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Abstract:

Objective: The present study aims to investigate the possible protective effects of lavender flowers powder and oil alone to healthy rats and against azathioprine induced toxicity of immune in rats.

Methods: Forty two male Sprague-Dawley rats in six groups (7 rats each) were divided to main groups: Normal control group: Basil diet (BD), Positive control group: BD + azathioprine (25mg/kg), and four subgroups :Subgroup1 :BD + lavender powder (200 mg/ kg/b.w/day) as experimental control group (pre-treated), Subgroup 2:BD + lavender oil (20 ml/kg/b.w/day) as experimental control group (pre-treated), Subgroup 3 : BD + lavender powder + azathioprine, Subgroup 4 :BD + lavender oil (20 ml/kg/b.w/ day)+ azathioprine.

Results: The results indicated that azathioprine intake showed significant decreases in serum alpha tumor necrosis factor ($-\alpha$ TNF), interleukin-6 (IL-6), immunoglobulin E (IgE). Furthermore, hepatic reduced glutathione and nitric oxide levels were diminished matched with a significant rise in the level of malondialdehyde. Administration of either lavender powder or oil alone and with treatment of oil to azathioprine-induced toxicity of immune rats produced potential role against damaging impact of azathioprine. Both powder and oil of lavender reduced oxidative stress, ameliorated most of changes in the hematological parameters, improved nitric oxide and immunoglobulin E production.

Conclusion: These results of enhanced hematological parameters and promoted immune system by pre/or treatment with lavender powder and oil alone and against azathioprine induced toxicity of immune in rats which, activities probably related to their potent antioxidative activity which due to their higher content of total phenolic compounds.

Key words: Lavender, Phenolic Compounds, Azathioprine, Haemotoxicity, TNF- α , IL-6, Malondialdehyde

Introduction:

Lavender (*Lavendula spica*) belonging to the family of Lamiaceae, is a natural herb, and the name of *lavender* is derived from the Latin “lavare”, lavender has a long history of medicinal uses, also lavender is best known for its popular use in the fragrance industry,. Many varieties of lavender are cultivated around the world. Today there is a rekindled interest in lavender for aromatherapy (Barrett, 1996 and Nomura *et al.*, 2016).

Medicinal properties of this plant is from its flowers, contain oil which, shows its antibacterial and antifungal properties against many species of bacteria, especially when antibiotics have no effect or action on the body, but the exact mechanisms are yet to be established. When talking about its use in aromatherapy, it is well documented for the treatment of abrasions, burns, stress, headaches, in promotion of new cell growth, skin problems, painful muscles and boosting an immune system (Babar *et al.*, 2015). This oil is used in the treatment of primary dysmenorrheal and has shown some promising results in one of the randomized, double-blind clinical trials (Han *et al.*, 2006 and Ou *et al.*, 2012).

Lavender oil possesses not only antibacterial and antifungal activity, but is also known to have astringent and anti-inflammatory properties, as well as accelerate wound healing and reduce scarring (Hammer *et al.*, 1999 & Cavanagh and Wilkinson, 2005). A great advantage of essential oils is that their use not associated with long-term genotoxic risk. Some of them show an antimutagenic activity that could well be linked to an anticarcinogenic activity (Manosroi *et al.*, 2006). The pro-oxidant activity of essential oils or some of their constituents is very efficient in reducing local tumor volume or tumor cell proliferation by apoptotic and necrotic effects (Tsuneki *et al.*, 2005). Furthermore essential oil of lavender has significant protection against increase of blood glucose as well as enhancement in antioxidant enzymes activities in diabetic rats. Treatment with lavender oils induced a decrease of lipoperoxidation as an increase of antioxidant enzyme activity (Sebai *et al.*, 2013). In addition, lavender's essential oil has activity in smooth muscle *in vivo*, supporting its

historical use as a digestive aid, the phytochemical components presented in lavender have potent analgesic and anticarcinogenic activities (Catherine *et al.*, 2001).

Hydrodistillation dried leaves and flowers of lavender identified by GC-MS analyses were alpha-fenchone 39.2%, myrtenyl acetate 9.5%, alpha-pinene 6.1%, camphor 5.9% and 1,8-cineole 3.8% in the flowers. (Kirmizibekmez *et al.*, 2009). Likewise, the principal compounds in lavender oil are reported by (Sebai *et al.*, 2013) as following: D-Fenchone (29.28%), Camphor (15.97%), α -pinene (23.18%), Camphene (7.83%), Limonene, (2.71%) Linalool, (2.01%) Eucapur (3.29%), Endobornyl Acetate (1.03%).

