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## Protective effect of almond oil and primrose oil on neurochemical and lipid profile in ovariectomized rats

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## ABSTRACT

**Introduction:** Ovariectomies rats were used to assess the preventive effects of almond and primrose oils on their lipid and neurochemical profiles.

**Methods:** The experimental groups were as follows: Group 1: A negative control group. Group 2: Rats given an oral dose of almond oil (800 mg/kg/d) for 30 days. Group 3: Rats given an oral dose of primrose oil (500 mg/kg/d) for 30 days. Group 4: Untreated ovariectomized rats. Group 5: Ovariectomized rats given an oral dose of almond oil (800 mg/kg/d) for 30 days. Group 6: Ovariectomized rats given an oral dose (500 mg/kg/d) of primrose oil daily for 30 days.

**Results:** Oral administration of almond and primrose oils significantly decreased mean (P < 0.05) serum total cholesterol (TC), triacylglycerol (TG), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C) concentrations and raised high-density lipoprotein cholesterol (HDL-C) in the ovariectomized groups compared to group 4 (P < 0.05). They also increased leptin and estradiol (E2) concentrations in groups 5 and 6. Administration of oils showed a marked increase in noradrenalin, dopamine, and 5-hydroxytyramin levels and a marked decrease in PGE2 and COX-2 levels (P < 0.05). Rats given almond and primrose oils revealed minor capillary congestion in the hippocampus in brain sections.

**Conclusion:** Administration of almond or primrose oils may improve central nervous system functions and decrease the risk of cardiovascular illnesses. They also might be effective against atherosclerosis, inflammation, endocrine disorders, and cognitive impairments for women who undergo surgical menopause prior to their natural menopause.

*Implication for health policy/practice/research/medical education:* 

Almond and primrose oils improved the lipid and neurochemical parameters in ovariectomized rats and ameliorated the histological changes in the rat hippocampal brain tissue. These essential oils might be recommended to physicians as for the treatment of cardiovascular disorders and mood and memory defects in ovariectomized women.

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## Introduction

Women over 50 now live roughly the third of their lives in an oestrogen-deficient state (1). Growing health issues like osteoporosis, cardiovascular disease, cancer, and neurological diseases are linked to this natural aging process in women. Rodents display age-related cognitive loss just like humans do, making them suitable research subjects. The impact of female sex hormones on cognition is possible (2). Following menopause, oestrogen deprivation causes a variety of atypical symptoms, such as osteoporosis and weight gain (3,4). In the hippocampus, in particular, it causes apoptosis, neuronal death, and cognitive impairment (5). As a result, numerous investigations have concentrated on creating treatment approaches like hormone replacement and comprehending their principles (6-8).

Menopausal women's claimed memory problems may be primarily caused by drops in steroid hormone levels, especially estradiol (E2) (9). During the menopause transition, many women express concerns about changes to their cognitive performance(10).

Changes in the morphology and neurochemistry of the cortex and hippocampus have been linked to ovarian removal. E2 prevents ovariectomy-induced fast declines in

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hippocampal CA1 pyramidal cell dendritic spine density in rats (11).

Estrogens have a significant impact on adult females' cognitive functioning, and their absence has been linked to mood swings (12) and memory problems (13). These findings show that the lack of estrogenic activities on the cells that innervate the affected cells, resulting in compensatory reactions in the target cells, may be the cause of alterations in cell shape brought on by ovariectomy. In fact, decreased cholinergic activity in the cortex and hippocampus is a consequence of oestrogen depletion (14).

A good source of nutrients linked to the functioning of the brain includes vitamin E, as well as mono- and poly-unsaturated fatty acids (PUFAs), arginine, and potassium, which are all present in almond replacement treatment. As RRR-tocopherol, almonds are one of the foods with the highest vitamin E content. Approximately 49% of almonds are made up of oils, of which 62% are mono-unsaturated oleic acid (an omega-9 fatty acid), 24% are poly-unsaturated linoleic acid (an essential omega-6 fatty acid), and 6% are palmitic acid (a saturated fatty acid) (11). In addition, they are abundant in monounsaturated fat, dietary fibre, B vitamins, and important minerals. Additionally, phytosterols found in almonds (Prunus dulcis) are thought to have cholesterol-lowering effects. By preventing the absorption of cholesterol, phytosterols serve to regulate blood levels of TC, lowdensity lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (LDL-C), which reduces the risk of cardiovascular disease (12).

