



Research Article

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Effects of Olive Oil On a Neurochemical Parameters and Histological Structure in Cerebral Cortex Region in Male Albino Rats

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ABSTRACT

Olive oil is the major component of the Mediterranean diet and has rich history of nutritional and medicinal uses which indicate that, olive oil has the Enhanced memory and antidepressant properties. This study aims to determine the effect of olive oil on the histological structure as well as, the levels of neurochemical include epinephrine (E), dopamine (DA) and 5-hydroxyindoleacetic acid (5-HIAA) in the cerebral cortex region of male albino rats. Animals of the treated groups were given olive oil orally at the dose of 3 mL/kg daily for 3 weeks. Brain neurochemical parameters results showed that administration of olive oil increased the levels of neurotransmitter in cerebral cortex region. From the data finding in the current work the olive oil has a neuroprotective effects. So, it could be used as a therapeutic substance for the treatment of depression and loss memory. Olive oil contains antioxidants which have a protective function in preserving the memory and protective the cerebral cortex region in brain.

KEYWORDS: Olive oil, neurochemical parameters, cerebral cortex region

INTRODUCTION

The plant kingdom is an important source of many organic compounds with medicinal properties (1). virgin olive oil is considered important to human health and has the characteristics of biological and therapeutic, because it contains unsaturated fatty acids, vitamins (A, B, C, D, E), antioxidants, phenolic acids, alcohols Aliphatic, the turbine and squalene (2-34) extra virgin olive oil is produced by the press or centrifuge directly.

The olive tree is considered a blessed tree mentioned in the Holy Quran and Sunnah. virgin Olive oil has been cultivated in the Mediterranean region for more than a thousand years. (5).

Olive oil Composed from triacylglycerols by 97%, components is Gelesredek (Vsvoulidat, Pigment carbohydrate, flavor compounds and the enzyme lipase), trace amounts of element metal (iron, magnesium, calcium, sulfur, phosphorus, sodium, potassium, copper) and a quantity of water materials which constitute 3% of the installation of olive oil.

Olive oil contains Polyunsaturated Fatty Acids such as Oleic Acid, Linoleic acid (6-7-8) and Saturated fatty acids including palmitic acid and stearic acid. The most material non-saponification (hydrocarbon - Tokovirollat- sterols and phenols), which inhibit the oxidation of lipids and thereby prevents be free of cracks that cause cell destruction (9).

Olive oil contain high concentrations of multiple Alvilah compounds and flavonoids that remove free radicals and activate antioxidant enzymes such as Glutathin Peroxides and Catalaes (10). Olive oil is the antagonist of concern by increasing antioxidant enzymes such as glutathione reductase in a large rat age (11).

Olive oil contains omega-3 fatty acids, which play an important role in maintaining the membranes of nerve cells and their functions. Olive oil is the antagonist of depression because of the presence of linoleic acid and omega-3 fatty acid, which works to reduce the inflammatory cytokines and thus protect the body from stress research has shown that low levels of fatty acids (omega-3 and omega-6) in the food intake instrumental in the emergence of depression (12-13).

The olive oil is a common oil use, especially in the Arab countries and regions of the Mediterranean Sea and contributes to the olive oil in the prevention of neurological disorders and improves cognitive performance (14) olive oil has ability to cross the blood brain barrier to the presence of viable compounds soluble in fat (15). Research has shown that a high amount of fatty acids, monounsaturated in eating foods protect against age-related cognitive decline and maintain the memory (16). Olive oil works to protect nerve cells from oxidation and increasing nerve conduction in the central nervous system (17-18).

Virgin olive oil and leaves are used for treatment in folk medicine, the aim of the work is to examine the effect of chronic administration of olive oil on epinephrine (E), dopamine (DA) and 5-hydroxyindoleacetic acid(5-HIAA) contents in the cerebral cortex region in brain and histological structure of cerebral cortex of male albino rats.

MATERIALS AND METHODS

2. Materials and Method

2.1. Materials used

a. Animals used

Experiments of this research was conducted on a group of male albino rats ranges weights of (70g -90g) from 5-7 weeks which obtained and experimental in King Fahd Center for Medical Research, King Abdulaziz University in Jeddah. The experiment developed were in private rooms with metal cages with food availability (diets dry balanced), water and lighting (12 hours of darkness and 12 hours lighting), temperature ranging from 22-25°C.

2.1b. Olive Oil

Olive oil (*OleaEuropaea.L*) was obtained from the local markets in Jeddah, Saudi Arabia.

2.2. Experimental Design

2.2.1 brain neurochemical parameters study

Young male rats divided into:

- The first group (control group): were given male rats (n=6) distilled water for a 3 week and was killed in the beginning of the experiment
- Group 2 (chronic treatment with olive oil):

It was given the male rats (24 rats) olive oil (3 ml / day) through oral tube (19) Succession 3 weeks, and after that six of the rats were killed after the end of 1, 2 and 3 weeks, compare the results of this group to the control group.

2.2.2. Histological study

Young male rats of this group was divided (12 rat) to 2 main groups:

- The first group (control group): were given male rats distilled water and was killed after the end treatment for histological study.

• Group B (chronic treatment with olive oil): Rats (n=6) were given this group (3 ml / day olive oil) through the oral tube for 3 consecutive weeks and killed after the end treatment for histological study.