Azathioprine (6-1-Methyl-4-nitroimidazol thiopurine) is used as an immunosuppressant drug usually corticosteroids (Gaston, 2001). It is used to protect rejection in organ transplants and it is used in treatment of auto-immune diseases (Conti *et al.*, 2003). Also it is used to prevent renal graft rejection, and hepatic transplantation (Heneghan and McFarlane 2002). Due to its anti-inflammatory activities, azathioprine is used to treat rheumatoid arthritis, bowel disease, biliary cirrhosis, lupus nephritis and multiple sclerosis (Lin *et al.* 2000). In addition, the medicinal effects of azathioprine include pancreatitis, gastrointestinal disturbances, rashes, muscle and joint pains, fever, chills, tachycardia, hypotension and renal dysfunction (Sweetman and Martindale 2005). Azathioprine treatment inhibits infections of bacteria, viral, and inhibition phagocytosis (Drath and Kahan 1984).

Although a growing number of investigations have been conducted in the last years, there is a lack of more substantial data on the mechanisms and effects of lavender action. Therefore, the current study assessed to investigate the possible impact of lavender flowers powder and oil alone to healthy rats and against azathioprine induced toxicity on rats by changes in biochemical and hematological parameters.

Materials and Methods:

Materials:

Azathioprine (Azamun) [®]:

Azathioprine tablets 50 mg purchased from El-Nasr Pharmaceutical Chemicals Co. "ADWIC" Egypt.

Lavender (*Lavendula spica*) flowers:

Dried lavender flowers and oil were purchased from local markets Cairo, Egypt.

Rats:

Forty two male albino rats of Sprague Dawley strain 115 ± 10 g were purchased from National research centre, Giza, Egypt.

Methods:

Chemical analysis:

Determination of antioxidant activity (%):

Antioxidant activity (%) was determined according to (A.O.A.C. 2007)

Determination of phenolic compounds:

Phenolic compounds were determined by HPLC according to the method of (Goupy *et al.*, 1999).

Experimental design:

Animals were housed in cages at room temperature and a photoperiod of 12 h light-dark cycle. In this experiment forty two rats were divided into six groups ($n=7$). Animals were permitted for free standard laboratory diet and drinking tap water *ad libitum*, experiment period for 28 days rats. Rats were randomly as follows:

The first main groups were divided into:

Normal control group: Basil diet (BD) only.

Positive group: BD+ Azathioprine[®] (25mg/kg) dissolved in saline. (Matsumoto *et al.* 1990) to induce toxicity, served as (untreated) group.

The subgroups were divided into:

Subgroup 1: Received basil diet (BD)+lavender flowers powder (200 mg/kg/ b.w/ day/orally) and served as experimental control group, pre- treated.

Subgroup 2: Received basil diet (BD) + lavender oil (20 ml/kg/b.w/day/orally) and served as experimental control group, pre-treated.

Subgroup 3: Received basil diet (BD) + lavender flowers powder (200 mg/ kg/b.w/day) + Azathioprine, and served as treated group.

Subgroup 4: Received basil diet (BD) + lavender oil (20 ml/kg/b.w/day)+ Azathioprine, and served as treated group.

Blood and tissue sampling:

At the end of the experimental period, animals were fasted overnight. They were slightly anesthetized with diethylether and sacrificed. Blood samples were collected. Each blood sample was divided into 2 portions: one portion put into EDTA tubes to hematological parameters determination, while others was left to clot then centrifuged, clear serum was separated for determine (TNF- α), (IgE) and (IL-6). Liver was dissected out and washed with saline, dried, weighted and subjected to homogenization according to **Lin et al. (1998)**, centrifuged at 3000 rpm. The supernatant was separated to determined levels of malondialdehyde (MDA), nitric oxide (NO) and glutathione (GSH) according to **Ohkawa et al., (1979)**, **Stocks and Donnandy (1971)** and **Beutler et al. (1963)** respectively.

Determination of complete blood count and indices:

Red blood cells (RBCs) count, hematocrite (Hct) value, total haemoglobin (Hb) value, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC), platelets (PLT) count and leucocyte parameters (white blood cells (WBCs), lymphocytes, monocytes and granulocytes count according to **Drabkin (1949)** and **Mc Inory, (1954)**.

Statistical analysis:

Results of the biochemical estimations are reported as mean \pm S.E. (Standard Error) The total variation was analyzed by performing one-way analysis of variance. "LSD test" (Least Significant Difference) was used for determining significance (**Sümbüloğlu et al., 1998**). Probability levels of less than 0.05 were considered significant.

Results and Discussion:

Total phenols and antioxidant activity (%) content of lavender, (on dry weight basis) were shown in Table (1). It could be noticed from the

results that lavender powder had total phenols (4761.28 mg/100gm) and antioxidant activity 89.13%. These result at accordance with (Sebai *et al.*, 2013) who reported that antioxidant capacity, radical-scavenging activity of lavender against DPPH radical increased significantly in a dose-dependant manner. Polyphenolic compounds are very important constituents, by virtue of their antioxidant activity in activating lipid free radical chains and preventing hydroperoxide.

