

## Hematological, biochemical and histopathological changes in the rabbits treated with prednisone and olive oil

Ahmed D. Latif

Collage of Medicine- University of Wasit

### التغيرات الدموية , الكيموحيوية والنسجية في الأرانب المعالجة بالبردنسلون وزيت الزيتون.

احمد ظاهر لطيف الحسيني

كلية الطب/جامعة واسط

#### المستخلص

الهدف من الدراسة الحالية لملاحظة تأثير زيت الزيتون والبردنسلون على التغيرات المصلية والنسجية في الأرانب والمقارنة بينهما.

المواد وطرق العمل: تم تقسيم عشرين أرنباً ذكراً ناضجاً وبصرة عشوائية إلى أربعة مجاميع (5 أرنباً لكل مجموعة) وتم معاملتها كالتالي:

المجموعة الأولى: أعطيت ماء مقطر 2مل/كغم وزن/يوم/تجريع وحقن عضلي بالسالين 2مل/كغم/يوم.

المجموعة الثانية: أعطيت ماء مقطر 2مل/كغم وزن/يوم/تجريع وحقن عضلي بالبردنسلون 2ملغم/كغم/يوم.

المجموعة الثالثة: أعطيت زيت الزيتون 2مل/كغم وزن/يوم/تجريع وحقن عضلي بالسالين 2مل/كغم/يوم.

المجموعة الرابعة: أعطيت زيت الزيتون 2مل/كغم وزن/يوم/تجريع وحقن عضلي بالبردنسلون 2ملغم/كغم/يوم.

بعد 14 يوم أخذت عينات من الدم لحساب كريات الدم الحمراء , الهيموكلوبين , وكريات الدم الحمراء المرصوفة إضافة لقياس مستوى الدهون في الدم. بعدها قُتلت الحيوانات وأخذت عينات من القلب والرئة و الأمعاء لملاحظة التغيرات النسجية.

النتائج: زيت الزيتون والبردنسلون بالجرعة المستخدمة ولمدة 14 يوم سببت تغيرات واضحة في عدد كريات الدم الحمراء ومستوى الهيموكلوبين في دم الأرانب, بينما حجم الخلايا المرصوفة لم يظهر اختلافاً معنوياً.

أظهرت التغيرات النسجية تأثيراً واضحاً في المجموعة الأولى مقارنةً ببقية المجاميع.

الاستنتاجات: زيت الزيتون له تأثير في التقليل من التغيرات الحاصلة في الأرانب من جراء المعالجة بالبردنسلون.

## Abstract

**Aim:** the purpose of this study was to investigate the effect of olive oil on the serological and histological changes in rabbits after treatment. And compared the effect of olive oil with of prednisolone.

**Materials and Methods:** Twenty male rabbits were randomly divided into four groups. Grop-1 control group C. (n = 5) received Distilled water 2 ml /kg b.w./ day / orally and intramuscularly (i.m) injection of normal saline 2 ml /kg b.w./ day.

Group-2 first treated T1. (n=5) received Distilled water 2ml/kg /day / orally and injected prednisolone 2 mg/kg/day/ i.m .

Group-3 second treated T2. (n=5) received 2ml /kg/day /orally Olive oil and i.m. injected of normal saline 2 ml/kg/day.

Group-4 third treated T3. (n=5) received olive oil 2ml/kg/day/orally and prednisolone 2mg /kg/day/i.m .

After 14 days, blood samples were obtained for Red Blood Cell count (RBCc); Hemoglobin (Hb); Pack cell volume (pcv) and serological evaluation of serum lipids.

Animal were sacrificed and samples from Heart, lung and small intestine (Ileum) were obtained for Histopathological study.

**Results:** olive oil and prednisolone with 2mg/kg/day for fourteen days induce significant changes in the RBCc, Hb and serum lipids of the rabbits. While PCV% not induce any change.

Histopathological examination scores were significantly in T1 compared to other groups.

**Conclusion:** olive oil if effective in reducing damage in prednisolone – Treated rabbits.

**Key word:** Olive oil, prednisolone, hematological, biochemical & histopathological changes.

## Introduction

Prednisolone is potent anti-inflammatory glucocorticoids, which inhibits the activation of various immune competent cells (1). Used as immunosuppressive drugs to prevent rejection following organ transplantation (2). They are used as a part of endocrine therapy in breast and prostate cancer and as anti- edema agents in brain tumors (3). Pretreatment with glucocorticoids could have organ protective effects (4). (5) indicate that prednisolone sodium phosphate at a dose 1.5 mg/ kg b.w/day/orally to old male mice for

8 weeks can improve cardiac function in mice with insignificant difference in body and heart weight. Also it is important type of therapeutic agent for the treatment of allergic disease such as bronchial asthma (6). (7) indicate the dilatation effect of prednisolone was most obvious after 15 day of nitrogen dioxide inhalation. Its treatment might improve bronchodilator responses in chronic obstructive pulmonary disease (8). While (9) suggest that intra- arterial steroid injection therapy may be potentially useful in severe intestinal disease.

On the other hand, olive oil is widely consumed in Mediterranean region and may have health benefits that include modification of the immune and inflammatory responses (10 ; 11). Analysis of olive oil was determined its component: palmitic, palmitoleic, myristic, myristoleic, stearic, oleic, linoleic, linolenic, Arachidic and Eicosanoic (12). (11) reported the chief active components of olive oil include oleic acid, phenolic constituents and squalene. The main phenolics include hydroxytyrosol oil. Most human studies used olive oil as a reference (13). (14) recorded that consumption of virgin olive oil, could provide beneficial effects in stable coronary heart disease patients as an additional intervention to the pharmacological treatment. Olive oil has been reported to inhibit atherosclerosis development and protective effect in cardiovascular disease (15; 16; 17 and 18). While (19) reported that dietary olive oil prevented the development of aberrant crypt foci and colon carcinomas in rats, suggesting that olive oil may have chemopreventive activity against colon carcinogenesis.

Olive oil could improve intestinal damage and reduce inflammation in experimental ulcerative colitis (20). (21) recorded that type of diet can induce changes in the cholesterol and phospholipids ratio. (12) and (22) suggest that olive oil associated with a reduced serum lipids.

## Material and Methods

Twenty, male, local rabbits (1000 – 1400 gm body weight) were fed concentrated pellets diets and green Leaves with drinking water along the period of experiment *ad libitum*.

