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Protective Effect of Sumac and Terebinth Extracts Against the Negative Effects of Breast Cancer on Cardiac Tissues of in Rats

Efecto protector de los extractos de zumaque y terebinto contra los efectos negativos del cáncer de mama en los tejidos cardíacos de ratas

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ABSTRACT

Due to the toxic side effects of chemotherapeutic drugs used in breast cancer, interest in medicinal plants has increased in order to develop alternative cancer drugs. The experimental model of this study was created to observe the remedial impacts of the Terebinth (*Pistacia terebinthus* L.) and the Sumac (*Rhus coriaria* L.) plants against the negative effects of 7,12-Dimethylbenz[a]anthracene induced breast cancer on cardiac tissues in rats. For this purpose, the levels of malondialdehyde were analyzed the indicator of the oxidative stress breast cancer will cause on cardiac tissues, the catalase, glutathione transferase and superoxide dismutase enzymes, glutathione, which holds and important place among antioxidant impacts and proteins. At the end of the study, it was determined that there was an increase in malondialdehyde levels, a decrease in glutathione and protein amounts, and a decrease in antioxidant enzyme levels in rats treated with cancer-induced 7,12-Dimethylbenz[a]anthracene.

Key words: Breast cancer; cardiac; antioxidant

RESUMEN

Debido a los efectos secundarios tóxicos de los fármacos quimioterapéuticos utilizados en el cáncer de mama, ha aumentado el interés en las plantas medicinales para desarrollar fármacos alternativos contra el cáncer. El modelo experimental de este estudio se creó para observar los efectos terapéuticos de las plantas de terebinto (*Pistacia terebinthus* L.) y zumaque (*Rhus coriaria* L.) contra los efectos negativos del cáncer de mama inducido por 7,12-Dimethylbenz[a] anthracene en el tejido cardíaco de ratas. Para ello, se analizaron los niveles de malondialdehído, indicador del estrés oxidativo que el cáncer de mama causa en el tejido cardíaco; las enzimas catalasa, glutatión transferasa y superóxido dismutasa; y el glutatión, que desempeña un papel importante entre los antioxidantes y las proteínas. Al finalizar el estudio, se observó un aumento en el nivel de malondialdehído, una disminución en los niveles de glutatión y proteínas en las ratas con 7,12-Dimethylbenz[a] anthracene inducido por cáncer, y una disminución en los niveles de enzimas antioxidantes.

Palabras clave: Cáncer de mama; cardíaco; antioxidante

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INTRODUCTION

As some medicine used in breast cancer treatments, which chemotherapeutic treatment leads, may have toxicity and side effects that render chemotherapy unsuccessful, a leaning on medical plants for the purposes of alternative cancer medicine development has increased [1]. In fact, some of these drugs are known to have cardiotoxic effects. Anthracyclines such as Doxorubicin, Epirubicin, Daunorubicin and Idarubicin are the most commonly used clinically [2].

However, patients treated with Anthracyclines (Doxorubicin equivalent dose of 385 mg/m2, 19 trials; n = 660) had a 5.4% decrease in Left Ventricular Ejection Fraction (LVEF) compared to the placebo group [3], suggesting that they are not as toxic as previously thought. In other words, cumulative dose has been reported as the only significant risk factor for cardiotoxicity of doxorubicin [4].

Pistachia terebinthus L. and *Rhus coriaria* L. are also plants used for this purpose that belong to the Anacardiaceae (cashews) family of plants [5]. It is known that the *P. terebinthus* has different biological activities and that it is utilized in asthma and bronchitis treatments within Turkey as antiseptics, moreover, that they are used in various traditional treatments similarly to its usage for burns. It was reported owing to its abundance of secondary compounds found in fruits and/or resins, this plant has high antioxidant, antimicrobial, anti-inflammatory, and cytotoxic effects [5].

