COMPARATIVE STUDY ON WATER MELON, COLOCYNTH AND CANTALOUPE SEEDS AS USED FOR TREATMENT OF HEPATOINTOXICATED RATS

By

**** Mohamed Said Mahmoud Elmahdy**

Supervised By

*** Prof. Dr. Mohammed Samir El. Dashlouty, *Dr.Ehab salah EL-Din Mohammed**

* Nutrition and Food Science Dept., Home Economics Faculty, Menoufia University, ** Dept of Field studies and research,l Nutrition Institute, Cairo Egypt

ABSTRACT

This study was carried out using watermelon (*Citrullus lanatus*) seeds, colocynth (*Citrullus colocynthis*) seeds, and Cantaloupe (*Cucumis melo var. cantalupensis*) seeds in diets of hepatointoxicated rats.

The present work aimed to evaluate the effect of separate mentioned seeds & their mixture (as 7.5%) on amelioration the hepatic disorder of CCL4 injected rats considering, some physiological parameters and, histological structure.

Male albino rats were distributed into 6 groups each of 5 rat in which means of rats weight for all groups were nearly equal; first main group negative control, second main group the hepatic rats - which were divided was into 6 groups (5rats / group) were fed on several seeds diets (7.5%). for 28 days. Biological (Bodyweight gain, feed intake and feed efficiency ratio) were calculated at the end of experiments. Aspartate aminotransferase (AST), glutamic alanintransaminase (ALT), alkaline phosphatase (ALP), total protein (T.P), albumin(Alb), superoxide dismutase (SOD), glutathione peroxidase (GPX), catalase (CAT), serum total cholesterol, triglycerides, HDL cholesterol, creatinine, urea; fasting blood sample were taken for the determination of glucose. Liver & kidney of all animals were carefully removed to be examined histologically.

Treatment groups fed on seeds diets revealed significant improvement of all the liver and kidneys function markers.Total cholesterol and serum triglycerides levels reduced while HDL-c increased in hepatic rats. Antioxidation, enzymes, BWG, FI, FER and also histological structure.were better for seeds dites groups, specially the watermelon seeds 7.5%.

Key words: watermelon seeds, colocynth seeds, cantaloupe seeds – serum glucose, liver function, kidney function, triglycerides, cholesterol, lipoproteins.

دراسة مقارنة على بذور البطيخ والحنظل والكنتالوب عند إستخدامها فى علاج الفئران المصابة بالتسمم الكبدى .

الباحث

**** محمد سعيد محمود المهدى**

تحت إشراف

*** محمد سمير الدشلوطى ،* إيهاب صلاح الدين محمد**

* قسم التغذية و علوم الأطعمة - كلية الاقتصاد المنزلى- جامعة المنوفية

** قسم الدراسات الميدانية والبحوث- المعهد القومى للتغذية

الملخص العربى

تم إجراء الدراسة الحالية لمعرفة تأثير بذور بعض النباتات (بذور البطيخ ، وبذور الحنظل وبذور الكنتالوب)على الخلل الفسيولوجى المحدث فى كبد الفئران المصابة بواسطة رابع كلوريد الكربون . تم إستخدام ٣٠ فأر ألبينو ذكور أوزانهم ١٣٩.٢±١٠جم وتم تقسيمهم إلى ٦ مجموعات متساوية إحداهما كمجموعة ضابطة سالبة أما المجموعات الأخرى فتم إحداث تسمم بالكبد فيها بالحقن تحت الجلد برابع كلوريد الكربون المخلوط مع زيت البرافين ٥٠% بالحجم بنسبة ٢ ملجم / كجم من وزن الجسم مرتين أسبوعيا ولمدة أسبوعين . وأضيفت البذور المستخدمة بنسبة ٧.٥% لكل منها من الوجبة الأساسية على هيئة مسحوق ناعم وتم قياس نشاط إنزيمات الكبد (ALP, GPT,GOT) والبروتين الكلى والألبيومين والجلوبيولين ونسبة الألبيومين على الجلوبيولين والبيليروبين الكلى والبيليروبين المباشر والغير مباشر وإنزيمات مضادات الأكسدة (سوبر أوكسيد ديسموتيز (SOD) ، والكتاليز (CAT) والجلوتاثيون بيروكسيديز (GPX) ودهون الدم (الكوليسترول الكلى ، والجليسريدات الثلاثية ، واللبيوبروتينات ، (HDL-c, LDL-c, VLDL-c) ووظائف الكلى (اليوريا والكرياتينين وحمض اليوريك). وكذلك إجراء الفحص الهستوباثولوجى لكل من الكبد والكلى . وقد أظهرت نتائج هذه الدراسة أن تناول هذه البذور نتج عنه تحسن فى وظائف الكبد والكلى ودهون الدم.

الكلمات الكاشفة : بذور البطيخ – بذور الحنظل – بذور الكنتالوب – مستوى جلوكوز الدم — وظائف الكبد – وظائف الكلى – الكوليسترول – الجلسريدات الثلاثية – ا للبيوبروتينات.