All membrane structures in the body depend on essential fatty acids used to make prostaglandins, which control the immune system. Skin rashes, hair loss, and reduced immunity can all be symptoms of a prostaglandin shortage (15). Gamma linolenic acid is one of the most significant unsaturated fatty acids involved in the formation of advantageous prostaglandins. Numerous medical investigations have concentrated on evening primrose oil and gamma-linolenic acid (GLA). According to some of these research results, taking supplements of evening primrose oil can increase natural immunity, lower cholesterol and blood pressure, as well as treat eczema, diabetes, osteoporosis, and premenstrual syndromes (13).

Dietary lipids are now understood to have direct impacts on the brain rather than affecting their effects on cardiovascular functions. Normal cell membrane composition and normal brain function both depend on omega-3 PUFAs. There is universal agreement that the lack of omega-3 fatty acids in rodents impairs learning and memory, despite the wide variation in the design of tests to assess the action of various dietary components on cognitive functions (16). Humans' dietary deficiencies in omega-3 fatty acids have been linked to an increased risk of a number of mental illnesses, including schizophrenia, attention deficit disorder, dyslexia, dementia, depression, and bipolar disorder (17).

Vitamin E, known as tocopherol, has also been linked to cognitive function, with declining serum levels of vitamin E being linked to deteriorating memory function in older people (18). Vegetable oils, almonds, green leafy vegetables, and fortified cereals are rich sources of vitamin E, which has been found to increase lifespan in elderly mice as well as mitochondrial function and neurological performance. Through the analysis of the rats' neurochemical profiles, this study sought to understand the impact of almond oil or primrose oil on rats cognitive performance after ovariectomies.

## Materials and Methods

## Animals

A total of 36 female albino rats of the Sprague Dawley strain with body weights ranging from 200 to 220 g were purchased from the animal breeding unit of the National Research Centre, Giza, Egypt. The rats were allowed free access to water ad libitum and were fed a standard pellet diet. They were housed for at least one week before starting the experiment. Animals were housed in polypropylene cages ( $47 \times 34 \times 18$  cm) in an air-conditioned room with 55% of humidity, controlled temperature ( $25 \pm 2^{\circ}$ C), and automatic lighting (alternative 12 hours periods of light and dark) throughout the duration of the study. The study follows the protocols approved by the local institutional animal ethics committee of Ain Shams University.

## Chemicals

All chemicals, including the kits, were purchased from a local distributor (Sigma chemical) in Cairo, Egypt. Almond oil and primrose oil were purchased from Nefertiti company for natural oils and herbs in Cairo, Egypt.

#### Ovariectomy

Nembutal (40 mg/kg) was injected intraperitoneally to anaesthetize the rats. From the hip to the lowest rib, the fur on both sides of the body was shaved. 1.5 cm inferior to the palpable rib cage, a 1.5 cm incision was used to execute bilateral ovariectomies. The incision was closed by suturing the muscles and stapling the skin after the removal of the ovaries and surrounding adipose tissue. The animals were placed on paper towels in a cage that was kept at a constant temperature while the antibiotic gel was given to the wound.

#### Experimental design

Animals were divided into 6 groups of 6 animals each.

- Group 1: Rats were fed on a basal diet (BD) and served as a negative control group with oral administration of distilled water.
- Group 2: Rats received an oral dose of almond oil (800 mg/kg/d) for 30 days (18).

- Group 3: Rats received an oral dose of primrose oil (500 mg/kg/d) for 30 days.
- Group 4: Untreated ovariectomized rats received an oral administration of distilled water.
- Group 5: Ovariectomized rats received an oral dose of almond oil (800 mg/kg/d) for 30 days.
- Group 6: Ovariectomized rats received an oral dose of (500 mg/kg/d) of primrose oil daily for 30 days.

## Blood parameters

After 24 hours of fasting following the final treatment, animals were weighed and then slaughtered by decapitation at the end of the experiment. Blood samples were drawn into sterile, dry centrifuge tubes and allowed to clot at room temperature for 15 minutes. Blood serum was then separated by centrifuging at 1000 g for 10 minutes. Using a Pasteur pipette, the serum was gently aspirated into dry, clean Eppendorf tubes and then stored at -20°C until analysis. For tissue analyses, the brain was removed and weighed.