Moreover, studies reporting on the fact that the fruit extracts of *P. terenbithus* L. are utilized for anticarcinogen, antioxidant, antimicrobial, and anti-mutagenic purposes are present [6]. On the other hand, it is known that alongside the culinary application of the *R. coriaria* plant, its many therapeutic properties were also highlighted [7].

For instance, it is known that the plant has effective antioxidant activity due to the phenolic compounds contained in it [8]. *R. coriaria* extracts were reported to positively impact various diseases such as atherosclerosis related to reactive oxygen types in the body (ROS) [9], insulin resistance, type II diabetes [10], cardiovascular diseases [7], osteoarthritis [11], hepatocyte toxicity [12], and DNA damage [13].

A study inspecting the impact of the *R. coriaria* plant on breast cancer reported that by inducing the autophagic cell death of the plant and senescence, the plant holds strong anti-breast cancer activity, and that it may be a candidate to be used against cancer as a hopeful alternative or a supporting treatment [14] On another study inspecting cancer, it was demonstrated that *R. coriaria*, as a vivo, inhibits tumor growth and metastasis [15].

Although the literature has focused on the active compounds contained in *P. terebinthus* (Terebinth) and *R. coriaria* (Sumac) to understand their anticancer properties, in our study, we thought that examining the effects of *P. terebinthus* and *R. coriaria* as the main material on cancer cells would contribute to the literature due to the difficulty of purification stages and limited use of active compounds.

For this reason, in this study, the healing properties of *Pistacia terebinthus* L. *subsp. Palaestina* (Terebinth) and *Rhus coriaria* L. (Sumac) plants were tried to be correlated against the negative effects affecting the nearby cardiac tissue by examining their antioxidant effects in an experimentally created breast cancer model in rats.

MATERIALS AND METHODS

The collecting plants and preparing of extracts

From plants, *Pistacia terebinthus L.* subsp. *Palaestina* (Boiss.) was collected from the Elazığ/Center Obuz village while *Rhus coriaria L.* was collected nearby Elazığ/Harput in their seed seasons (between the months August-November 2017). The second volume of Davis' [16] work titled "Flora of Turkey" was utilized for the diagnosis of the plants.

Plant materials were dried in a sunless location (in the shade) in order to separate their seeds, afterwards, they were conserved in a cool environment until the experiment was conducted. 20 grams (g) of the seed parts of each plant were weighed, followed up by the addition of 1000 mL of sinkwater (20 mg/kg) and homogenization through the use of a blender. (Waring brand, USA) Afterwards, they were left to rest under 40 °C for 1 hour (h) within a drying oven (Memmert brand, Germany), after which they were put through a sieve and given to rats as drinking water.

Animal experiment, experimental design and preparation of tissue homogenates

Animals and experimental protocols used in the study were approved by the Local Animal Experiments Ethics Committees of Firat University (Elazig, 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).

66 female Sprague-Dawley rats (*Rattus norvegicus*) were utilized in the study Sixty-six healthy female Sprague-Dawley rats, 8 weeks old, were obtained from the Firat University Experimental Research Center (Elazig, Turkey). The experiments were completed after 16 weeks.

Rats were separated into 6 groups:

Group 1: C (n=7): Being the control group, cancer was not formed and the group was only fed with the basic diet [(The control group was not added 7,12-Dimethylbenz[a]anthracene (DMBA)].

Group 2: S (n=7): (*Rhus coriaria:* Sumac) was given.

Group 3: T (n=7): (*Pistacia terebinthus* subsp. *Palaestina*: Terebinth) was given.

Group 4: DMBA (n=15): 80 mg/kg DMBA was given to female rats through gavage [17] and their feeding with the basic diet was ensured.

Group 5: DMBA+S (n=15)**:** DMBA (80 mg/kg) + S (*Rhus coriaria:* Sumac) extract were given.

Group 6: DMBA+T (n=15): DMBA (80 mg/kg) + T (*Pistacia terebinthus* subsp. *Palaestina:* Terebinth) extract were given.

