

Effects of *Pistacia terebinthus* L. Subsp. *palaestina* and *Rhus coriaria* L. Plants on Some Biochemical Parameters of Brain Tissue of Sprague-Dawley Rats in Experimental Breast Cancer Model

Figen Erdem ERISIR¹, Oguz Ayhan KIRECCI², Okkeş YILMAZ³, Ayse Dilek ÖZSAHİN⁴

^{1,3}Fırat University, Faculty of Science, Department of Biology, Elazığ, ²Bitlis Eren University, Hizan Vocational School, Bitlis, ⁴Bitlis Eren University, Faculty of Science, Department of Biology, Bitlis

¹https://orcid.org/0000-0002-0499-9339, ²https://orcid.org/0000-0003-2205-4758, ³https://orcid.org/0000-0002-8276-4498

⁴https://orcid.org/0000-0002-1832-7082

✉: molekuler@gmail.com

ABSTRACT

In this study, the therapeutic effects of *Pistacia terebinthus* L. subsp. *Palaestina* (terebinth) and *Rhus coriaria* L (sumac) plants on DMBA-induced breast cancer in 66 female Sprague-Dawley rats were investigated through biochemical analysis. The rats were divided into 6 groups as Control, DMBA (7.12-Dimethylbenzanthracene), PT (terebinth), RC (sumac), PT+DMBA and RC+DMBA. DMBA was administered to 8-week-old rats via gavage, a single dose of 80 mg/kg according to body weight. Aqueous extracts of terebinth and sumac were given orally to rats in antioxidant groups 3 days a week.

In biochemical studies, changes in activities of the antioxidant enzymes CAT (catalase), GST (glutathione transferase), and SOD (superoxide dismutase) in brain tissues as well as total protein, MDA (malondialdehyde), GSH (glutathione), fatty acid, and vitamin levels were determined. Total protein levels generally reduced in the DMBA group compared to the control group ($p<0.05$) while the levels of the MDA in the DMBA brain tissue groups elevated compared to the control group and reduced in antioxidant groups ($p<0.01$; $p<0.001$). Cholesterol levels and lipophilic vitamins were determined by HPLC. Their grades were different in the DMBA and antioxidant groups. Fatty acids were analyzed by GC. As a result of analysis, fatty acids such as palmitic, palmitoleic, stearic, oleic, linoleic, arachidonic, and docosahexaenoic were high in the tissues examined ($p<0.01$; $p<0.001$). The fatty acid levels were also found to vary in the DMBA and antioxidant tissue groups. These data suggest that *Pistacia terebinthus* and *Rhus coriaria* plants can be used against breast cancer and to reduce its negative outcomes, and studies should be continued for their safe medical application.

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Sprague-Dawley Sıçanlarda Deneysel Meme Kanseri Modelinde *Pistacia terebinthus* L. Subsp *palaestina* ve *Rhus coriaria* L. Bitkilerinin Beyin Dokusunun Bazı Biyokimyasal Parametreleri Üzerindeki Etkileri

ÖZET

Bu çalışmada, dişi 66 Sprague-Dawley ratında DMBA ile indüklenen meme kanserine karşı *Pistacia terebinthus* L. subsp *Palaestina* (terebinth) ve *Rhus coriaria* L. (sumak)'nin iyileştirici etkileri biyokimyasal olarak incelendi. Sıçanlar, Kontrol, DMBA (7.12-Dimetilbenzantrasene), PT (menengiç), RC (sumak), PT+DMBA ve RC+DMBA olmak üzere 6 gruba ayrıldı. DMBA, vücut ağırlıklarına göre, tek doz 80 mg/kg olacak şekilde, gavaj yoluyla, 8 haftalık dişi Sprague-Dawley sıçanlara uygulandı. Antioksidan gruplarındaki ratlara oral yolla menengiç ve sumak'ın sulu ekstraktları verildi. Biyokimyasal çalışmalarda beyin dokusunda antioksidan enzimler olan CAT (katalaz), GST (glutasyon transferaz) ve SOD (süperoksit dismutaz) aktivitelerindeki değişiklikler, total protein, MDA,

