atherosclerosis in apolipoprotein E – deficient mice .Agric Food Chem2006;5:4970-4971.
21 Sakamura et al. Conjugated serotonins related to cathartic activity in safflower seeds(Carthamus tinctorius L.)AgricBiolChem 1978;42:1805-1806.
22 Kruawan K, Kagsadalampai K. Antioxidant activity, Phenolic compound contents and antimutagenic activity of some water extract of herbs. Thai J Pharm Sci 2006;30: 28-35.
23 Cai Y et al. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. Life Sci 2003;74,2157-2184.
24 Calomme M et al. Inhibition of bacterial mutagenesis by citrus flavonoids. Planta .Med.1996; 62,222-226.
25 Aja PM et al. Evaluation of antidiabetic and liver enzymes activity of aqueous extract of Moringaoleifera and Bridelia ferruginea leaves in alloxan induced albino rats.Int J Biochem Res Rev. 2013;3(3): 248-258

26 Parivash R et al. Hepatoprotective and hypolipidemic effects of Carthamus tinctorius oil in alloxan induced type -1 diabetes rats. J Herb .Med .Pharmacol 2014;2:107-111.

27 Takahashi T, Miyazawa M. Potent α glucosidase inhibitors from safflower (Carthamus tintorius L.) Seed .Phytother Res 2012;26:722-726.

28 Mandade R. Protective effect of carthamus tinctorius on streptozotocin induced diabetic complications in rats and the possible morphological changes in the liver and kidney. Int. J .of Sci. Inn and Dis 2012; 5: 502-510.

29 Zhu HB et al .Therapeutic effects of hydroxysafflower yellow A on focal cerebral ischemic injury in rats and its primary mechanism. J Asian Nat ProdRes 2005;7: 607-613

30 Li HX et al .Effects of the Carthamin yellow from Carthamus tintorius L. on hemorhogical disorders of blood stasis in rats. Food ChemToxicol2009;47: 1797- 180.

31 Bae CS et al. Effects of Safflower (Carthamus tinctorius L.)seed powder on osteoporosis. Korean J Electron Microscopy. 2002;32: 258-290

32 Tae HY et al. Inhibitory effects of carthamus tinctorius L. seed extract on bone resorption mediated by tyrosine kinase, cox-2 (cyclooxygenase) and prostaglandin E2. The American journal of Chinese medicine 2002; 3 (1)95-108.

33 Kim HJ et al. Bone protecting effects of safflower seeds in overrectomized rats. Calcif Tissue Int 2002;71:88-94.

34 Wu S et al. Carthamus red from carthamus tinctorius L. exerts antioxidant and hepatoprotective effects against CCl4-induced liver damage in rats via the Nrf2 pathway. J Ethnopharmacol 2013;148-570.

35 Arpornsuwan T et al. The effects of the extract from Carthamus tinctorius L. on gene expression related to cholesterol metabolism in rats. Songklanakarin. J Sci .Technol 2010; 32, 129-136.

36 Wang CY et al. Activation of PPARϒ is required for hydroxysafflor yellow A Carthamus tinctorius to attenuate hepatic fibrosis induced by oxidative stress. Phytomedicine 2013; 20:592-599.

37 Teerakul A et al. Effects of Carthamus tinctorius L. solvent extract on antiproliferation of human colon cancer (SW 620 cell line) via apoptosis and the growth promotion of lymphocytes. Songhlanakarin J SciTechnol 2012;34(1): 45-51

38 Jia, et al.Carthamus tinctorius enhances the antitumor activity of dentritic cell vaccines via polarization Th 1 cytokines and increase of cytotoxic T Lymphocytes. Evidence based complementary and alternative medicine vol 2011, article ID 27 of a herbal 4858,10 Pages http://dx.doi.org/10.1093/ecam/nen068.

39 .Wings TY et al. The inhibitory effect of a herbal Formula comprising ginseng and carthamus tinctorius on breast cancer. L ifesciences 2004 ;76 (2):191-20

40 Izuru A. et al.Safflower polysaccharides activate the transcription factor NF-Nb viaTLR4and induce cytokineproduction by macrophages.International. pharmacology 2002; 2:1155-1162.