In order to form breast cancer, DMBA, a type of carcinogen, was utilized. And through gavage (Genject brand, TURKEY), [(depending on the rat's weight, an amount of 80 mg/kg that was dissolved in a mixture of olive oil and Dimethyl Sulfoxide (DMSO)] it was applied onto 8 weeks old female Sprague-Dawley rats [17]. The experiments were completed after 16 weeks. The cardiac tissues of the animal groups were homogenized through the Tris-HCL (pH 7,4) tampon and were centrifuged (Hettich Zentaifugen, Germany) under + 4°C at 150 cps for 15 second (s) in order to remove the tissues from their pellets, yielding the supernatant part.

For the determination of antioxidant enzyme activities such as malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD) through total protein analysis, catalase (CAT), glutathione-S-transferase (GST), this supernatant part was utilized [18].

Determination of protein levels

The total protein content in the tissues was conducted through a method determined by Lowry *et al*. [19] in a spectrophotometer (Shimadzu UV mini 1240 brand, USA).

Determination of MDA

Lipid peroxide level in tissue homogenate (MDA-TBARS) was calculated using thiobarbituric acid reagent according to the method of Ohkawa *et al*. [20].

The measurement of GSH content

1 mL of 10% trichloroacetic acid (TCA) was added to the obtained supernatant (1 mL) in order to precipitate the proteins. The mixture was left to wait in this manner in room temperature for 10 minutos (min) and was later centrifuged at 75 counts per s (cps) for 10 s .Upon the precipitation of the proteins through this method, the supernatant part was transferred into another test tube, followed up by the addition of 2 mL 0.3 M NA_2HPO_4 solution and 1 mL 150 µM Ellman's reagent [5,5'-dithiobis-(2-nitrobenzoic acid) or DTNB] solution onto it, and was then mixed. Once the resulting yellow color properly stabilized in room temperature after 5-10 s, measurement was conducted through a spectrometer at 412 nm [21].

Enzyme activities (SOD, CAT, GST)

Superoxide dismutase activity was determined through the method that utilizes the inhibition of adrenochrome oxidation that forms through the epinephrin-xanthine and xanthine oxidase systems as a foundation [22]. For the determination of the catalase enzyme activity, the most commonly used method in literature, a UV method SOD that, as its foundation, utilizes the measurement of the absorbance values of hydrogen peroxide (H_2O_2) at a wavelength of 240 nm [23]. The glutathione-S-transferase activity was determined through the measurement of its activity in 100 mM potassium phosphate tampon (pH 6.5), 1 mM 1-chloro-2,4-dinitrobenzane (CDNB) and 1 mM GSH at 340 nm [24].

Statistical analysis

One-way analysis of variance (ANOVA) and the Post Hoc Tukey-HSD test were used to determine the differences between the groups. Results are presented as mean ± S.E.M. SPSS/PC program (Version 15.0; SPSS, Chicago, IL) was used for statistical analysis. The conclusions were depicted with average ± standard errors.

RESULTS AND DISCUSSION

Protein values

The cardiac tissue total protein analyses of rats who had breast cancer artificially developed in them through DMBA were depicted in TABLE I. When compared to the C group, all groups excluding the S group (DMBA, DMBA+T, DMBA+S, and T) demonstrated statistical decreases (P<0.05). On the other hand, a significant increase was detected in the Sumac (S) group (P<0.01). When the groups with added DMBA are compared to the DMBA group, it can be observed that both the DMBA+S and the DMBA+T groups demonstrated distinct increases (P<0.05). (TABLE I).