2.3.-Measurement of neurochemical parameters in the cerebral cortex of the brain:

Rats were slaughtered abruptly and then taken brain carefully then cut lengthwise into halves on a glass then cerebral cortex region was separated depending on the mode (20). Neurochemical analysis was performed to estimate concentrations of epinephrine (E), dopamine (DA) and 5-hydroxyindoleacetic acid(5-HIAA) in the cerebral cortex region of rats by HPLC-EC method as reported by (21).

Preparations cerebral cortex for histological study:

Taking the head of rats and the anatomy of the rat skull very carefully to get the cerebral cortex then washed with a saline solution to remove blood and impurities outstanding, Part of the cerebral cortex was cut and fixed in 10% neutral buffered formalin and processed for light microscopic study to get paraffin sections of 5 μ m thickness. Sections were stained with Haematoxylin and Eosin (H&E) at the King Fahd Medical Research Center (22).

Statistical analysis:

The expression of neurotransmitters content under study as an average arithmetic + standard error of the mean + S.E.M then compared the groups treated group using (t -test) (23) and then calculate the percentage of difference compared to the control group.

RESULT

3-1: neurochemical parameters result

The daily intake of olive oil at a dose (3 ml / day) cause a rise significantly in the content of E in the cerebral cortex after the first, second and third week. The results recorded the highest significant increase in the cerebral cortex (21.04%) after the third week table (1).

The daily intake of olive oil at a dose (3 ml / day) cause a rise significantly in the content of DA in the cerebral cortex after the first, second and third week. The results recorded the highest significant increase in the cerebral cortex (98.66%) after the third week table (2)

The daily intake of olive oil at a dose (3 ml / day) cause a rise significantly in the 5-hydroxyindoleacetic acid(5-HIAA) content in the cerebral cortex after the 1st, 2nd and 3rd week of treatment. It has been found that the highest significant increase of the content of 5-HIAA in the cerebral cortex area (97.56%) after the first week.

Table (1): Effect of chronic oral administration of olive oil (3ml/kg b.wt.) on epinephrine (E) content in the Cerebral cortex region of male albino rat.

Time of decapitation		Cerebral cortex mean \pm S.E.
1 week	C	56.443 \pm 0.216
	T	62.667 \pm 0.558
	%	11.03 *
2 weeks	C	55.777 \pm 0.585
	T	64.333 \pm 0.494
	%	15.34 *
3 weeks	C	55.493 \pm 0.105
	T	67.167 \pm 0.601
	%	21.04 *

- Statistical analyses were performed between control (C=6) and treated (T=6) animals by using paired *t* ' test.
% : Percentage of change from control.

Table (2): Effect of chronic oral administration oral of olive oil (3mL/ daily) on dopamine (DA) content in the different brain areas of male albino rat.

Time of decapitation		Cerebral cortex mean \pm S.E.
1 week	C	61.240 \pm 0.214
	T	68.000 \pm 0.365
	%	11.04 *
2 weeks	C	61.240 \pm 0.214
	T	84.333 \pm 0.494
	%	37.71 *
3 weeks	C	60.488 \pm 0.044
	T	120.167 \pm 0.601
	%	98.66 *

- Statistical analyses were performed between control (C=6) and treated (T=6) animals by using paired t' test.
% : Percentage of change from control.

Table (3): Effect of chronic oral administration oral of olive oil (3mL/kg daily) on 5-hydroxyindoleacetic acid (5-HIAA) content in the different brain areas of male albino rat.

Time of decapitation		Cerebral cortex mean \pm S.E.
1 week	C	61.240 \pm 0.214
	T	67.667 \pm 0.333
	%	10.49 *
2 weeks	C	61.240 \pm 0.214
	T	97.833 \pm 0.307
	%	59.75 *
3 weeks	C	60.488 \pm 0.044
	T	119.500 \pm 0.764
	%	97.56 *

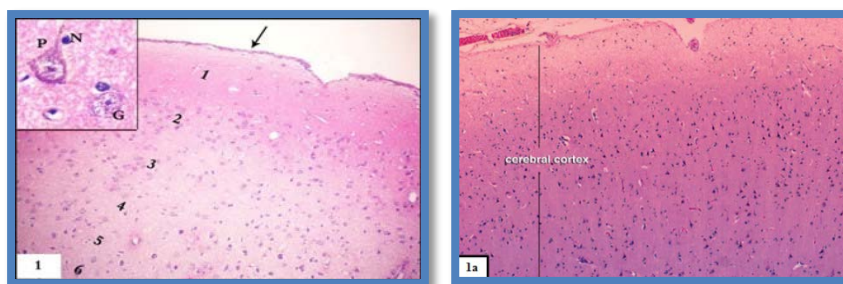
- Statistical analyses were performed between control (C=6) and treated (T=6) animals by using paired t' test.
% : Percentage of change from control.

3-2: Histological examination result

In the control group, Cross-section of Light microscope (LM) sector accidental in the cerebral cortex area of the brain male albino rats of the control group showing six classes a molecular layer, the external granular layer, the external Pyramidal layer, the internal granular layer, the internal ganglionic layer and multi-form layer (H & E, 40) (24).

