processes

MDPI

Article

Phytochemical Profile and Cosmeceutical Potential of Leaf Extracts of Two Species of the Anacardiaceae Family from the Mediterranean Scrubland: *Pistacia lentiscus* L. and *Pistacia atlantica* Desf.

Mouna Belkessam [1,2,*], Manon Genva [2], Ahmed Kouki [1], Louise Vilain [2], Moussa Ahmed-Alem [1], Marouane Mohaddab [2,3], Pierre Leonel K. Tafokeu Taguimjeu [2,4], Safia El-Bok [5], Mossadok Ben-Attia [1,†] and Marie-Laure Fauconnier [2,†]

1 Laboratory of Environment Biomonitoring (LR01/ES14), Group on "Ecological Risk of Pharmaceuticals & Pesticides", Faculty of Sciences of Bizerta, University of Carthage, Zarzouna 7021, Tunisia
2 Laboratory of Chemistry of Natural Molecules, Gembloux Agro-Bio Tech, University of Liège, Passage des Déportés 2, 5030 Gembloux, Belgium
3 Laboratory of Agrifood and Health, Faculty of Sciences and Techniques, Hassan First University of Settat, BP 577, Settat 26000, Morocco
4 Department of Organic Chemistry, Faculty of Science, University of Yaoundé I, Yaoundé P.O. Box 812, Cameroon
5 Laboratory of Biodiversity, Biotechnologies and Climate Change (LR11/ES09), Faculty of Sciences of Tunis, University of Tunis El-Manar, Tunis 2092, Tunisia
* Correspondence: mouna.belkessam@uliege.be; Tel.: +32-470950753
† These authors contributed equally to this work.

Abstract

Skin aging involves oxidative stress, inflammation, and hyperpigmentation, prompting growing interest in plant-based treatments. *Pistacia lentiscus* L. and *Pistacia atlantica* Desf. (Anacardiaceae), North African pharmacopoeia species with recognized phytotherapeutic and cosmeceutical properties, were analyzed to elucidate these biological activities through their phytochemical composition and in vitro antioxidant, anti-inflammatory, and anti-hyperpigmentation potentials. Leaves were successively extracted with hexane, ethyl acetate, and methanol. The methanolic leaf extract of *P. atlantica* exhibited the highest total phenolic content (430.28 ± 0.01 mg GAE/g), while *P. lentiscus* showed the highest flavonoid content (230.00 ± 0.01 mg QE/g). LC–MS/MS analysis identified thirteen major phenolic compounds, including methyl gallate and myricitrin. Biological assays revealed that *P. lentiscus* exhibited the strongest antioxidant activity (IC_{50} = 5.19 ± 0.01 µg/mL) and the highest ferric-reducing power, whereas *P. atlantica* showed strong inhibition of protein denaturation (139.10 ± 0.55 µg/mL). Both extracts displayed potent anti-lipoxygenase activity (IC_{50} = 22.53 ± 0.05 and 22.67 ± 0.04 µg/mL, respectively), as well as anti-tyrosinase effects (IC_{50} = 39.80 ± 0.08 and 38.25 ± 0.02 µg/mL, respectively). Altogether, these findings underscore the cosmetic potential of these *Pistacia* species and support their use as valuable raw materials for the development of dermatological treatments.

Keywords: anti-inflammatory activity; anti-tyrosinase activity; fatty acids; phenolic compounds; *Pistacia*

check for updates

Academic Editor: Ibrahim Abu-Reidah

Received: 17 October 2025
Revised: 9 November 2025
Accepted: 14 November 2025
Published: 17 November 2025

Citation: Belkessam, M.; Genva, M.; Kouki, A.; Vilain, L.; Ahmed-Alem, M.; Mohaddab, M.; Taguimjeu, P.L.K.T.; El-Bok, S.; Ben-Attia, M.; Fauconnier, M.-L. Phytochemical Profile and Cosmeceutical Potential of Leaf Extracts of Two Species of the Anacardiaceae Family from the Mediterranean Scrubland: *Pistacia lentiscus* L. and *Pistacia atlantica* Desf. *Processes* **2025**, *13*, 3712. https://doi.org/10.3390/pr13113712

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Skin aging and pigmentary disorders represent major challenges in dermato-cosmetics today. These phenomena are multifactorial, involving oxidative stress, inflammation,

hydration loss, and the appearance of pigmentary spots [1]. Faced with these issues, in many cultures, especially in North Africa, skin tone uniformity, particularly on the face, neck, and arms, constitutes an essential aesthetic criterion [2]. This aspiration for clearer and more homogeneous skin, often reinforced by social pressures and historical stigmas, has naturally led to an increasing demand for hyperpigmentation treatments [3–5]. However, this demand raises significant concerns regarding the safety of products used.

Many products marketed for skin lightening indeed contain potentially dangerous substances, such as steroids, mercury, or hydroquinone, responsible for serious side effects, including skin disorders like exogenous ochronosis or damage related to prolonged exposure to heavy metals [6]. This safety issue therefore makes the search for natural active ingredients capable of protecting and regenerating the skin, while being safer, essential. Within this context, the development of innovative dermocosmetic solutions based on plant-derived compounds has become a major research priority.