INTRODUCTION:

The liver is one of the largest solid organs of the body. It is located in the upper right part of the abdomen. Most of the organ lies under cover of the rib cage. Its major function include processing the food that passes through the gut and converting it into energy that can be utilized by the body. It is also apowerful detoxification center that handles many chemicals, alcohol, poisons and toxins as well as drugs and clears the blood. The liver also makes bile and stores it in a small pouch like organ called the gallbladder. This bile helps in digestion especially fats **(Mandel, Ananya 2013).**

Watermelon (*Citrullus lanatus*) is of the cucurbitaceae family. As a member of the cucurbitaceae, watermelon is related to the cantaloupe, squash and pumpkin and other plants that grows on vines on the ground. Watermelon is a good source of carotenoid and lycopene. Lycopene has been found to be protective against a growing list of cancer **(Cho *et al.*, 2004).** Watermelon is also expectedly high in citrulline; an amino acid the body make use of to make another amino acid, arginine (used in the urea cycle to remove ammonia from the body) **(Collins *et al.*, 2007)**. Watermelon is delectable, thirst-quencher which helps quench the inflammations that contributes to conditions like asthma, atherosclerosis, diabetes, colon cancer and arthritis. Cucurbit seeds are source of food particularly protein and oil **(Hassan *et al*., 2008).**

Egusi (*Colocynthis citrullus* L.) kernels contain 52.0% oil, 28.4% protein (60% in defatted flour), 2.7% fiber, 3.6% ash, and 8.2% carbohydrate. They are good sources of essential amino acids, especially arginine, tryptophan and methionine, vitamins B_1, B_2, and niacin, and S, Ca, Mg, Mn, K, P, Fe, and Zn. The oil contains mostly oleic (15.9%) and linoleic (62.8%) acids. Protein isolates that differ in gel electrophoretic patterns and amino acid content can be prepared from the flour in one- or two-step water and sodium hydroxide extractions. The water and oil holding capacities of the flour are 0.7 and 2.6 ml/g, respectively. Thick (mayonnaise-type) emulsions form in the alkaline pH range, and a stable foam forms at pH 5.0. Nutritionally, lysine is the most limiting amino acid (chemical score, 52.4) **(Akobundu *et al.*, 2006)**.

Cantaloupe contains a lot of nutritions. It contains various vitamins, minerals and unsaturated fats. It contains vitamin C, fiber, carbohydrate, potassium, sodium, calcium, phosporus, iron, niacin, protein, polyunsaturated fat and absolutely a lot of water.
It also has a high betacarotene, it can fight free radicals and absolutely prevent from cancer and tumor. Cantaloupe is good for someone who has a diet program, because it can fill stomach longer. Besides has high

betacarotene, it also contains vitamin A that good for eyes's health **(Anon, 2013)**.

AIM OF THE STUDY:

This study aims to examine the effect of water melon, colocynth and cantaloupe seeds on body weight gain feed intake, feed efficiency ratio, antioxidant enzymes such as GPX, SOD & CAT, liver function, kidney function, blood glucose & lipids, and histological properties of liver& kidney in hepatointoxicated rats were in the scope of this investigation.

MATERIALS AND METHOD:

Material:

Watermelon seeds (*Citrullus lanatus*), colocynth seeds (*Citrullus colocynthis*), and Cantaloupe seeds (*Cucumis melo var. cantalupensis*) were obtained from the ministry of Agricalture.

Carbon tetra chloride (CCL_4) was obtained from El-Gomhoria Company for chemicals, Cairo, Egypt, as a toxic chemical for liver poisoning according to **(Passmore and Eastwood, 1986)**. At the same time, CCL_4 was mixed with paraffin oil by equal volumes and used for induction of liver disease.

Rats: Thirty (30) adult male albino rats, Sprague Dawley strain, mean weight 139.2±10 g were obtained from Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt. Rats were housed in wire cages under the normal laboratory conditions and fed on basal diet for 7 consecutive days as adaptation period. Diets were introduced to rat in a special non-scattering feeding cup to avoid loss of food and contamination. Tap water was provided to rats by means of glass tubes projecting through wire cages from inverted bottles supported to one side of the cage.

Methods:

Experimental design: Thirty (30) (Sprague - Dawley strain) male albino rats were distributed into 6 groups each of 5 rat in which means of rats weight for all groups were nearly equal. All rats were housed in wire cages and fed on the experimental diets for 4 weeks according to the following groups:

Group (1): Control negative group (-ve), in which normal rats were fed on basal diet for 28 days.

Group (2): Control positive (+ve), in which hepatotoxicity rats which were injected by CCL_4 were fed on basal diet for 28 days.

Group (3): CCL_4 hepatotoxicity rats were fed on basal diet containing 7.5% watermelon seeds for 28 days.

Group (4): CCL_4 hepatotoxicity rats were fed on basal diet containing 7.5% colocynth seeds for 28 days.

Group (5): CCL_4 hepatotoxicity rats were fed on basal diet containing 7.5% cantaloupe seeds for 28 days.

Group (6): CCL_4 hepatotoxicity rats were fed on basal diet containing 7.5% equalized combination of all plants for 28 days.

Rats were weighted at the beginning of the experimental then weekly and at the end of the experimental; consumed feed calculated each day.

Diet: The basal diet was prepared according to **AIN** (**1993).**The vitamin mixture was prepared according to **AIN (1977**). The salt mixture was prepared according to **AIN (1977).**

Organ weights: The organs (liver – Heart- kidney –Spleen – and Lungs) were excised, rinsed in chilled saline solution, then blotted on filter paper, and weighed separately to calculate the absolute and relative organs weight.