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(malondialdehit) GSH (glutatyon), yağ asidi ve vitamin düzeyleri belirlendi. Toplam protein seviyelerinin genellikle DMBA grubunda kontrole göre azaldığı gözlemlendi ($p<0.05$). DMBA beyin dokusu gruplarındaki MDA seviyeleri kontrol grubuna göre arttığı; antioksidan gruplarında azaldığı saptandı ($p<0.01$; $p<0.001$). Kolesterol seviyeleri ve lipofilik vitaminler HPLC ile belirlendi. DMBA ve antioksidan gruplarında bunların derecelerinin farklı olduğu görüldü. Yağ asitleri GC ile analiz edildi. Analiz sonucunda dokularda palmitik, palmitoleik, stearik, oleik, linoleik, araşidonik, dokosaheksaenoik gibi yağ asitlerinin yüksek olduğu bulundu ($p<0.01$; $p<0.001$). Bu yağ asidi seviyeleri DMBA ve antioksidan doku gruplarında değişiklikler gösterdi. Bu veriler, *Pistacia terebinthus* ve *Rhus coriaria* bitkilerinin meme kanseri ve olumsuzluklarına karşı bir uygulama olarak kullanılabilmesi, güvenli tıbbi uygulaması için çalışmaların sürdürülmesi önerilir.

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INTRODUCTION

International Agency for Research on Cancer reports that breast cancer is the most common cancer diagnosed among women and this cancer type is one of leading causes of death in them (Globocan, 2018; Sheokand et al., 2019).

The mortality rate of female breast cancer is 11.6% all over the world (Globocan, 2018). In the majority of countries (154 countries), breast cancer is the most common cancer in women in terms of new cases. The mortality profile among women was more heterogeneous, and breast cancer is the leading cause of cancer deaths in 103 countries (Globocan, 2018).

Some chemotherapy medications (paclitaxel, cyclophosphamide, carboplatin, and cisplatin) have also been commonly used in breast cancer treatments (Guerrero et al., 2010). Breast cancer cells tend to resist chemotherapeutic agents with different signal responses (Mundhe et al., 2015).

Epidemiological studies on diet and cancer have led to investigate anticarcinogenic agent-like nutraceuticals (Sheokand et al., 2019). Most cancer treatments include surgery, radiotherapy, chemotherapy, and immunotherapy. New chemotherapeutic agents and molecular-targeted drugs contribute to cancer treatment, but their toxicity and drug resistance result in the failure of chemotherapy. Therefore, researchers strive to discover few toxic and efficient bio-components for cancer therapy. In this regard, some herbs have played a leading role as an alternative in the discovery of new cancer preventative molecules (İçen et al., 2015).

Among medicinal plants, *Pistacia terebinthus* L. and

Rhus coriaria L. species belong to the Anacardiaceae family, which is used in alternative medicine. Extracts obtained from *Rhus coriaria* are used as pharmaceuticals (Verzele et al., 1985). It is reported that *R. coriaria* has anti-cancer activity and is a promising alternative treatment candidate (El Hasasna et al., 2016).

The effects of *Pistacia terebinthus* subsp. *palaestina* (terebinth), that it has the high antioxidant capacity and antioxidant properties, and effects of *Rhus coriaria* (sumac), that it has a chemotherapeutic treatment potential with its strong anti-breast cancer activity on biochemical parameters in brain tissue in DMBA-induced breast cancer model in rats were aimed in this work.

MATERIALS and METHODS

Animals and experimental protocols used in the study were approved by the Local Animal Experiments Ethics Committees of Fırat University (Elazığ, Turkey). Animal maintenance and experimental protocols were carried out in accordance with the NIH Guide for the Care and Use of Laboratory Animals (NIH publication no. 12.10.2016/181). Sixty-six healthy adult female Sprague-Dawley rats, aged 8 weeks were obtained from Fırat University Experimental Research Center (Elazığ, Turkey). The animals were kept in the polycarbonate cages with a 12-h/12-h day/night cycle, at temperature of $22\pm 3^{\circ}\text{C}$, with humidity of 45% to 65%. Throughout the experiment, the animals were regularly fed with a commercial diet (Elazığ Food Corporation, Elazığ, Turkey) *ad libitum*.