Rabbits were acclimatized for 7 days before the beginning of the study. Then randomly divided into four groups (each group consist of five rabbits) and handled as follows for 2 weeks:

- 1- Group C: rabbits of this group were received 2ml/kg/day/ orally/distilled water; and 2mg/kg/day/ intramuscularly injection (i.m) normal saline. And served as control group.
- 2- Group T1: rabbits of this group were treated with 2 ml/kg/ day/ orally/ Distilled water and 2mg/ kg/ day/ i.m/ prednisolone.
- 3- Group T2: rabbits of this group were treated with 2 ml/ kg/ day/ orally olive oil and 2 ml/ kg/ day/ i.m/normal saline.
- 4- Group T3: rabbits of this group were treated with 2 ml/ kg/ day/ orally /olive oil and 2 mg/ kg/day / i.m /prednisolone.

Fasting blood samples were collected from marginal ear vein at the end period of experiment for measurement Biochemical and Hematological analysis to determine the Red Blood Cell (RBC) count, Hemoglobin (Hb), packed cell volume (pcv %), cholesterol, Triglycerides and Lipoprotein.

Were determined in the clinical laboratory of AL- Karama hospital\ Kut, according to the previously reported methods (23; 24; 25)

### **Histopathological examination**

Specimens from heart, lung and small intestine (Ileum) were taken immediately after scarifying animals, Histological section were prepared and stained in the clinical Laboratory of AL- Karama hospital, according to (26).

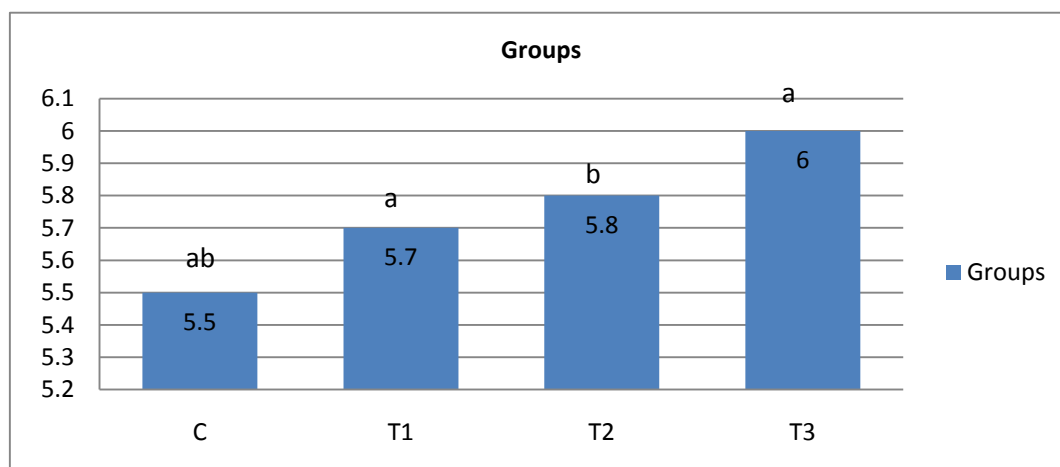
## Results

**1-Red blood cell count ( $\times 10^6$  / ml) and hemoglobin level (gm/dl):** Both RBC count in table (1); Fig. (1) and Hb level in table (1); fig (2) male rabbits in (T1) recorded significant increased, while the other treated recorded insignificant increased in comparison with control group ( $P < 0.05$ ). On the other hand, T3 recorded the highest significant ( $P < 0.05$ ) mean value when compared with T2.

**Table (1): Hematological and biochemical effect of the prednisolone and olive oil in the different group of experimental male rabbits**

	Groups of Animals tests	C	T1	T2	T3
1	RBC count ( $\times 10^6$ /ml)	ab $5.5 \pm 0.11$	a $5.7 \pm 0.13$	b $5.8 \pm 0.25$	a $6.00 \pm 0.13$
2	Hb level (gm/dl)	ab $10.3 \pm 0.14$	a $10.6 \pm 0.21$	b $10.8 \pm 0.29$	a $11.0 \pm 0.18$
3	PCV%	a $20.5 \pm 0.4$	a $20.0 \pm 0.1$	a $20.5 \pm 0.2$	a $21.2 \pm 0.3$
4	Serum cholesterol concentration (mg/dl)	a $58.5 \pm 0.25$	b $72.8 \pm 1.33$	c $71.2 \pm 0.15$	d $79.0 \pm 0.4$
5	Serum Triglycerides concentration (mg/dl)	a $50.2 \pm 0.12$	b $64.5 \pm 0.22$	c $63.0 \pm 0.2$	d $67.8 \pm 0.18$
6	Serum high density Lipoprotein concentration (mg/dl)	a $37.9 \pm 0.22$	b $38.1 \pm 0.1$	c $42.5 \pm 0.18$	d $41.2 \pm 0.28$
7	Serum low density Lipoprotein concentration (mg/dl)	a $15.5 \pm 0.15$	b $21.4 \pm 0.19$	c $26.5 \pm 0.28$	d $24.5 \pm 0.21$

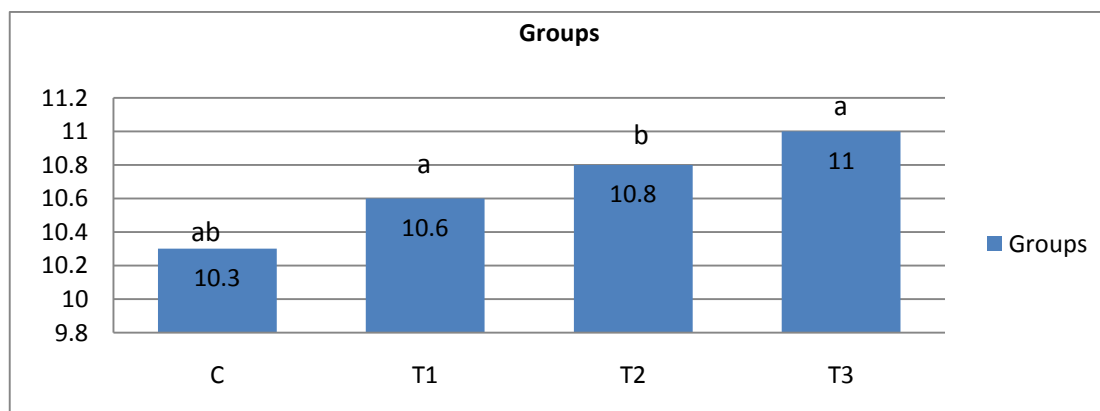
- The value represents  $\bar{M} \pm S.E.$
- The different small letters show significant effect while the same letters show insignificant effect between groups. ( $P < 0.05$ ).