Serum was used to estimate lipid profile, TC (19), triacylglycerols (TG) (20), and HDL-C (21). Finally, serum the LDL-C was calculated using the equation of [total cholesterol-(triglycerides/5)-HDL-cholesterol], and VLDL-C was calculated using the equation of (22). Also, the estimation of E2 was done by using the rat/mouse E2 ELISA kit (Calbiotech Co., USA). The assay steps were followed according to the manufacturer's pamphlet and serum leptin was estimated using Diagnostic system Laboratory, Inc., Active Leptin ELISA Kit, Catalog No. DSL-10- 24100.

Tissue homogenate for the quantitative determination of rat cyclooxygenase-2 (COX-2) and rat prostaglandin E2 (PGE2) concentrations was done by the ELISA kits; 100 mg brain tissue slices were rinsed with  $1 \times$  PBS (phosphatebuffered saline) homogenized in 1 mL  $1 \times$  PBS and stored overnight at -20°C. After two freeze-thaw cycles were performed to break the cell membrane, the homogenates were centrifuged for 5 minutes at 5000 g, 2-8°C. The supernatant was removed and assayed immediately. The sample was centrifuged again after thawing, then the concentrations of noradrenaline (NA), dopamine (DOP), and 5-hydroxytriptamine (5-HT) were determined in the selected brain regions using high-performance liquid chromatography with electrochemical detection (HPLC-ED).

## Histological examination

Brain samples were dehydrated in increasing alcohol series for 48 hours, embedded in paraffin wax, and fixed for 48 hours in 10% buffered formalin. Hematoxylin-eosin (H&E) was used to stain slices that were around 5 mm thick in order to examine general morphology. An expert histologist who was not informed of the experimental groups performed histological evaluations using an Olympus BX 51 photomicroscope (Tokyo).

## Statistical analysis

The mean and standard deviation (SD) of 10 replicate measurements were used to express the data. One-way analysis of variance (ANOVA) was used in statistical analysis to determine whether there were any notable differences between the various groups (23). When P < 0.05, the findings were deemed significant. Version 16 of the statistical analysis program SPSS Modeler was used for all calculations.

## Results

## Biochemical measurements

#### TC, TG, LDL-C, HDL-C, and VLDL-C in serum

The mean concentrations of serum TC, TG, LDL-C, and VLDL-C were significantly high (P < 0.05) in ovariectomized rats group compared to the control group, and also when compared with the groups 2 and 3 (Table 1). Supplementation with almond and primrose oils to rats of groups 5 and 6 caused significant improvement in the concentrations of TC, TG, LDL-C, and VLDL-C. There was also a significant decrease in the HDL-C in ovariectomized rats of group 4 compared to the control

Table 1. Effect of almond oil ar	id primrose oil on the serum	lipid parameters in healthy	and ovariectomized rats

Groups	TC (mg/dL)	TG (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)
Group 1	91 ± 0.89ª	105.15 ± 1.10 <sup>a</sup>	20.49 ± 0.36°	50.294 ± 1.24ª	21.03 ± 0.22 <sup>a</sup>
Group 2	$90 \pm 0.90^{\circ}$	110.14 ± 1.15 <sup>b</sup>	$21.66 \pm 0.31^{b}$	47.197±0.34 <sup>b</sup>	22.02 ± 0.23 <sup>b</sup>
Group 3	80 ± 0.53 <sup>b</sup>	96.43 ± 0.78°	19.12 ± 0.20 <sup>cd</sup>	43.752±0.62°	19.28 ± 0.15°
Group 4	103 ±0.69°	118.20±1.60 <sup>d</sup>	18.15 ±0.41 <sup>d</sup>	57.710±0.36 <sup>d</sup>	23.64 ±0.18 <sup>d</sup>
Group 5	97 ±0.38 <sup>d</sup>	106.20±0.95d	18.79 ±0.36 <sup>d</sup>	57.596±0.52 <sup>d</sup>	21.24 ±0.24 <sup>d</sup>
Group 6	96 ±0.41 <sup>e</sup>	100.40±1.40 <sup>e</sup>	18.96 ±0.40 <sup>e</sup>	56.707±0.04 <sup>d</sup>	20.08 ±0.48 <sup>e</sup>

TC, Total cholesterol; TG, Triacylglycerols; HDL-C, High-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; VLDL-C, very low-density lipoprotein-cholesterol.