Histological examination showed that the cerebral cortex, the area is divided into six layers, namely:

Control group

**Fig (1-1a):** Cross-section of Light microscope (LM) sector accidental in the cortex area of the brain male albino rats of the control group

1. Molecular layer and the layer containing a few small neurons.

2. The external granular layer contain a large number of small granule cells.
3. The external Pyramidal layer.
4. The internal granular layer.
5. The internal Gangilionic layer contain a number of large ganglion cell.
6. The multiform layer contain three different types of cells.

Treatment group

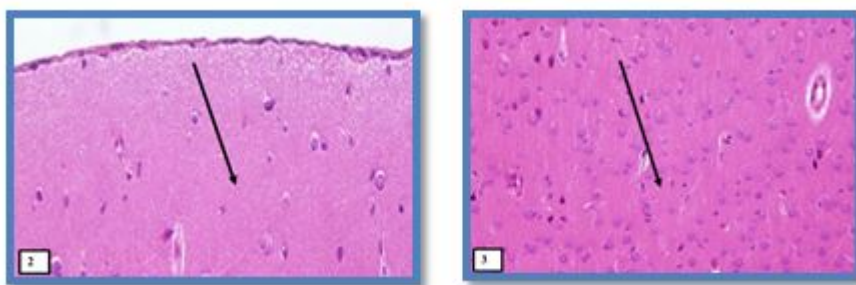


Fig (2): Cross-section of (LM) in the first layer of cerebral cortex explain the small number of neurons (arrow) (H & E, 40).

Fig (3): Cross-section of (LM) in the external granular layer it is thin layer consists of a few small crowded neurons (arrow) (H & E, 40).

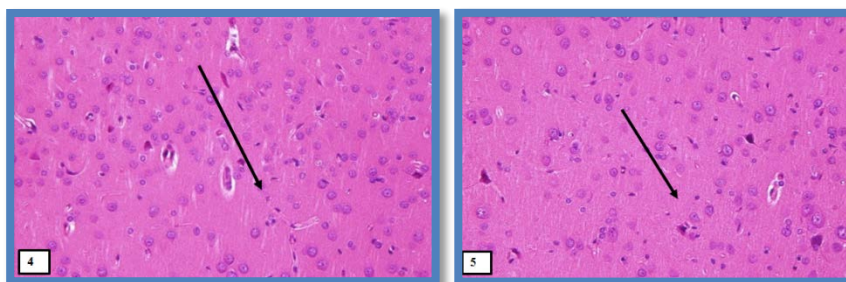


Fig (4): Cross-section of (LM) in the external pyramidal layer consists pyramidal neurons medium-sized (arrow) (H & E, 40).

Fig (5): Cross-section of (LM) in the internal granular layer consists a small-sized nerve cells irregularly (arrow) (H & E, 40).

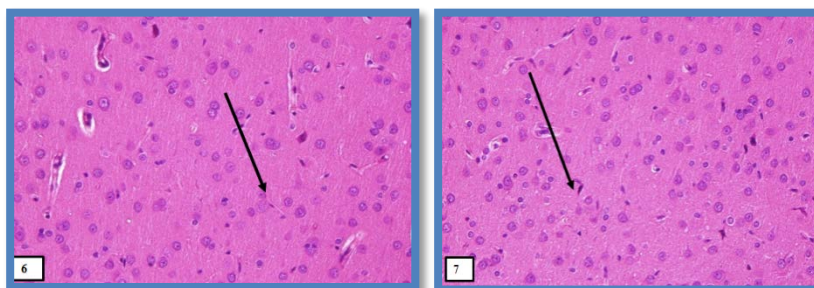


Fig (6): Cross-section of (LM) in the internal Gangilionic layer consists of a large pyramidal cells (arrow) (H & E, 40).

Fig (7): Cross-section of (LM) in multiform cell layer consists of tow kind of cells multiform cell and a small spindle neurons (arrow) (H & E, 40).

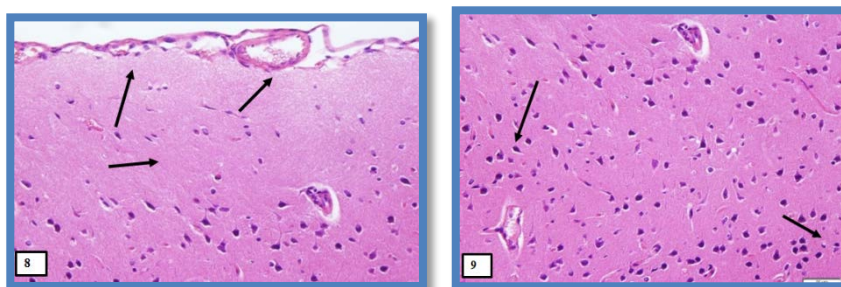


Fig (8): Cross-section in the molecular layer of connective tissue show a thin membrane that surrounds the cortex, blood vessel and neurons are clear few number (arrow) (H & E X100).

Fig (9): Cross-section in the external granule layer neurons show crowded (arrow) (H & E X100).

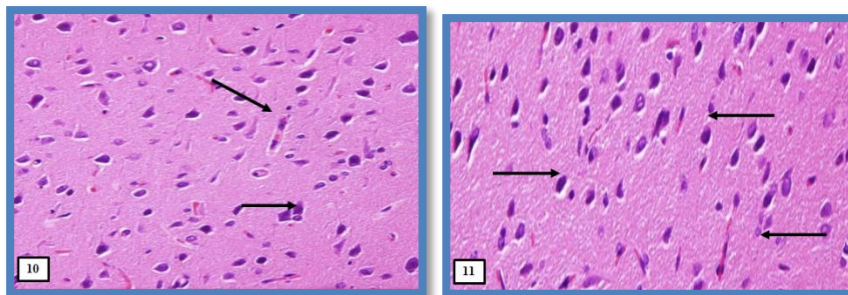


Fig (10): Cross-section in the internal granular layer neurons appear small size and irregular (arrow) (H & E X100).