TABLE I
Protein levels of cardiac tissue (mg/g)

GROUPS	PROTEIN (mg/g)
C	59.87±6.12
S	65.25±2.17 [c]
T	58.01±7.37 [a]
DMBA	57.65±2.58 [b]
DMBA+S	59.13±4.02 [a,b]
DMBA+T	58.85±3.51 [a,b]

*d: P<0.001; c: P<0.01; b: P<0.05; a: P>0.05. * The 2nd letters in the *DMBA+S and the DMBA+T groups; are statistical values that communicate the comparison conducted between these two groups according to the DMBA group
S: Sumac (*Rhus coriaria*)
T: Terebinth (*Pistacia terebinthus* subsp. *Palaestina*)

In a study inspecting the protein values in breast cancer conducted by Dong *et al.* [25], determined that GSTP1 protein levels are very low in the human breast cancer cell line MCF-7. This study is parallel with the study in the literature in that it demonstrated a decrease in protein levels even though it was not statistically meaningful in the DMBA-caused breast cancer group. Additionally, our treatment groups (DMBA+S and DMBA+T) demonstrated increases compared to the DMBA group.

MDA values

The MDA levels in cardiac tissues were demonstrated in TABLE II. Relative to the C group, the DMBA, DMBA+T, and DMBA+S groups demonstrated significant increases (P<0.001) while the S group demonstrated a distinct decrease (P<0.001), and the T group demonstrated a smaller decrease (P<0.05). (TABLE II).

TABLE II MDA levels of cardiac tissue (nmol/gr)	
GROUPS	**MDA (nmol/gr)**
Control	89.80±36.05
S	65.94±4.80 ^{d}
T	86.78±6.96 ^{a}
DMBA	138.28±25.14 ^{d}
DMBA+S	105.87±21.17 ^{d,d}
DMBA+T	113.01±11.03 ^{d,c}

*d: P<0.001; c: P<0.01; b: P<0.05; a: P>0.05. * The 2nd letters in the *DMBA+S and the DMBA+T groups; are statistical values that communicate the comparison conducted between these two groups according to the DMBA group.
S: Sumac (*Rhus coriaria*)
T: Terebinth (*Pistacia terebinthus* subsp. *Palaestina*)

The characterization with High-Performance Liquid Chromatography (HPLC) of *P. terebinthus*' raw extracts revealed that it is rich in terms of luteolin and luteolin-7-glucozoid. It was reported that by eliminating the free radicals of these secondary metabolites, it demonstrates strong antioxidant activity with protective properties against the risk of cancer [26].

A previously conducted study investigated the tumor growth inhibiting effects luteolin, which is abundantly contained in *P. terebinthus*, on breast cancer cell lines (MDA-MB-231) with negative estrogen receptors (ER), and reported at the end that it suppresses the contribution of 3H, which depicts luteolin's cell growth inhibition, that it stops the cell cycle in the G2/M and S phases, and that it has apoptotic activity.

In conclusion, it was reported that luteolin effectively suppressed the MDA-MB-231 ER-negative breast cancer cell growth, and that it has anticancer activity due to its demonstration of inhibitive effects on cancer cell survival [27]. The anticancer effect of *Rhus coriaria*, on the other hand, was inspected on a three-type breast cancer cell line (MDA-MB-231, MCF-7, and T47D) level.

The ethanolic extract of *R. coriaria* (RCE), depending on time and concentration, was reported to stop the cell cycle in the G1 phase and inhibit the proliferation of these cell lines by inducting senescence [14].

In a previously conducted study, Hamdy *et al*. [28] measured the reducing activity effects of Hesperidin (HES), which is a flavanone glycoside, as well as Cyperus esculentus tubers (Tiger Nut (TN)) on cancer formed by DMBA. To this end, when the MDA levels in the serum are compared to the control group, while the DMBA and DMBA+TN groups demonstrated meaningful increases, a comparison with DMBA revealed that the DMBA+HES group demonstrated decreases of significant levels.

Another study examining the protective effects of Berberine, an alkaloid found in plants, on DMBA-induced breast cancer in female Sprague Dawley rats reported significant increases in MDA in the DMBA-treated groups. The study reported that pre- and post-treatment with Berberine provided significant protection against DMBA-induced increases in MDA [29].