Biochemical analysis Blood:

At the end of the 4 weeks, the animals were anesthetized with diethyl ether. Incisions were made into the abdomen and blood samples were obtained from the portal vein into (EDTA) centrifuge tubes. Plasma was separated by centrifugation at 4000 r .p. m for 10 minutes. The collected samples were analyzed for the biochemical parameters. Enzymatic colorimetric method used to determine, Aspartate aminotransferase GOT (AST) and alkaline phosphate GPT (ALT) activities were measured according to method described by **Henry (1974) and Yound (1975)**. Alanine determination of (ALP) procedure based on colorimetric determination was preformed according to the method of **IFCC** (**1983).** Serum total protein (TP) assessed according to **(Henry, 1974),** serum albumin (Alb) according to **(Doumas *et al*., 1971),** serum total bilirubin (T.Bil) according to **Doumas *et al*., (1973),** serum direct bilirubin (D.Bil) according to **Chary and Sharma (2004),** Serum in direct bilirubin (Ind.Bil) according to **Chary and Sharma (2004)**. Determination of SOD carried out according to **(Sun *et al*., 1988),** GPX according to **Zhao, (2001)** and CAT according to **Diego (2011)**. Determination of Cholesterol performed according to **Allain (1974),** triglycerides according to **Fossati and Prencipe(1982),** high density lipoprotein (HDL) cholesterol according to **Lopez (1977)**. Low density lipoprotein (LDL-c) & very low density lipoprotein (VLDL-c) assessed according to **Lee and Nieman (1996).**Creatinine was determined according to the method described by **Bohmer (1971),** Urea according to the method described by **Patton and Crouch (1977)** and serum glucose according to **Yound (1975) and Tietz (1976)**.

Histological examination: Specimens of the internal organs (Liver & kidney) were taken immediately after sacrificing rats and immersed in 10% neutral buffered formalin. The fixed specimens were then trimmed

and dehydrated in ascending grades of alcohol, cleared in xylene, embedded in paraffin, sectioned (4-6 Mm thickness), stained with hematoxylin and eosin and examined microscopically **(Carleton, 1979)**.

Statistical analysis: The data were statically analyzed using a computerized costat program by one way ANOVA. The results are presented as mean ± SD. Differences between treatments at $p \leq 0.05$ were considered significant **(S.A.S, 1985)**.

RESULTS AND DISCUSSION:

In Table (1) The effect of watermelon seeds, colocynth, cantaloupe seeds, and the combination of all on body weight gain (BWG %), feed intake (FI) and feed efficiency ratio (FER) of CCL4 injectted in rats is shown. Data illustrate in hepatic rats a gradual increase in relative BWG, FI, & FER when feeding on watermelon seeds, colocynth, cantaloupe seeds & mixture seeds levels 7.5%. The statistical analysis showed significant positive relations between treatments and BWG, FI, & FER. These results are in agreement with those reported by **Bakr (2009); Nazeah (2012) & Shehata, (2012) for hepatic rats**.

Table (2) Effect of watermelon seeds, colocynth, cantaloupe seeds, and the combination of all on organ weight (g) of carbontetrachloride (CCL4) injected rats. Data illustrate that in hepatic rats a gradual increase took place in relative organs weight. When watermelon seeds, colocynth, cantaloupe seeds & mixture seeds level 7.5% diets lowered such weights. The statistical analysis showed a significant positive correlation between treatments and organs ratio. These results are in agreement with those reported by **Bakr (2009); Nazeah (2012) & Shehata, (2012) for hepatic rats**.

Table (3) reflects the effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on glutamic oxaloacetic transaminase (GOT or AST), glutamic pyruvate transaminase (GPT or ALT), alkaline phosphatases (ALP) ,(GOT)/ (GPT) or (AST/ALT), total protein (g/L), albumin (mg/dl), globulin (mg/dl), Albumin (mg/dl) / globulin (mg/dl), Total bilirubin (mg/dl), direct bilirubin (mg/dl) & indirect bilirubin (mg/dl) of CCL_4 injected rats. AST level in hepatic rats fed control diet was 170.00±3.653 U/L. The decrease of aspartame amino transferase (AST) level 7.5% also, alanine amino transferase (ALT) level was recorded. Alkaline phosphates (ALP), total protein (g/l) & albumin (mg/dl), total bilirubin, direct bilirubin & indirect bilirubin improved when rats feed on seeds but the best transactions when fed to rats watermelon seeds. These results are in agreement with those reported by **Sevcan *et al.*, (2011)** studied the effect of Diyarbakır watermelon (*Citrullus lanatus* cv: Sürme) juice on lipid peroxidation status in rat liver, kidney and brain.

Administration of carbon tetrachloride along with watermelon juice or ursodeoxycolic acid (UDCA) significantly reduces serum markers of liver damage, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TB) and decreases albumin when compared to the control group.These results are in agreement with those reported by **Madhavi *et al.*, (2012)**, they found that the significant decrease in serum ALT, AST and ALP levels treated groups which were increased due to CCl4 induced liver damage are comparable with standard drug. Histopathological study of liver tissue ravealed the hepatoprotective activity of *Citrullus lanatus* seed oil. This was also found for hepatointoicated rats by CCL_4. These results are in agreement with those reported by **Arshed, Iqbal*, et al.*, (2011),** Based on the results it could be concluded that *Citrullus colocynthis* alcoholic extract reduces the inflammation and protect the hepatocytes.