One of the groups was the control group. The other

groups were DMBA group (n=15), *Pistacia terebinthus* group (PT) (n=7), *Rhus coriaria* group (RC) (n=7), DMBA+ *Pistacia terebinthus* group (DMBA+PT) (n=15), DMBA+ *Rhus coriaria* group (DMBA+RC) (n=15). In the DMBA group 80 mg kg⁻¹ 7.12-dimethylbenz(a)anthracene was administered as a single dose according to Mundhe et al., (2015).

Pistacia terebinthus and *Rhus coriaria* extracts of 20 mg kg⁻¹ were added to 500 mL drinking water of the rats once per week (Chakraborty et al., 2009; Saglam et al., 2014). These treatments continued for 16 weeks and then each subject was decapitated with ether. Their brain tissue samples were dissected and stored at -85°C until biochemical analyses.

Preparation of homogenates

Tissue samples were homogenized in Tris-HCl buffer (pH 7.4) and centrifuged at 9050xg at 4°C for 15 min. Supernatants were gathered, processed, and stored at -70°C until they were used to identify MDA, glutathione (GSH), antioxidant enzymes (CAT, SOD and GST), and total protein. The pellets were used for ADEK vitamins, cholesterol, and fatty acid analysis.

Determination of MDA-TBA level

Lipid peroxidation was calculated as specified by Ohkawa et al., (1972).

Determination of GSH level in tissue samples

Reduced glutathione (GSH) was measured according to Ellman's (1959).

Lipid extraction

Hexane-isopropanol (3:2 v v⁻¹) was used for lipid extractions of tissue samples according to Hara and Radin (1978). Fatty acids in the lipid extracts were converted into methyl esters including 2% sulphuric acid (v v⁻¹) in methanol (Christie, 1999). Analysis of fatty acid methyl ester was performed in a Shimadzu GC-17A instrument gas chromatograph equipped with a flame ionization detector (FID) and a 25 m, 0.25 mm i.d. permabond fused-silica capillary column (Macherey-Nagel, Germany). The oven temperature was set between 145-215°C, 4°C/min. Temperatures Injector and FID were 240 and 280°C, respectively.

The results were calculated as mg/g tissue.

Saponification and extraction

Alpha-tocopherol and cholesterol were obtained from the lipid extracts according to Sanchez-Machado et al., (2004). They were identified by HPLC device.

Total protein assay

Total protein of the brain tissue was measured according to Lowry et al., (1951). For this purpose,

BSA (Bovin serum albumin) was used as standard. The absorbance was measured at 750nm as spectrophotometric.

Antioxidant Enzymes Analysis

Superoxide dismutase (SOD) (EC 1.15.1.1) activity was performed in terms of its capacity to inhibit the oxygen-dependent oxidation of adrenalin (epinephrine) to adrenochrome by xanthine oxidase plus xanthine (Panchenko et al., 1975).

Glutathione S-transferase (GST) (EC 2.5.1.18) activity was determined spectrophotometrically at 340 nm (Bell et al., 1985). As a result of decomposition of hydrogen peroxide (H₂O₂) with catalase, the decrease in absorbance at 240 nm was utilized to calculate catalase activity (Aebi, 1984).

Statistical analysis

One-way analysis of variance (ANOVA) and Post Hoc Tukey-HSD test were used to determine differences between the groups. Results are presented as mean ±S.E.M. Values were considered statistically significant at the level of p<0.05. The SPSS/PC program (Version 15.0; SPSS, Chicago, IL) was used for the statistical analysis.

RESULTS and DISCUSSION

Protein Values

Table 1 shows protein values of the brain tissue. When compared with the control group, a significant decrease (p<0.05) was observed in the DMBA group, but the changes in other groups were not statistically significant (p>0.05).