GSH values

The changes in the GSH levels of cardiac tissues were depicted in TABLE III. When compared to the C group, while the GSH levels of the S and T groups demonstrated clear increases (P<0.05, P<0.001), with the DMBA group being in the lead, the DMBA+S and DMBA+T groups, in order, demonstrated decreases of varying degrees (P<0.05, P<0.001). The GSH levels of groups with added DMBA, when compared to the DMBA group; demonstrated a more distinct increase in the DMBA+S group while demonstrating smaller increases in the DMBA+T group (P<0.001, P<0.05).

TABLE III GSH values of the cardiac tissue (µg/gr)	
GROUPS	**GSH (µg/gr)**
C	397.27±19.09
S	456.57±12.83 ^{d}
T	414.32±23.76 ^{b}
DMBA	344.60±40.63 ^{d}
DMBA+S	374.86±56.41 ^{b,b}
DMBA+T	351.07±38.80 ^{d,a}

*d: p<0.001; c: p<0.01; b: p<0.05; a: p>0.05. * The 2nd letters in the *DMBA+S and the DMBA+T groups; are statistical values that communicate the comparison conducted between these two groups according to the DMBA group.
S: Sumac (*Rhus coriaria*)
T: Terebinth (*Pistacia terebinthus* subsp. *Palaestina*)

Reduced GSH prevents or limits tissue damage by scavenging free radicals in the cell [30]. Therefore, a decrease in the GSH levels of cancer groups demonstrate the beginning of oxidative stress [31]. In a previously conducted study, Hamdy *et al.* [28] measured the reducing activity effects of HES, which is a flavanone glycoside, as well as Tiger Nut (TN) on cancer formed by DMBA.

In the study by Hamdy *et al.* [28], serum GSH levels showed significant decreases in DMBA and DMBA+TN levels compared to the control group, while they showed significant increases in the DMBA+HES group compared to the DMBA group.

In a breast cancer study where Berberine was applied, it was reported that GSH activities showed regeneration as a result of pre- and post-treatment [29]. This study is similar to other studies in terms of decreases in GSH activity.

Antioxidant enzymes activities

The CAT, GST, and SOD enzyme levels in cardiac tissues were depicted in TABLE IV. When compared to the C group, the CAT and GST enzymes, with the DMBA group being the lead, demonstrated clear decreases of varying degrees in the DMBA+S and DMBA+T groups (P<0.05, P<0.01, P<0.001). On the other hand, when the S and T groups are compared to the control group; while the S and T groups demonstrated decreases in the CAT enzyme, the GST and SOD enzymes were observed to increase in varying levels. When compared to the DMBA group, the enzyme levels of the groups with added DMBA, with the DMBA+S group being the lead, demonstrated distinct increases (P>0.05, P<0.05, P<0.01, P<0.001).

TABLE IV
CAT, GST and SOD activities of cardiac tissue

GROUPS	CAT (µg/g/1dk)	GST (µg/g/1dk)	SOD (% İnhibisyon)
C	995.89±54.81	9.32±0.43	56.15±5.19
S	893.65±82,70 [b]	9.79±0.98 [b]	77.24±4.04 [d]
T	886.99±66.05 [c]	9.35±0.65 [a]	73.81±5.76 [d]
DMBA	879.01±58.44 [d]	9.02±0.82 [d]	58.43±6.23 [a]
DMBA+S	978.62±68.10 [c,c]	9.22±1.55 [d,a]	60.66±8.93 [b,d]
DMBA+T	959.72±89.54 [b,c]	9.09±2.16 [d,a]	70.83±5.28 [b,b]

*d: p<0.001; c: p<0.01; b: p<0.05; a: p>0.05. * The 2nd letters in the *DMBA+S and the DMBA+T groups; are statistical values that communicate the comparison conducted between these two groups according to the DMBA group.
S: Sumac (*Rhus coriaria*)
T: Terebinth (*Pistacia terebinthus* subsp. *Palaestina*)

Enzyme antioxidant defense systems such as reduced SOD, CAT and glutathione peroxidase prevent tissue damage by clearing free radicals in the cell. By metabolizing free radicals, SOD turns superoxide anions into H_2O_2, protecting cells from lipid peroxidation [30, 31]. Catalase, on the other hand, fulfills this goal by turning H_2O_2 into H_2O and O_2 [32].