Table (4): reflects Effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on SOD (U/L) & CAT enzyme (mmol/L) & GPX (Ng/ml.) of hepatointoxicated rats. Serum SOD in control (+) group was 17.64±1.216 (U/L). In hepatic rats fed different seeds of watermelon showed pronounced ment a improve. The table illustrates maximum improves of serum (CAT), (GPX), & SOD when rats fed on rat watermelon seeds diet.These results are in agreement with those reported by **Habibur *et al.*, (2013)** reported that *Citrullus lanatus* is a well known fruit (watermelon) of family Curcubitacea. The fruit is consumed for cooling effect. Moreover, so many literature suggests that it contains important phytoconstituetns like vitamine C, minerals etc. Moreover, literature is available for its pharmacological activities like anti-oxidant, laxative, antimicrobial, diurectic etc. Its seeds contain fatty acids and have phenolic and triterpinoids. The seeds extract showed so many pharmacological activities.

Table (5) results shows the effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on serum total cholesterol & triglycerides (TG), high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), veryLow density lipoprotein cholesterol (VLDL-c) & atherogenic index (AI) of CCL4 injected rats. Pronounced decreases. Data revealed of serum (T.c), (TG), (LDL-c), (VLDL-c) & (AI) when feed on rat watermelon seeds, while HDL was raised. These results are in agreement with those reported by **Zamani *et al.*, (2007)** reported that the pulp and the seeds of *Citrullus colocynthis* were assessed for their effects on the lipid profile of hyperlipidemic New Zealand rabbits. In the experimental groups that received the pulp of *C. colocynthis* or 100 mg/kg of seeds, the lipid profiles were significantly reduced when compared to the control group ($P<0.05$). Moreover, these results are in agreement with those reported by **Aruna *et al.*, (2012),**

consumption of *C. lanatus* 'sentinel' extract led to lower body weight and fat mass without influencing lean mass. *C. lanatus* 'sentinel' extract administration decreased plasma cholesterol concentrations that was attributed to reductions of intermediate-/low-density lipoprotein cholesterol. Plasma concentrations of monocyte chemo attractant protein-1 and interferon-gamma were decreased and those of interleukin-10 were increased in mice consuming *C. lanatus* 'sentinel' extract. Intake of *C. lanatus* 'sentinel' extract resulted in reductions of atherosclerosis in both aortic arch and thoracic regions.Also these results are in agreement with those reported by **Talabani and Tofiq (2012),** who found significant drop in serum total cholesterol and triglyceride observed at 120 h after first administration of colocynth seeds oil. They found that the suggestion of *Citrullus colocynthis* oil as a treatment for hyperlipidemia.

IN Table (6) The effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on urea (mg/dl), creatinine (mg/dl) and uric acid of hepatointoxicated rats is shown. Serum creatinine level for rats fed control diet was 0.50±0.004 mg/dl. marked decrease of serum creatinine was observed, along with the feeding of hepatic rats on watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds. Urea& Uric acid showed a paralled decreases when rats fed on mentioned seeds. But the best transactions recorededwhen rat fed on the mixture seeds. Howerer these results (table 6) disagree with that reported by **Al-Ghaithi *et al*., (2004)** who found that *Citrullus colocynthis* (Handal) plant extract did not have any effect on blood urea nitrogen (BUN).

Table (7) show the effect of watermelon seeds, colocynth, cantaloupe seeds, and the combination of all on serum glucose in CCL_4 injected rats. Results illustrate a pronounced decrease of blood glucose level followed feeding on watermelon seeds, colocynth, cantaloupe seeds, and the combination of all. Data proved the desirable the effect of feed seeds on blood glucose. Blood glucose was lower in the all supplemented diets compared to control (+ve). Group G6 (mixture of all seeds) revealed lowest values compared to others groups.

These results are in agreement with those reported by **Oryan *et al*., (2014),** they found that *C. colocynthis* was able to reduce blood glucose significantly compared with the control diabetic group ($P<0.05$).

Histopathologically (photo1-12), where pronounced changes took place in liver & kidneys structures due to injection with CCL_4. **Oryan *et al*., (2014),** they found that injection with alloxan resulted in severe necrotic changes in the pancreatic islets, especially in the central area of the islets. Liver of the treated diabetic rats revealed significant changes due to diabetes mellitus mean while, improvement of the hepatic tissue compared to those of the untreated diabetic rats recorded when inflicted rats recered extract of colocynth.

In present work (photos 1-12) supplementing with seeds improved liver and kidneys structures such improvement was achieved by feeding hepatic rats with 7.5% watermelon seeds, colocynth, cantaloupe seeds, and

mixture of all seeds. Anyhow microscopically, liver & kidney of rat from control (-ve) group showed normal structures (Photo 1&7).While, hepatic rat from control (+ve) group showed atrophy and vacuolations in liver & kidney .Meanwhile, liver & kidney of rat from all groups showed no histopathological changes indicating regaining of original structure.