Table 1. Protein content of brain tissue (mg g⁻¹)
Çizelge 1. Beyin dokusunun protein içeriği (mg g⁻¹)

GROUPS	PROTEIN (mg g ⁻¹)
C	30.97±0.76
DMBA	27.88±0.50 ^b
PT	31.11±1.13 ^a
PT+DMBA	29.95±0.55 ^a
RC	30.01±0.59 ^a
RC+DMBA	29.29±0.37 ^a

d: p<0.001; c: p<0.01; b: p<0.05; a: p>0.05

The findings of the present study indicated that total protein levels of brain tissue significantly decreased in the DMBA group compared to the control group (p<0.05). Also, the differences in the other groups were not statistically significant (p>0.05). In another study, DMBA administration decreased total protein, albumin, and globulin levels while organoselenium compounds significantly increased total protein and albumin levels (Özdemir et al., 2007). In a study, the effects of cat's claw (*Uncaria tomentosa*), rosemary (*Salvia rosmarinus*), and hops (*Humulus lupulus*)

plants against hepatic toxicity induced by 7.12-DMBA were determined (El Kholy et al., 2013). As a result of the DMBA applications, serum and liver total proteins, total albumin, and globulin amounts significantly decreased. There was a significant decrease in serum total proteins, total albumin, globulin and liver total protein in the DMBA group. On the other hand, in addition to serum albumin and globulin, a remarkable improvement was observed in serum and hepatic total protein with the supplementation of these plants to rats treated with DMBA (El Kholy et al., 2013). In this study, total protein decreased with the application of DMBA. When DMBA and plant extracts were applied together, it was understood that the total protein content increased.

MDA Values

Table 2 shows MDA values of the brain tissue. While a significant decrease was found in MDA values of RC, PT+DMBA and RC+DMBA groups ($p<0.01$; $p<0.001$), there was a significant increase in the MDA value of DMBA group ($p<0.05$). However, the difference in the PT group was insignificant ($p>0.05$).

Table 2. MDA contents of the brain tissue (nmol gr⁻¹)
Çizelge 2. Beyin dokusunun MDA içeriği (nmol gr⁻¹)

GROUPS	MDA (nmol gr ⁻¹)
C	170.70±12.74
DMBA	181.13±6.66 ^b
PT	174.02±17.42 ^a
PT+DMBA	140.01±8.08 ^c
RC	110.79±9.37^d
RC+DMBA	132.31±7.98 ^c

d: $p<0.001$; c: $p<0.01$; b: $p<0.05$; a: $p>0.05$

When the MDA level of the brain tissue was examined in the present study, an important increase was observed in the DMBA group when compared to the control group ($p<0.05$). There were significant decreases in some antioxidant groups ($p<0.01$; $p<0.001$). The amount of malondialdehyde detected in the circulation is higher in advanced stages of breast cancer than the value reported in its early stages (Zarrini et al., 2016). It was also stated that the amount of the MDA determined in breast cancer patients was higher than the value of the control group patients (Coughlin, 2018). In the present study, the increase in the amount of the MDA in the DMBA groups was associated with oxidative stress. Oxidative stress plays a role in the development and metastasis of breast cancer (Jeziarska-Drutel et al., 2013). It was also determined that the MDA level decreased in the antioxidant groups. *P. terebinthus* are effective in the fight against oxidative stress.

GSH Values

Table 3 shows GSH values of the brain tissue. When examining GSH values based on the control group, it was found that there was a significant decrease in the DMBA, PT, PT+DMBA and RC+DMBA groups ($p<0.001$; $p<0.01$), but no statistically significant difference in the RC group ($p>0.05$).

Table 3. GSH values of the brain tissue (µg gr⁻¹)
Çizelge 3. Beyin dokusunun GSH değerleri (µg gr⁻¹)

GROUPS	GSH (µg gr ⁻¹)
C	121.91±6.69
DMBA	96.15±1.77 ^c
PT	106.64±7.24 ^b
PT+DMBA	99.82±3.36 ^c
RC	126.46±13.68 ^a
RC+DMBA	92.13±4.45^d

d: $p<0.001$; c: $p<0.01$; b: $p<0.05$; a: $p>0.05$

Glutathione level in brain tissue significantly decreased in the DMBA group ($p<0.01$). Likewise, a significant decrease ($p<0.001$) was detected in the RC+DMBA group. While GSH deficiency or a decrease in GSH/GSSG ratio causes an increased susceptibility to oxidative stress in advanced stage cancer. High GSH levels in most cancer cells support the antioxidant capacity and thus the defense mechanism against oxidative stress (Traverso et al., 2013). The fact that the amount of glutathione in the brain tissue in the DMBA groups was less than the amount of the control group is evidence of oxidative stress in the cancer groups.

