Study the Potentials Antitoxicity Effects of extract on Rats Induced Carthamus tinctorius by Heterocyclic Compounds Containing Nitrogen

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ABSTRACT

The purpose of this paper was to investigate the study potentials antitoxicity effects of *Carthamus tinctorius* (CT) extract on some organs of rats induced by heterocyclic compounds containing nitrogen and spreading nutritional awareness of the benefits of medicinal plants and how to use them. Forty-two (42) Sprague-Dawley white male albino rats, each weighing 215±10g; rats were divided into 6 groups, every 7 rats in each group fed on a certain diet for 28 days. CT extract and vitamin C will be used at 100 mg/kg of rats' weight, while melamine will be used at 2%. Polyphenols are a large family of naturally occurring organic compounds and have gained a lot of importance because of their potential use as prophylactic and therapeutic agents in many diseases. We determined some significant changes about levels of bioelements in rats' brain and testes tissues exposed to the CT extract. The results clarified that the groups fed on CT extract were the best compared to the other groups, especially the (-Ve). Based on current information, the pharmacological functions, including the brain and testes protective effects of polyphenols, can be effectively exploited in the development of new drugs to treat various human brain and testes diseases.

Keywords: Polyphenols; brain; testes; antioxidant; cyanuric.

INTRODUCTION

Lifestyle-related diseases of stroke, cancer, heart disease, diabetes, kidney disease, hypertension, and so on have been considered to be associated with reactive oxygen species (ROS), including free radicals. In the brain diseases such as ischemia, Parkinson's disease, Alzheimer's disease, dementia, and posttraumatic epilepsy, reactive oxygen species are thought to be related to the induction or progression of these diseases. From these facts, it is needed to find nutrients and food with effective antioxidant activity against oxidative damage to delay aging and to prevent various diseases **(Akbar, 2020)**. ROS are generated from diverse cellular processes or external sources such as chemicals, pollutants, or ultraviolet (UV) irradiation. Accumulation of radicals causes cell damage that can result in degenerative diseases. Antioxidants remove radicals by

eliminating unpaired electrons from other molecules **(Kim *et al.*, 2019)**.

Carthamus tinctorius, also known as safflower, is a highly branched and thistle-like annual plant belonging to the *Compositae* family. CT has a long history of use as a food colorant, dye, and traditional medicine for the treatment of brain and testes diseases. In previous studies, phytochemical investigation of this plant reported the presence of polyphenols, such as Gallic acid, Chlorogenic acid, Catechin, Methyl gallate, Coffeic acid, Syringic acid, Pyro catechol, Rutin, Ellagic Acid, Coumaric acid, Vanillin, Ferulic acid, Naringenin, Quercetin, Cinnamic acid, Kaempferol, and Hesperetin **(Mani *et al.*, 2020)** and **(Baek *et al.*, 2021)**.

The brain is highly sensitive and vulnerable to oxidative damage due to its high oxygen demand and very limited antioxidant capacity. Once cerebral ischemia/reperfusion (I/R) is initiated, a large number of ROS are produced and attack various cellular macromolecules, resulting in DNA double-strand breakage, protein oxidation, lipid peroxidation and ultimately cell death **(Choi *et al.*, 2018)**. Antioxidant strategies aimed at exhausting excess free radicals have achieved effective protection against cerebral I/R injury. Thioredoxin (Trx), glutathione (GSH) and Nrf2 systems are three major antioxidant systems responsible for removing overproduced free radicals. Glutathione, a thiol-based antioxidant present in millimolar concentrations in the brain, plays a vital role in modulating redox homoeostasis **(Choi *et al.*, 2018)**. GSH depletion is involved in multiple neurological diseases, including cerebral ischemic stroke, whereas the administration of GSH reduces the infarct volume and ameliorates brain damage.

Moreover, Trx is another important antioxidant system that catalysis thiol-disulphide oxido-reductions in DNA synthesis, defends against oxidative injury and inhibits apoptosis. In particular, Trx binds to apoptosis signal-regulating kinase-1 (ASK-1) and inhibits subsequent apoptosis in cerebral I/R injury **(Wang *et al.*, 2018)**. In addition, Nrf2 is a central regulator that modulates redox homoeostasis by binding to its antioxidant response elements (AREs) in the promoter regions of target genes

in response to oxidative stress. In cerebral I/R injury, the functions of multiple antioxidant systems are seriously damaged, and the brain is vulnerable to the excess oxygen free radicals that aggravate cerebral damage **(Tian *et al.*, 2021)**.

The testes are two oval-shaped organs in the male reproductive system. They're contained in a sac of skin called the scrotum. Structures within the testes are important for the production and storage of sperm until they're mature enough for ejaculation. The testes also produce a hormone called testosterone. Spermatogenesis is an elaborate process of germ cell proliferation and differentiation which leads to the production and release of spermatozoa from the testis. This complex process is dependent upon hormonal stimulation as well as dynamic interactions between the Sertoli cells and the germ cells of the seminiferous epithelium **(Sengupta *et al.*, 2019)**. Sertoli cells secrete hormonal and nutritive factors into the adluminal compartment which create a specialized microenvironment that fosters the development and viability of resident germ cells. In addition, Sertoli cells form sites of attachment to germ cells that provide efficient paracrine signaling mechanism between these cells as well as physical support to developing germ cells. The intricate regulation and cellular interactions that occur in the testis provide multiple distinct targets by which toxicants can disrupt spermatogenesis **(Ni *et al.*, 2020)**.

A vast number of heterocyclic derivatives observed in natural products have been reported. On the other side, they find increasing applications as superconductors, optoelectronics, light emission diodes LEDs, and non-linear optical (NLO) chromophores. Besides, their pharmacological profiles as antimicrobial, antifungal, antiinflammatory, antiproliferative and antioxidant agents have led to an enduring interest in the development of various methods for their synthesis **(Omar, 2020)**. Functional groups containing heteroatom-heteroatom bonds (X–X, where X = N, O, S, and P) have been identified in natural products isolated from a variety of sources. The diverse structures and reactivities of these motifs have captured the attention of chemists and chemical biologists. Indeed, many metabolites containing such linkages are used clinically; including the Nnitrosourea-

containing chemotherapeutic streptozotocin **I**, the isoxazolidinone-containing antibiotic D-cycloserine **II**, and the nitro group-containing antibiotic chloramphenicol **III**. X–X bond containing functional groups can be essential for the activity of natural products **(Awakawa *et al.*, 2021)** and **(Chen *et al.*, 2021)**.