In the study by Handy et al. [28], serum SOD, CAT and GSH-Px activities showed significant decreases in DMBA and DMBA+TN levels compared to the control group, while they showed significant increases in the DMBA+HES group compared to the DMBA group. In the berberine study, regenerations in SOD and CAT activities were also reported as a result of pre- and post-treatment [29]. Another similar study regarding GST activation in breast cancer conducted by Kadam and Abhang [33] recorded a significant decrease in the GST levels of breast cancer patients due to increased oxidative stress. This study is similar to previous studies in terms of decreases in antioxidant enzymes.

CONCLUSION

As a result of this study, an increase in MDA levels, an indicator of lipid peroxidation, was detected in DMBA groups, especially compared to the C group, and a decrease was detected in antioxidant-added DMBA groups, especially in the sumac group. The findings also support literature on antioxidant enzyme activities, which are indicators of cancer. These results suggest that terebinth and sumac extracts may play a role in counteracting the oxidative effects of breast cancer on other organs.

However, it's important to note that our results require molecular and pathological support before these plant extracts or their ingredients can be used in pharmaceuticals or similar dietary supplements.

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Conflicts of Interest

The authors declare no conflict of interest.

Data availability statement

Data are available on reasonable request for corresponding author.

BIBLIOGRAPHIC REFERENCES

[1] Sheokand S, Navik U, Bansal AK. Nanocrystalline solid dispersions (NSD) of hesperetin (HRN) for prevention of 7, 12-dimethylbenz [a] anthracene (DMBA)-induced breast cancer in Sprague-Dawley (SD) rats. Eur. J. Pharm. Sci. [Internet]. 2019; 128:240-249. doi: https://doi.org/qb78

[2] McGowan JV, Chung R, Maulik A, Piotrowska I, MalcolmWalker J, Yellon DM. Anthracycline chemotherapy and cardiotoxicity. Cardiovasc. Drugs Ther. [Internet]. 2019; 31 (1): 63–75. doi: https://doi.org/f9xtdv

[3] Jeyaprakash P, Sangha S, Ellenberger K, Sivapathan S, Pathan F, Negishi K. Cardiotoxic effect of modern anthracycline dosing on left ventricular ejection fraction: a systematic review and meta-analysis of placebo arms from randomized controlled trials. J. Am. Heart Assoc. [Internet]. 2021; 10(6):e018802. doi: https://doi.org/grcdwx

[4] Torti FM, Bristow MR, Howes AE, Aston D, Stockdale FE, Carter SK, KOHLER M, BROWN Jr. BW, BILLINGHAM ME. Reduced cardiotoxicity of doxorubicin delivered on a weekly schedule: Assessment by endomyocardial biopsy. Ann. Intern. Med. [Internet]. 1983; 99(6):745–749. doi: https://doi.org/qb79

[5] Topçu G, Ay M, Bilici A, Sarıkürkcü C, Öztürk M, Ulubelen A. A new flavone from antioxidant extracts of *Pistacia terebinthus*. Food Chem. [Internet]. 2007; 103(3):816-822. doi: https://doi.org/cbfc3g

[6] Germano MP, Pasqualo RD, D'Angelo V, Catania S, Silvari V, Costa C. Evaluation of Extracts and Isolated Fraction from *Capparis spinosa* L. Buds as an Antioxidant Source. J. Agric. Food Chem. [Internet]. 2002; 50(5):1168-1171. doi: https://doi.org/ffwkb3

[7] Shabbir A. *Rhus coriaria linn*, a plant of medicinal, nutritional and industrial importance: A review. J. Anim. Plant. Sci. [Internet]. 2012 [cited 22 Jun 2025]; 22(2):505-512. Available in: https://goo.su/5SsMVUf

[8] Mizushima N, Levine B. Autophagy in mammalian development and differentiation. Nat. Cell Biol. [Internet]. 2010; 12:823-830. doi: https://doi.org/cvnkcz