The main phenolic acids identified in lavender powder are presented in Fig. (1). The results showed that lavender powder was higher contents of *P-Oh*-benzoic, benzoic, epicatechen, salicylic, ellagic, chlorogenic, pyrogallol which were recorded 1267.70 , 1209.08, 873.39, 622.52, 538.01, 220.68 and 174.76 ppm respectively. Furthermore several studies demonstrated that lavender has been extensively reported for its essential oil content (Roberto *et al.*, 2003). Likewise, the antioxidant capacity of the plant extracts is mainly dependent on action of phenolic compounds presented in oil (Ramarathnam *et al.*, 1997 and Pitchersky and Gang, 2000). Antiradical activities associated with phenolic compounds which founded in herbs depends on their molecular structure; that is, on the availability of phenolic hydrogens, which caused the formation of phenoxyl radicals related to hydrogen donation (Ramarathnam *et al.*, 1997 and Ugwu *et al.*, 2013).

Data recorded in Table (2) illustrated that azathioprine induction to rats caused significant decrease in weight gain, feed intake and FER in comparison to normal control and experimental control (pre-treated) groups. But no significant difference in body weight gain, feed intake and FER between experimental control groups (pre-treated) with lavender powder and oil and treated group which consumed lavender oil in azathioprine-induced toxicity of immune in rats which, produced significant increase in weight gain, feed intake and FER. The drug of azathioprine, used from long time since 1960 to damage the immune system. In fact like various other drugs have diverse effects. The toxicity of azathioprine is related to production of free radicals in the organ and the body of different subjects (Park and Lee, 2008 and Watanabe *et al.*, 1979). The reduction that observed in body weight gain of rats after azathioprine induction were similar to the work of (Amouoghli *et al.*, 2009 and Hooshang *et al.*, 2013) who reported that azathioprine caused

side effects in different tissues which, resulted to reduce weight of experimental animals.

Pre-administration with lavender flower powder and oil alone (pre-treated) into rats produced good effects in serum (α -TNF), (IL-6) and (IgE) levels which comparable to normal control rats (Table 3). On the other hand, oral administration of azathioprine (25 mg/kg/rats) to rats caused significant decreases in serum (α -TNF), (IL-6) and (IgE) levels when compared to normal control and experimental groups (pre-treated).

Treatment with lavender powder to azathioprine-induced toxicity of immune rats resulted in non significant increases in serum (α -TNF-), (IgE) and significant decrease in serum levels of (IL-6) when compared to normal control rats. Oral intake of lavender oil to azathioprine intoxicated rats showed improvement in (α -TNF), (IL-6) and (IgE) levels compared to normal rats. These results in parallel with the finding of (Watanabe *et al.*, 1979) who demonstrated that oral use of azathioprine associated with cell necrosis and mitochondrial proliferation. However previous studies have well established that lavender essential oil excellent source of phenolic compounds (Matosa *et al.*, 2009).

The statistical data in Table (4) predicted that, oral administration of lavender powder or oil alone (pre-treated) into normal rats produced good effects in hepatic NO levels as normal control, increase GSH and decrease MDA levels compared with normal control group. Whereas, induction with azathioprine (untreated) group resulted in significant increase in hepatic MDA level and significant decrease in hepatic GSH and NO contents compared to normal control and experimental controls groups.

In comparison with azathioprine treated rats with lavender powder and oil significantly ameliorated hepatic GSH, NO and MDA levels towards the normal levels of the controls. But as expected that induction of azathioprine to rats produces oxidative stress that has a more damage as observed by reduction in GSH and NO levels. Nitric oxide (NO) considered as free radical gas with a short-term effect action that arise From L-arginine and it is the key factor mediator in different body functions like immune system (Dixit and Parvizi, 2001). These results agree with the earlier report of (Hooshang *et al.*, 2013) who demonstrated that oral administration of azathioprine causes the reduction in nitric

oxide levels and weaken immune system. Furthermore, these molecules, are the primal source of antioxidant ability by scavenging free radicals as hydroxyl radical (OH) which is the major cause of lipid peroxidation (Kumazawa *et al.*, 2002). For instance, researchers from China have discovered that lavender essential oil helps the body to produce three most powerful antioxidants, glutathione, catalase, and SOD within 22 hours of using lavender essential oil. Moreover, scientists in Romania found that just seven days of inhaling lavender essential oil protect cells from damage that can lead to cancer (Hancianu *et al.* 2013). In addition (Sebai *et al.*, 2013) stated that treatment with lavender oils induced a decrease of lipoperoxidation as an increase of antioxidant enzymes activity.