1,3,5-triazine-2,4,6-triamine, also called **cyanuramide** or **triamino-triazine**, is a colorless crystalline substance belonging to the family of heterocyclic organic compounds, which are used principally as a starting material for the manufacture of synthetic resins. 1,3,5-triazine-2,4,6-triamine is rich in nitrogen, a property that is like protein. The misuse of 1,3,5-triazine-2,4,6-triamine, namely the adulteration of various food products with the chemical, raised significant public health and food safety concerns in the first decade of the 21st century **(Albiol, 2020)**. 1,3,5-triazine-2,4,6-triamine is an organic base commercially synthesized from urea with an intermediate step producing cyanic acid. The reaction also results in the formation of other byproducts, including cyanuric acid, ammeline, and ammelide. 1,3,5-triazine-2,4,6-triamine is 66% nitrogen by molecular weight. It is combined with formaldehyde by industry to produce 1,3,5-triazine-2,4,6-triamine resin, a very durable thermosetting plastic, and 1,3,5-triazine-2,4,6-triamine foam, a polymeric cleanser. Other commercial products containing 1,3,5-triazine-2,4,6-triamine include countertops, dry erase boards, fabrics, glues, housewares, and flame retardants. 1,3,5-triazine-2,4,6-triamine is also one of the major components in pigment yellow 150, which is a colorant for inks and plastics. It is also a derivative of arsenical drugs, and Melarsoprol is one such drug used for the treatment of African trypanosomiasis **(Liu *et al.*, 2020)**. 1,3,5-triazine-2,4,6-triamine is not metabolized by animals and is rapidly eliminated in the urine. More than 90% of ingested 1,3,5-triazine-2,4,6-triamine is toxicity can be classified as acute or chronic. 1,3,5-triazine-2,4,6-triamine has low acute toxicity; the LD_{50}, the lethal dose of a compound that would result in death in 50% of the tested animals, for 1,3,5-triazine-2,4,6-triamine in rats is 3.161 g/kg body weight. Long-term exposure to 1,3,5-triazine-2,4,6-triamine reduces fertility and results in fetal toxicity in animal studies **(Rajpoot *et al.*, 2020)**.

The aims of the present paper were thus to presenting a comprehensive overview of the morphological properties, and therapeutic potential of *Carthamus tinctorius* extract and antioxidants with a view to their traditional and popular uses in different parts of the world, development of new drugs to treat various human diseases, return to nature by activating the use of remedies of natural origin instead of therapies of chemical origin, and spreading awareness and nutritional education of the benefits of medicinal plants and how to use them.

MATERIALS AND METHODS

Materials:

1. Basal diet was installed its ingredients, minerals and vitamins mixtures were purchased from AL-Gomhoryia Co., Tanta - Gharbia - Egypt.

Table (1): Composition of basal diet

Ingredients	Amount
Casein*	10%
Corn oil	10%
Mineral's mixture	4%
Vitamin's mixture	1%
Fiber	4%
Corn starch	71%
Total	100%

From: **(Busserolles *et al.*, 2002) *12.3 g of casein gives 10.0 g protein**

The minerals mixture, which was used in this experiment, can be seen from table (2) as recommended by **(Hegsted *et al.*, 1941)**.

Table (2): Composition of mineral's mixture

Ingredients	Amount
$CaCo_3$	30.0
KH_2PO_4	32.25
$CaHPO_4$- H_2O	7.50
$MgSO_4$- $7H_2O$	10.2
NaCl	16.66
Fe ($C_6H_2O_7$)- $6H_2O$	2.75
KI	0.08
$MnSo_4$- $4H_2O$	0.50
$ZnCI_2$	0.025
$CuSO_4$- $5H_2O$	0.03
Total	100.00

The vitamins mixture can be seen from table (3) as recommended by **(Muller, 1964)**.

Table (3): Composition of vitamin's mixture

Ingredients	Amount
Vitamin A	200.00 IU*
Vitamin D	100.00 IU*
Vitamin E	10.00 IU*
Vitamin K_3	0.50 IU*
Vitamin C	20.00 mg
Vitamin B_{12}	2.00 mg
B_1	50.00 mg
B_2	1.00 mg
B_6	0.40 mg
Calcium pantothenic	4.00 mg
Nicotinic acid	4.00 mg
Choline chloride	200.00 mg
Folic acid	0.20 mg
P-amino- benzoic acid	10.00 mg
Biotin	0.02 mg
Corn starch	Up to 1000 mg

***1 IU equal 1.02 mg, 1 ppm = 0.0001%**

2. *Carthamus tinctorius* **[**The detailed animal experiment design after modeling, the T2DM rats were daily oral administrated with **safflower** (120 mg/kg) or metformin (90 mg/kg) or normal saline for eight weeks. The dose of metformin is based on the daily dose conversion in humans (1.0g/d) **(Lee *et al.*, 2020)]** was purchased from Surour herbal Co., Tanta -Gharbia - Egypt.
3. 1,3,5-triazine-2,4,6-triamine powder **[Melamine**, the current limit set by the FDA for melamine in food is 2.5 parts per million, calculated on the basis of ingestion by a person weighing 60 kg **(deQuirós *et al.*, 2019)**. Rats were administered 0%, 0.0001%, 0.001%, 0.01%, 0.02%, or 0.05% BBN in experiment 1 in the drinking water in light-shielded bottles; and 0%, 0.3%, 1.0%, or 3.0% melamine in experiment 2 in the basal diet (CRF-1; Oriental Yeast, Tokyo, Japan) for 2 days or 4 weeks **(Yamada *et al.*, 2020)]** was purchased from AL-Gomhoryia Co., Tanta - Gharbia - Egypt.
4. **Animals:** Forty-two (42) Sprague-Dawley white male albino rats, each weighing 215±10g, were used in this investigation obtained from serum and vaccine center. All rats were housed in group cages under conditions of controlled temperature (22-24°C) and illumination (12-h light cycle starting at 6 AM) for at least seven days before experiments.
5. **Animals and experimental design:** Rats were housed individually in well-aerated cages under hygienic laboratory conditions. Animals were housed at the Institute of Ophthalmology, Cairo University, and fed for one week on standard died for adaptation before the beginning of the experiment **(Abhari *et al.*, 2016)**. Rats were divided into 6 groups, every 7 rats in each group fed on a certain diet for 28 days as follows:
    a. **Group (1) (Negative or normal group) (-Ve):** Fed on basal diet only, as control negative.
    b. **Group (2) (Positive group) (+Ve):** Fed on basal diet plus 2% of 1, 3, 5-triazine-2, 4, 6-triamine powder, as

control positive and the infection continues throughout the period of the experiment.

c. **Group (3) (-Ve) + *Carthamus tinctorius* extract:** Fed on basal diet plus 100 mg/ kg of rats of *Carthamus tinctorius* extract.
d. **Group (4) (+Ve) + *Carthamus tinctorius* extract:** Fed on basal diet plus 2% of 1, 3, 5-triazine-2, 4, 6-triamine powder plus100 mg/ kg of rats of *Carthamus tinctorius* extract.
e. **Group (5) (-Ve) + Vitamin C:** Fed on basal diet only plus plus100 mg/ kg of rats of vitamin C.
f. **Group (6) (+Ve) + Vitamin C:** Fed on basal diet plus 2% of 1, 3, 5-triazine-2, 4, 6-triamine powder plus100 mg/ kg of rats of vitamin C.

Methods:

1) **HPLC conditions:** High-density chromatography was used to identify the phenolic compounds in *Carthamus tinctorius* extract **(Table 4)**. HPLC analysis was carried out using an Agilent 1260 series at the National Research Center - Cairo. The separation was carried out using Eclipse C18 column (4.6 mm x 250 mm i.d., 5 µm). The mobile phase consisted of water (A) and 0.05% trifluoroacetic acid in acetonitrile (B) at a flow rate 1 ml/min. The mobile phase was programmed consecutively in a linear gradient as follows: 0 min (82% A); 0 - 5 min (80% A); 5 - 8 min (60% A); 8 - 12 min (60% A); 12 - 15 min (82% A); 15 - 16 min (82% A) and 16 - 20 (82%A). The multi-wavelength detector was monitored at 280 nm. The injection volume was 5 µl for each of the sample solutions. The column temperature was maintained at 40 °C.