All values are expressed as the mean of 6 rats ± standard deviation.

There is a significant difference between means having different letters in the same column (P < 0.05).

Groups 1 to 6: Control group receiving normal diet, rats receiving almond oil (800 mg/kg/d), rats receiving primrose oil (500 mg/kg/d), untreated ovariectomized rats, ovariectomized rats receiving almond oil (800 mg/kg/d), ovariectomized rats receiving (primrose oil 500 mg/kg/d) daily for 30 days, respectively.

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group, while treatment with almond and primrose oils increased (P < 0.05) the concentration of HDL-C (Table 1).

## *Leptin and E*<sup>2</sup> *concentrations in serum*

There was a significant increase (P < 0.05) in serum leptin and E2 in groups 2 and 3 compared to negative control group. On the other hand, a significant decrease (P < 0.05) was observed in leptin and E2 in ovariectomized rats group. Also, almond and primrose oils significantly increased their concentrations in groups 5 and 6 when compared with the control group and also ovariectomized rats group (Table 2).

# *Neurotransmitters concentrations (NA, DOP, and 5-HT) in brain areas*

The levels of brain NA, DOP, and 5-HT were significantly decreased in the ovariectomized group compared to the control group. In addition, almond oil and primrose oil were effective on the levels of NA, DOP, and 5-HT in the hippocampus area, 4 weeks after the administration of oils (P<0.05) (Table 3).

**Table 2.** Effect of Almond oil and Primrose oil on Leptin and Estradiol

 Concentration in healthy and ovariectomized rats

Parameter	Leptin (pg/mL)	Estradiol-2 (pg/mL)	
Group 1	6.048±0.06ª	1.672 ± 0.01ª	
Group 2	6.156±0.04ª	1.76 ± 0.03 <sup>b</sup>	
Group 3	5.418±0.08 <sup>b</sup>	2.04 ± 0.02°	
Group 4	4.351±0.07°	$1.26 \pm 0.04^{d}$	
Group 5	5.016±0.06°	$1.41 \pm 0.03^{e}$	
Group 6	5.179±0.08 <sup>d</sup>	$1.32 \pm 0.01^{f}$	

All values are expressed as the mean of 6 rats  $\pm$  standard deviation (*P* < 0.05) significant. There is a significant difference between means having different letters in the same column (*P* < 0.05).

Groups 1 to 6: Control group receiving normal diet, rats receiving almond oil (800 mg/kg/d), rats receiving primrose oil (500 mg/kg/d), untreated ovariectomized rats, ovariectomized rats receiving almond oil (800 mg/kg/d), ovariectomized rats receiving (primrose oil 500 mg/kg/d) daily for 30 days, respectively.

## Changes in PGE2 and COX2 concentrations

The levels of brain PGE2 and COX2 were significantly increased in the ovariectomized group (4) compared to the control group. Also, almond oil and primrose oil decreased (P<0.05) the levels of PGE2 and COX2 (Table 3).

## Histopathological studies

Sections of the cortex and cerebrum stained with hematoxylin and eosin were examined under a light microscope. The usual complete histological structure of the cerebral cortex was discovered in the control group, and no vascular injury or haemorrhages were noted (Figures 1A-1C). Transverse slices of the hippocampus that had undergone ovariectomy demonstrated neuronal degeneration. The regular arrangement of cell layers was disrupted. Larger cells with surrounding vascular gaps, localised gliosis in the cerebral cortex, and pyknotic neurons were present (Figures 1D and 1E). Figures 1F-1I show brain slices from animals that were given almond oil and primrose oil treatments had modest blood vessel congestion in the normal hippocampus.

#### Discussion

According to the study's findings, untreated ovariectomized rats had significantly higher serum levels of TC, TG, LDL cholesterol, and VLDL cholesterol, with lower levels of HDL cholesterol. According to certain investigations (24), ovariectomy raised TC and LDL-C levels, which facilitated the growth of atherosclerosis and CHD. In a rat model of ovariectomized rats, this study looked at the efficacy of almond and primrose oils in avoiding an increase in serum TC. Rats administered almond and primrose oils were chosen for this investigation because of their high antioxidant content. Plasma lipids are benefited from PUFAs (n-6 and n-3 series). The n-3 series primarily affect triglycerides, while the n-6 series are effective at lowering cholesterol (25).