Table (1): Effect of watermelon seeds, colocynth, cantaloupe seeds, and the combination of all on body weight gain (BWG %), feed intake (FI) and feed efficiency ratio (FER) of CCL4 rats

Parameter / Groups	BWG (%) M±SD	FI (g) M±SD	FER M±SD
(G1) Control (-)	48.00^{a} ± 3.654	25.00^{b} ± 1.750	0.069^{a} ± 0.0006
(G2) Control (+)	12.00^{d} ± 1.546	11.00^{e} ± 1.440	0.038^{f} ± 0.0003
(G3)Watermelon seeds 7.5%	47.00^{a} ± 1.381	26.00^{a} ± 1.550	0.065^{b} ± 0.0004
(G4) Colocynth Seeds 7.5%	35.00^{b} ± 1.930	25.00^{b} ± 1.840	0.050^{c} ± 0.0002
(G5) Cantaloupe Seeds 7.5%	26.00^{c} ± 2.553	23.00^{c} ± 1.750	0.040^{e} ± 0.0002
(G6) Mixture of all seeds 7.5%	25.00^{c} ± 2.701	18.00^{d} ± 1.660	0.049^{d} ± 0.0003
LSD	1.5453	0.2685	2.7389

Means in the same row with different litters are significantly different at ($P \leq 0.05$).

Table (2): Effect of watermelon seeds, colocynth, cantaloupe seeds, and the combination of all on organ weight (g) of carbontetrachloride (CCL4) injected rats

Parameter / Groups	Liver mean± SD	Heart Mean± SD	Kidneys Mean± SD	Spleen Mean± SD	Lungs Mean± SD
(G1) Control (-ve)	3.27^{e} ± 0.003	0.23^{e} ± 0.002	0.53^{f} ± 0.002	0.15^{f}± 0.002	0.53^{f} ± 0.0040
(G2) Control (+ve)	4.15^{a} ± 0.007	0.37^{a} ± 0.006	0.88^{a} ± 0.007	0.29^{a} ± 0.004	0.83^{a} ± 0.0070
(G3) Watermelon seeds 7.5%	3.40^{d} ± 0.004	0.31^{d}± 0.003	0.68^{e} ± 0.003	0.18^{e} ± 0.002	0.61^{c} ± 0.0035
(G4) Colocynth seeds 7.5%	3.80^{b} ± 0.005	0.32^{c} ± 0.004	0.73^{c} ± 0.004	0.23^{c} ± 0.003	0.59^{d} ± 0.0030
(G5) Cantaloupe seeds 7.5%	3.70^{c} ± 0.003	0.33^{b}± 0.005	0.75^{b} ± 0.006	0.26^{b} ± 0.004	0.66^{b} ± 0.0056
(G6) Mixture of all seeds 7.5%	3.80^{b} ± 0.006	0.31^{d} ± 0.003	0.69^{d} ± 0.005	0.20^{d} ± 0.001	0.57^{e} ± 0.0050
LSD	0.00297	0.00267	0.0034	0.0022	0.00269

Means in the same row with different litters are significantly different at ($P \leq 0.05$).

Table (3): Effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on (GOT or AST), (GPT or ALT), (ALP) and

(AST/ALT), total protein (g/), Albumin (mg/dl), globulin (mg/dl), Albumin (mg/dl) / globulin (mg/dl), Total bilirubin (mg/dl), direct bilirubin (mg/dl) & indirect bilirubin (mg/dl) of CCL_4 injected rats

Parameter / Groups	AST (U/L) Mean ± SD	ALT (U/L) Mean ± SD	Alkaline Phosphatase ALP (U/L) Mean ± SD	AST(U/L) / ALT(U/L) Mean ± SD	Total Protein (g/L) Mean ± SD	Albumin (mg/dl) Mean ± SD	Globulin (mg/dl) Mean ± SD	Alb/Glb Mean ± SD	Total Bilirubin (mg/dl) Mean ± SD	Direct Bilirubin (mg/dl) Mean ± SD	Indirect Bilirubin (mg/dl) Mean ± SD
(G1) Control (-ve)	95.00^{f} ± 2.660	30.00^{e} ± 3.250	248.00^{f} ± 4.320	3.17^{d} ± 0.053	5.30^{a} ± 0.269	3.80^{a} ± 0.170	1.50^{b} ± 0.229	2.53^{a} ± 0.051	0.20^{e} ± 0.0025	0.10^{c} ± 0.012	0.10^{d} ± 0.01
(G2) Control (+ve)	170.00^{a} ± 3.653	46.00^{a} ± 4.360	596.00^{a} ± 5.520	3.70^{a} ± 0.018	4.60^{b} ± 0.255	2.00^{b} ± 0.189	2.60^{a} ± 0.136	0.77^{e} ± 0.005	0.50^{a} ± 0.007	0.20^{a} ± 0.016	0.30^{a} ± 0.026
(G3) Watermelon Seeds 7.5%	102.25^{e} ± 2.563	32.00^{d} ± 3.550	251.80^{e} ± 4.550	3.20^{d} ± 0.022	4.90^{ab} ± 0.912	3.52^{a} ± 0.104	1.38^{b} ± 0.180	2.55^{a} ± 0.108	0.20^{e} ± 0.001	0.10^{c} ± 0.014	0.14^{c} ± 0.016
(G4) Colocynth Seeds 7.5%	131.40^{c} ± 4.566	36.20^{b} ± 2.660	402.40^{d} ± 3.640	3.63^{b} ± 0.095	5.08^{ab} ± 0.820	3.48^{a} ± 0.118	1.60^{b} ± 0.499	2.18^{c} ± 0.104	0.32^{c} ± 0.002	0.10^{c} ± 0.013	0.22^{b} ± 0.018
(G5) Cantaloupe Seeds 7.5%	134.60^{b} ± 3.542	37.00^{b} ± 4.550	470.00^{c} ± 6.330	3.64^{b} ± 0.085	5.04^{ab} ± 0.756	3.40^{a} ± 0.654	1.64^{b} ± 0.569	2.07^{d} ± 0.004	0.23^{d} ± 0.003	0.10^{c} ± 0.011	0.13^{c} ± 0.023
(G6) Mixture of all seeds 7.5%	120.80^{d} ± 5.540	34.80^{c} ± 3.025	583.60^{b} ± 6.650	3.47^{c} ± 0.066	5. 10^{ab} ± 0.451	3.60^{a} ± 0.129	1.50^{b} ± 0.171	2.4^{b} ± 0.038	0.38^{b} ± 0.004	0.16^{b} ± 0.015	0.22^{b} ± 0.025
LSD	2.0774	1.364	2.1688	0.0579	0.5258	0.3847	0.3402	0.08356	0.0038	0.0034	0.11195