Table (4) Phenolic compounds in *Carthamus tinctorius* extract		
	Area	**Conc. (µg/ml=µg/g)**
Gallic acid	255.38	1538.50
Chlorogenic acid	137.36	649.76
Catechin	ND	ND
Methyl gallate	6.87	5.21
Caffeic acid	11.23	26.02
Syringic acid	18.96	51.46
Pyrocatechol	85.89	395.81
Rutin	5.48	41.72
Ellagic acid	26.22	186.22
Coumaric acid	65.60	67.40
Vanillin	ND	ND
Ferulic acid	28.28	68.11
Naringenin	41.78	120.75
Quercetin	7.27	28.45
Cinnamic acid	13.75	7.93
Kaempferol	ND	ND
Hesperidin	10.92	18.80

2) **Biological evaluation:** During the experiment period, the consumed diet was recorded everyday feed intake (FI), and body weight was recorded every three days. Biological evaluation of the different diets was carried out by determination of the percentage of body weight gain and feed efficiency ratio **(Chapman *et al.*, 1959)**, Using well-known equations.

3) **Biochemical analysis:** At the end of the experiment, the rats were fasted overnight and serially anesthetized with diethyl ether. Blood was collected in clean dry centrifuge tubes from the hepatic portal vein, these tubes containing 3.1% sodium citrate solution (1:10v/v) to prepare serum and plasma, respectively **(Higgins *et al.*, 2020)**. Blood samples were centrifuged for 15 minutes at 3000 rpm to separate the serum. Serum was carefully separated and transferred into

dry clean Eppendorf tubes and kept frozen at 20° C until analysis **(Turchiano *et al.*, 2013)**. Serum total cholesterol (TC), triglyceride (TG) and high density lipoprotein cholesterol (HDL-c) were determined by using enzymatic colorimetric methods **(Chu *et al.*, 2019)** respectively. The determination of low density lipoprotein cholesterol (LDL-c) was calculated as mg/dl **(Sampson *et al.*, 2020)** equation**:**

LDL-c (mg/dl) = Total cholesterol - [HDL-c + VLDL-c]

While very low density lipoprotein cholesterol (VLDL-c) was carried out according to **(Bijland *et al.*, 2010)** and **(Sibal *et al.*, 2010)** equation:

VLDL-c (mg/dl) = Triglycerides/5

Determination of Glucose was carried out by the enzymatic colorimetric method **(Pinheiro *et al.*, 2020)**. Protein fractions (TP, Alb and Glb were determined by electrophoresis in blood serum **(Janků *et al.*, 2011)**. Blood samples for complete blood count were collected for determination of CBC variables **(Herrick *et al.*, 2020)**, **(Zong *et al.*, 2020)** and **(Narduzzi *et al.*, 2021)**. Determination of minerals in brain tissues **(Cemek *et al.*, 2014)**. Determination of minerals in testes tissues **(Abdel-All *et al.*, 2021)**.

RESULTS AND DISCUSSION

Table (5): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the glucose of rats induced by heterocyclic compounds containing nitrogen

Groups	Glucose (mg/dl)
-Ve	98.00 ± 7.40^{b}
+Ve	140.33 ± 5.80^{a}
G1	90.00 ± 8.50^{b}
G2	94.33 ± 9.90^{b}
G3	112.00 ± 10.10^{ab}
G4	118.00 ± 8.50^{ab}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

Results from the table (5) concerning to antitoxicity activity of polyphenols on the glucose of rats induced by heterocyclic compounds containing nitrogen. Respecting for **glucose** in (-Ve) group was 98.00±7.40, while (+Ve) group was 140.33±5.80. It's

clear that glucose for control (+Ve) was higher than control (-Ve), and others groups 90.00±8.50, 94.33±9.90, 112.00±10.10 and 118.00±8.50, respectively; all groups were lower values as compared with control (+Ve), but G1 and G2 showed high significant P<0. 01 compared to control (+Ve). These results were agreed with **(Yan *et al.*, 2020)** who said that *Carthamus tinctorius* extract decreased glucose levels and improved insulin sensitivity in rats, suggesting the anti-hyperglycemia effects of *Carthamus tinctorius* extract.

Table (6): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the lipids profile of rats induced by heterocyclic compounds containing nitrogen

Groups	TC (mg/dl)	TG (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
-Ve	63.00 ± 1.53^{b}	69.00 ± 3.61^{c}	17.00 ± 0.58^{ab}	32.20 ± 2.71^{a}	13.80 ± 0.72^{bc}
+Ve	70.67 ± 2.19^{a}	145.00 ± 6.11^{a}	11.00 ±0.57^{c}	30.67 ± 2.34^{b}	29.00 ± 1.22^{a}
G1	47.00 ± 1.53^{c}	63.00 ± 5.29^{c}	19.67 ± 1.20^{a}	14.73 ± 1.33^{c}	12.60 ± 1.06^{c}
G2	49.00 ± 1.15^{c}	65.33 ± 3.18^{c}	19.33 ± 1.86^{a}	16.60 ± 1.97^{bc}	13.07 ± 0.64^{bc}
G3	66.33 ± 2.03^{ab}	94.33 ± 4.71^{bc}	16.00 ± 2.00^{ab}	31.80 ± 3.01^{ab}	18.87 ± 3.34^{ab}
G4	68.00 ± 1.73^{ab}	102.00± 5.58^{b}	15.67 ± 0.88^{b}	31.60 ± 1.72^{ab}	20.40 ± 2.72^{b}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

Table (6) depicts antitoxicity activity of polyphenols on the lipids profile of rats induced by heterocyclic compounds containing nitrogen. Regarding **total cholesterol** in (-Ve) group was 63.00±1.53, while (+Ve) group was 70.67±2.19. It's clear that total cholesterol for control (+Ve) was higher than control (-Ve), and others groups 47.00±1.53, 49.00±1.15, 66.33±2.03 and 68.00±1.73, respectively; all groups were lower values as compared with control (+Ve), but G1 and G2 point to very high significant P<0.001 compared to control (+Ve). As for

triglyceride in (-Ve) group was 69.00±3.61, while (+Ve) group was 145.00±6.11. It's clear that triglyceride for control (+Ve) was higher than control (-Ve), and others groups 63.00±5.29, 65.33±3.18, 94.33±4.71 and 102.00±5.58, respectively; all groups were lower values as compared with control (+Ve), but G1 and G2 showed very high significant P<0.001 compared to control (+Ve), while G4 point to high significant P<0.01 compared to control (+Ve). Concerning **HDL-c** in (-Ve) group was 17.00±0.58, while (+Ve) group was (11.00±0.57). It's clear that HDL-c for control (+Ve) was lower than control (-Ve), and others groups 19.67±1.20, 19.33±1.86, 16.00±2.00 and 15.67±0.88, respectively; all groups were higher values as compared with control (+Ve), but G1 and G2 showed a significant P<0.05 compared to control (+Ve), while G4 point to high significant P<0.01 compared to control (+Ve). In connection with **LDL-c** in (-Ve) group was 32.20±2.71, while (+Ve) group was 30.67±2.34. It's clear that LDL-c for control (+Ve) was lower than control (-Ve), and others groups 14.73±1.33, 16.60±1.97, 31.80±3.01and 31.60±1.72, respectively; G1 and G2 were lower values as compared with control (+Ve), while G3 and G4 recorded non-significant differences, as compared to control (+Ve). But G1 only point to very high significant P<0.001 compared to control (+Ve). With reference to **VLDL-c** in (-Ve) group was 13.80±0.72, while (+Ve) group was 29.00±1.22. It's clear that VLDL-c for control (+Ve) was higher than control (-Ve), and others groups 12.60±1.06, 13.07±0.64, 18.87±3.34 and 20.40±2.72, respectively; all groups were lower values as compared with control (+Ve), but G1 revealed to very high significant P<0.001 compared to control (+Ve), while G4 point to high significant P<0.01 compared to control (+Ve). Our results showed that *Carthamus tinctorius* extract decreased serum (TC), (TG), (LDL-c) and (VLDL-c) and increased the level of (HDL-c) that compatible with **(Du *et al.*, 2021)**. The plasma level of both lipid peroxides and anti-oxidized LDL-c autoantibody titers decreased concomitantly with the reduction of lesion formation. Serotonin derivatives were detected as both intact and conjugated metabolites in the plasma of C57BL/6J mice fed on 1.0% *Carthamus tinctorius* extract diet. These findings demonstrate that