Data presented in Table (5) showed that oral administration of both experimental control groups (pre-treated) with lavender powder and oil produced insignificant changes in total white blood cells, lymphocytes, monocytes and granulocytes counts when compared to normal control rats. In the contrary, azathioprine oral administration into rats induced significant decreases in total white blood cells, lymphocytes counts.

Treatment with lavender powder to azathioprine-induced toxicity of immune to rats significantly improved white blood cells, lymphocytes counts ($p < 0.05$), that were reduced by azathioprine induction but it insignificantly in monocytes and granulocytes count $P < 0.05$. While oral administration of lavender oil to azathioprine-induced toxicity of immune to rats resulted in insignificantly in white blood cells, lymphocytes, monocytes and granulocytes counts when compared with normal control rats. These results are consistent with other data attributed that the reduction in RBCs, WBCs and platelets counts to bone marrow depression related to the incorporation of 6-TGNs into DNA. Bone marrow served as the major source of all blood cells, including lymphocytes (Ghonime *et al.*, 2011).

Data recorded in Table (6), showed that oral administration of either lavender powder or oil only to rats revealed insignificant changes in Hb, RBCs, Hct, MCV, and Plt counts when all compared with normal control rats. While, azathioprine (25mg/kg) induced significant decreases in Hb, RBCs count Hct values, MCV values and Plt count.

Treatment with lavender powder to intoxicated rats with azathioprine resulted non significant difference in Hb, RBCs, Hct, MCV and Plt count when compared to normal control rats. Treatment with lavender oil to azathioprine intoxicated rats caused non significant changes in Hb and RBCs count and significant increase in Hct, MCV and Plt count when compared to normal control rats. In the present study, azathioprine induction caused significant anemia (reduced RBC, Hb, Hct), leucopenia and thrombocytopenia since the RBCs, WBCs and platelets counts decreased significantly in the blood of rats treated with azathioprine. The alteration observed in hematological parameters on positive (untreated) group corresponds to previous study by (Colombel *et al.*, 2000) who reported that azathioprine caused liver toxicity in the form of anemia, leucopenia, thrombocytopenia, vascular diseases and idiosyncratic cholesterol in patients treated with azathioprine.

Lavender, natural herb, rich in phenolic compounds, knowing to possess biological activities such as antioxidant, free radical scavenging, anti-platelet aggregation and vascular muscle cell proliferation (Fuhrman and Aviram 2001). The current investigation explains antioxidative properties, which supported by data in Table (1&2), demonstrated that lavender contain major phenolic compounds with high antioxidant activity, that responsible for boost immune system against azathioprine in rats as well as, confirmed by co-administration of either lavender flower or oil alone (pre-treated) to healthy rats or to the azathioprine-induced rats provided a marked correction effects on all biochemical and hematological parameters.

Table (1): Total phenolic content (mg/100g) and antioxidant activity radical % of lavender

Parameters	Content
Total phenolic content (mg/100g)	4761.28
Antioxidant activity (%)	89.13

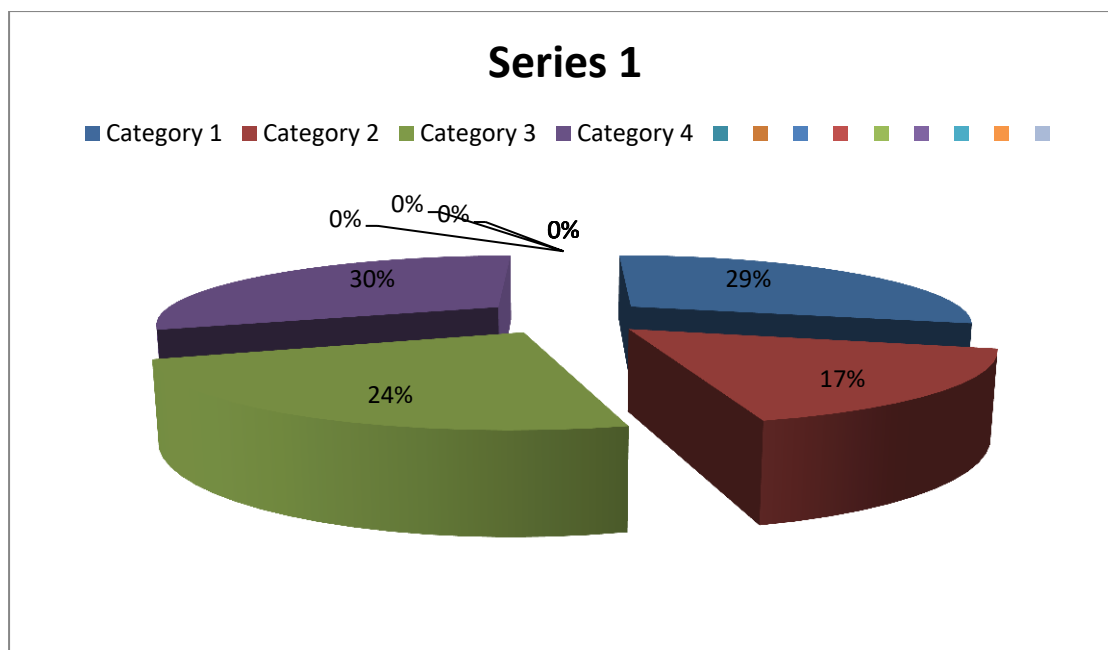


Fig. (1): Phenolic compounds of lavender flowers

Table (2): Effect of lavender powder and oil on weight gain, Daily feed intake and food efficiency ratio (FER).