Means in the same row with different litters are significantly different at ($P \leq 0.05$).

Table (4): Effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on SOD (U/L) & CAT (mmol/L) & GPX (Ng/ml.) of hepatointoxicated rats

Parameter / Groups	SOD (U/L)	CAT (Mmol/L) Mean ± SD)	GPX (Ng/ml)
(G1) Control (-ve)	40.85^{a} ± 1.444	63.72^{a} ± 13.160	32.20^{a} ± 0.767
(G2) Control (+ve)	17.64^{e} ± 1.216	16.79^{e} ± 0.934	14.65^{f} ± 1.130
(G3) Watermelon Seeds 7.5%	31.49^{b} ± 1.272	64.34^{a} ± 1.830	29.04^{b} ± 0.967
(G4) Colocynth Seeds 7.5%	27.04^{c} ± 1.490	36.19^{c} ± 1.721	24.33^{c} ± 1.781
(G5) Cantaloupe Seeds 7.5%	27.04^{c} ± 1.560	52.87^{b} ± 1.562	20.10^{d} ± 1.076
(G6) Mixture of all seeds 7.5%	23.95^{d} ± 1.527	26.54^{d} ± 0.836	16.08^{e} ± 1.195
LSD	0.2573	0.7499	0.6228

Means in the same row with different litters are significantly different at ($P \leq 0.05$).

Table (5): Effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on serum total cholesterol & Triglycerides (TG), high density lipoprotein cholesterol (HDL-c) & Low density lipoprotein cholesterol (LDL-c), veryLow density lipoprotein cholesterol (VLDL-c) & atherogenic index (AI) of CCL4 injected rats

Parameter / Groups	T.C (mg/dl) Mean± SD	T.G (mg/dl) Mean± SD	(HDL-c) (mg/dl) Mean± SD	(LDL-c) (mg/dl) Mean± SD	(VLDL-c) (mg/dl) Mean± SD	AI Mean ± SD
(G1) Control (-ve)	115.00^{b} ± 1.553	65.00^{e} ± 1.855	43.00^{c} ± 1.560	59.00^{b} ± 0.018	13.00^{e} ± 0.183	1.67^{c} ± 0.027
(G2) Control (+ve)	195.00^{a} ± 1.365	132.00^{a} ± 0.140	29.00^{e} ± 1.130	139.60^{a} ± 0.098	26.40^{a} ± 1.002	5.72^{a} ± 0.026
(G3) Watermelon Seeds 7.5%	97.40^{e} ± 1.020	83.40^{c} ± 0.162	56.70^{a} ± 1.602	24.02^{e} ± 0.012	16.68^{c} ± 0.028	0.72^{d} ± 0.016
(G4) Colocynth Seeds 7.5%	97.80^{e} ± 0.982	120.00^{b} ± 0.095	55.40^{b} ± 1.056	18.40^{f} ± 0.011	24.00^{b} ± 0.016	0.77^{d} ± 0.014
(G5) Cantaloupe Seeds 7.5%	105.00^{c} ± 1.23	77.60^{d} ± 0.204	31.20^{d} ± 1.860	58.28^{c} ± 0.138	15.52^{d} ± 0.019	2.37^{b} ± 0.184
(G6) mixture of all seeds 7.5%	101.25^{d} ± 1.575	76.80^{d} ± 0.950	56.00^{ab} ± 0.198	29.89^{d} ± 0.029	15.36^{d} ± 0.183	0.81^{d} ± 0.031
LSD	0.4654	1.288	1.0760	0.0978	0.6956	0.1203

Means in the same row with different litters are significantly different at (P≤ 0.05).