According to our findings, therapy with almond oil significantly reduced the lipid profile changes caused by exposure to ovariectomy. Additionally, it was discovered

Groups	NA (ng/mg)	DOP (ng/mg)	5-HT (ng/mg)	PGE3 (ng/mg)	COX-2 (ng/mg)
Group 1	490 ± 5.64ª	379 ± 3.66ª	411 ± 3.6ª	17.65 ± 0.36°	17.37 ± 0.14ª
Group 2	494 ± 3.78 <sup>a</sup>	370 ± 3.78 <sup>b</sup>	422 ± 2.32°	14.99 ± 0.12 <sup>b</sup>	$16.31 \pm 0.11^{b}$
Group 3	494 ± 2.75°	374 ± 2.75 <sup>b</sup>	412 ± 2.24ª	15.51 ± 0.11 <sup>b</sup>	$16.03 \pm 0.10^{\text{b}}$
Group 4	$393 \pm 3.34^{b}$	316 ± 3.24°	$310 \pm 3.94^{b}$	24.86 ± 0.47°	26.32 ± 0.65°
Group 5	420 ± 3.24 <sup>c</sup>	$332 \pm 3.34^{d}$	331 ± 2.67°	22.45 ± 0.23 <sup>d</sup>	$23.11\pm0.31^{d}$
Group 6	432 ± 2.15 <sup>d</sup>	339 ± 2.15 <sup>e</sup>	343 ± 2.43 <sup>d</sup>	$20.98 \pm 0.12^{\circ}$	$21.60 \pm 0.19^{\circ}$

NA, noradrenaline; DOP, dopamine; 5-HT, 5-hydroxytryptamine; COX-2, cyclooxygenase-2; PGE2, prostaglandin E2.

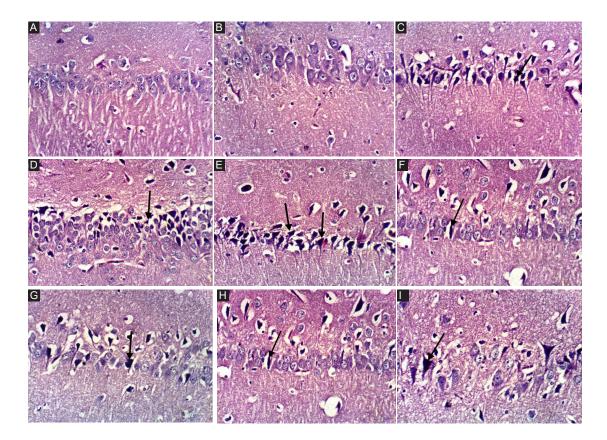
All values are expressed as mean of 6 rats  $\pm$  standard deviation (*P* < 0.05) significant.

There is a significant difference between means having different letters in the same column (P < 0.05).

Groups 1 to 6: Control group receiving normal diet, rats receiving almond oil (800 mg/kg/d), rats receiving primrose oil (500 mg/kg/d), untreated ovariectomized rats, ovariectomized rats receiving almond oil (800 mg/kg/d), ovariectomized rats receiving (primrose oil 500 mg/kg/d) daily for 30 days, respectively.

that evening primrose oil had positive impacts on lipid profiles and transaminase activity while receiving isotretinoin medication (26). In addition, in recent years, PUFAs have been advocated as a dietary modification to lower serum cholesterol (27). Almond oil is the main component of almonds that mediates its ability to decrease cholesterol (28). Almond oil showed a large reduction in cholesterol and TG levels. Almond oil includes a number of small components, including tocopherols, which may have beneficial biological effects (29). These substances have been shown to decrease cholesterol buildup in the arteries and shield the structural integrity of lipoproteins (30). Since almonds primarily contain oleic and linoleic acids, which are rich in unsaturated fatty acids and are poor in saturated fatty acids, cholesterol reduction associated with almond oil consumption has primarily been attributed to increased LDL-C receptor activity and increased bile acid and cholesterol excretion, as well as decreased absorption of cholesterol and bile acid (31). Almond oil is a great source of  $\alpha$ -tocopherol, which may improve the activity of many enzymes, including those involved in lipid decomposition. Additionally, almonds' polyphenolic components have recently undergone characterization and were discovered to have antioxidant properties (32). In particular, it causes apoptosis, neuronal death, and cognitive impairment in the hippocampus when oestrogen levels are low during menopause period (5). As a result, numerous investigations have concentrated on creating treatment approaches like hormone replacement and comprehending their principles (6-8). The ovariectomized rats group in the current study had significantly lower levels of leptin and E2. When compared to the control group and the ovariectomized rats group, the injection of almond and primrose oil considerably boosted their concentrations.