serotonin derivatives of *Carthamus tinctorius* extract are absorbed into circulation and attenuate atherosclerotic lesion development possibly because of the inhibition of oxidized LDL-c formation through their strong anti-oxidative activity **(Koyama *et al.*, 2006)**.

Table (7): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the protein fractions of rats induced by heterocyclic compounds containing nitrogen

Groups	TP (mg/dl)	Alb (mg/dl)	Glob (mg/dl)
-Ve	3.93 ± 0.41^{bc}	1.53 ± 0.08^{bc}	1.43 ± 0.43^{c}
+Ve	5.03 ± 0.47^{a}	2.30 ± 0.31^{a}	3.07 ± 0.41^{a}
G1	3.43 ± 0.20^{c}	1.27 ± 0.12^{c}	1.63 ± 0.23^{bc}
G2	3.87 ± 0.52^{bc}	1.73 ± 0.12^{bc}	1.90 ± 0.55^{bc}
G3	4.10 ± 0.38^{b}	1.83 ± 0.03^{b}	2.27 ± 0.38^{b}
G4	4.53 ± 0.35^{ab}	1.97 ± 0.09^{ab}	2.40 ± 0.38^{ab}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

The outcome of our study of the table (7) can be summarized as follows: with reference to **total protein** in (-Ve) group was 3.93±0.41, while (+Ve) group was 5.03±0.47. It's clear that TP for control (+Ve) was higher than control (-Ve), and others groups 3.43±0.20, 3.87±0.52, 4.10±0.38 and 4.53±0.35, respectively; all groups were lower values as compared with control (+Ve), but G1 point to very high significant P<0.001 compared to control (+Ve), while G3 showed high significant P<0.01 compared to control (+Ve). Concerning **albumin** in (-Ve) group was 1.53±0.08, while (+Ve) group was 2.30±0.31. It's clear that Alb for control (+Ve) was higher than control (-Ve), and others groups 1.27±0.12, 1.73±0.12, 1.83±0.03 and 1.97±0.09, respectively; all groups were lower values as compared with control (+Ve), while G1 revealed to very high significant P<0.001 compared to control (+Ve), but G3 refer to high significant P<0.01 compared to control (+Ve). With regard to **globulin** in (-Ve) group was (1.43±0.43), while (+Ve) group was 3.07±0.41. It's clear that Glb for control (+Ve) was higher than control (-Ve), and others groups 1.63±0.23, 1.90±0.55, 2.27±0.38 and 2.40±0.38, respectively; all groups were lower values as compared with control (+Ve), just G3 refer to high significant P<0.01 compared to control (+Ve). At the time of writing, there were no reports in

the literature demonstrating potential effects of *Carthamus tinctorius* on the protein fractions. Therefore, we explored the mechanisms underlying *Carthamus tinctorius* decreased of protein fractions (TP, Alb, and Glob) via antioxidant action of polyphenols for *Carthamus tinctorius*. While, dietary supplementation with antioxidants such as vitamin C could prevent oxidative protein denaturation, and consequently, improve nutrient digestibility and feed efficiency **(Ibrahim *et al.*, 2020)** and **(Amer *et al.*, 2020)**.

Table (8): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the blood complete count of rats induced by heterocyclic compounds containing nitrogen

Groups	Hb (g/dl)	RBCs (mm^3)	Hematocrit %	Platelets (mm^3)
-Ve	12.93 ± 0.03^{ab}	4.97 ± 0.52^{d}	37.40 ± 3.12^{bc}	645.67 ± 46.97^{a}
+Ve	11.70 ± 0.98^{c}	7.47 ± 0.23^{a}	22.30 ± 1.68^{e}	447.00 ± 25.79^{d}
G1	13.23 ± 1.06^{ab}	5.27 ± 0.58^{bc}	42.30 ± 3.38^{b}	601.67 ± 35.25^{b}
G2	13.70 ± 0.36^{a}	5.23 ± 0.12^{c}	43.80 ± 1.14^{a}	602.62 ± 37.21^{ab}
G3	12.23 ± 0.48^{b}	6.27 ± 0.09^{ab}	28.93 ± 0.96^{d}	552.45 ± 32.11^{c}
G4	12.67 ± 0.64^{ab}	6.17 ± 0.12^{b}	33.13 ± 1.24^{c}	590.67 ± 33.82^{bc}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

Table (8) refers to antitoxicity activity of polyphenols on the complete blood count of rats induced by heterocyclic compounds containing nitrogen. Point to **hemoglobin** in (-Ve) group was 12.93±0.03, while (+Ve) group was 11.70±0.98. It's clear that hemoglobin for control (+Ve) was lower than control (-Ve), and others groups 13.23±1.06, 13.70±0.36, 12.23±0.48 and 12.67±0.64, respectively; all groups were higher values as compared with control (+Ve), when G2 refer to a significant $P<0.05$ compared to control (+Ve). But G3 showed a high significant $P<0.01$ compared to control (+Ve)**.** In connection with

red blood cells in (-Ve) group was 4.97±0.52, while (+Ve) group was 7.47±0.23. It's clear that RBC for control (+Ve) was higher than control (-Ve), and others groups 5.27±0.58, 5.23±0.12, 6.27±0.09 and 6.17±0.12, respectively; all groups were lower values as compared with control (+Ve), when G2 point to very high significant P<0.001 compared to control (+Ve). When G4 showed high significant P<0.01 compared to control (+Ve). Apropos **hematocrit** in (-Ve) group was (37.40±3.12), while (+Ve) group was 22.30±1.68. It's clear that hematocrit for control (+Ve) was lower than control (-Ve), and others groups 42.30±3.38, 43.80±1.14, 28.93±0.96 and 33.13±1.24, respectively; all groups were higher values as compared with control (+Ve), while G1 point to high significant P<0.01 compared to control (+Ve). When G2 showed a significant P<0.05 compared to control (+Ve), but G4 refer to a very high significant P<0.001 compared to control (+Ve). With reference to **platelets** in (-Ve) group was 645.67±46.97, while (+Ve) group was 447.00±25.79. It's clear that PLT for control (+Ve) was lower than control (-Ve), and others groups 601.67±35.25, 602.62±37.21, 552.45±32.11 and 590.67±33.82, respectively; all groups were higher values as compared with control (+Ve), while G1 point to high significant P<0.01 compared to control (+Ve). When G3 refer to very high significant P<0.001 compared to control (+Ve). Therefore, *Carthamus tinctorius* extract administration might provide the additional benefit of increasing blood fluidity by lowering blood viscosity, which can be of great value in the prevention of hemorheological disorder-associated diseases in at risk patients. Meanwhile, the mild activities of antiplatelets aggregation and anti-coagulation induced by *Carthamus tinctorius* extract should be considered, if these relatively untoward symptoms occurred when the hemorrhagic patients ate food colored by *Carthamus tinctorius* extract. However the small amounts used in food are highly unlikely to cause adverse effects **(Zhao *et al.*, 2014)**.