Table (6): Effect of watermelon seeds, colocynth, cantaloupe seeds, and mixture of all seeds on urea (mg/dl), creatinine (mg/dl) and uric acid of hepatointoxicated rats

Parameter / Groups	Urea (mg/dl) Mean ± SD	Creatinine (mg/dl) Mean ± SD	Uric Acid (mg/dl) Mean ± SD
(G1) Control (-ve)	18.00^{d} ± 2.448	0.20^{d} ± 0.001	1.10^{c} ± 0.039
(G2) Control (+ve)	26.00^{a} ± 3.798	0.50^{a} ± 0.004	2.50^{a} ± 0.222
(G3) Watermelon Seeds 7.5%	23.75^{b} ± 3.654	0.34^{b} ± 0.003	1.16^{c} ± 0.024
(G4) Colocynth Seeds 7.5%	19.60^{cd} ± 2.650	0.34^{b} ± 0.002	1.14^{c} ± 0.053
(G5) Cantaloupe Seeds 7.5%	20.80^{c} ± 1.650	0.34^{b} ± 0.004	1.52^{b} ± 0.040
(G6) Mixture of all seeds 7.5%	19.00^{d} ± 1.965	0.26^{c} ± 0.001	1.04^{c} ± 0.023
LSD	1.591	0.00250	0.1397

Means in the same row with different litters are significantly different at (P≤ 0.05).

Table (7): Effect of watermelon seeds, colocynth, cantaloupe seeds, and the combination of all on serum glucose in CCL_4 injected rats

parameter / Groups	Serum Glucose (mg/dl) Mean± SD
(G1) Control (-ve)	**122.40^{f} ± 4.658**
(G2) Control (+ve)	**205.00^{a} ± 7.660**
(G3) Watermelon Seeds 7.5%	**157.80^{d} ± 5.665**
(G4) Colocynth Seeds 7.5%	**175.40^{c} ± 6.550**
(G5) Cantaloupe Seeds 7.5%	**186.00^{b} ± 5.450**
(G6) Mixture of all Seeds 7.5%	**153.60^{e} ± 3.660**
LSD	**2.550**

Means in the same row with different litters are significantly different at ($P \leq 0.05$).

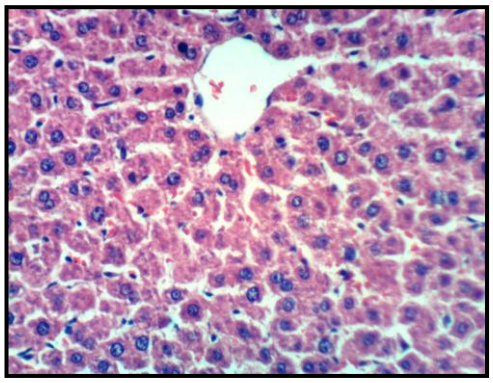

Photo (1): Liver of rat from group 1(control negative) showing the normal histological structure of hepatic lobule **(H & E X 400).**

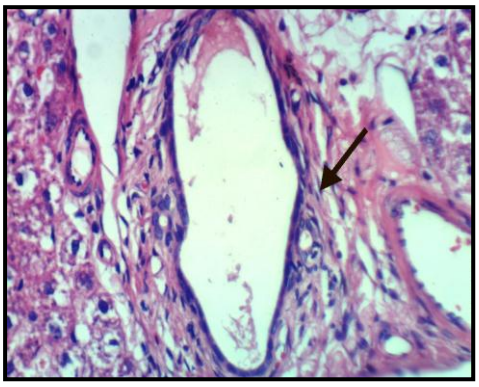

Photo (2): Liver of rat from group 2 (control positive) showing cystic dilatation of bile duct and fibroplasia in portal triad **(H & E X 400).**

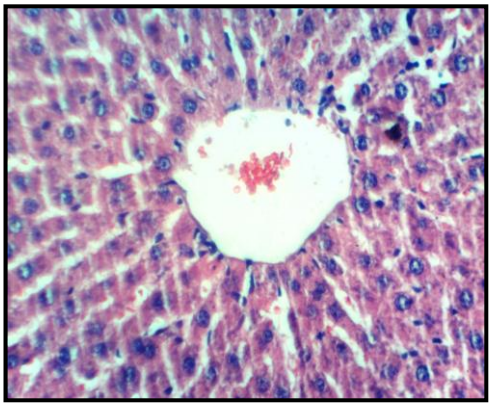

Photo (3): Liver of rat from group 3 (watermelon seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

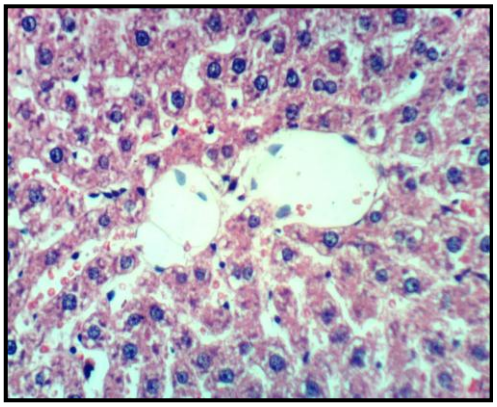

Photo (4): Liver of rat from group 4 (colocynth seeds 7.5%) showing no histopathological changes **(H & E X 400).**