Groups Parameters	Normal control	Lavender (200 mg/kg/ b.w.)	lavender oil (20 ml/kg/ b.w.)	Azathioprine (25 mg/kg)	Lavender powder + Azathioprine	Lavender oil + Azathioprine
Weight gain (g)	91.76± 8.11	83.59± 6.11	85.13± 7.13	75.64± 8.11*	88.77± 9.17	93.44± 9.17
Daily feed intake (g)	17.94± 2.20	16.80± 2.03	16.66± 2.32	13.94± 2.20*	16.65± 2.21	17.08± 2.92
Food efficiency ratio	0.097± 0.03	0.085± 0.02	0.083± 0.04	0.063± 0.06*	0.085± 0.03	0.091± 0.04

Each value represent the mean± SD. Significant with control group

*p< 0.05

Table (3): Effect of lavender powder and oil on tumor necrosis factor-alpha, interleukin-6, immunoglobulin E in rats.

Groups Parameters	Normal control	Lavender (200 mg/ kg/b.w.)	lavender oil (20 ml/ kg/ b.w.)	Azathioprine (25mg/kg)	Lavender powder + Azathioprine	Lavender oil + Azathioprine
Tumor necrosis factor-alpha (pg/mf)	95.14 ± 2.18	95.89± 8.39	97.14± 7.14	70.55± 5.98*	89.00± 9.01	92.10± 7.6
Interleukin-6 (pg/mf)	9.61± 3.82	8.81± 3.5	9.79± 3.4	5.14± 4.01*	6.5± 2.54*	8.0± 3.4
Immunoglobulin E (IgE) (IU/mf)	34.56 ± 3.2	32.4± 4.0	33.7± 5.4	28.0± 3.4*	34.73± 7.4	35.0± 3.4

Each value represent the mean± SD Significant with control group
*p< 0.05

Table (4): Effect of lavender powder and oil on hepatic nitric oxide (NO), GSH and MDA in rats

Groups Parameters	Normal Control	Lavender (200 mg/ kg/ diet)	Lavender oil (20 ml/ kg/diet)	Azathioprine (25mg/kg)	Lavender powder + Azathioprine	Lavender oil + Azathioprine
Nitric oxide (NO) (nmol/g)	1.85± 0.4	1.80± 0.4	1.82± 0.9	1.5± 0.33*	1.7± 0.3	1.8± 0.74
GSH (mg/g)	29.8± 1.9	27.4± 1.5	34.9± 1.2	20.4± 1.8*	27.0± 1.2	29.5± 1.2

MDA	70.6±	69.5±	66.7±	110.0±	90.4±	85.2±
(nmol/g)	13.6	10.2	9.4	18.2*	7.8*	13.2

Each value represent the mean± SD. Significant with control group * P<0.05

Table (5): Effect of lavender powder and oil on white blood cells, lymphocyte, monocyte and granulocyte counts in rats.

Groups Parameters	Normal Control	Lavender (200mg / kg/diet)	Lavender oil (20 ml/kg/ diet)	Azathioprine (25mg/kg)	Lavender powder + Azathioprine	Lavender oil + Azathioprine
White blood cells (×103/μL)	8.61± 0.82	7.81± 0.5	7.79± 0.4	4.14± 0.01*	5.5± 0.3*	6.3± 0.7
Lymphocyte (×103/μL)	6.2± 0.01	5.5± 0.3	6.0± 0.1	3.5± 0.9*	4.6± 0.1*	5.5± 0.01
Monocyte (×103/μL)	5.9± 0.67	5.5± 0.19	5.7± 0.01	4.2± 0.9*	4.9± 0.3	5.0± 0.01
Granulocyte counts (×103/μL)	1.5± 0.99	1.2± 0.75	1.3± 0.2	0.85± 0.04*	1.1± 2.0	1.2± 0.9

Each value represent the mean± SD. Significant with control group * P<0.05

Table (6): Effect of lavender powder and oil on haemoglobin (Hb), Red blood cells (RBCs) haematocrit (Hct)%, mean corpuscular volume (MCV) and platelet (Plt) in rats