Fig (11): Cross-section in the ganglion cell layer show neurological and axes clear (arrow) (H & E X100)

The effect of chronic treatment with olive oil (3 ml / day) in the cerebral cortex area when the treatment of male albino rats with olive oil at dose (3 ml / day) for three weeks cerebral cortex show connective tissue, a thin membrane that surrounds the cortex, blood vessel clear and neurons are clear few in number, the neurons are clear and crowded and small and irregular, large pyramidal cells clear and obvious axons (Figs 7,8,9,10, and11).

Cross-section of (LM) in the cortex area of the brain male albino rats of the group treated with olive oil for 3 weeks

DISCUSSION

The olive oil is considered as a commonly used, especially in the Arab countries and the regions of the Mediterranean Sea. The olive oil contributes in the prevention of certain neurological disorders and improves cognitive performance (14-22). Olive oil has the ability to cross the blood brain barrier due to the presence of viable compounds such as antioxidants and unsaturated fats, such as polyphenols, oleic acid, linoleic acid and vitamin E which is soluble in fat (15,23-35). Research has shown that the high amount of fatty acids, monounsaturated in the intake of foods protects against age related cognitive decline and preserve the memory (16-25,36-42).

Result from the current study showed that, the daily intake of olive oil caused an increase in E, DA and 5-HIAA contents in the cerebral cortex area after treatment, this is in compatible with the previous studies, suggesting that the olive oil rich in fatty acids such as omega-3 and omega-6, which enters in the composition of the nerve cell

membrane and help the nerve cell to perform its functions and working to improve memory and support of the central nervous system and increase the level of epinephrine, norepinephrine, dopamine, gamma-aminobutyric acid and serotonin

It was found that virgin olive oil works as anti-depressant because it contains antioxidant phenolic by increasing content nervous dopamine and 5-hydroxyindoleacetic acid in cerebral cortex (11-26), which play a significant role in reduction of the depression (27,43-49). The olive oil stimulate the production of neurotransmitters in the cells that secrete it such as acetylcholine, norepinephrine, dopamine, gamma-aminobutyric acid and serotonin, which has an important role in learning and memory (28,50-57).

The study of the (29-30,58-64) shows that omega-3 works to stimulate the production and secretion of dopamine in the frontal cortex and hippocampus.

Recent studies have shown that omega-3 acid plays an important role in organizing the work of the cells producing dopamine and serotonin (31,65-72).

It found that olive oil works to increase the release and re-uptake the dopamine, epinephrine and norepinephrine (26) this corresponds to the current study that daily treatment with olive oil for 3 consecutive weeks led to a rise in the total content of epinephrine, norepinephrine, dopamine and GABA in a few different areas of the brain during the treatment period.

From the previous studies found that olive oil contains a high content of antioxidants and monounsaturated fatty acids such as oleic acid and linoleic acid (32,79,73). These acids is working to increase the concentration of calcium free ions Ca^{+2} by calcium accumulate in the endoplasmic of granulocytes and production of inositol and 1, 4, 5-triphosphate leading to the opening of calcium channels and the entry of calcium into neuron cells. The oleic and linoleic acids work on the phosphorylation of protein-tyrosine kinases, which lead to the production of some important enzymes such as tryptophan hydroxylase, carboxylic acid L aromaticamino acid decarboxylase, tyrosine hydroxylase, and dopamine β -hydroxylase which lead in the formation of neurotransmitters monounsaturated and stored monoamines in the vesicles which contain high amounts of energy. The linoleic acid increase the formation and release of neurotransmitters such as NE, E, DA and GABA and re-uptake (33).

The study showed that the chronic oral administration of olive oil (3 ml / day) for three weeks led to a significant increase in neurotransmitter content. This is may be due to the effect of oleic acid and Linoleic acid which works to increase the formation, release and re-uptake of neurotransmitters.

Diet that contains olive oil works to increase nerve conduction and protect nerve cells from oxidative stress, reduce the impact of free radicals and the effects of aging in the central nervous system (17-18).phenol compound found in olive oil,play an important role in protecting nerve membranes and the safety blood brain barrier, Previous studies had shown that eating foods contain polyphenols work to improve cognition in learning difficulties associated with aging memory, lower incidence of Alzheimer's disease by reducing oxidative damage in the brain and increase the concentration of E and NE (34).

Studies have shown that the polyphenols, vitamin E and unsaturated fats have antioxidant significant effects in some brain cells, especially the hippocampus cells (35). It was found that the use of olive oil frequently works as a stimulant for the mind through reduced cell death in the hippocampus (36).

Results of current histological study showthat the tissue of the cerebral cortex area is not affected by a daily treatment with olive oil at a dose (3ml / day) for three weeks succession may be due to the presence of omega acid 3, which has an important role in maintaining the nervous tissue (13).