[9] Zargham H, Zargham R. Tannin extracted from Sumac inhibits vascular smooth muscle cell migration. Mcgill. J. Med. [Internet]. 2008 [cited 14 Jun 2025]; 11(2):119–123. Available in: https://goo.su/k7oMA

[10] Anwer T, Sharma M, Khan G, Iqbal M, Ali MS, Alam MS, Safhi MM, Gupta N. *Rhus coriaria* ameliorates insulin

resistance in non-insulin-dependent diabetes mellitus (NIDDM) rats. Acta Pol. Pharm. [Internet]. 2013 [cited 02 May 2025]; 70(5):861-867. Available in: https://goo.su/m2yIU9

[11] Panico A, Cardile V, Santagati NA, Messina R. Antioxidant and protective effects of Sumac Leaves on Chondrocytes. J. Med. Plants Res. [Internet]. 2009 [cited 15 Jun 2025]; 3(11):855–861. Available in: https://goo.su/71x5EJ

[12] Pourahmad J, Eskandari, MR, Shakibaei R, Kamalinejad M. A search for hepatoprotective activity of aqueous extract of *Rhus coriaria* L. against oxidative stress cytotoxicity. Food Chem. Toxicol. [Internet]. 2010; 48(3):854-858. doi: https://doi.org/d2q4ff

[13] Chakraborty A., Ferk F, Simić T, Brantner A, Dušinská M, Kundi M, Hoelzl C, Nersesyan A, Knasmüller S. DNA-protective effects of sumach (*Rhus coriaria* L.), a common spice: results of human and animal studies. Mutat. Res. Fund. Mol. Mech. Mutagen. [Internet]. 2009; 661(1-2):10-17. doi: https://doi.org/ftn2tn

[14] Hasasna H, Athamneh K, Al Samri H, Karuvantevida N, Al Dhaheri Y, Hisaindee S, Ramadan G, Al Tamimi N, AbuQamar S, Eid A, Iratni R. *Rhus coriaria* induces senescence and autophagic cell death in breast cancer cells through a mechanism involving p38 and ERK1/2 activation. Sci. Rep. [Internet]. 2015; 5: 13013. doi: https://doi.org/f7mj5z

[15] El Hasasna H, Saleh A, Al Samri H, Athamneh K, Attoub S, Arafat K, Benhalilou N, Alyan S, Viallet J, Al Dhaheri Y, Eid A, Iratni R. *Rhus coriaria* suppresses angiogenesis, metastasis and tumor growth of breast cancer through inhibition of STAT3, NFκB and nitric oxide pathways. Sci. Rep. [Internet]. 2016; 6:21144. doi: https://doi.org/qb8b

[16] Davis PH, Cullen J, Coode MJE. Polygonaceae. Flora of Turkey and the East Aegean Islands, 2 nd ed. Edinburgh: Edinburgh University Press; 1967.

[17] Mundhe NA, Kumar P, Ahmed S, Jamdade V, Mundhe S, Lahkar M. Nordihydroguaiaretic acid ameliorates cisplatin induced nephrotoxicity and potentiates its anti-tumor activity in DMBA induced breast cancer in female Sprague–Dawley rats. Int. Immunopharmacol. [Internet]. 2015; 28(1):634–642. doi: https://doi.org/f7rvfb

[18] Demir E, Yılmaz Ö. The Effect of Bitter Almond Oil on The Some Alterations in Liver Tissue of Experimental Diabetic Rats. Van Vet. J. [Internet]. 2015 [cited 15 Jun 2025]; 26(1):17-23. Available in: https://goo.su/JvGKDX

[19] Lowry OH, Rosenbrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin-phenol reagent. J. Biol. Chem. [Internet]. 1951 [cited 15 Jun 2025]; 193(1):265-275. Available in: https://goo.su/kwZeb31

[20] Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal. Biochem. [Internet]. 1979; 95(2):351–358. doi: https://doi.org/bktx4x