**Figure (1): The effects of prednisolones and olive oil on RBC count (X10<sup>6</sup> / ml) in male rabbits.**

**.The values represent M± S.E**

**.The different small letters show significant effect while the same small letters show insignificant effect between different groups (P<0.05).**



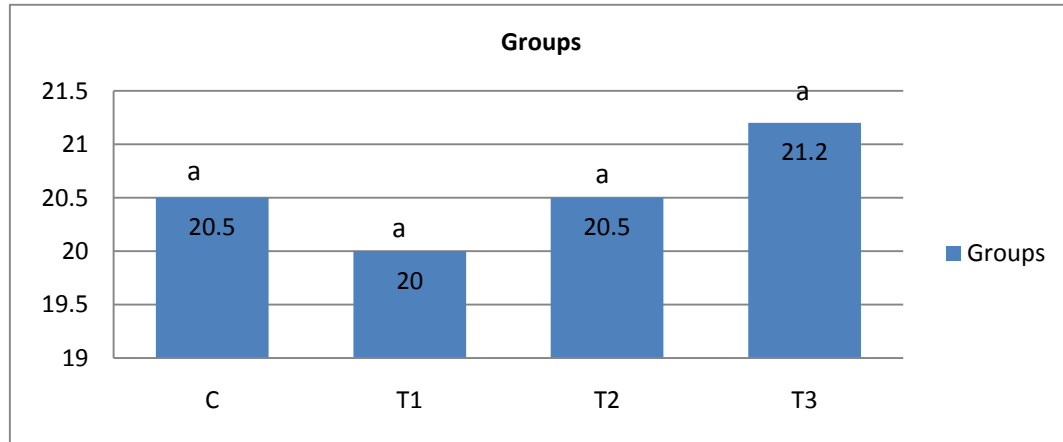
**Figure (2): The effect of prednisolone and olive oil on Hb level (gm/dl) in male rabbits.**

**.The values represent M± S.E**

**.The different small letters show significant effect while the same small letters show insignificant effect between different groups (P<0.05).**

### 1- Pack cell volume (%)

As shown in table (1); fig. (3); PCV% recorded insignificant differences ( $P < 0.05$ ) in the experimental groups when compared with each other.



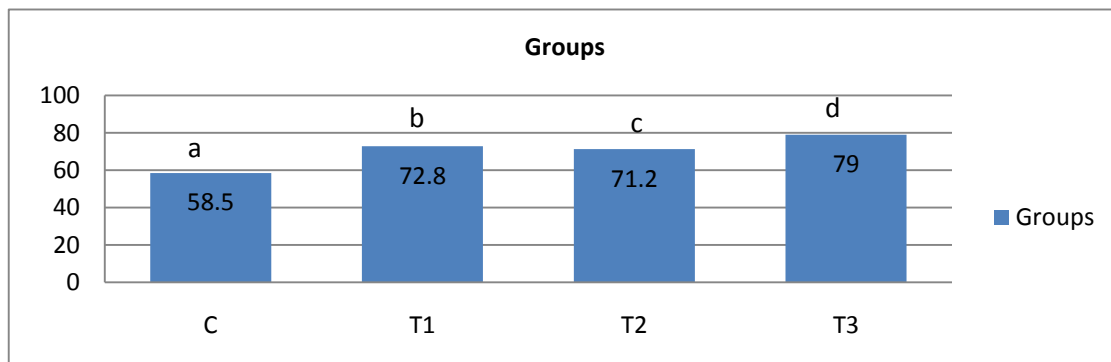
**Figure (3): the effect of prednisolone and olive oil on PCV (%) in male rabbits.**

.The values represent  $M \pm S.E$

.The different small letters show significant effect while the same small

### 2- serum cholesterol and serum triglycerides concentration (mg/dl):

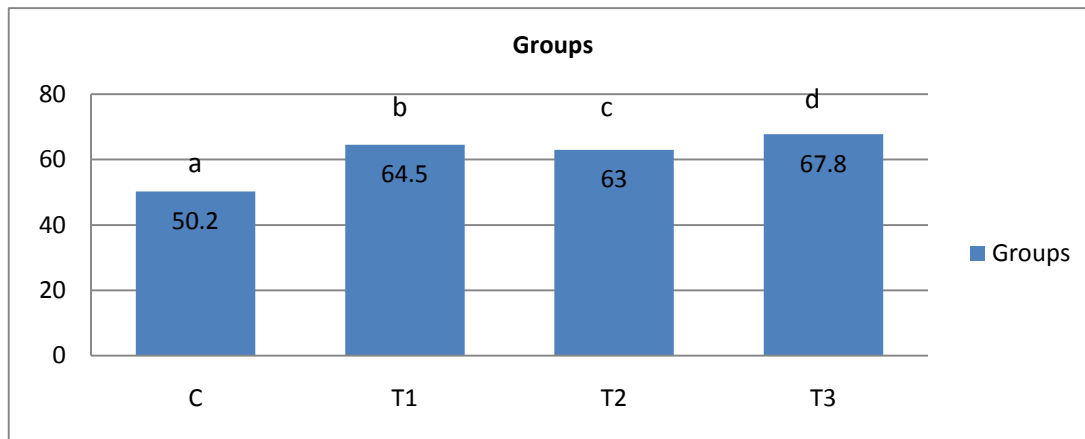
Both serum cholesterol concentrations (mg/dl) in fig (4) and serum triglyceride concentration (mg/dl) in figure (5) showed that T3 recorded the highest significant ( $P < 0.05$ ) concentration followed by T1 and T2 respectively.



**Figure (4): The effect of prednisolone and olive oil on serum cholesterol concentration (gm/dl) in male rabbits.**

.The values represent  $M \pm S.E$

.The different small letters show significant effect while the same small letters show insignificant effect between different groups ( $P < 0.05$ ).