The results of the (37) study shows an increase in the activity of antioxidant enzymes in rats exposed to reoxygenation hypoxia and treated with olive oil while retaining neurons form compared to non-treated rat with olive oil

Studies by the electron microscope shown that the lack of omega-3 intake in the early stages of growth led to a significant decrease in the number of dopamine vesicles in pre-synaptic cells (38-39).

As well as lower level of docosahexaenoic acid (DHA acid) leads to changes in the size of nerve cells that affect learning, memory, auditory responses, olfactory and changes in the growth of nervous system in the cerebral cortex region and the emergence of aggressive behavior in rats deprived of foods containing omega-3 fatty acids for 15 weeks after weaning (29).current study find that olive oil maintained the integrity of the tissue of the cerebral cortex area throughout the treatment period

CONCLUSION AND RECOMMENDATIONS

olive oil have biological properties including several antioxidant compounds,oleic acid and. , vitamins E ,A and K, important minerals (including iron, calcium, magnesium and potassium) and amino acids.therefore an important role in improving the development and functaion of the brain, protect the nervous cells, maintain memory, prevention of Alzheimer's disease and anti-depressants. It is recommended to use it use a day regularly with meals

REFERENCES

- 1- Tyler, V. E.; Brady, L. R. and Robbers, J. E. (1988): Pharmacognosy. 9thed. *Lea and Febiger*. Philadelphia. pp: 175.
- 2- Garcia, A.; Brenes, M.; Romero, C.; Garcia, P. and Garrido, A. (2002): Study of phenolic compound on virgin olive oils of the Picual Variety. *Eur. Food. Res. Technol.* 215: 407-412.
- 3- Stark, A. H. and Madar, Z. (2002): Olive oil as functional food: epidemiology and nutritional approaches. *Nutr. Rev.* 6:170-176.
- 4- Trichopoulou, A.; Corella, D.; Marti'Nez-Gonza'Lez, M. A.; Soriguer, F. and andOrdovas, J. M. (2006): The Mediterranean diet and cardiovascular epidemiology. *Nutr. Rev.* 64 (10): 13-19.
- 5- Migahid, A. M. (1996): Flora of Saudi Arabia. 4thEd.King Saud University Press. Riyadh.
- 6- Brouwer, I. A. (2004): Dietary alpha-linolenic acid is associated with reducedrisk of fatal coronary heart disease. *J. Nutr.*13(4): 919-922.
- 7- Buckner, G. (2004): Microcirculation, vit E and omega -3fatty acids: an overview. *Adv. Exp. Med. Biol.* 415:195-208.
- 8- Borges I J. R.; Moreira, E. A.; Filho, D. W. ; de Oliveira, T. B.; da Silva, M. B. and Frode, T. S. (2007): Proinflammatory and oxidative stress markers in patients with periodontal disease. *Mediatorsinflamm.* 5.
- 9- Tuck, K. L.; and Hayball, P. J. (2002): Major phenolic compounds in olive oil: metabolism and health effects. *J. Nutr. Biochem.* 13(11): 636-644.
- 10- Visioli, F.; Wolfram, R.; Richard, D.; Abdullah, M. and Crea, R. (2009): Olive phenolics increase glutathione levels in healthy volunteers. *J. Argri. Food chem.* 57(5): 1793-1796.
- 11- Pitozzi, V.; Jacomelli, M.; Zaid, M.; Luceri, C.; Bigagli, E.; Lodovici,M.; Ghelardini, C.; Vivoli, E.; Norcini, M.; Gianfriddo, M.; Esposto,S.; Servili, M.; Morozzi, G.; Baldi, E.; Bucherelli, C.; Dolara, P. andGiovannelli, L. (2010): Effects of dietary extra-virgin olive oilonbehaviour and brain biochemical parameters in ageing rats.*Br. J. Nutr.* 103(11): 1674-1683.
- 12- Maes, M.; Christophe, A.; Bosmans, E.; Lin, A. and Neels, H. (2000): In humans, serum polyunsaturated fatty acid levels predict the response of proinflammatory cytokines to psychologic stress. *Biol. Psychiatry.* 47(10): 910-920.
- 13- Sirtori, C. R.; Anderson, J. W. and Arnoldi, A. (2007): Nutritional andnutraceuticalconsiderations for dyslipidemia. *Future Lipidology.* 2(3): 313-339.
- 14- Khalatbary, A. R. (2013): Olive oil phenols and neuroprotection. *Nutr. Neurosci.* 16(6): 243-249.
- Mitchell, R. W.; Edmundson, C. L.; Miller, D. W. and Hatch, G. M. (2009): On the mechanism of oleate transport across human brain microvessel endothelial cells. *J. Neurochem.* 110(3): 110:1049-1057.
- 15- Solfrizzi, V.; Panza, F.; Torres, F.; Mastroianni, F. Del Parigi, A.; Venezia, A. andCapurso, A. (1999): High monounsaturatedfatty acids intake protects against age-related cognitive decline.*Neurology.* 52(8): 1563-1569.