According to the current study, the amount of acetylcholine in the hippocampus and frontal cortex after long-term almond administration was positively connected with memory retention, indicating the role of acetylcholine in the memory-enhancing effects of long-term almond administration (33). The cortex and hippocampus have undergone morphological and neurochemical changes as a result of ovarian removal. E2 prevents the fast declines in hippocampal CA1 pyramidal



**Figure 1.** (A) Hippocampus of rat from negative control group showing no histopathological changes (H & E ×400). (B) Hippocampus of rat from group 2 (healthy rats administered almond oil) showing no histopathological changes (H & E ×400). (C) Hippocampus of rat from group 3 (healthy rats administered primrose oil) showing no histopathological changes (H & E ×400). (D, E) Hippocampus of rat from ovariectomized group 4 showing necrosis, pyknosis, and atrophy of hippocampus neurons (H & E ×400). (F, G) Hippocampus of rat from group 5 (ovariectomized rats administered Almond oil) showing pyknosis of some hippocampus neurons (H & E ×400). (H) Hippocampus of rat from group 6 (ovariectomized rats administered primrose oil) showing pyknosis of some hippocampus neurons (H & E ×400). (I) Hippocampus of rat from group 6 (ovariectomized rats administered primrose oil) showing pyknosis of sporadic hippocampus neurons (H & E ×400). (I) Hippocampus of rat from group 6 (ovariectomized rats administered primrose oil) showing pyknosis of sporadic hippocampus neurons (H & E ×400). (I) Hippocampus of rat from group 6 (ovariectomized rats administered primrose oil) showing pyknosis of sporadic hippocampus neurons (H & E ×400). (I) Hippocampus of rat from group 6 (ovariectomized rats administered primrose oil) showing pyknosis of sporadic hippocampus neurons (H & E ×400).

cell dendritic spine density that occur in rats after ovariectomy (11).

Fruits, seeds, and whole grains are abundant sources of phytoestrogens. These phytoestrogens consist of coumestans, lignans, and isoflavones. Similar to endogenous oestrogen in chemical structure, phytoestrogens bind to oestrogen receptors and influence glucose and lipid metabolism, as well as calcium absorption (34) to enhance cognition, neuronal survival, reproductive behaviour, emotion, and sexual differentiation (35).

The current study showed that in rats with oestrogen deficiency, the phytoestrogens in almond and primrose oils reduced the risk of obesity. In this study, ovariectomy lowered serum leptin concentrations; however, supplementation with almond and primrose oils counteracted this impact by raising circulating leptin levels. Rat colon leptin receptor expression is decreased after ovarian removal but is restored with 17-estradiol therapy (36), supporting our findings. Furthermore, 17-beta-estradiol (E2) ovariectomized in mice hippocampal neurons enhances spine synapse density and promotes long-term potentiation. E2 enhances hippocampus-dependent memory, which is consistent with these positive effects on the cellular level (37).

The ovariectomized group had much lower levels of the brain chemicals NA, DOP, and 5-HT than the control group did. Additionally, 4 weeks following the administration of the oils, a significant raise in the levels of NA, DOP, and 5-HT were seen in the hippocampal area, demonstrating the effectiveness of almond oil and primrose oil on these markers. According to the current study, female albino rats given oral doses of almond and primrose oils had significantly higher levels of DOP, gamma-aminobutyric acid (GABA), and 5-HT in various brain regions, including the cerebellum, striatum, cerebral cortex, hypothalamus, brain stem, and hippocampus. The increased levels of NA, DOP, 5-HT, and GABA in the various CNS regions of albino rats could be attributed to the Ca2+/calmodulin binding being inhibited, which is crucial for the release of neurotransmitters. The release of 5-HT and NA into the extracellular environment was interestingly enhanced by the addition of linoleic acid to these cells (37).