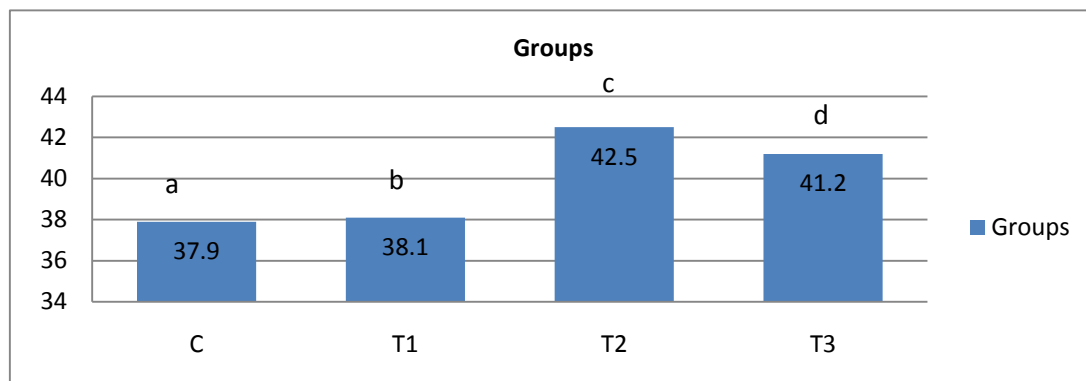
**Figure (5): The effect of prednisolone and olive oil on serum triglycerides concentration (gm/dl)**

.The values represent  $M \pm S.E$

.The different small letters show significant effect while the same small letters show insignificant effect between different groups ( $P < 0.05$ ).

### 3- serum high density and serum low density lipoprotein concentration (mg/dl):

Both serum high density in fig (6) and serum low density lipoprotein in fig (7) showed that T2 recorded the highest significant ( $P < 0.05$ ) concentration followed by T3 and T2 respectively.

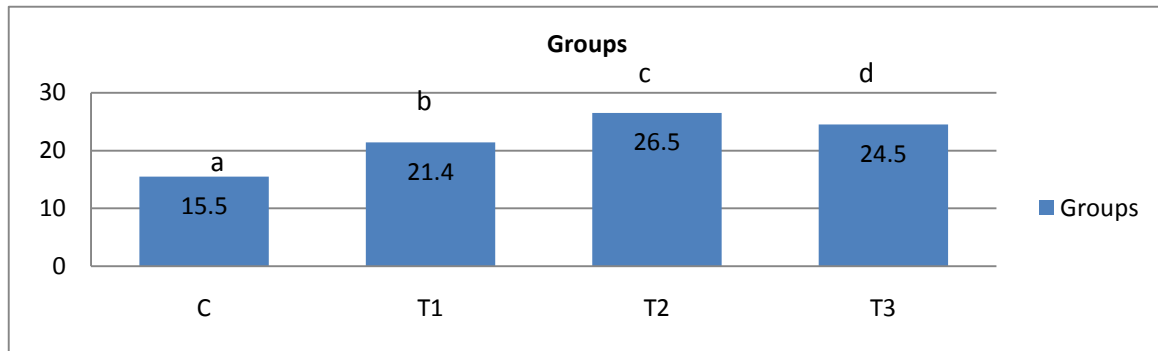


**Figure (6): The effect of prednisolone and olive oil on serum high density lipoprotein concentration (gm/dl):**

.The values represents  $M \pm S.E$

.The different small letters show significant effect while the same small letters show insignificant effect between different groups ( $P < 0.05$ ).





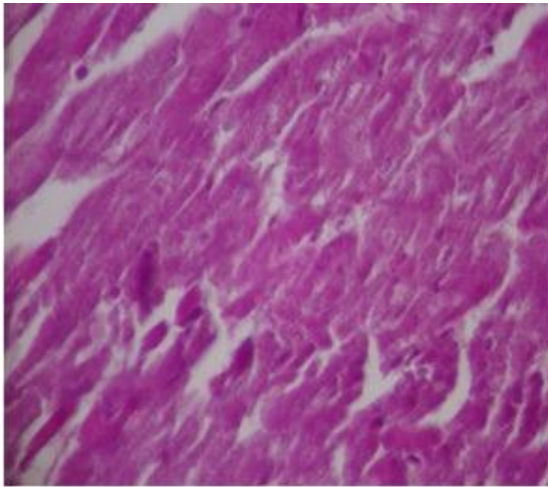
**Figure (7): The effect of prednisolone and olive oil on serum- low density lipoprotein concentration (gm\dl):**

.The values represent  $M \pm S.E$

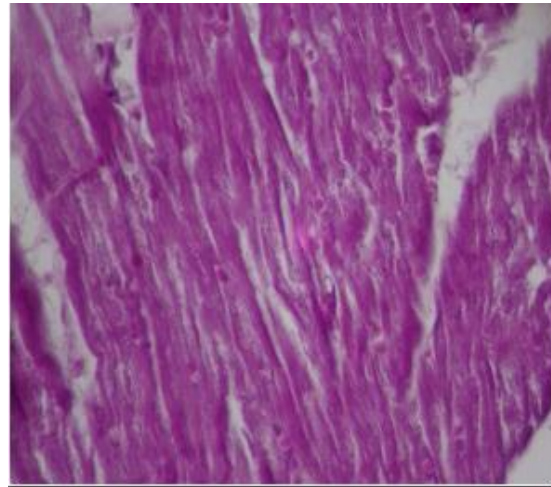
.The different small letters show significant effect while the same small letters show insignificant effect between different groups ( $P < 0.05$ ).