- 16- Schaffer, S., Podstawa, M., Visioli, F., Bogani, P., Müller, W. E. and Eckert, G. P. (2007): Hydroxytyrosol-rich olive mill wastewater extract protects brain cells invitro and exvivo. *J. Agric. Food Chem.* 55:5043-5049.
- 17- Valente, T.; Hidalgo, J.; Bolea, I.; Ramirez, B.; Angles, N.; Reguant, J.; Morello, J. R.; Gutierrez, C.; Boada, M. and Unzeta, M. (2009): A diet enriched in polyphenols and polyunsaturated fatty acids, LMN diet, induces neurogenesis in the subventricular zone and hippocampus of adult mouse brain. *J. Alzheimer's Dis.* 18(4): 849-865.
- 18- Brai, B. I. C.; Adisa, R. A. And Odetola, A. A. (2014): Hepatoprotective Properties of Aqueous Leaf Extract of *Persea Americana*, Mill (Lauraceae) 'Avocado' Against CCL4-Induced Damage in Rats. *Afr. J. Tradit. Complement Altern. Med.* 11(2): 237-244
- 19- Glowinski, J. and Iversen, L.L. (1966) Regional studies catecholamines in the rat brain I. The disposition of [3H] norepinephrine, [3H] dopamine and [3H] dopa in various regions of the brain. *Journal of Neurochemistry*, 13,655-669.
- 20- Haider S, Saleem S, Shameem S, Ahmed SP, Parveen T, Haleem DJ. Is anorexia in thioacetamide-induced cirrhosis related to an altered brain serotonin concentration. *Polish Journal of Pharmacology.* 2004;56(1):73-78.
- 21- Harris, H.F. (1900): On the rapid conversion of haematoxylin into haematin staining reactions. *Journal of Applied Microscopy and Laboratory Methods*, 3, 777.
- 22- Hill, H. B. (1971): Principles of medical statistic. 9th ed. Oxford Univ. press.
- 23- Ross M, Pawlina W (2011) *Histology: A Text and Atlas* (6th ed.). Lippincott Williams & Wilkins. p. 646.
- 24- Logan, A. C. (2003): Neurobehavioural aspects of omega-3 fatty acids: possible mechanisms and therapeutic value in major depression. *Altern. Med. Rev.* 8(4): 410- 425.
- 25- Perveen, T.; Hashmi, B. M.; Haider, S.; Tabassum, S.; Saleem, S. and Siddiqui, M. A. (2013): Role of Monoaminergic System in the Etiology of Olive Oil Induced Antidepressant and Anxiolytic Effects in Rats. *ISRN Pharmacol.* 1-5.
- 26- Hasler, G. (2010): Pathophysiology of depression: do we have any solid evidence of interest to clinicians?. *World Psychiatry.* 9(3):155-161.
- 27- Hasselmo, M. E. (2006): The role of acetylcholine in learning and memory. *Curr. Opin. Neurobiol.* 16(6): 710-715.
- 28- DeMar JC, Jr.; Ma, K.; Bell, J. M.; Igarashi, M.; Greenstein, D. and Rapoport, S. I. (2006): One generation of n-3 polyunsaturated fatty acid deprivation increases depression and aggression test scores in rats. *J. Lipid Res.* 47(1):172-180.
- 29- Russo-Neustadt, A. A. and Chen, M. J. (2005): Brain-derived neurotrophic factor and antidepressant activity. *Curr. Pharm. Des.* 11(12): 1495-1510.
- 30- Zimmer, L.; Dellion-Vaancassel, S.; Durand, G.; Guilloteau, D.; Bodard, S.; Besnard, J. C. and Chalon, S. (2000): Modification of dopaminergic neurotransmission in the nucleus accumbens of rats deficient in n-3 polyunsaturated fatty acids. *J. Lipid Res.* 41:32-40.
- 31- Perez-Jimenez, F.; Ruano, J.; Perez-Martinez, P.; Lopez-Segura, F. and Lopez-Miranda, J. (2007): The influence of olive oil on human health: Not a question of fat alone. *Mol. Nutr. Food Res.* 51(10):1199-1208.
- 32- Bawazir, A. E. (2011): Chronic effect of olive oil on some neurotransmitter contents in different brain regions and physiological, histological structure of liver and kidney of male albino rats. *World J. Neuroscience.* 1: 31-37.
- 33- Chen, Z. H.; Yoshida, Y.; Saito, Y.; Sekine, A.; Noguchi, N. and Niki, E. (2006): Induction of adaptive response and enhancement of PC12 cell tolerance by 7-hydroxycholesterol and 15-deoxy-delta(12,14)-prostaglandin J2 through up-regulation of cellular glutathione via different mechanisms. *J Biol Chem.* 281:14440-14445
- 34- De la Puerta, R.; Dominguez, M. E. M.; Ruiz-Gutierrez, V.; Flavill, J. A. and Hoult, J. R. S. (2001): Effects of olive oil phenolics on scavenging of reactive nitrogen species and upon nitric neurotransmission. *Life Sci.* 69:1213-1222.
- 35- O'Keefe, J. and Dostrovsky, J. (1971): The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely moving rat. *Brain Res.* 34(1):171-175.
- 36- González-Correa, J. A.; Muñoz-Marín, J.; Arrebola, M. M.; Guerrero, A.; Narbona, F.; López-Villodres, J. a. and De La Cruz, J. P. (2007): Dietary virgin olive oil reduces oxidative stress and cellular damage in rat brain slices subjected to hypoxia-reoxygenation. *Lipids.* 42(10):921-929.
- 37- Sapolsky, R. M. (2000): The possibility of neurotoxicity in the hippocampus in major depression: a primer on neuronal death. *Biol Psychiatry.* 48(8): 755-765.