Antioxidant Enzymes Activities

Catalase, glutathione S transferase and superoxide dismutase enzyme levels of the brain tissue were examined (Table 4). When the catalase enzyme was examined in the groups, the analysis revealed that the amount of enzyme decreased in all groups and this decrease was more significant in the RC+DMBA group ($p<0.001$). When the GST enzyme of the groups was compared with the value of the control group, it was observed that while the DMBA group showed a significant decrease ($p<0.001$), no statistical differences were found in the other treatment groups ($p>0.05$).

SOD enzyme activities were calculated as % inhibition and unit. There was a significant decrease in PT+DMBA and RC+DMBA groups ($p<0.01$) and a significant increase in the PT group in terms of the SOD level ($p<0.05$); whereas, there was no statistical difference in the RC group ($p>0.05$).

Antioxidant enzymes have important tasks against the negative effects of free radicals in cells. GST, one of these enzymes, is effective in the detoxification of carcinogenic and reactive oxygen species (Shokrzadeh

et al., 2019). It has been reported that the GSTP1 protein level is very low in the human breast cancer cell line MCF-7 (Dong et al., 2019). Similarly, in the study, it was determined that the GST activity in the

brain tissue was lower in the DMBA groups than the control group and this finding is compatible with the literature.

Table 4. CAT, GST and SOD activities of brain tissue
 Çizelge 4. Beyin dokusunun KAT, GST ve SOD aktiviteleri

GROUPS	Catalase ($\mu\text{g}^{-1}\text{ml}^{-1}\text{dk}$)	Glutathione Transferase ($\mu\text{g}^{-1}\text{ml}^{-1}\text{dk}$)	Superoxide dismutase (% Inhibition)	Superoxide dismutase (Unit)
C	202.79±17.20	14.72±1.21	32.65±2.41	16.72±1.26
DMBA	156.77±4.85 ^c	8.45±0.43^d	28.60±0.87 ^b	14.91±0.56 ^b
PT	152.32±20.52 ^c	13.82±1.77 ^a	36.58±3.07 ^b	19.72±1.95 ^b
PT+DMBA	165.90±5.93 ^b	14.07±0.93 ^a	25.76±1.15 ^c	13.23±0.55 ^c
RC	166.18±10.90 ^b	11.91±1.23 ^b	30.46±1.38 ^a	15.68±0.72 ^a
RC+DMBA	152.08±6.53^d	13.36±0.77 ^a	25.74±0.84 ^c	13.34±0.35 ^c

d: p<0.001; c: p<0.01; b: p<0.05; a: p>0.05

Another enzyme, CAT, acts as a protector against damage that occurs under oxidative stress conditions. Catalase frequently decreases in tumor tissues compared to normal tissues. Available data indicate that catalase activity severely reduces in human breast carcinoma cell line MCF-7 cells compared to normal healthy ones (Glorieux et al., 2018). In the present study, it was concluded that the level of catalase in the brain tissues was lower in the DMBA groups than the control group. The results of the present study are consistent with the literature.

In a study investigating the role of superoxide dismutase (SOD), an important member of enzymatic antioxidants in breast cancer, it was found that metformin significantly reduced the ROS levels and upregulated the SOD isoforms (Sharma and Kumar, 2018). The results of the present study indicated that the SOD level in the brain tissue was lower in the DMBA groups when compared to the control group. In the antioxidant groups, higher levels of the SOD enzyme activity were determined.

Cholesterol levels and ADEK vitamins

Table 5 shows cholesterol levels and vitamins A, D, E, K in brain tissue. When the groups were examined in terms of these variables, it was detected that while a significant increase was found in the levels of D3, α -tocopherol, and β - Sterol (p<0.01; p<0.001), a significant decrease was found in the levels of δ -tocopherol, ergosterol, and stigmasterol (p<0.05); however, no statistical difference was seen in the level of D2 (p>0.05).

The PT group showed a significant increase in terms of α -tocopherol, D2, cholesterol, ergosterol, β -sterol levels (p<0.01; p<0.001) and a significant decrease in stigmasterol level (p<0.05).