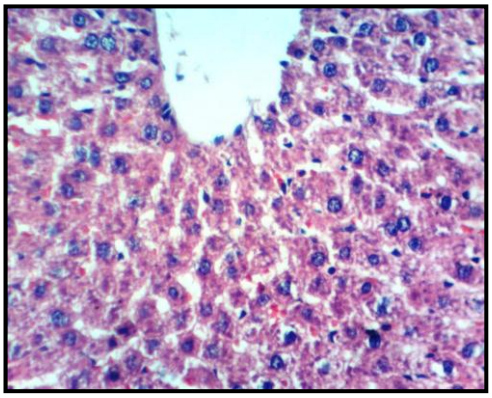

Photo (5): Liver of rat from group 5 (cantaloupe seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

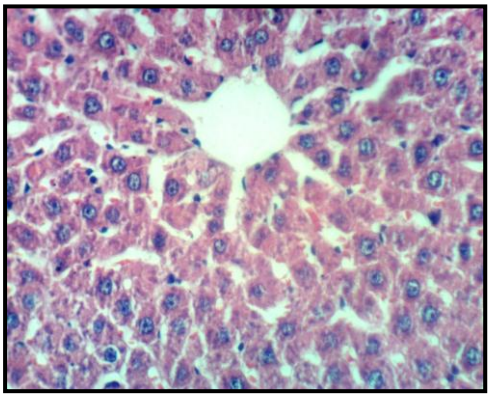

Photo (6): Liver of rat from group 6 (mixture of all seeds) showing no histopathological changes **(H & E X 400)**.

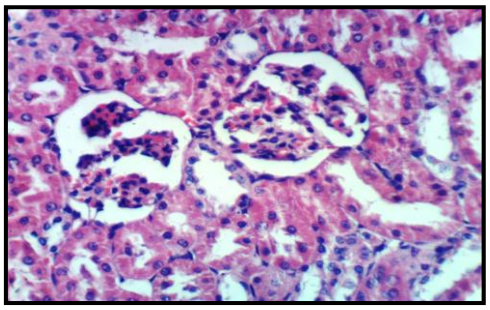

Photo (7): Kidney of rat from group 1(control negative) showing thenormal histological structure of renal parenchyma **(H & E X 400)**.

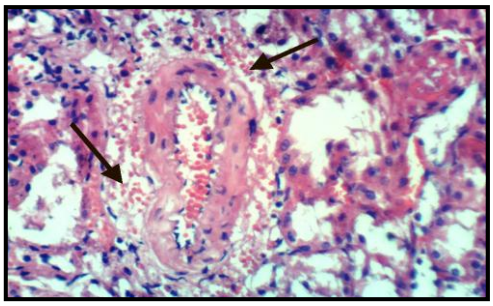

Photo (8): Kidney of rat from group 2 (control positive) showing perivascular haemorrhage **(H & E X 400)**.

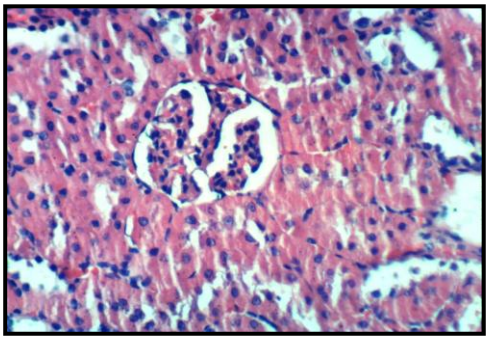

Photo (9): Kidney of rat from group 3 (watermelon seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

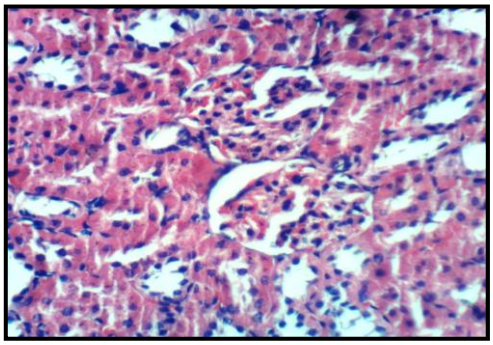

Photo (10): Kidney of rat from group 4 (colocynth seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

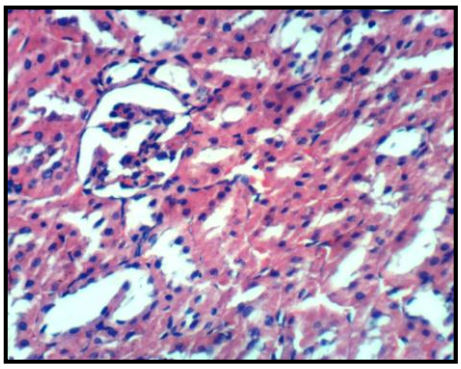

Photo (11): Kidney of rat from group 5 (cantaloupe seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

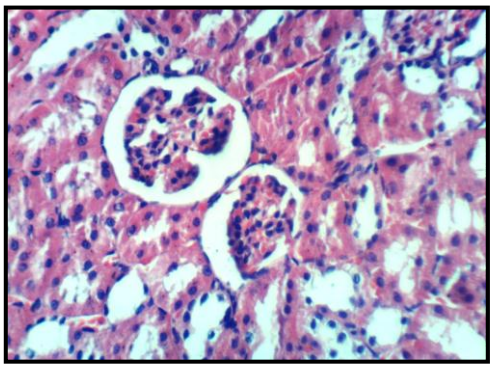

Photo (12): Kidney of rat from group 6 (mixture of all seeds) showing no histopathological changes **(H & E X 400)**.

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