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## Effect of hydrocortisone and olive oil on phagocytes

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# Abstract :

This study organized to realize the side effect of hydrocortisone therapy which administrated by thigh muscle injection on phagocytic cells, and inhibit their functions. Fifteen laboratory male white mice was distributed into three groups used in this study, each group consist of five animals . 1st group administrated by normal saline orally for ten days, while 2nd group injected in thigh muscle by 1mg/kg of the therapy for ten days, and the 3rd group injected in thigh muscle by 1mg/kg of the therapy for ten days then administrated orally by 0.5 ml / 100 of olive oil for anther ten g days.

The Results of the study agree with other studies and investigate side effect of the therapy which cause inhibition to the activity of phagocytic cells and decrease in their number in 2nd group, whenever in 3rd group the study discover the benefit of olive oil to reactivate the whole of immune system and especially the phagocytic cells and increase their number.

### المستخلص

اجريت هذه الدراسة للتعرف على الأثر السلبي لعقار الهيدروكوتزون المعطى عن طريق الحقن بعضلة الفخذ على الخلايا البلعمية بشكل عام وتثبيط عمل تلك الخلايا في اجراء عملية البلعمة ، حيث اجريت الدراسة على خمسة عشرة حيوان من ذكور الفئران البيض من نوع Mus musculus والتي وزعت على ثلاث مجاميع وبواقع خمس عشرة حيوان من ذكور الفئران البيض من نوع Mus musculus والتي وزعت على ثلاث مجاميع وبواقع خمس حيوانات لكل مجموعة ، جرعت المجموعة الأولى ( مجموعة السيطرة ) بالمحلول الملحي الفسلجي ولمدة عشرة حيوانات لكل مجموعة ، جرعت المجموعة الأولى ( مجموعة السيطرة ) بالمحلول الملحي الفسلجي ولمدة عشرة اليام، فيما حقنت المحموعة الثانية بعقار الهيدروكوتزون في منطقة الفخذ بجرعة قدرها 19 / mg الحداث الضرر وكمجموعة سيطرة سالبة ولمدة عشرة اليام ، بينما حقنت الثالثة بعقار الهيدروكوتزون في منطقة الفخذ بجرعة قدرها 100 / kg الحداث الضرر وكمجموعة سيطرة الملحي الفرة عشرة الفخذ بجرعة قدرها 100 / kg الملحي ولمدة عشرة المرام وقد جامت المجموعة الأولى ( مجموعة الثالثة بعقار الهيدروكوتزون في منطقة الفخذ بحرعة قدرها 100 / kg الحداث الضرر وكمجموعة سيطرة الملحي ولمدة عشرة الضرر الميدروكوتزون في منطقة الفخذ بحرعة قدرها 100 / kg الملحي ولمدة عشرة ايام ، بينما حقنت الثالثة بعقار الهيدروكوتزون في منطقة الفخذ بجرعة قدرها 100 / kg ولمدة عشرة ايام الحرى. وكمجموعة الذي المالبي للعقار على الخلايا البلعمية وقد تم تثبيط وقد جاءت النتائج متوافقة مع عدد من الدراسات حيث لوحظ الأثر السلبي للعقار على الخلايا البلعمية وقد تم تثبيط وقد جاءت النتائج متوافقة مع عدد من الدراسات حيث لوحظ الأثر السلبي للعقار على الخلايا البلعمية وقد تم تثبيط وقد جاءت النتائة وقلة اعدادها في المجموعة الثانية بينما لوحظ زيادة اعدادها في المجموعة مع زيادة في فاعليتها في المجموعة من الدراسات حيث لوحظ الأثر السلبي العقار على الخلايا البلعمية وقد تم تثبيط وقد جاءت النتائج من الدراسات حيث لوحظ الأثر السلبي للعقار على الخلايا البلعمية وقد تم تثبيط وقد جاءت النتائج ملوا وقلة اعدادها في المجموعة مع زيادة اعدادها في المجموعة مع زيادة في فاعليتها في المجموعة الثائلة .

# Introduction

Phagocytosis is a spontaneous intracellular or non specialized action which by the phagocytes can swallow and destroy the microorganisms and particulate materials . Damaged cell secretes chemotactants which collectively Attracts phagocytes to damage position via a process known as chemotaxis which considered as the phagocytosis first step of (1).Hydrocortisone is one of therapeutic family called corticosteroids, interning the cell and bind with a special receptors in the cytoplasm. Then complex of therapy and receptor move to interring the nucleus and unite with DNA which respond and act to transcript a certain mRNA works to produce the desired action in the cytoplasm (2). In spite of the importance of hydrocortisone in many medical cures, But it is certain that there are a number of negative effects resulting from the use of this drug on the immune system of the body in general and on the effectiveness of macrophages in particular(3).