The PT+DMBA group showed a significant increase in terms of α -tocopherol, K2, β -Sterol levels and a significant decrease in amounts of K1, cholesterol, δ -

tocopherol, and stigmasterol (p<0.001; p<0.01).

A significant decrease was found in the RC group in terms of K1, cholesterol, and δ -tocopherol levels (p<0.001); on the other hand, the same group had a significant increase in stigmasterol, β -Sterol, and retinol levels; besides, no statistical difference was found in the changes of K2, D2, D3, α -tocopherol, and ergosterol levels (p>0.05).

While there was a significant increase in D3, α -tocopherol levels of the RC+DMBA group, a significant decrease was detected in its cholesterol and δ -tocopherol amounts (p<0.001; p<0.01).

Some diseases are related to vitamin levels. A study reported that there was a relationship between breast cancer and vitamin D concentrations in both animal models and cell lines (De La Puente-Yagüe et al., 2018). In addition, high amounts of 25-hydroxyvitamin D cause a significant decrease in the postmenopausal incidence of breast cancer (Abbas et al., 2009). And lipophilic vitamins are important for many physiological events especially in immunity.

Vitamin D induces apoptosis, stimulates cell differentiation, and provides inhibition of angiogenesis, invasion and metastasis with its anti-inflammatory and antiproliferative properties (De La Puente-Yague et al., 2018). There is a correlation between vitamin D deficiency and different types of diseases including oncological diseases such as breast, colorectal, and prostate cancer (Garland et al., 2006).

Fatty Acids Values

The PT group showed a significant decrease in 15:1, 16:1, 18:0, 18:1, 24:0, 24:1 levels (p<0.01; p<0.001) and had a significant increase in 14:0, 22:0 levels (p<0.05) (Table 6).

There was a significant decrease in the PT+DMBA group in terms of 15:1, 16:1, 17:1, 18:0, 18:1, 18:2 levels (p<0.001; p<0.01; p<0.05); whereas, a significant increase was found in 18:1, 22:0, 24:1

levels of this group. Moreover, no statistical significance was found in the changes of 14:0, 16:0, 17:0 levels ($p>0.05$).

A significant increase was found in the RC group in terms of 14:0, 18:2, 22:0 levels; on the other hand, there was a significant decrease in this group's 16:1,

18:1 and 24:1 fatty acid amounts ($p<0.001$; $p<0.05$).

While there was a significant decrease in 15:1, 16:1, 18:0, 18:1, 18:2, 24:1 levels in the RC+DMBA group ($p<0.01$); a significant increase was observed in 16:0, 18:1 and 22:0 levels.

Table 5. Cholesterol and A, D, E, K vitamins values of the brain tissue ($\mu\text{g g}^{-1}$)

Çizelge 5. Beyin dokusunun kolesterol ve A, D, E, K vitemin değerleri ($\mu\text{g g}^{-1}$)

Vitamins/Sterols	CONTROL	DMBA	PT	PT+DMBA	RC	RC+DMBA
K-2	3.72±0.25	3.95±0.36 ^a	3.95±0.39 ^a	5.11±0.46 ^b	4.19±0.38 ^a	4.74±0.29 ^b
δ -Tocopherol	5.71±0.99	4.03±0.62 ^b	4.63±0.44 ^a	3.79±0.14 ^c	3.24±0.43 ^c	3.45±0.27 ^c
D-2	1.02±0.12	1.40±0.19 ^a	1.98±0.49 ^c	1.29±0.12 ^a	0.96±0.21 ^a	0.94±0.14 ^a
D-3	0.36±0.05	0.94±0.11 ^c	0.68±0.32 ^a	0.57±0.07 ^a	0.47±0.08 ^a	1.27±0.16^d
α -Tocopherol	10.87±1.23	22.95±3.69 ^c	33.08±3.98^d	27.47±4.30^d	10.14±1.14 ^a	20.16±1.73 ^c
Ergosterol	20.25±5.03	15.93±1.78 ^b	25.59±1.76 ^b	21.85±1.67 ^a	17.16±1.73 ^a	21.81±1.51 ^a
K-1	2.69±0.23	1.38±0.25^d	2.72±0.18 ^a	2.18±0.17 ^b	1.27±0.31^d	2.49±0.19 ^a
Cholesterol	1038.55±2.77	847.31±0.60^d	1121.57±3.61^d	940.22±0.57^d	984.90±2.46^d	940.30±0.73^d
Stigmasterol	6.71±3.21	1.95±0.51 ^b	1.81±0.33 ^b	1.02±0.32 ^c	14.95±8.21 ^c	5.33±4.46 ^a
β -Sterol	0.15±0.11	8.95±3.62^d	2.37±0.73 ^b	1.24±0.29 ^b	5.94±1.27 ^c	1.18±0.25 ^b
Retinol	0.03±0.002	0.03±0.001 ^a	0.02±0.005 ^a	0.03±0.007 ^a	0.06±0.015 ^c	0.03±0.001 ^a