Groups Parameters	Normal Control	Lavender (200 mg/kg)	Lavender oil (20 ml/ kg/ diet)	Azathioprine (25mg/kg)	Lavender powder +	Lavender oil +
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		/diet)			Azathiopr ine	Azathiopr ine
HB (g/dl)	15.08± 2.18	14.99± 1.3	14.14± 1.4	13.55± 1.98*	14.5± 3.5	14.9± 2.6
RBCs (×106/μL)	7.61± 1.82	6.01± 0.5	7.79± 0.4	5.14± 4.01*	6.8± 0.5*	7.33± 2.2
Hct (%)	39.1± 9.5	37.9± 8.5	38.2± 9.5	34.6± 9.5*	38.5± 8.9	39.8± 9.5
MCV (fL)	60.6± 9.5	59.9± 8.5	61.9± 9.5	48.9± 3.5*	59.9± 9.9	63.1± 9.5
Plt (×103/μL)	880.36± 33.5	870.53± 43.5	885.43± 44.9	680.19± 23.5*	750.65± 43.8*	820.23± 33.2

Each value represent the mean± SD.
group *p< 0.05

Significant with control

Reference:

A.O.A.C. (2007). Official methods of analysis. 17th edition. Association of Official Analytical Chemists, Washington DC. USA.

Amouoghli, T. B.; Mohajeri, D. G.; Mousavi F. F.; Khodadadi, A.; Alizade, S.B. and Reihani, B. (2009). Biochemical and Pathological Study of Protective Effect of Vitamin E in Azathioprine -Induced Hepatotoxicity in Rat. J. Bio. Sci., 9(4): 339-44.

Barrett, P. (1996). Growing and using lavender. a Storey Country Wisdom Bulletin. US. Amazon's Book Store. 12:31.

Beutler, E.; Duron, O. and Kelly, M.B. (1963). Determination of reduced glutathione in tissue homogenate. J. Lab Clin. Med. 61, 882.

Catherine, J. C.; Kathi, J. and Kemper, A. (2001). The Longwood Herbal Task Force, The Center for Holistic Pediatric Education and Research. Longwood Herbal Task Force. (7) 2:32.

Cavanagh, H.MA. and Wilkinson, J.M. (2005). Lavender essential oil: A review. Aust. Infect. Control, 10, 35–37.

- Colombel, J.F.; Ferrari, N. and Debuysere, H. (2000).** Genotypic analysis of thiopurine S-methyltransferase in patients with Crohn's disease and severe myelosuppression during azathioprine therapy. *Gastroenterology*, 118(6):1025-30.
- Conti, F.; Emmanuel, M.E. and Calmus, Y. (2003).** Immunosuppressive therapy in liver transplantation. *J. Hepatol*; 39(5):664-678.
- Dixit, V.D. and N. Parvizi, (2001).** Nitric oxide and the control of reproduction. *Animal Reproduction Science*, 65: 1-16.
- Drabkin, D. (1949).** The standardization of hemoglobin measurements. *Am. J. Med. Sci.*, 21 (7): 710.
- Drath, D.B. and Kahan, B.D. (1984).** Phagocytic cell function in response to immunosuppressive therapy. *Arch Surg* 1984; 119(2):156-60.
- Fuhrman, B. and Aviram, M., (2001).** Flavonoids protect LDL from oxidation and attenuate atherosclerosis. *Curr Opin Lipidol*, 12:41–48.
- Gaston, R.S. (2001).** Maintenance immunosuppression in the renal transplant recipient: an overview. *Am. J. Kidney Dis*; 38(6 Suppl 6):S25-35.
- Ghonime, M., Eldomany, R. and Abdelaziz, A., (2011).** Evaluation of immunomodulatory effect of three herbal plants growing in Egypt. *Immunopharmacol Immunotoxicol*. 33(1):141-5.
- Goupy, P.; M. Hugues; P. Boivin and J. Amiot (1999).** Antioxidant composition and activity of barley (*Hordeumvulgare*) and malt extract and of isolated phenolic compounds. *J. Sci. Food Agric.*, 79: 1625-1634.
- Hammer, K.A.; Carson, C.F.; Riley, T.V. (1999).** Antibacterial activity of essential oils and other plant extracts. *J. Appl. Microbiol*, 86, 985–990.
- Han, S.H.; Hur, M.H.; Buckle, J.;Choi, J. and Lee, M.S. (2006).** Effect of aromatherapy on symptoms of dysmenorrhea in college students: a randomized placebo-controlled clinical trial. *J Altern Complement Med* ; 12(6): 535-41.