Olive oil considered as one of the most important component in the meals of the Mediterranean basin and the middle east(4). Using of olive oil had been increased around whole the world and in wide rate specially in the latest centuries, that because Its high nutritional value and its ability to enhance the overall health of the body(5). Many of resent studies improve that the usage of olive oil was successful to treat a number of ailments ( In particular some cancers and atherosclerosis ), in addition to being effective in enhancing the immune system in general and it is also a powerful antioxidant (6). As we have available scientific sources that indicate the importance of olive oil in stimulating the immune system and as

an attempt to discourage the adverse effects of the action or reduction of hydrocortisone (7).

### Aim of the study:

The aim of this study was to discover the side effect of hydrocortisone therapy which injected in thigh on the phagocytic cells, and trying to treat this side effect by use oral administration of olive oil.

## Materials and methods :

According to Basic histology (8), a staining method used to stain phagocytes to studding their immunological activity where the animals were taken in groups , each group include five mice distributed as follows:

G1: control group was administrated by 1ml normal saline for 10 days.

G2: 2<sup>nd</sup> group was injected by 1ml/kg of hydrocortisone in thigh muscle for 10 days (9).

G3: 3<sup>rd</sup> group was injected by 1ml/kg of hydrocortisone in thigh muscle for 10 days , then administrated via oral dosage of olive oil to 10 days (10).

After that the samples was collected ( the peritoneal fluid ) and stained via gemza stain to produce the slides (11). Then three Repetitions to each group were done.

200 devourer and non-devourer phagocytic cells were collected, (cells which contain gemza stain granules inside their cytoplasm Considered as devourer cells) and the percentage of devourer cells by the following equation :-

Number of devourer phagocytic cells

% devourer cells =	
	×
100	

#### 100

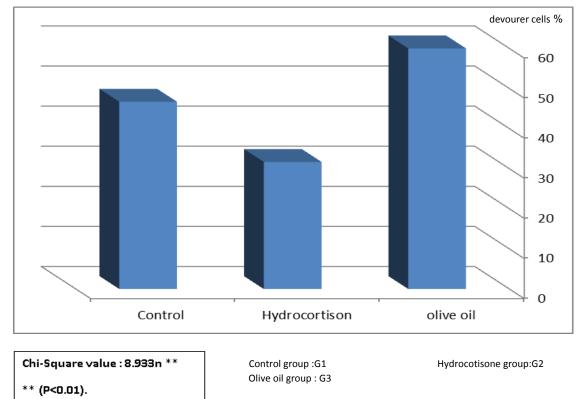
200 (total number)

### **Statistical Analysis**

The Statistical Analysis System-SAS (2012) program was used to effect of difference groups s in study percentage . Chi-square test was used to significant compare between percentage in this study (12).

### **Results and discussion :-**

The slides were examined under light microscope whereby the devourer and non-devourer phagocytic cells collected to all groups, and results showed a presence of a highly significant decrease in number of devourer phagocytic cells at p< 0.01 in G2 comparing with G1, and even there was a highly significant increase in their number at p> 0.01 in G3 comparing with G1 (figure 1).



# Figure 1: percentage of devourer phagocytic cells.

Results of slides enhance the results above , where examination of the photos of first group (G1) shown the normal state of phagocytes when they phagocytose stain granules (fig. 2) , where they show the phagocytic pseudopodia when it Surrounding the stain granules (the target ) to swell it , while the examination of the photos of second group (G2) discover the disability of phagocytes to swell the closely stain granules (fig. 3), and the photos of third group (G3) shown the rise in number of phagocytes and increase in their activity (fig. 4).

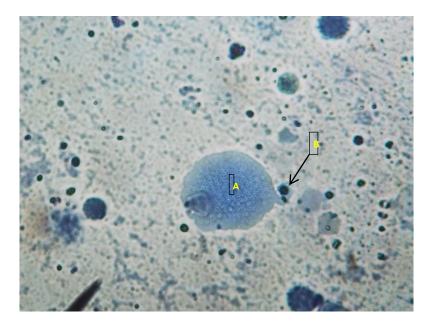


Fig. (2): show normal state of phagocyte and their pseudopodia (A) engulf stain granules (B) (G1)

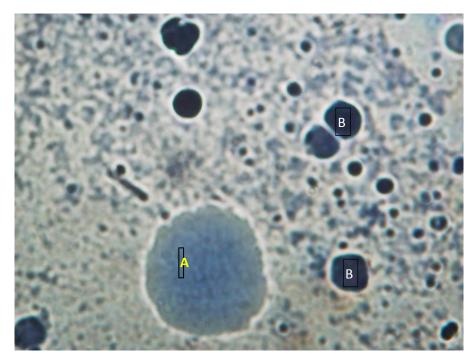


Fig. (3) :show disability of phagocyte (A) to swell stain granules (B) (G3).