[21] Elman GI. Tissue Sulfhydryl Groups. Arch. Biochem. Biophys. [Internet]. 1959; 82(1):70-77. doi: https://doi.org/bz2vt8

[22] Pinho RA, Andrades ME, Oliveira MR, Pirola AC, Zago MS, Silveira PC, Dal-Pizzol F, Moreira JCF. Imbalance in SOD/CAT activities in rat skeletal muscles submitted to treadmill training exercise. Cell Biol. Int. [Internet]. 2006; 30(10):848-853. doi: https://doi.org/c66kdh

[23] Aebi, H. Catalase Invitro. Meth. Enzymol. [Internet]. 1984; 105:121-126. doi: https://doi.org/dnf7v9

[24] Bell JG, Cowey CB, Adron JW, Shanks AM. Some effects of vitamin E and selenium deprivation on tissue enzyme levels and indices of tissue peroxidation in rainbow trout (*Salmo gairdneri*). Br. J. Nutr. [Internet]. 1985; 53:149–157. doi: https://doi.org/fmnrbk

[25] Dong X, Yang Y, Zhou Y, Bi X, Zhao N, Zhang Zet, Li L, Hang Q, Zhang R, Chen D, Cao P, Yin Z, Luo L. Glutathione S-transferases P1 protects breast cancer cell from adriamycin-induced cell death through promoting autophagy. Cell Death Differ. [Internet]. 2019; 26:2086-2099. doi: https://doi.org/qb8k

[26] Kavak D, Altıok E, Bayraktar O, Ülkü S. *Pistacia terebinthus* extract: As a potential antioxidant, antimicrobial and possible β- glucuronidase inhibitor. J. Mol. Catal. B. Enzym. [Internet]. 2010; 64(3-4):167-171. doi: https://doi.org/fgcckh

[27] Lee EJ, Oh SY, Sung MK. Luteolin exerts anti-tumor activity through the suppression of epidermal growth factor receptor-mediated pathway in MDA-MB-231 ER-negative breast cancer cells. Food Chem. Toxicol. [Internet]. 2012; 50(11):4136-4143. doi: https://doi.org/f39z23

[28] Hamdy SM, Sayed O, Latif AKMA, Abdel-Aziz AM, Amin AM. Hesperidin and tiger nut reduced carcinogenicity of DMBA in female rats. Biomed. Pharmacother. [Internet]. 2016; 83:718-724. doi: https://doi.org/qb8n

[29] Karnam KC, Ellutla M, Bodduluru LN, Kasala ER, Uppulapu SK, Kalyankumarraju M, Lahkar M. Preventive effect of berberine against DMBA-induced breast cancer in female Sprague Dawley rats. Biomed. Pharmacother. [Internet]. 2017; 92:207-214. doi: https://doi.org/gbtzg3

[30] Ramírez-Expósito MJ, Urbano-Polo N, Dueñas B, Navarro-Cecilia J, Ramírez-Tortosa C, Martín-Salvago MD, Martínez-Martos JM. Redox status in the sentinel lymph node of women with breast cancer. Upsala J. Med. Sci. [Internet]. 2017; 122(4):207-216. doi: https://doi.org/qb8p

[31] Beutler E. Nutritional and metabolic aspects of glutathione. Annu. Rev. Nutr. [Internet]. 1989; 9:287–302. doi: https://doi.org/fhz9sk

[32] Coughlin SS. Oxidative Stress, Antioxidants, Physical Activity, and the Prevention of Breast Cancer Initiation and Progression. J. Environ. Health Sci. [Internet]. 2018 [cited 15 Jun 2025]; 4(2):55-57. Available in: https://goo.su/iD0dEk

[33] Kadam CY, Abhang SA. Evaluation of serum levels of reduced glutathione, glutathione-stransferase and nitric oxide in breast cancer patients undergoing adjuvant chemotherapy. Int. J. Cur. Res. Rev. 2013 [cited 15 Jun 2025]; 5(13):51-57. Available in: https://goo.su/nS7Oq