d: $p<0.001$; c: $p<0.01$; b: $p<0.05$; a: $p>0.05$

Table 6. Fatty acids values of brain tissue (%)

Çizelge 6. Beyin dokusunun yağ asidi değerleri (%)

Fatty Acids	CONTROL	DMBA	PT	PT+DMBA	RC	RC+DMBA
14:0	0.11±0.006	0.12±0.005 ^a	0.14±0.01 ^b	0.11±0.008 ^a	0.13±0.01 ^b	0.10±0.005 ^a
15:1	2.27±0.05	1.79±0.13 ^c	1.94±0.15 ^b	1.47±0.10^d	2.02±0.17 ^a	1.47±0.07^d
16:0	17.62±0.26	17.15±0.11 ^b	17.97±0.15 ^a	17.64±0.17 ^a	17.94±0.16 ^a	18.04±0.13 ^b
16:1. n-7	1.03±0.05	0.81±0.02^d	0.93±0.05 ^b	0.76±0.04^d	0.88±0.03 ^b	0.73±0.03^d
17:0	0.32±0.02	0.29±0.009 ^b	0.32±0.01 ^a	0.34±0.02 ^a	0.33±0.002 ^a	0.32±0.01 ^a
18:0	16.41±0.29	9.13±2.29 ^c	10.85±3.27 ^c	11.94±2.41 ^c	16.91±0.37 ^a	14.63±1.63 ^b
18:1. n-7	15.25±4.82	12.97±3.20 ^b	9.12±3.76 ^c	19.59±1.60 ^c	3.17±0.12^d	21.42±0.13 ^c
18:1. n-9	20.31±0.34	17.82±0.63 ^b	16.41±0.92 ^b	16.97±0.44 ^b	20.69±0.14 ^a	17.30±1.21 ^b
18:2. n-6	0.90±0.04	0.75±0.02 ^c	0.90±0.06 ^a	0.87±0.04 ^b	1.18±0.29^d	0.79±0.02 ^c
22:0	0.30±0.03	0.33±0.02 ^a	0.42±0.07 ^b	0.48±0.01 ^c	0.57±0.05^d	0.40±0.02 ^b
24:0	1.36±0.19	0.45±0.07^d	0.43±0.11^d	0.44±0.02^d	0.38±0.04^d	0.79±0.22 ^c
24:1	0.68±0.07	0.68±0.04 ^a	0.50±0.04 ^d	0.78±0.19 ^c	0.48±0.02^d	0.60±0.03 ^c

d: $p<0.001$; c: $p<0.01$; b: $p<0.05$; a: $p>0.05$; myristic acid (14:0); pentadecanoic acid (15:0); pentadecenoic acid (15:1); palmitic acid (16:0); palmitoleic acid (16:1 n-7); heptadecanoic acid (17:0); heptadecenoic acid (17:1); stearic acid (18:0); oleic acid (18:1 n-9); linoleic acid (18:2 n-6); linolenic acid (18:3 n-3); behenic acid (22:0); nervonic acid (24:1); saturated fatty acids (SFA); monounsaturated fatty acids (MUFA); polyunsaturated fatty acids (PUFA); unsaturated fatty acids (USFA)

Polyunsaturated fatty acids in cholesterol esters, phospholipids, and triglycerides are affected by oxidation caused by free radicals and participate in chain events that cause damage to biomolecules. Brain tissue has a large amount of cholesterol. The present results of the study indicated that the level of cholesterol in the brain tissue of cancerous rats decreased in the groups containing plant extracts than in the control group and plant extracts reversed this situation.