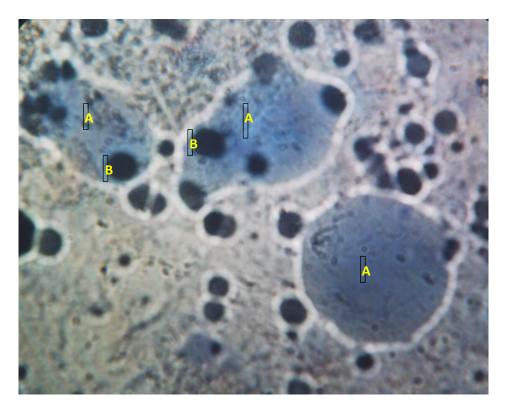


Fig. (4): show increase in number and activity of phagocytes (A) to stain granules (B) (G3).

It has been observed that corticosteroids in general, including hydrocortisone, reduce inflammatory response, Inflammation is defined as the natural response of the body to any damage in the tissues and is in three stages, , The first leakage of a large amount of liquid resembling plasma to outside the capillaries to the affected area and clot in there . Second, the migration of white blood cells to the damage zone. Third, start repairing the damaged tissue, and cortical sugars adversely affect all these steps (13).

More specifically, corticosteroids of all types preserve the particle walls of lysosomes , which prevents the secretion of enzymes that specialized to secret in inflammatory response. It also reduces the permeability of the capillaries. which reduces the accumulation and leakage of fluids and proteins in the inflammation zone, and reduces accumulation the and efficiency of white blood cells and

macrophages the sites of at inflammation, which causes the weakening of the process of phagocytosis of pathogens or wastes resulting from the vital functions of cells (14).

Corticosteroids also cause a decrease in the production of interleukins such as IL-1, prostaglandins and Leukotrienes by damaged cells (15).

It has also been found that corticosteroids cause a weakening of antibody formation, as well as a decrease in the number of macrophages lymphocytes, and circulating eosinophilic leukocytes in the bloodstream with weakness and lack in the lymphatic tissues, All result in a weakening of the body's immune system (16).

As for the G3 group treated with hydrocortisone and then olive oil, using of erythrodiol in olive oil has been improved and increased the susceptibility of macrophages to gene expression specific production of ABDA1 protein which aid in Disposal of circulating cholesterol in the bloodstream (17).

The administration of olive oil to a number of volunteers has enhanced the effectiveness of immune cells in general and phagocytic cells in particular by 44% of what is in the control group (18). Phenolic materials had the most prominent effect of other components in stimulating and improving the immune cells' performance of phagocytosis and elimination of foreign bodies, pathogens and dead cell residues (19).

Al-Saleh (20) Confirmed that the repairing act of olive oil when used to treat the damage caused by exposure to increased alcohol is due to of concentrations the enzyme glutathione (GSH) in addition to increasing the effectiveness and impact of both enzymes GST and GSH-Px These two enzymes are the main source of anti-oxidant stress and the primary removal of damage caused Out.

The positive effect of olive oil is the result of the presence of high amounts of tyrosol and hydroxy terosol, which are natural phenols that preserve the integrity of the biological membranes and preserve them from damage, these phenols have antioxidant properties with great ability to sweep many types of free radicals, have the ability to block the chains of peroxides that lead to Reactive oxygen species (ROS) production (21).

# References

1-

Lostra,M.D.;Pastelin,R.;Camacho,A.; Monroy,B.;Aguilar,A.E.(2001) Zinc interaction on macrophages and lymphocytes response .J.Trace. Elem. Med. Biol. 15(1):5-10.

2- Buchman Al. Side effect of corticosteroid therapy. J. Clin. Gastroenterol 2001; 33(4): 289 -94 .

3- Gray CR, David SL. Pharmocology Board Review series 3rd edition: Williams and Wilkins. Baltimore Maryland. 1998; 21201-436.