### Histopathological change:

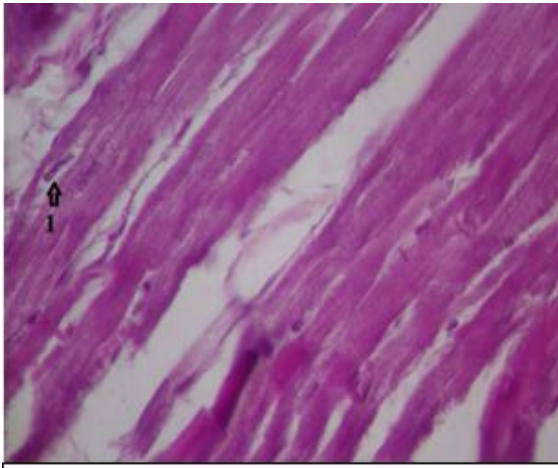
#### 1-Heart tissue:



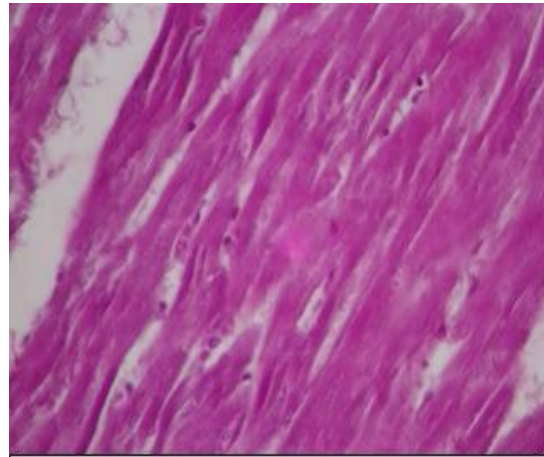
**Figure (8): Section of heart from control male rabbit showed normal heart tissue (H&E,X100).**



**Figure (9): Section of heart from T1 male rabbit showed cardiac damage and fibrosis with infiltration of neutrophil cell (H&E,X100).**

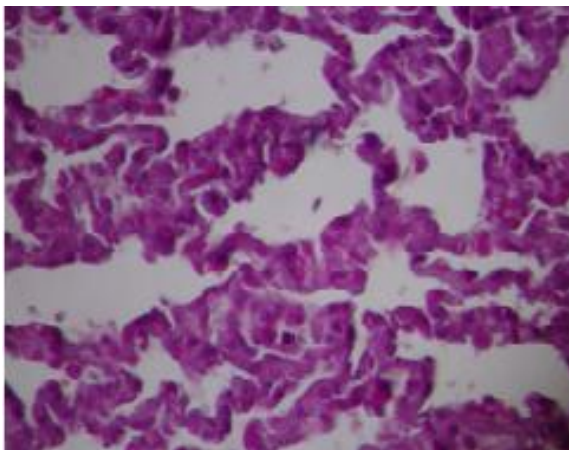


**Figure (10):** Section of heart from T2 male rabbit showed normal heart tissue; cardiac muscle with centrally located nuclei (1).(H&E,X100).

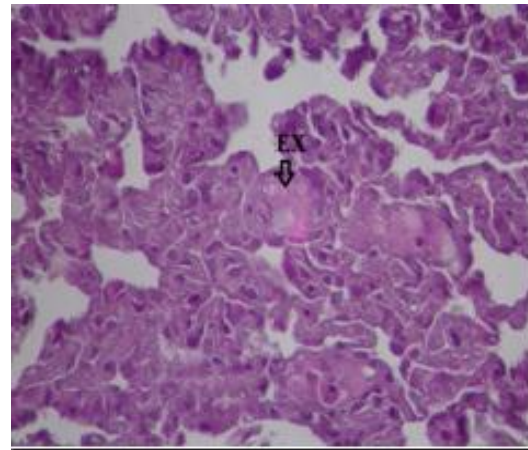


**Figure (11):** Section of heart from T3 male rabbit showed normal heart tissue; cardiac muscle with centrally located nuclei (H&E,X100).

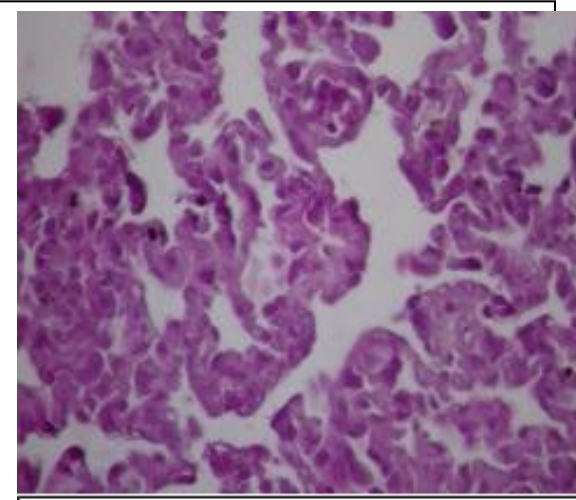
## 2-Lung tissue:



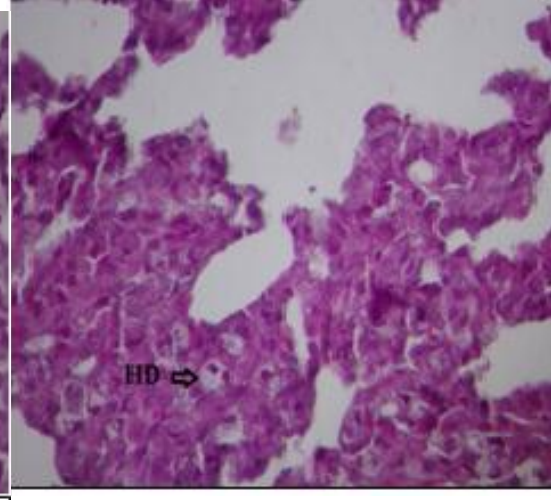
**Figure (12):** Section of lung from control male rabbit showed normal pulmonary tissue (H&E,X100)



**Figure (13):** Section of lung from TI male rabbit showed Mild exudation (EX) in the alveolar wall, inflammation with increase number of neutrophils and showed alveolar collapse (H&E,X100).