Lipids are substances with a wide structural diversity covering many cytological and pathological metabolisms such as breast cancer.

Most lipids act as secondary messengers, as in tumors. In this way, lipids can be used for

pathophysiology, therapy, and diagnosis of diseases. Changes in lipid metabolism can be detected in cancer cells in the early stages of malignancy (Kawashima et al., 2013).

In a study on the development of human breast cancer cells and lipid profile, it was reported that omega-6 polyunsaturated fatty acids (n-6 PUFA) promoted development of breast tumor and metastasis while long-chain n-3 polyunsaturated fatty acids exhibited suppressive effects. In addition, the ratio of n-6 to n-3 fatty acids was seen as an important factor in the control of tumor growth. Dietary intake of n-3 PUFA may alter breast cancer risk factors. The addition of fish oil n-3 PUFAs such as eicosapentaenoic acid (20:5 n-3, EPA) and

docosahexaenoic acid (22:6 n-3, DHA) to culture media or animal diets suppress tumor cell proliferation and increase apoptosis by multiple mechanisms (Ge et al., 2002).

Linoleic and linolenic acids are known as essential fatty acids. The essential fatty acid consists of $\Delta 6$ and $\Delta 5$ desaturase enzymes. $\Delta 6$ desaturation is added to this acid. As a result of the activities of these enzymes, γ -linoleic, eicosatrienoic, arachidonic, docosapentaenoic, and docosahexaenoic acids formed. Researchers reported that linoleic acid and linolenic acid should be taken with diet and arachidonic acid would be synthesized from 18:2 and 18:3 (Rule et al., 1994). Polyunsaturated fatty acids are important structural components by imparting fluidity and selective permeability to membranes (Horrobin 1993).

CONCLUSION

Oxidative stress occurs if antioxidants cannot scavenge free oxygen radicals (Zarrini et al., 2016), resulting in cancer and other chronic diseases. Breast cancer develops as a result of abnormal changes that occur in breast cells (Kumar et al., 2013). Treatment options for breast cancer include surgery, radiotherapy, chemotherapy, and immunotherapy. New chemotherapeutic agents and molecular-targeted drugs contribute to cancer treatment. However, the toxicity of these drugs and the drug resistance prevent chemotherapy from achieving the desired result. Less toxic and more effective bio-compounds have gained importance for treatment. Medicinal plants have come to the fore for the development of new anticancer agents (İçen et al., 2015).

Pistacia terebinthus L. and *Rhus coriaria* L. are species belonging to the Anacardiaceae family (cashew family) and they are used in alternative medicine. Extracts derived from *Rhus coriaria* are used as pharmaceuticals (raw materials of medicines) (Verzele et al., 1985). *R. coriaria* has an anticancer activity and is a promising alternative treatment candidate (El Hasasna et al., 2016). *Pistacia terebinthus* L. fruit extracts are used for anticarcinogenic, antioxidant, antimicrobial, and antimutagenic purposes in alternative medicine (Germano et al., 2002; Tesoriere et al., 2007; Kulisic et al., 2012). This study revealed the effects of *P. terebinthus* and *R. coriaria* on some biochemical parameters of brain tissue of rats with experimentally-induced breast cancer.

The results of the present study showed that the herb suspensions exerted anti-cancer effects and consequently may alleviate brain damage caused by DMBA-induced breast cancer. However, it was observed that they were not sufficiently effective especially on enzymatic activities at molecular level. In the light of the findings of the present study, it is concluded that these plants can be used for follow-up

and treatment of cancer patients. *Pistacia terebinthus* and *Rhus coriaria* plants can be used in the fight against oxidative stress in breast cancer. Both plants can give positive results in similar cancer cases.

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The authors declare no conflict of interest. This study complies with research and publishing ethics and rules.

Researchers Contribution Rate Declaration Summary

The authors declared that they contributed equally to the article.

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