- Hancianu, M. (2013).** Neuroprotective effects of inhaled lavender oil on scopolamine-induced dementia via anti-oxidative activities in rats. *Phytomedicine*, 15; 20(5): 446-52.
- Heneghan, M.A. and McFarlane, I.G. (2002).** Current and novel immunosuppressive therapy for autoimmune hepatitis. *Hepatology*, 35(1):7-13.
- Hooshang, j.; Mahmood, N.; Mojtaba, P.; Eskandarzadeh, H.N.; Kargar J. H.; Farzam, M. and Rahmanian, E. (2013).** Antioxidant Effects of Ginseng Root Extract Against Side Effects of Azathioprine on the Rat Ovary. *World Journal of Zoology* 8 (4): 425-431.
- Kirmizibekmez, H.; Demirci, B. and Yeşilada, E. (2009).** Chemical composition and antimicrobial activity of the essential oils of *Lavandula stoechas* L. ssp. *stoechas* growing wild in Turkey. *Nat Prod Commun* ;4(7):1001-6.
- Kumazawa, S.; Taniguchi, M.; Suzuki, Y.; Shimura, M.; Kwon, M.S. and Nakayama, T. (2002).** Antioxidant activity of polyphenols in carob pods. *J Agric Food Chem.*, 50:373–377.
- Lin, C.C.; Hsu, Y.F. and Lin, T.C., (1998).** Antioxidant and hepatoprotective activity of punicalagin and punicalin on carbon tetrachloride induced liver damage in rats. *J Pharm Pharmacol.* 50(7):789-94.
- Lin, Y.T.; Yang, Y.H. and Tsai, M.J. (2000).** Long-term effects of azathioprine therapy for juvenile rheumatoid arthritis. *J. Formos Med Assoc*; 99(4):330-5.
- Manosroi, J.; Dhumtanom, P.; Manosroi, A. (2006).** Antiproliferative activity of essential oil extracted from Thai medicinal plants on KB and P388 cell lines. *Cancer Lett*, 235, 114–120.
- Matosa, F., Miguela, M.G., Duarte, J., Venâncio, F. and Moiteiro, C. (2009).** Antioxidant capacity of the essential oils from *Lavandula luisieri*, *L. stoechas* subsp. *lusitanica*, *L. stoechas* subsp. *lusitanica* x *L. luisieri* and *L. viridis* grown in Algarve (Portugal). *J. Essent Oil Res*, 21:327–336.

- Matsumoto, K., Sekita, K. and Ochiai, T., (1990).** Evaluation of immunotoxicity testings using azathioprine-treated rats: the International Collaborative Immunotoxicity Study (Azathioprine). *Eisei Shikenjo Hokoku*, 108:34-9.
- Mc Inory, I. (1954).** Amicro heamatocrit for determining the packed cell and hemoglobin concentration on capillary blood. *J. Clin., Path.*, (7): 32.
- Nomura, S.; Maeyama, K. and Ito, K. (2016).** Enhancement of Autonomic Stress Response and Reduction of Subjective Stress by Lavender Inhalation During a Short-term Calculation Task, *Advanced Biomedical Engineering* 5: 7–12.
- Ohkawa, H.; Ohishi, N. and Yagi,K. (1979).** Assay for lipid peroxidation in animal tissues by thiobarbituric acid reaction annals of *Biochemistry*. 95:351- 358.
- Ou, M.C.; Hsu, T.F.; Lai, A.C.; Lin, Y.T. and Lin, C.C. (2012).** Pain relief assessment by aromatic essential oil massage on outpatients with primary dysmenorrhea: a randomized, double-blind clinical trial. *J Obstet Gynaecol Res*; 38(5): 817-22.
- Park, S.W. and S.M. Lee, (2008).** Antioxidant and prooxidant properties of ascorbic acid on hepatic dysfunction induced by cold ischemia/reperfusion. *Eur. J. Pharmacol.*, 580(3): 401-6.
- Pitchersky, E. and Gang, D. R. (2000).** Genetics and biochemistry of secondary metabolite in plants: An evolutionary perspective. *Trends Plant Science*. 5: 445-459.
- Ramarathnam, N.; Ochi, H. and Takeuchi, M. (1997).** Antioxidant defense system in vegetable extracts. In: *Natural Antioxidants; Chemistry, Health Effects and Application*. Shahidi F (eds). Champaign IL. AOAC Press. pp 76-87.
- Roberto, F.; Vieira, N.; Renee, J.; Grayer, T. and Alan, J. P. (2003).** Chemical profiling of ocimum americanum using external flavonoids. *Phytochemistry*; 63: 555-567.
- Sebai, H.; Selmi, S.; Rtibi, K.; Souli, A.; Gharbi, N. and Sakly, M. (2013).** Lavender (*Lavandula stoechas* L.) essential oils attenuate hyperglycemia and protect against oxidative stress in alloxan-induced