4- Awney, H. (2010) The effect of green tea and olive oil on the mutagenic activity of heterocyclic amines extracted from common food consumed in Saudi Arabia. International Journal of Food Sciences and Nutrition

5- Monteleone, E., Caporale, G., Carlucci, A. and Pagliarini E. (1998) Optimisation of extra virgin olive oil quality Journal of the Science of Food and Agriculture, 77, 31-37.

6- Bawazir, A. E.(2011) Chronic effect of olive oil on some neurotransmitter contents in different brain regions and physiological, histological tructure of liver and kidney of male albino rats, World Journal of Neuroscience, 1.31-37.

7- Bowers,J.M.(2002).Nutrition and immunity :You are what you eat . ACRIA Update ;11 (2).

8- Junqueira, L. and Carneiro, J. (2005). Basic histology .Text and atlas.11th ed. McGraw- Hill companies, p: 266-415.

9- Al – Kaisy . Kawkab. S. N. (1995).Changes in thymocytes associated with hydrochlorazone and interleukin-2 injections in white mice. PhD thesis, College of Science, University of Baghdad.

10- Al-Thwani A. N., Sanaa J. Kahdum, Dalia A. Hamodi(2013). Effect of Olive Oil Extract on some Biochemical Parameters in Alloxan Induced Diabetic Mice Iraqi Journal of Biotechnology,Vol.12, No.1, 36-43.

11- Adam K.M.G., J. Paul and V. Zaman .1979. Medical and Veterinary Protozoology. An Illustrated Guide. Churchill Livingstone Edinburg, London. P:173.

12-SAS. 2012. Statistical Analysis System, User's Guide. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N.C. USA.

13- Annane, D., Sébille, V., Charpentier, C., et. al. (2002, August). Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. Journal of the American Medical Association, 288(7), 862–871

14- De Benedictis, F. M., Teper, A., Green, R. J., et al. (2001). Effects of 2 inhaled corticosteroids on growth. Archives of Pediatric and Adolescent Medicine, 1248-1254, (11) 155.

15- Matfin, G., Kuenzi, J. A, & Guven, S. (2005). Disorders of endocrine control of growth and metabolism. In C. M. Porth, Pathophysiology: Concepts of altered health states (7th ed., pp. 961–985). Philadelphia: Lippincott Williams & Wilkins .

16- Matfin, G., Kuenzi, J. A, & Guven,
S. (2005). Disorders of endocrine control of growth and metabolism. In
C. M. Porth, Pathophysiology:
Concepts of altered health states (7th ed., pp. 961–985). Philadelphia:
Lippincott Williams & Wilkins.

17- Limei Wang, Sarah Wesemann, Liselotte Krenn, Angela Ladurner, Elke H. Heis Verena M. Dirsch and Atanas G. Atanasov. (2017). Erythrodiol, an Olive Oil Constituent Increases the Half-Life of ABCA1 and Enhances Cholesterol Efflux from THP-1-Derived Macrophages. Frontiers in Pharmacology. Volume 8. Article 375

18- Helal, O., Berrougui, H., Loued, S., and Khalil, A. (2013). Extra-virgin olive oil consumption improves the capacity of HDL-C to mediate cholesterol efflux and increases ABCA1 and ABCG1 expression in human macrophages. Br. J. Nutr. 109, 1844-1855.

19- Farras, M., Valls, R. М., Fernandez-Castillejo, S., Giralt, M., Sola, R., Subirana I., et al. (2013). Olive oil polyphenols enhance the expression of cholesterol fflux related genes in vivo in humans. А randomized controlled trial. J. Nutr Biochem. 24. 1334–1339. doi: 10.1016.

20- Al-Salih, M. N. Mustsfa, (2016). Effect of Ethanol in Histopathological Lesions Production and Biochemical Veriaties in liver and Kidney of White Rats Ratus Norvegicus and Treating By Natural Therapies (Camel Milk & Olive Oil) and Chemical Therapies (Zinc Acetate). PhD thesis. Tikrit University, College of Sciences.

21- MACHOWETZ A., POULSEN H. E., GRUENDEL S., WEIMANN A., FITO'M., MARRUGAT J., DE LA TORRE **SALONEN** J.T., R., J., NYYSSÖNEN K., MURSU S., GADDI NASCETTI A., KIESEWETTER H., BÄUMLER H., SELMI H., KAIKKONEN J., ZUNFT H. J-F., COVAS M-I., KOEBNICK C .: Effect of olive oils on biomarkers of oxidative DNA stress in Northern and Southern Europeans. FASEB. J., 2007, 21, 45-52. 2011; 101 - 104.