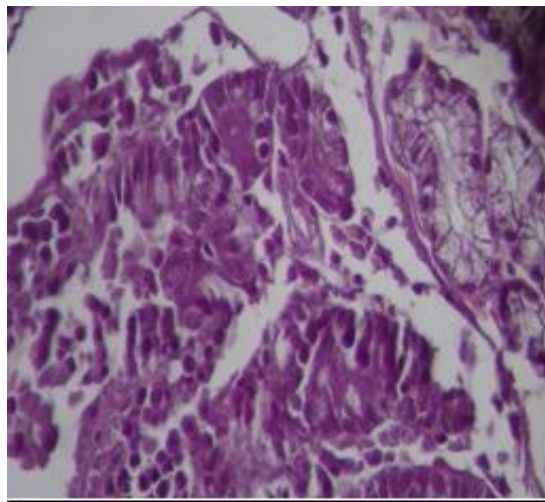


**Figure (14):** Section of lung from T2 male rabbit showed normal pulmonary tissue (H&E,X100).

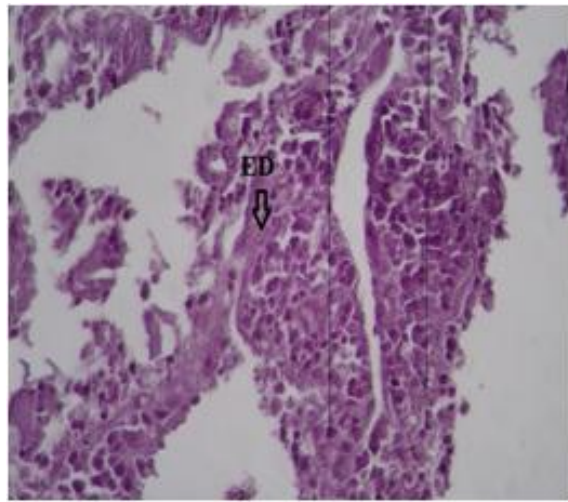


**Figure (15):** Section of lung from T3 male rabbit showed Hydropic degeneration (HD) of few cells in the alveolar wall, with present number of neutrophil cell (H&E,X100).

### 3-Ileum:

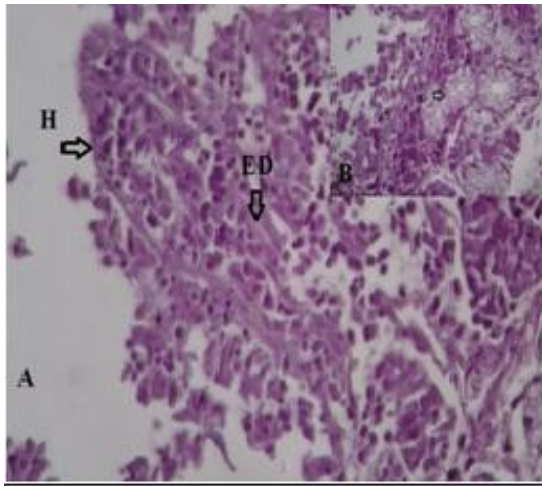


**Figure (16):** Section of Ileum from control male rabbit showed normal Villus tissue (H&E,X100).

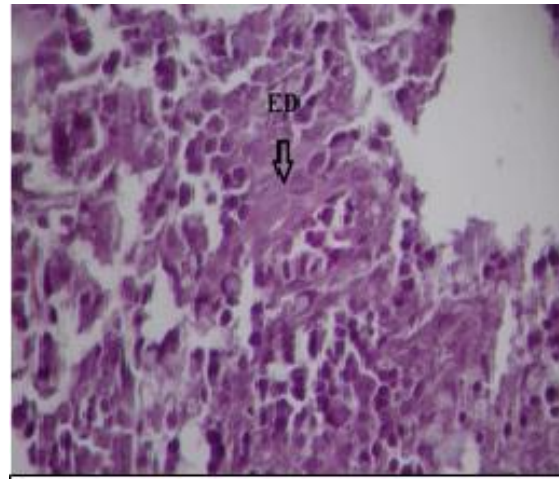


**Figure (17):** Section of Ileum from T1 male rabbit showed normal villus tissue with mild edema (H&E,X100).





**Figure (18):** Section of Ileum from T2 male rabbit showed hyperatrophy of villus tissue (H) with mild edema (ED), and showed normal intestinal glands (IG)



**Figure (19):** Section of Ileum from T3 male rabbit showed normal Villus tissue with mild edema (H&E,X100).

## Discussion

The results of the present study clearly demonstrate that oral administration of olive oil and intramuscular injection of prednisolone for 2 weeks in the experimental animal (rabbits) increased the hematological and Biochemical parameters. Prednisolone is a potent anti-inflammatory glucocorticoid which inhibits the activation of various immune competent cells (1). Has a preventive effect against apoptosis and induce improved hemoglobin concentration, Hematocrit Value (4; 27)(28) have reported that Glucocorticoids exert Mino on hemoglobin and erythrocyte formed Elements of blood content of blood.

The results in the present study confirmed by (29) and (30) showed that cortisone does induce abnormal increases in the serum cholesterol.(31) have reported that lung histological changes included interstitial edema and inflammation with polymorph nuclear cell with alveolar edema and intra alveolar hemorrhage in prednisolone with a dose 25 mg/kg B.w. Inhaled corticosteroids have been shown to decrease the number of eosinophils but increase neutrophils (32). Longer inhalation of prednisolone enhances contraction of trachea and bronchi (7). Methyl prednisolone lead to complete maintenance of in vivo and in vitro respiratory mechanics in mild lesion, prevented

collagen increment and avoided elastogenesis (31). Increasing concentration of prednisolone resulted in increasing suppression of Muscin secretion (33). (34) reported that rapid effect of prednisolone is mainly indirect, possibly by inhibition of allergen-induced cytokine release. Moreover, (35) reported that female adult rabbits received a single injection of prednisolone at a dose 4 mg\ kg B.w. on day 14 fat globules were present in the arterioles and some small and large arterioles were completely occluded.(5) showed that prednisolone induced cardiac damage and fibrosis. Prednisolone at a dose 10 microg/L decrease responses of muscle to the nerve fiber stimulation by 21 % (36). And caused increased volume density of abnormal myofibril (37). (9) reported that intra-arterial steroid injection may be potentially useful in sever intestinal Bchcets disease; colon ulcer improved markedly and the frequency of bloody stools decreased immediately.

Olive oil is native to the Mediterranean have wide range of therapeutic effects that may be due to its components such as &- Tocopherol, polyphenols and other phenolic compounds that are not present in other oil (38).(18) recorded that olive oil was more effective than its isolated components in improving lipid profile, elevating High density lipoprotein, and diminishing low diminishing low density Lipoprotein cholesterol concentration.

The results in the present study confirmed by (17);(22) they have reported olive oil caused significant increase in Triglyceride, Low density lipoprotein, high density lipoprotein. While (39) have reported that no difference in serum cholesterol and serum Lipid composition in piglets treated with olive oil. Olive oil did not change total low density Lipoprotein or high density Lipoprotein, cholesterol and triglycerides (13; 40).

Oleanolicacin in the olive oil may contribute to the cardioprotective effect (16). Dietary olive oil prevented the development of aberrant crypt foci and colon carcinomas in rats (19). Although Argchidonic acid regulates the synthesis of phospholipids in the intestine with antioxidant activity that improve histology of colon and decreasing inflammation (10 ; 20). Antioxidants are believed to be responsible for a number of olive oils biological activities such as induce apoptosis and cell differentiation and down regulates the expression of cyclooxygenase-2, phenols in the olive oil are capable to scavenging free radicals (41; 42).