- 38- Ikemoto, A.; Nitta, A.; Furukawa, A.; Ohishi, M.; Nakamura, A.; Fujii, Y. and Okuyama, H. (2000): Dietary n-3 fatty acid deficiency decreases nerve growth factor content in rat hippocampus. *Neurosci. Lett.* 285(2): 99-102.
- 39- Ghaderi N, Taymoori P, Yousefi F, Nouri B. The prevalence of Cigarette Smoking among adolescents in Marivan City- Iran: Based on health belief model (HBM). *International Journal of Pediatrics.* 2016. 4(9), pp. 3405-3414.
- 40- Sharifi G, Bakhtevvari MH, Samadian M, Alavi E, Rezaei O. Endoscopic Surgery in Nonhydrocephalous Third Ventricular Colloid Cysts: A Feasibility Study. *World Neurosurg.* 2015 Aug;84(2):398-404. doi: 10.1016/j.wneu.2015.03.033. Epub 2015 Mar 28.
- 41- Samadian M, Bakhtevvari MH, Nosari MA, Babadi AJ, Razaee O. Trigeminal Neuralgia Caused by Venous Angioma: A Case Report and Review of the Literature. *World Neurosurg.* 2015 Sep;84(3):860-4. doi: 10.1016/j.wneu.2015.04.063. Epub 2015 May 9.
- 42- Bakhtevvari MH, Sharifi G, Jabbari R, Shafizad M, Rezaei M, Samadian M, Rezaei O. Giant leaking colloid cyst presenting with aseptic meningitis: Review of the literature and report of a case. *World Neurosurg.* 2015 Dec;84(6):1997-2001. doi: 10.1016/j.wneu.2015.06.064. Epub 2015 Jul 2.
- 43- Rabieepour S, Ebrahimi M, Sadeghi E. Relationship between sexual health and contraception methods in women. *Journal of Mazandaran University of Medical Sciences.* 2015. 25(130), pp. 30-39
- 44- Ghazavi A, Abbasi E, Nikibakhsh A, Sadeghi E, Sadeghimanesh J. Comparison of prophylactic effect of clobazam and diazepam in children with simple febrile convulsion (SFC). *International Journal of Tropical Medicine.* 2016. 11(2), pp. 21-23
- 45- Anbari K, Sahraei N, Ahmadi SAY, Baharvand P. Barriers of breast cancer screening from the viewpoint of women in Khorramabad (West of Iran). *Research Journal of Pharmaceutical, Biological and Chemical Sciences.* 2016. 7(6), pp. 2044-2049
- 46- Nejad DB, Azandeh S, Gholami MR, Gharraei AM, Zhaleh M. Superficial palmar arch with Persistent median artery. *Journal of the Anatomical Society of India.* 2016. 65(2), pp. 175-176
- 47- Sane S. The Effect of intrathecal fentanyl on Bi-spectral index during spinal anesthesia in patients with lower limb orthopedic surgery. *Journal of Global Pharma Technology.* 2016. 8(12), pp. 435-440
- 47- Sane S, Khoshkbar M, Abbasyvash R, Mahoori AR. Evaluation of the effect of preoperative oral Tizanid in on the rate of anesthetic consumption & hemodynamic changes in TIVA (total intravenous anesthesia). *Journal of Global Pharma Technology.* 2016. 8(12), pp. 441-446
- 49- Farhadifar F, Molina Y, Taymoori P, Akhavan S. Mediators of repeat mammography in two tailored interventions for Iranian women Health behavior, health promotion and society. *BMC Public Health.* 2016. 16(1)
- 50- Macoie AA, Nikibakhsh AA, Vatan AE, Rasmi Y. Comparing the serum total antioxidant capacity in children suffering from Henoch-Schönlein purpura in both active and remissive phase of the illness. *Acta Medica Mediterranea.* 2015. 31(7), pp. 1405-1409.
- 51- Sadeghi E, Gozali N, Tabrizi FM. Effects of energy conservation strategies on cancer related fatigue and health promotion lifestyle in breast cancer survivors: A randomized control trial. *Asian Pacific Journal of Cancer Prevention.* 2016. 17(10), pp. 4783-4790
- 52- Darvishi M, Sadeghi SS. Evaluation of association of helicobacter pylori infection and coronary heart disease (CHD) among CCU patients. (2016) *Journal of Pure and Applied Microbiology*, 10 (4), pp. 2621-2626.
- 53- Valizadeh R, Taymoori P, Yousefi F, Rahimi L, Ghaderi N. The effect of puberty health education based on health belief model on health behaviors and preventive among teen boys in Marivan, North West of Iran. *International Journal of Pediatrics.* 2016. 4(8), pp. 3271-3281
- 54- Farhidnia N, Memarian A. Congenital anomalies following use of isotretinoin: Emphasis on its legal aspects. *Med Leg J.* 2017 Mar;85(1):33-34. doi: 10.1177/0025817216668720. Epub 2016 Sep 25.
- 55- Mehrpisheh S, Mosayebi Z, Memarian A, Kadivar M, Nariman S, Ostadrahimi P, Dalili H. Evaluation of specificity and sensitivity of gastric aspirate shake test to predict surfactant deficiency in Iranian premature infants. *Pregnancy Hypertens.* 2015 Apr;5(2):182-6. doi: 10.1016/j.preghy.2015.01.006. Epub 2015 Feb 21.
- 56- Ameri M, Memarian A, Behtash N, Karimi Zarchi M. The importance of re-examination with deep biopsies in diagnosing cervical malignancies despite multiple negative pathology reports: A case report. *Int J Surg Case Rep.* 2015;14:48-9. doi: 10.1016/j.ijscr.2015.07.010. Epub 2015 Jul 21.
- 57- Memarian A, Ameri E, Aghakhani K, Mehrpisheh S, Ameri M. The epidemiology of lower extremities injuries in Iranian population. *Iran J Public Health.* 2016 Jul;45(7):960-1.