Table (9): Continue potentials antitoxicity effects of *Carthamus tinctorius* extract on the blood complete count of rats induced by heterocyclic compounds containing nitrogen

Groups	MCV	MCH (pg)	MCHC (g/l)	Total leukocyte count %
-Ve	76.67 ± 8.96^{a}	23.93 ± 2.79^{a}	31.33 ± 0.09^{a}	21.02 ± 1.49^{b}
+Ve	53.50 ± 1.76^{e}	17.60 ± 0.64^{f}	21.47 ± 0.50^{d}	13.52 ± 3.40^{e}
G1	67.20 ± 4.22^{b}	20.97 ± 1.32^{d}	31.77 ± 0.09^{a}	23.28 ± 6.01^{a}
G2	68.13 ± 2.09^{ab}	21.30 ± 0.54^{b}	31.67 ± 0.09^{a}	17.70 ± 0.55^{cd}
G3	56.80 ± 4.44^{d}	18.70 ± 0.40^{e}	25.67 ± 1.46^{c}	19.88 ± 3.02^{c}
G4	58.60 ± 2.30^{c}	20.37 ± 0.59^{c}	27.73 ± 0.92^{b}	16.81 ± 3.29^{d}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

For table (9) explain antitoxicity activity of polyphenols on the complete blood count of rats induced by heterocyclic compounds containing nitrogen. Point to **MCV** in (-Ve) group was 76.67±8.96, while (+Ve) group was 53.50±1.76. It's clear that MCV for control (+Ve) was lower than control (-Ve), and others groups 67.20±4.22, 68.13±2.09, 56.80±4.44 and 58.60±2.30, respectively; all groups were higher values as compared with control (+Ve), when G1 refer to high significant P<0.01 compared to control (+Ve). But G4 showed very high significant P<0.001 compared to control (+Ve). In connection with **MCH** in (-Ve) group was 23.93±2.79, while (+Ve) group was 17.60±0.64. It's clear that MCH for control (+Ve) was lower than control (-Ve), and others groups 20.97±1.32, 21.30±0.54, 18.70±0.40 and 20.37±0.59, respectively; all groups were higher values as compared with control (+Ve), when G2 point to high significant P<0.01 compared to control (+Ve). When G4 showed very high significant P<0.001 compared to control (+Ve). Apropos **MCHC** in (-Ve) group was 31.33±0.09, while (+Ve) group was 21.47±0.50. It's clear that MCHC for control (+Ve) was lower

than control (-Ve), and others groups 31.77±0.09, 31.67±0.09, 25.67±1.46 and 27.73±0.92, respectively; all groups were higher values as compared with control (+Ve), while G1 and G2 point to a significant P<0.05 compared to control (+Ve). When G3 showed very high significant P<0.001 compared to control (+Ve), but G4 refer to high significant P<0.01 compared to control (+Ve). With reference to **total leukocyte count** in (-Ve) group was 21.02±1.49, while (+Ve) group was 13.52±3.40. It's clear that TLC for control (+Ve) was lower than control (-Ve), and others groups 23.28±6.01, 17.70±0.55, 19.88±3.02 and 16.81±3.29, respectively; all groups were higher values as compared with control (+Ve), while G1 point to a significant P<0.05 compared to control (+Ve). When G3 refer to very high significant P<0.001 compared to control (+Ve). As erythrocyte indices like mean cell volume (MCV), mean cell hemoglobin (MCH) and mean cell hemoglobin concentration (MCHC), in experiment, correlated with RBC, hemoglobin and hematocrit values **(Karimungi and Joshi, 1996)**, then *Carthamus tinctorius* extract administration might provide the additional benefit of increasing blood fluidity by lowering blood viscosity, which can be of great value in the prevention of hemorheo-logical disorder-associated diseases in at risk patients **(Zhao *et al.*, 2014)**. *Carthamus tinctorius* extract predicted by spectrum-effect relationship analysis had good blood-activating effect. Therefore, spectrum-effect relationship analysis is an effective approach for seeking active components in herbs **(Wang *et al.*, 2019)**.

Table (10): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the brain tissue minerals of rats induced by heterocyclic compounds containing nitrogen

Groups	Brain Na^{+} (mg/l)	Brain K^{+} (mg/l)	Brain Ca^{++} (mg/l)	Brain P^{+++} (mg/l)
Ve-	63.00 ± 3.51^{b}	1.50 ± 0.04^{c}	1.24 ± 0.05^{bc}	1.44 ± 0.41^{c}
Ve+	52.00 ± 4.04^{c}	1.16 ± 0.03^{f}	1.65 ± 0.04^{a}	1.20 ± 0.21^{d}
G1	54.00 ± 3.51^{bc}	1.28 ± 0.05^{e}	1.43 ± 0.05^{ab}	1.15 ± 0.05^{e}
G2	68.33 ± 4.26^{ab}	1.62 ± 0.06^{b}	1.15 ± 0.04^{c}	1.65 ± 0.09^{b}
G3	59.00 ± 5.03^{bc}	1.37 ± 0.06^{d}	1.42 ± 0.03^{b}	1.26 ± 0.04^{cd}
G4	75.33 ± 3.84^{a}	1.70 ± 0.07^{a}	0.84 ± 0.07^{d}	1.83 ± 0.05^{a}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

The outcome of our study of table (10) can be summarized antitoxicity activity of polyphenols on the brain tissue minerals of rats induced by heterocyclic compounds containing nitrogen. For **Na^{+}** in (-Ve) group was 63.00±3.51, while (+Ve) group was 52.00±4.04. It's clear that Na^{+} for control (+Ve) was lower than control (-Ve), and others groups 54.00±3.51, 68.3±4.26, 59.00±5.03 and 75.33±3.84, respectively; all groups were higher values as compared with control (+Ve), but G4 point to a significant P<0.05 compared to control (+Ve). As for **K^{+}** in (-Ve) group was 1.50±0.04, while (+Ve) group was 1.16±0.03. It's clear that K^{+} for control (+Ve) was lower than control (-Ve), and others groups 1.28±0.05, 1.62±0.06, 1.37±0.06 and 1.70±0.07, respectively; all groups were higher values as compared with control (+Ve), but G2 showed high significant P<0.01 compared to control (+Ve), while G4 point to a significant P<0.05 compared to control (+Ve). Concerning **Ca^{++}** in (-Ve) group was 1.24±0.05, while (+Ve) group was 1.65±0.04. It's clear that Ca^{++} for control (+Ve) was higher than control (-Ve), and others groups 1.43±0.05, 1.15±0.04, 1.42±0.03 and 0.84±0.07, respectively; all groups were lower values as compared with control (+Ve), but G2 showed very