- diabetic rats. Département des Sciences de la Vie, Laboratoire de Physiologie Animale, Faculté des Sciences de Tunis, Tunis 1060, Tunisia.
- Stocks, J. and Donnandy, J. (1971).** The autoxidation of human red cell lipids induced by hydrogen peroxide. Br. J. Haematol., 20: 95-111.
- Sümbüloğlu, K. and Sümbüloğlu, V. (1998).** Biyoistatistik, 8th edition, HatibogluYayinevi, Ankara, p. 76-86.
- Sweetman, S.C. (2005).** Martindale: The Complete Drug Reference. 34th edn. London: Pharmaceutical Press.
- Tsuneki, H.; Ma, E.L.; Kobayashi, S.; Sekizaki, N.; Maekawa, K.; Sasaoka, T.; Wang, M.W.; Kimura, I. (2005).** Antiangiogenic activity of beta-eudesmol in vitro and in vivo. Eur. J. Pharmacol., 512, 105–115.
- Ugwu, M.N.; Umar, I.A.; Utu-Baku, A.B.; Dasofunjo, K.; Ukpanukpong, R.U.; Yakubu, O.E. and Okafor, A.I. (2013).** Antioxidant status and organ function in streptozotocin-induced diabetic rats treated with aqueous, methanolic and petroleum ether extracts of ocimum basilicum leaf. Journal of Applied Pharmaceutical Science Vol. 3 (4 Suppl 1), pp. S75-S79.
- Watanabe, A.; Hobara, N.; Tobe, K.; Endo, H. and Nagashima, H. (1979).** Biochemical and morphological study on hepatotoxicity of azathioprine in rat. Acta. Med. Okayama, 33(1): 5-14.

تأثير اللافندر (سحوق زهور وزيت) على فئران التجارب المصابة بالازاثيوبيرين المثبط للمناعة

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الملخص :

الهدف: تهدف الدراسة الحالية الى فحص التأثير الوقائى المحتمل لمسحوق زهور وزيت اللافندر على الفئران السليمة ضد الازاثيوبيرين المسبب للسمية فى المناعة بالفئران.

الطرق : اجريت هذه التجربة على عدد ٤٢ من ذكور الفئران قسمت إلى ٦ مجموعات كل مجموعة (٧ فأر) لمدة ٢٨ يوما. وقد قسمت الى مجموعتين رئيسيتين: المجموعة الضابطة السالبة: تناولت الوجبة الاساسية، المجموعة الضابطة الموجبة: تناولت الوجبة الاساسية بجانب عقار ازاثيوبيرين بجرعة ٢٥ ملجم لكل كجم من وزن الفار والاربع مجموعات الفرعية: المجموعة الفرعية ١: تناولت الوجبة الاساسية مع مسحوق زهور اللافندر بجرعة ٢٠٠ ملجم لكل كجم من وزن الفار. والمجموعة الفرعية ٢: تناولت الوجبة الاساسية مع ٢٠ مل زيت اللافندر لكل كجم من وزن الفار واعتبرت كلا من المجموعتين، مجموعات ضابطة تجريبية (قبل المعالجة)، والمجموعة الفرعية ٣: تناولت الوجبة الاساسية مع مسحوق زهور اللافندر وأزاثيوبيرين، والمجموعة الفرعية ٤: تناولت الوجبة الاساسية مع ٢٠ مل زيت اللافندر وأزاثيوبيرين

النتائج: أظهرت النتائج أن تناول عقار ازاثيوبيرين أدى الى انخفاض معنوى فى مستوى عامل نخر الورم الفا الانترلويكين و الغلوبولين المناعى فى السيرم، وأيضا انخفاض مستويات الجلوتاثيون وأكسيد النترىك مع الزيادة المعنوية فى مستوى المالنوالدهيد بالكبد، وقد ادى تناول كلا من مسحوق زهور وزيت اللافندر بمفردهم وباستخدام المعالجة بالزيت فى الفئران المصابة بالسمية فى المناعة بالازاثيوبيرين والذى كان له دورا فعالا فى الاقلال من التأثير المدمر لعقار ازاثيوبيرين ، وقد أظهرت النتائج ان كلا من مسحوق وزيت اللافندر ساعدا على انخفاض الضغط التأكسدى و تحسن أغلب التغيرات

فى مؤشرات صورة الدم الكاملة و تعزيز مستوى اكسيد النتريك، ومستوى انتاج الغلوبولين المناعى E .

الخلاصة: من خلال النتائج المتحصل عليها والتي أظهرت تحسنا فى مؤشرات صورة الدم الكاملة وتعزيز جهاز المناعة باستخدام قبل / المعالجة بمسحوق وزيت الالفندر بمفردهم و ضد سمية المناعة بالازاثيوبيرين فى الفئران والذى يرجع الى النشاط المضاد للاكسدة نتيجة لمحتواه المرتفع من المركبات الفينولية الفعالة.