## References

- 1- **Ehrmantraut, S.; Laschke, M.; Merkel, D.; Scheuer, C.; Willnecker, V.; Meyer-Lindenberg, A.; Menger, M. and Naumann, A. (2010).** Preoperative Steroid Administration inhibits Angiogenic host tissue response to porous polyethylene (Medpor ) Implants. *European cells and Materials*. 19: 107- 116.
- 2- **Vethe, N.; Midtvedt, K.; Asberg, A.; Amundsen, R. and Bergan, S. (2011).** Drug interactions and Immunosuppression in organ transplant recipients. *Tidsskr Nor Laegeforen*. 131 (20): 2000- 2003.
- 3- **Kluza, E., Heisen, M.; Schmid, S.; Daisy, W.; Schaft, V.; Raymond, M.; Romeny, B.; Gustav, J. and Nicolay, K. (2011).** Multi- Parametric assessment of the anti angiogenic effects of Liposomal glucocorticoids. *Angiogenesis*. 14: 143- 153.
- 4- **Ozisik, M.; Pinar, K.; Tuncer, S.; Yildirim, V.; Kilinc, K. and Gol, K. (2005).** Beneficial effect of Methyl Prednisolone on cardiac Myocytes in a rat Model of severe brain injury. *Tohoku J. Exp. Med*. 207:119- 124.
- 5- **Bauer, R.; Mac- Gowan, G.; Blain, A.; Bushby, K- and Straub, V. (2008).** Steroid treatment causes deterioration of myocardial Function in the 6- sarcoglycan-deficient mouse model for dilated, cardiomyopathy. *Cardiovascular Research*. 79, 652- 661.
- 6- **Hashimoto, M.; Shinozaki, Y. and Katori, M. (1993).** Immediate inhibitory effect of Methyl prednisolone Suleptanate (U. 67590 A) on antigen- induced Cutaneous and airway anaphylactic responses in guinea- pigs. *Br. J- pharmacol*. 108: 604- 612.
- 7- **Fedin, A.; Kuzubova, N.; Danilov, L.; Lebedeva, E.; Potnikova, T. and Krivchenko, A. (2010).** Broncholytic effect of prednisolon in the rats inhaled with nitrogen dioxide- *Russ Fiziol Zhim Schenova*- 96 (3): 292- 300
- 8- **Corden, Z. and Rees, P. (1998).** The effect of oral corticosteroids on bronchodilator responses in Cop D. *Respir. Med*. 92 (2): 279- 282.
- 9- **Toda, K.; Shiratori, Y.; Yasuda, M. Enya, M.; Uematsu, T.; Shimazaki, M.; Fukutomi, Y.; Kato, T. and Moriwaki, H. (2002).** Therapeutic effect of intraarterial prednisolone injection in sever intestinal Behcets disease. *J. Gastroenterol*. 37 (10): 844- 848.
- 10- **Camuesco, D.; Galvez, J.; Nieto, A.; Comalada, M.; Elena, M.; Concha, A; Xaus, J. and Zarzuelo, A. (2012).** Dietary olive oil Supplemented with Fish oil rich in EpA and DHA (n- 3) poly un saturated fatty acids, Attenuates colonic inflammation in rats with DSS- Induced colitis .*J. of nutrition*- 687- 694.
- 11- **Waterman, E. and lockwood, B. (2007).** Active components and clinical Application of olive oil. *Alternative Medicine Review*. 12 (4): 331- 342.

- 12-Priora, R.; Summa, D.; Frosa, S.; Margaritis, A.; Di- Giuseppe, D.; Iapucci, C.; Ieri, F.; pulcinelli, F.; Romani, A.; Franconi, F. and Di- Smplicio, P. (2012). Administration of Minor polar compound Enriched Extra virgin olive oil Decreases platelet aggregation and the plasma concentration of Reduced Homocysteine in rats. J. of Nutrition. Nutrition and disease. 36- 41.
- 13-Pfeuffer, M.; Fielitz, K.; Laue, C.; Winkler, P.; Rubin, D.; Helwig, U.; Giller, K.; Kammann, J.; Schwedhelm, E. and Schrezenmeir, J. (2011). CLA does not impair endothelial function and decreases body weight as compared with safflower oil in overweight and obese male Subjects. J. Am. Coll Nutr. 30 (1): 19- 28.
- 14- Fito, M.; Claelellas, M.; Torre, R.; Marti, J.; Munoz, D.; Schroder, H.; Alcantara, M. (2008). Anti-inflammatory effect of Virgin olive oil in stable coronary disease Patients: a randomized, cross over, Controlled Trial. Eur.J. Clin. Nutr. 62 (4): 570- 574.
- 15- Monahan, K.; Wilson, T. and Ray, C. (2012). Omega-3 fatty acid supplementation Augments Sympathetic Nerve activity Responses to physiological stressors in Human. J. Hypertension. 732- 738.
- 16- Simonsen, U.; Rodriguez, R.; Dalsgard, T.; Henrik, N. and Stankevicius, E. (2009). Novel approaches to improving endothelium- dependent nitric Oxide- mediated Vasodilatation. Pharmacological Reports. 61: 105- 115.
- 17-Tsantila, N.; Karantonis, H.; Perrea, D.; Theocharis, S.; Liopoulos, D.; Antonopoulou, S. and Demopoulos, C. (2007). Antithrombotic and Antiatherosclerotic properties of olive oil and olive pomace polar Extracts in rabbits. Mediators of inflammation. 36204- 36214.
- 18-Faine, L.; Rodrigues, H.; Galhardi, C.; Ebaid, G.; Diniz, Y.; Padovaini, C. and Novelli, E. (2006). Effects of olive oil and its minor constituents on serum lipids, Oxidative stress and energy metabolism in cardiac Muscle. Can. J. Physiol. Pharmacol. 84 (2): 239- 245.
- 19- Bartoli, R.; Fernandez, F.; Navarro, E.; Castella, E.; Mane, J.; Cabre, E. and Gassulla, M. (2000). Effect of olive oil on early and Late events of colon carcinogenesis in rats: Modulation of arachidonic acid metabolism and local prostaglandin E2 Synthesis. Gut. 46:191- 199.
- 20- Nieto, N.; Torres, M.; Rios, A. and Gil, A. (2012). Dietary polyunsaturated fatty acids improve Histological and Biochemical Alterations in rats with Experimental ulcerative colitis. J. of Nutrition. 11- 19.
- 21- Gomez- Ayala, A.; Lisbona, F.; Barrionuera, M.; Hartiti, S. and Campos, M. (1994). Effect of intestinal resection type of Dietary fat and time on biliary Lipid secretion in rats. Experimental physiology. 79: 25- 33.