- 58- Kazemi S, Khayati G, Faezi-Ghasemi M. β -galactosidase production by *Aspergillus niger* ATCC 9142 using inexpensive substrates in solid-state fermentation: Optimization by orthogonal arrays design. *Iranian Biomedical Journal*. 2016. 20(5), pp. 287-294
- 59- Rastegarian A, Jahromi MJ, Sanie MS, Kalani N. Comparing the anxiety of children when entering and leaving the operating room with and without the presence of parents. *Journal of Global Pharma Technology*. 2016. 8(6), pp. 42-46
- 60- Darvishi M. Antibiotic resistance pattern of uropathogenic methicillin-resistant staphylococcus aureus isolated from immunosuppressive patients with pyelonephritis. (2016) *Journal of Pure and Applied Microbiology*, 10 (4), pp. 2663-2667.
- 61- Sotoudeh A, Jahanshahi A, Zareiy S, Darvishi M, Roodbari N, Bazzazan A. The influence of low-level laser irradiation on spinal cord injuries following ischemia-reperfusion in rats. *Acta Cir Bras*. 2015 Sep;30(9):611-6.
- 62- Rashidpanah M, Abolghasemi J, Toosi MN, Salehi M. Investigating the different stages in the progress of cirrhosis using the Markov model. *Govaresh*. 2016. 21(3), pp. 157-166
- 63- Taymoori P, Molina Y, Roshani D. Effects of a randomized controlled trial to increase repeat mammography screening in Iranian women. *Cancer Nursing*. 2015. 38(4), pp. 289-297
- 64- Behnam Soboti , Shima Javadinia , Samileh Noorbaksh , Ramin Asgarian , Nastaran Khosravi , Azardokht Tabatabaee . Diagnostic value of the level of interleukins in cerebrospinal fluid in children meningitis. *Tehran Univ Med J* 2015, 72(12): 847-853.
- 65- Poorgholami F, Mansoori P, Montaseri Z, Najafi K. Effect of self care education with and without telephone follow-up on the level of hope in renal dialysis patients: A single-blind randomized controlled clinical trial. *International Journal of Community Based Nursing and Midwifery*. 2016. 4(3), pp. 256-264
- 66- Taheri L, Kargar Jahromi M, Hojat M. Comparison Patients and Staffs Satisfaction in General Versus Special Wards of Hospitals of Jahrom. *Glob J Health Sci*. 2015 Apr 2;7(6):95-100. doi: 10.5539/gjhs.v7n6p95.
- 67- Aghamohammadzadeh N, Niafar M, Dalir Abdolahinia E, Najafipour F, Gharebaghi SM, Adabi K, Abdolahinia ED, Ahadi, H. The effect of pioglitazone on weight, lipid profile and liver enzymes in type 2 diabetic patients. 2015. *Therapeutic Advances in Endocrinology and Metabolism*. 6(2), pp. 56-60.
- 68- Arazpour M, Samadian M, Bahramizadeh M, Joghtaei M, Maleki M, Ahmadi Bani M, Hutchins SW. The efficiency of orthotic interventions on energy consumption in paraplegic patients: A literature review. *Spinal Cord*. 2015 Mar;53(3):168-175. doi: 10.1038/sc.2014.227. Epub 2015 Jan 20.
- 69- Lubin AS, Snyderman DR, Ruthazer R, Bide P, Golan Y. Predicting high vancomycin minimum inhibitory concentration in methicillin-resistant *Staphylococcus aureus* bloodstream infections. *Clin Infect Dis*. 2011 Apr 15;52(8):997-1002. doi: 10.1093/cid/cir118.
- 70- Salari MH, Sohrabi N, Kadkhoda Z, Khalili MB. Antibacterial effects of enoxolone on periodontopathogenic and capnophilic bacteria isolated from specimens of periodontitis patients. *Iranian Biomedical Journal*. 2013. 7(1), pp. 39-42
- 71- Badri R, Shushizadeh MR A new method for the oxybromination of aromatic compounds with copper(II)bromide and potassium dichromate. 2005. *Phosphorus, Sulfur and Silicon and the Related Elements*. 180(2), pp. 533-536.
- 72- Badri R, Shushizadeh MR. An efficient tandem oxidative-protection reaction of benzylic alcohols to corresponding arylhydrazones and oximes. 2007. *Phosphorus, Sulfur and Silicon and the Related Elements*. 182(3), pp. 601-60
- 73- Khademvatan K, Alinejad V, Eghtedar S, Rahbar N, Agakhani N. Survey of the relationship between metabolic syndrome and myocardial infarction in hospitals of Urmia University of medical sciences. *Global journal of health science*. 2014. 6(7), pp. 58-65.