high significant P<0.001 compared to control (+Ve), while G3 point to high significant P<0.01 compared to control (+Ve). In connection with $\mathbf{P^{+++}}$ in (-Ve) group was 1.44±0.41, while (+Ve) group was 1.20±0.21. It's clear that P^{+++} for control (+Ve) was lower than control (-Ve), and others groups 1.15±0.05, 1.65±0.09, 1.26±0.04 and 1.83±0.05, respectively; G1 was lower value as compared with control (+Ve), while G2, G3 and G4 were higher. When G2 point to high significant P<0.01 compared to control (+Ve), G4 refer to a significant P<0.05 compared to control (+Ve). The results we obtained were in agreement with what he said calcium signaling assays indicated that *Carthamus tinctorius* could reduce the intracellular free Ca^{++} level. These findings demonstrate that *Carthamus tinctorius* could activate BK_{Ca} channels and inhibit Ca-L channels and reduce intracellular free Ca^{++} level, which are probably important for its vasodilatory effect **(Wang *et al.*, 2020)**. Traumatic Brain Injury (TBI) refers to the injury of cerebral tissue structure/function caused by various kinds of mechanical violence in the outside world **(Liu *et al.*, 2021)** and **(Yao *et al.*, 2021)**. *Carthamus tinctorius* has the potential to be utilized as a neuroprotective agent in cases of TBI. Firstly, TBI enables *Carthamus tinctorius* to distribute in the cerebral tissues of rats **(Bie *et al.*, 2010)**. Then, the antioxidant effect of *Carthamus tinctorius* in the brain of the TBI rats could explain the TBI improvement via increasing SOD, catalase and glutathione levels, while reducing MDA and oxidized glutathione (GSSG) levels **(Bie *et al.*, 2010)** and **(Wang *et al.*, 2016)**. Lastly, *Carthamus tinctorius* could increase mitochondrial ATPase (i.e., Na^{+}, K^{+}-ATPase, Ca^{++}-ATPase, and Mg^{++}-ATPase) and tissue plasminogen activator activities, while decreasing plasma plasminogen activator inhibitor-1 activity and MMP-9 expression in the hippocampus of TBI rats **(Wang *et al.*, 2016)**.

Table (11): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the testes tissue minerals of rats induced by heterocyclic compounds containing nitrogen

Groups	Testes Na^{+} (mg/l)	Testes K^{+} (mg/l)	Testes Ca^{++} (mg/l)	Testes P^{+++} (mg/l)
Ve-	74.00 ± 4.73^{f}	1.09 ± 0.02^{f}	3.05 ± 0.41^{a}	5.70 ± 0.26^{f}
Ve+	103.00 ± 1.15^{a}	2.21 ± 0.01^{a}	2.31 ± 0.41^{e}	7.13 ± 0.88^{a}
G1	78.00 ± 7.00^{e}	1.24 ± 0.04^{e}	2.91 ± 0.31^{ab}	5.93 ± 0.52^{e}
G2	91.67 ± 0.88^{b}	2.11 ± 0.02^{b}	2.45 ± 0.58^{d}	6.82 ± 0.67^{b}
G3	87.00 ± 3.06^{c}	1.85 ± 0.05^{c}	2.78 ± 0.28^{c}	6.61 ± 0.79^{c}
G4	82.33 ± 1.86^{d}	1.57 ± 0.03^{d}	2.88 ± 0.25^{b}	6.34 ± 0.49^{d}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

In the case of table (11) can be summarized antitoxicity activity of polyphenols on testes tissue minerals of rats induced by heterocyclic compounds containing nitrogen. For **Na^{+}** in (-Ve) group was 74.00±4.73, while (+Ve) group was 103.00±1.15. It's clear that Na^{+} for control (+Ve) was higher than control (-Ve), and others groups 78.00±7.00, 91.67±0.88, 87.00±3.06 and 82.33±1.86, respectively; all groups were lower values as compared with control (+Ve), but G2 refer to a high significant P<0.01 compared to control (+Ve) and G3 showed a very high significant P<0.001. As for **K^{+}** in (-Ve) group was 1.09±0.02, while (+Ve) group was 2.21±0.01. It's clear that K^{+} for control (+Ve) was higher than control (-Ve), and others groups 1.24±0.04, 2.11±0.02, 1.85±0.05 and 1.57±0.03, respectively; all groups were lower values as compared with control (+Ve), while G2 point to a high significant P<0.01 compared to control (+Ve), G3 refer to a very high significant P<0.001. Concerning **Ca^{++}** in (-Ve) group was 3.05±0.41, while (+Ve) group was 2.31±0.41. It's clear that Ca^{++} for control (+Ve) was lower than control (-Ve), and others groups 2.91±0.31, 2.45±0.58, 2.78±0.28 and 2.88±0.25, respectively; all groups were higher values as compared with control (+Ve), but G3 showed a very high significant P<0.001 compared to control (+Ve), while G4 point to a high significant

P<0.01 compared to control (+Ve). In connection with P^{+++} in (-Ve) group was 5.70±0.26, while (+Ve) group was 7.13±0.88. It's clear that P^{+++} for control (+Ve) was higher than control (-Ve), and others groups 5.93±0.52, 6.82±0.67, 6.61±0.79 and 6.34±0.49, respectively; all groups were lower values as compared with control (+Ve). When G2 point to a high significant P<0.01 compared to control (+Ve), G3 refer to a very high significant P<0.001 compared to control (+Ve). Vascular dilation and congestion found in the interstitial tissue have been described in *Carthamus tinctorius*–treated animals. These changes could be a consequence of the action of vasodilator substances like serotonin present in the *Carthamus tinctorius* extract, and this may be attributed to the lack of blood flow to the testicles and the nutrients it carries, especially the minerals, and this is consistent with what was stated in our study. Additionally, *Carthamus tinctorius* extract may induce production another vasodilator substances such as nitric oxide (NO) **(Mirhoseini *et al.*, 2012)**.

Table (12): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the organs weight of rats induced by heterocyclic compounds containing nitrogen

Groups	Brain weight (g)	Testes weight (g)
-Ve	2.00 ± 0.15^{c}	2.83 ± 0.19^{c}
+Ve	2.53 ± 0.18^{a}	3.30 ± 0.06^{a}
G1	1.73 ± 0.03^{d}	2.39 ± 0.16^{e}
G2	1.65 ± 0.07^{e}	2.73 ± 0.31^{d}
G3	2.13 ± 0.39^{bc}	2.97 ± 0.12^{b}
G4	2.33 ± 0.35^{b}	3.10 ± 0.15^{ab}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

Results in table (12) showed that **brain weight** in the normal rats group was 2.00±0.15, while the control positive group was 2.53±0.18. It's clear that brain weight for control (+Ve) was higher than control (-Ve), meanwhile in other groups weight were 1.73±0.03, 1.65±0.07, 2.13±0.39 and 2.33±0.35, respectively; all groups were lower values when compared with control (+Ve). But just G4 revealed to high significant P<0.01 compared to control (+Ve). Concerning to **testes weight** in the normal rats group was 2.83±0.19, while control positive group was 3.30±0.06. It's clear

that testes weight for control (+Ve) was higher than control (-Ve), while in others groups weight were 2.39±0.16, 2.73±0.31, 2.97±0.12 and 3.10±0.15, respectively; all groups were lower values when compared with control (+Ve). But just G3 refer to a high significant P<0.01 compared to control (+Ve). Some studies reported the toxic effects of *Carthamus tinctorius* on brain tissues. *Carthamus tinctorius* extract has been shown to reduce the cerebral infarction area and neurological deficits as well as expression of TNFα and IL-1β in ischemia-reperfusion (I/R) brain injury in rats **(Keshavarzi *et al.*, 2019)** and this is consistent with our current study. On the other hand, contradicted with our results **(Bahmanpour *et al.*, 2012)** who said, as the data showed the increase in the weight and volume of the testis. *Carthamus tinctorius* extract can promote the blood circulation and has antioxidant activity; therefore, through blood circulation in the testes, which would lead to gains in weight and volume in the testes. Increases in the weight and volume must be dependent on the improvement in spermatogenesis caused by the safflower extract; testes send more sperm to the epididymis, which of course will make it heavier and larger in weight and volume.