- 22- **St- onge, M.; Bosarge, A.; Goree, L. and Darnell, B. (2008).** Medium chain Triglyceride oil consumption as part of a weight loss- Diet not lead to an Adverse metabolic profile when compared to olive oil. *J. Am. Coll Nutr.* 27 (5): 547- 552.
- 23- **Green, J. (1994).** An Introduction to hemato physiology. 4<sup>th</sup>. ed. New. York.
- 24- **Coles, E. (1986).** Veterinary clinical pathology. 4<sup>th</sup>. ed. New. York.
- 25- **Von Losson Czy, T.; Ruter, H.; Bronsgi cest- Schoute, C.; Van. Gent and Hermus, R.(1978).** The effect of a fish diet on serum Lipids in healthy human Subjects. *Am. J. Clin. Nutr.* 31: 1340.
- 26- **Bancroft, J. and Stevens, A. (1996).** Theory and practice of histological Techniques. 4<sup>th</sup>. ed. New. York :Churchill Livingstone.
- 27- **Pyrrho, A.; Richemer, W.; Sweet, D. (2004).** Dexamethasone treatment improves morphological and hematological parameters in chronic experimental Schistomiasis. *Parasitol Res.* 92 (6): 478- 83.
- 28- **Goodman and Gilmans, (2008).** Manual of pharmacology and Therapeutics. MC Graw Hill Medical. 1014- 1031.
- 29- **Uchida, H.; Nakamura, Y.; Kaihara, M.; Norii, H.; Hanayama, Y.; sugiyama, H.; Maeshima, Y.; Yamaski, Y. and Makino, H. (2006).** Steroid pluse Therapy impaired endothelial function while increasing plasma high molecule adiponectin concentration in patients with IgA nephropathy. *Nephrol Dial Transplant.* 21: 3475-3480.
- 30- **Wang, G.; Moga, D.; Richemer, W.; Sweet, D.; Reger, S. and Thompsan, R. (1978).** Cortisone induced bone changes and its response to lipid clearing agents. *Clin. Orthop Relat. Res.* 130: 81- 85.
- 31- **Rocco, P.; Souza, A.; Faffe, D. Passaro, C.; Santos, F.; Negri, E.; Lima, J.; Contador, R.; Capelozi, V. and Zin, W. (2003).** Effect of corticosteroid on Lung Parenchyma Remodeling at an Early phase of Acute Lung Injury. *Am. J. of Respiratory and Critical care Medicine.* 168: 678- 684.
- 32- **Fukakusa, M.; Bergeron, C.; Tulic, M.; Fiset, P.; Laviolette, M.; Hamido, Q. and Chakir, J. (2005).** Oral corticosteroids decrease eosinophil and CC chemokine expression but increase neutrophil, IL- 8 and IFN- gamma- inducible protein 10 expressions in asthmatic air way mucosa. *J. Allergy Clin. Immunol.* 115 (2): 280- 286.
- 33- **Fergie, N.; Guo, L.; Sithole, J.; Pearson, J. and Birchall, J. (2003).** Influence of prednisolone on the secretion of mucin from the HT2,- MTX cell lin. *Clin. Otolaryngol Allied Sci.* 28 (1): 39- 42.



- 34- **Rudack, C. and Bachert, C. (2000).** Glucocorticoids rapidly inhibit allergen-induced expression of E- selectin in vitro in a mucosal Model of allergic rhinitis. *Allergy*. 55 (4): 363- 368.
- 35- **Fukui, K.; Kominami, R.; Shinohara, H. and Matsumoto, T. (2006).** Glucocorticoid induced micro- fat embolism in the rabbit: a scanning electron microscopic Study. *J. Orthop. Res.* 24 (4): 675- 683.
- 36- **Fedin, A.; Nekrasova, E.; Frolova, S.; Danilova, L.; Lebedeva, E. and IL Kovich, M. (2007).** Effect of prednisolone on Trachea smooth muscle of normal rats with fibrosing alveolitis. *Zh. EVOL Biokhim Fiziol.* 43 (4): 352- 356.
- 37- **Sasson, C.; Zhu, E.; Pham, H.; Nelson, R.; Fang, L.; Baker, M. and Caiozzo, V. (2008).** Acute effects of high- dose methyl prednisolone on diaphragm muscle function. *Muscle Nerve*. 36(3): 1161- 1172.
- 38- **Teres, S.; Barcelo, G.; Benet, M.; Alvarez, R.; Halver, J. and Escriba, P. (2008).** Oleic acid Content is responsible for the reduction in blood pressure induced by olive oil. *PNAS*. 105 (37): 13811- 13716.
- 39- **Ruiter, A.; Jongbloed, A.; Van Gent, C.; Danse, L. and Metz, S. (2012).** The influence of dietary Mackerel oil on the condition of organs and on blood Lipid Composition in the young growing pig. *The Amer. J. of clinical Nutrition*- 2159- 2166.
- 40- **Sigueira, J.; Smiley, D.; Newton, C.; Gosmanoy, A. (2011).** Substitution of standard soybean oil with olive oil. Based Lipid emulsion in parenteral nutrition: Comparison of vascular, metabolic and inflammatory effects. *J. Clin. Endocrinol metab.* 96 (10): 3207- 3216.
- 41- **ODowd, Y.; Driss, F.; Dong, P.; Gougerot, M.; pasguier, C. and EL- Benna, J. (2004).** Anti oxidant effect of Hydroxytyrosol, a polyphenol from olive oil. Scavenging of Hydrogen peroxide but not Superoxide an ion produced by human neutrophils. *Biochem pharmacol.* 68 (10): 2003-2008.
- 42- **Kadhim, A.; Muslim, B. (2002).** The Advance Econometrics Theory and Application. AL- Amel- Baghdad.