Depression's telltale signs and symptoms are brought on by the lack of 5-HT. Regarding the pathophysiology of depression, the 5-HT hypothesis is currently the mainstream theory (38). The regulation of several processes, including neurotransmission and signaling pathways by fatty acids and some of their metabolites in certain brain regions has an impact on emotional behaviour (39). The use of circulating lipids as biomarkers to predict response to medication needs more research, even if they can distinguish between those who are sad and those who are not.

Numerous investigations have shown that essential oils (EOs) have an impact on the serotonergic system. The

olfactory system and the respiratory system are the two separate mechanisms through which EO molecules may enter the brain and have an impact. Following inhalation, the molecules of the EOs would either enter the respiratory tract or directly affect the olfactory mucosa. These two delivery methods imply various underlying action mechanisms. Increased neurogenesis, hormone level regulation, activation of various brain regions, and changes in blood biochemistry are just a few of the multiple sets of responses that would be set off, which would eventually affect mood and emotion (40).

compared to the control group, the When ovariectomized group's levels of brain PGE2 and COX2 were considerably higher. Additionally, when compared to the ovariectomized untreated group, the levels of PGE2 and COX2 were significantly lower after the administration of primrose and almond oils. Plasma levels of a-linolenic acid and its metabolite dihomo-linolenic acid raises as a result of evening primrose oil administration. In the presence of cyclooxygenase, this molecule is converted to series 1 prostaglandins or oxidized by 15-lipoxygenase to 15-hydroxyeicosatrienoic acid. These substances possess both anti-inflammatory and anti-proliferative properties (41). The GLA concentration of evening primrose oil is principally responsible for its bioactivity. After ingesting evening primrose oil, GLA is quickly absorbed and subsequently converted directly to dihomogamma-linolenic acid (DGLA) and other prostaglandin precursors (42,43), bypassing the rate-limiting phase in the metabolism of linolenic acid. This acts on the prostanoid pathway.

Cells in the various levels of the cerebral cortex were found to be disorganized histologically in the group of ovariectomized rats in the current investigation. The cells' layering configuration was severely disturbed. The circulatory gaps around the cells were enormous, and the cells themselves seemed to be larger. The Purkinje cell layer was completely separated from the granular cell layer when visibility was high. These alterations are related to changes that occur in the hippocampus. Using quantitative histological methods, the morphometric evaluation demonstrated absolute increases in the number of injured cells in all brain regions of the ovariectomized rats group and significant interstitial edema. Our findings are supported by a recent research that found problems in the structure of cognitive function in addition to the loss of neurons in the hippocampus and hypothalamus as a result of hormonal changes brought on by aging (44). Primrose oil is more effective than almond oil at protecting against atherosclerosis, inflammation, and endocrine problems, and it may be required to do so for women who undergo surgical menopause prior to their natural menopause.

## Conclusion

The central nervous system was strengthened by almond or primrose oil, which may be safe for use as a sedative and reduce the risk of cardiovascular disorders. The use of almond and primrose oil as a preventative measure against atherosclerosis, inflammation, and endocrine disorders suggests the need for safeguards against cognitive impairments for women who undergo surgical menopause prior to their natural menopause. Because bitter almond oil and primrose oil include phytochemical components and EOs utilized for antioxidative and therapeutic purposes, they can be blamed for the favourable effects that were seen.

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## Authors' contribution

Sharaf EH and Kamel EA designed and performed all experiments and biochemical analyses. Sharaf EH and Hassan MM prepared and wrote the whole manuscript, interpreted and discussed the results. All authors read and approved the final manuscript for publication.

## **Conflict of interests**

The Authors declare that they have no conflict of interest.

## **Ethical considerations**

All authors declare that principles of laboratory animal care (National Institute of health guide for care and use of laboratory Animals) (NIH Publication No. 85-23 received 1985) were followed. All experiments have been examined and approved by the appropriate ethics committee, Cairo University (IACUC NO. 1552: on 3/12/2019).

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