Table (13): Potentials antitoxicity effects of *Carthamus tinctorius* extract on the biological evaluation of rats induced by heterocyclic compounds containing nitrogen

Groups	BWG %	FI (g/ day)	FER (g)
Ve-	16.10 ± 2.17^{e}	225.30 ± 8.08^{ab}	0.09 ± 0.06^{c}
Ve+	-22.44 ± 1.84^{f}	203.20 ± 2.33^{e}	-0.16 ± 0.03^{d}
G1	38.50 ± 2.98^{b}	210.40 ± 3.67^{d}	0.14 ± 0.04^{abc}
G2	30.60 ± 3.82^{c}	218.60 ± 6.22^{c}	0.15 ± 0.03^{ab}
G3	31.50 ± 2.42^{c}	216.10 ± 3.50^{cd}	0.19 ± 0.02^{a}
G4	25.50 ± 2.42^{d}	221.50 ± 2.93^{bc}	0.13 ± 0.03^{bc}

a=*p < 0 .05; b=**p < 0.01 and c= P < 0.001***

Results in table (13) indicated that the **body weight gain percentage** in the normal rats group was 16.10±2.17, while the control positive group was -22.44±1.84. It's cleared that BWG% for control (-Ve) was higher than control (+Ve). Other groups (-Ve + *Carthamus tinctorius* extract) (G3), (+Ve + *Carthamus tinctorius* extract) (G4), (-Ve + Vitamin C) (G5) and (+Ve +

vitamin C) (G6) were 38.50±2.98, 30.60±3.82, 31.50±2.42 and 25.50±2.42 respectively; G1, G2, G3 and G4 were highly value as compared with control (+Ve). When G2 and G3 showed a very high significant P<0.001 compared to (+Ve), but G1 showed a high significant P<0.01 compared to (+Ve). As for **Feed Intake** (FI) (g) in (-Ve) group was 225.30±8.08, while (+Ve) group was (203.20±2.33). It's clear that feed intake (g) for control (+Ve) was lower than control (-Ve), and other groups 210.40±3.67, 218.60±6.22, 216.10±3.50 and 221.50±2.93 respectively, all groups were highly value as compared with control (+Ve). Just G2 point to a very high significant compared to (+Ve). With regard to the **Feed Efficiency Ratio** (FER) in (-Ve) group was 0.09±0.06, while (+Ve) group was -0.13±0.03. It's clear that (FER) for control (+Ve) was lower than control (-Ve), and others groups 0.14±0.04, 0.15±0.03, 0.19±0.02 and 0.13±0.03 respectively, all groups were highly value as compared with control (+Ve). But just G3 revealed to a significant P<0.05 compared to (+Ve). **(Kucuk *et al.*, 2003)** stated that supplementation with 200 mg/kg diet of vitamin C, and not 100 mg/kg diet, resulted in increased FI, BW, and FER of rats. Ascorbic acid improved the feed efficiency by increasing the nutrient digestibility and controlling the deficiency of minerals and vitamins. *Carthamus tinctorius* extract inclusion improves the ingestive behavior (feeding and drinking) **(Amer *et al.*, 2021)** and **(Khelil-Arfa *et al.*, 2021)**.

HISTOPATHOLOGICAL OF BRAIN

Photo (1): Section of normal brain group 1 (Negative control) showed normal sized glial cells (Red arrows) surrounded by fibrillary stroma containing normal sized blood vessels (Blue arrow) (H&E X 100).

Photo (2): Section of brain group 2 (Plant) showed normal sized glial cells (Red arrow) surrounded by fibrillary stroma (Blue arrow) (H&E X 100).

Photo (3): Section of brain group 3 (Antioxidant) showed normal sized glial cells (Blue arrow) surrounded by fibrillary stroma (Red arrow) (H&E X 100).

Photo (4): Section of intoxicated brain group 4 (Positive control) showed congested dilated blood vessels (Red arrows) surrounded by an area of infarction (Blue arrow) (H&E X 40).

Photo (5): Section of intoxicated brain group 4 (Positive control) showed glial degeneration (Blue arrows) with congested blood vessels (Red arrow) (H&E X 100).

Photo (6): Section of brain group 5 (Intoxicated treated with plant) showed almost normal brain tissue (Red arrow) with focal degeneration (Blue arrows) (H&E X 100).

Photo (7): Section of brain group 6 (Intoxicated treated with antioxidant) showed an area of degenerated stroma (Red arrow) and another area of normal brain tissue (Blue arrow) (H&E X 100).

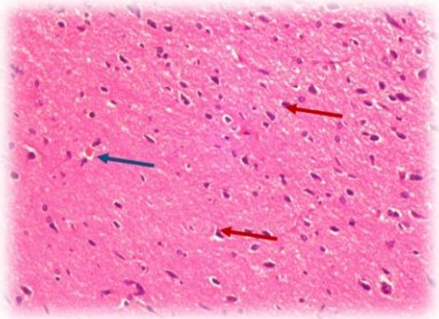
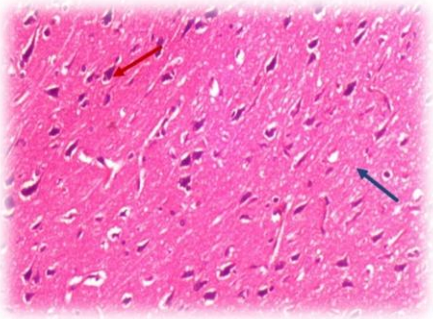


Photo (1)



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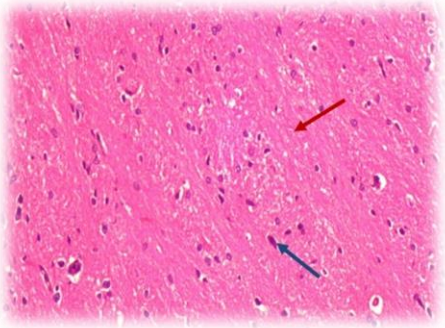

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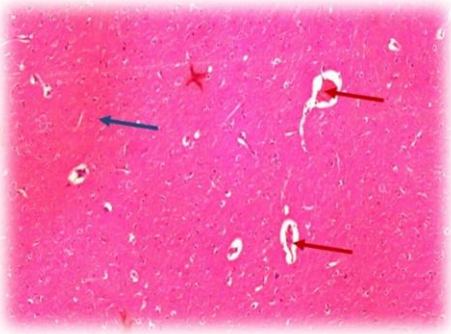

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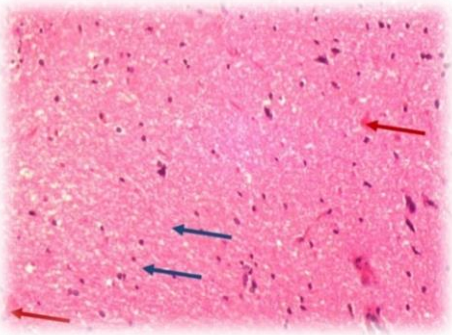

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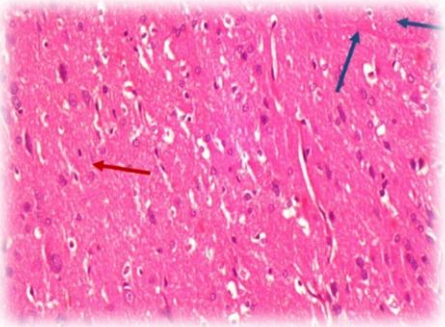

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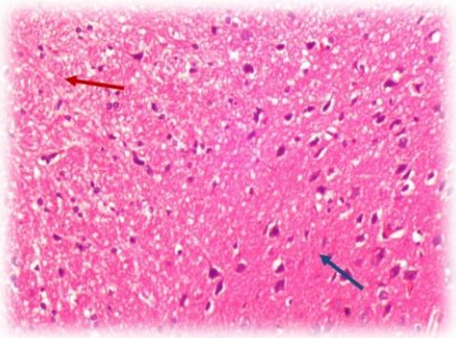


Photo (7)

HISTOPATHOLOGICAL OF TESTES

Photo (1): Section of testis of group 1 (Negative control) showed average sized seminiferous tubules lined with spermatocytes (Blue arrows) (H&E X 100).

Photo (2): Section of testis of group 2 (Plant) showed average sized seminiferous tubules lined with hypercellular spermatocytes (Blue arrows) (H&E X 100).

Photo (3): Section of testis of group 3 (Antioxidant) showed average sized seminiferous tubules with hypercellular spermatocytes (Blue arrows) (H&E X 100).

Photo (4): Section of testis of group 4 (Intoxicated positive control) showed destruction and disorganization with hyalinization of seminiferous tubules (Blue arrows) (H&E X 100).

Photo (5): Section of testis of group 5 (Intoxicated treated with plant) showed some disorganized seminiferous tubules without hyalinization or destruction (Green arrows) (H&E X 100)

Photo (6): Section of testis of group 6 (Intoxicated treated with antioxidant) showed focal disorganized seminiferous tubules without hyalinization or destruction (Blue arrow) surrounded by normal sized seminiferous tubules (Blue arrows) (H&E X 100).

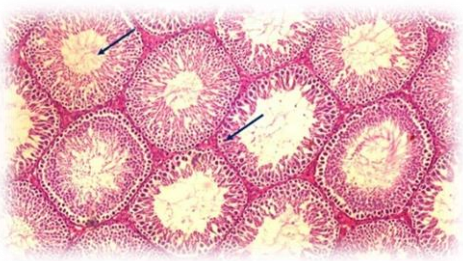
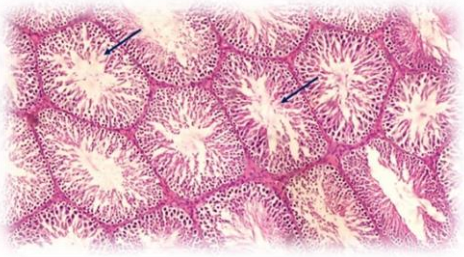


Photo (1)

Photo (2)



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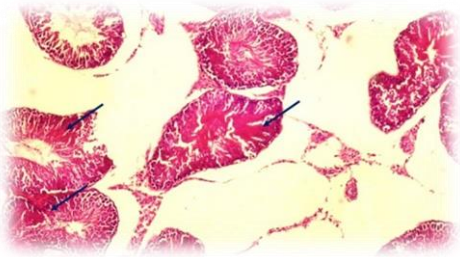

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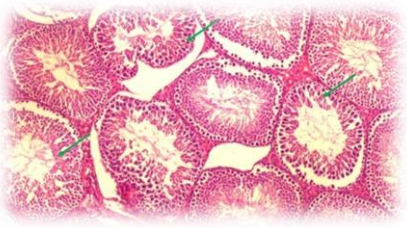

Photo (5)

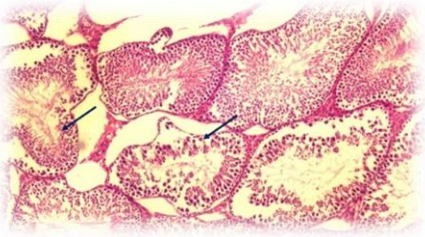

Photo (6)

CONCLUSIONS AND FUTURE PERSPECTIVES

This study was an attempt to provide a comprehensive overview on the morphological characteristics, and the therapeutic as well as the non-therapeutic potential of *Carthamus tinctorius* extract with a view towards its traditional and folk uses in different parts of the world. Hence, future studies should focus on the identification and characterization of the individual metabolites of the *Carthamus tinctorius* extract, which are essential for a thorough understanding of the pharmacological significance of polyphenols. Based on current information, the pharmacological functions, including the antioxidant, anti-inflammatory, anti-diabetic, brain and testes protective effects of *Carthamus tinctorius* extract, can be effectively exploited in the development of new drugs to treat various human diseases.

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الملخص العربى

دراسة التأثيرات المضادة للسمية المحتملة لمستخلص نبات *Carthamus tinctorius* على الجرذان التي تسببها المركبات الحلقية غير المتجانسة المحتوية على النيتروجين

ناصر نسيم عطية زهران

مستشفيات جامعة المنوفية – شبين الكوم – مصر

الهدف من هذه الدراسة هو دراسة التأثيرات المضادة للسمية المحتملة لمستخلص *Carthamus tinctorius* على بعض أعضاء الفئران التي تسببها المركبات الحلقية غير المتجانسة المحتوية على النيتروجين ونشر الوعي الغذائي بفوائد النباتات الطبية وكيفية استخدامها. أجريت الدراسة الحالية لتقييم تأثير مستخلص *CT* من خلال تحديد العناصر الحيوية ومستويات مضادات الأكسدة في أنسجة المخ والخصيتين لدى الفئران. اثنان وأربعون (42) من ذكور الجرذان البيضاء من نوع Sprague-Dawley، وزن كل منها 10±215 جم؛ تم تقسيم الفئران إلى 6 مجموعات، تغذت كل 7 فئران في كل مجموعة على نظام غذائي معين لمدة 28 يومًا. تم استخدام مستخلص *CT* وفيتامين C بوزن 100مجم/كجم من وزن الفئران ، بينما تم استخدام الميلامين بنسبة 2٪. البوليفينول هى عائلة كبيرة من المركبات العضوية الموجودة بشكل طبيعي وقد اكتسبت الكثير من الأهمية بسبب استخدامها المحتمل كعوامل وقائية وعلاجية في العديد من الأمراض. حددنا بعض التغييرات المهمة حول مستويات العناصر الحيوية في دماغ الجرذان وأنسجة الخصيتين المعرضة لمستخلص *CT*. وقد أوضحت النتائج أن المجموعات التي تم تغذيتها على مستخلص *CT* كانت الأفضل مقارنة بالمجموعات الأخرى وخاصة المجموعة (-Ve). استنادًا إلى المعلومات الحالية، يمكن استغلال الوظائف الدوائية، بما في ذلك التأثيرات الوقائية لمضادات الأكسدة، ومضادات الإلتهابات، ومضادات السكري، والدماغ والخصيتين للبوليفينول، بشكل فعال في تطوير عقاقير جديدة لعلاج أمراض الدماغ والخصيتين المختلفة.

الكلمات المفتاحية: البوليفينولات، المخ، الخصيتين، مضادات الأكسدة، سيانوريك.