Plant extracts are increasingly recognized as valuable sources of multifunctional bioactive molecules suitable for dermocosmetic applications. Previous research has established that numerous natural phytochemicals exhibit strong antioxidant performance [7] as well as marked anti-inflammatory properties by suppressing nitric oxide production, downregulating cyclo-oxygenase-2 expression, and limiting the release of pro-inflammatory cytokines [8]. As a recent example, benzylic alcohol derivatives isolated from *Moringa oleifera* seeds were shown to reduce lipopolysaccharide-stimulated nitric oxide generation through selective interaction with matrix metalloproteinase-9, thereby highlighting the therapeutic relevance of plant-derived compounds as effective anti-inflammatory agents [9]. Collectively, these bioactivities underline the crucial role of botanical ingredients in mitigating oxidative stress and chronic inflammation, two major biological drivers involved in skin aging and pigmentation disorders. Thus, plants represent promising candidates for the development of safe skin-lightening and anti-aging formulations.

Among natural candidates, Mediterranean plants of the Anacardiaceae family, particularly the genus *Pistacia*, are gaining increasing scientific interest due to their traditional dermatological uses in Africa and around the Mediterranean Basin [10–12]. *P. lentiscus* L. and *P. atlantica* Desf. are among the best-known *Pistacia* species, widely distributed throughout the Mediterranean and the Middle East [10]. They have been traditionally applied to treat various skin conditions, including eczema, wounds, and burns [11,13]. *P. lentiscus* mastic has also been used as a spice and cosmetic ingredient [14], whereas *P. atlantica* is recognized for its properties promoting wound healing and treating scabies, chapped lips, and hair loss [15]. Moreover, its resin and oil have demonstrated beneficial effects on wound contraction and cutaneous lesion maturation [16].

Extensive research has documented the multiple pharmacological activities of *P. lentiscus* and *P. atlantica*, revealing antibacterial [17,18], antioxidant [19,20], antidiabetic [21,22], anti-inflammatory [23,24], antitumoral [25,26], antihyperlipidemic [27], anti-acetylcholinesterase [28,29] and hepatoprotective [30,31]. Of particular relevance to cosmeceutical applications, wound-healing effects have also been demonstrated, confirming their potential for skin protection and regeneration [32,33]. However, despite this well-established diversity of biological activities, no comparative study has yet combined phytochemical profiling (using LC-MS/MS and GC-FID) with in vitro evaluation of antioxidant, anti-inflammatory, and anti-tyrosinase activities of *P. lentiscus* and *P. atlantica* leaves. This lack of integrated evidence, especially regarding their ability to modulate melanin synthesis through tyrosinase inhibition, a key mechanism in hyperpigmentation control, represents a significant knowledge gap in their cosmeceutical relevance.

The unique chemical composition of these species explains this richness of biological activities. Phytochemical studies have shown that *P. lentiscus* and *P. atlantica* are particu-

larly rich in diverse bioactive compounds including triterpenoids, flavonoids, phenolic compounds, tannins, fatty acids, and phytosterols, which may account for their potential therapeutic properties [34,35]. Interestingly, these compounds and their concentrations can vary depending to the plant's growth conditions and the extraction methods applied for their isolation [36]. Therefore, a detailed phytochemical investigation is crucial prior to evaluating their biological properties.

On this basis, the main objective of the present study aimed to establish a correlation between the traditional uses of *P. lentiscus* and *P. atlantica* leaf extracts and their in vivo effects, particularly in a cosmeceutical context. The phytochemical profiles of both species were first characterized through the quantification of total phenolic constituents using the Folin–Ciocalteu method and the measurement of total flavonoid contents using the aluminum chloride colorimetric method, followed by detailed analysis using Liquid Chromatography–Tandem Mass Spectrometry (LC-MS/MS) to identify the main phenolic compounds. In parallel, Gas Chromatography coupled with a Flame Ionization Detector (GC-FID) was used to highlight compounds with potential skin-hydrating effects. The biological activities were evaluated through several complementary approaches: antioxidant activity was assessed using DPPH free radical scavenging and Ferric Reducing Antioxidant Power (FRAP) assays; anti-inflammatory activity was determined by measuring lipoxygenase (LOX) enzyme inhibition and protein denaturation tests; and finally, anti-hyperpigmentation potential was explored through tyrosinase inhibition evaluation. We hypothesized that differences in the phytochemical composition of *P. lentiscus* and *P. atlantica* would translate into distinct biological profiles relevant to skin protection and pigmentation control.

2. Materials and Methods

2.1. Chemicals and Reagents

All chemicals and reagents utilized in the present study were of analytical grade. Detailed specifications are provided in Table S1 (Supplementary Materials).

2.2. Sample Collection

The leaves of *P. lentiscus* and *P. atlantica* were collected in 2022 during the productive stage in Algeria, in Bouira (6°22′00″ N, 3°53′00″ E) and Batna (35°33′00″ N, 6°10′00″ E), respectively. The botanical identification was conducted by Mohamed DRIDI, a senior agricultural engineer affiliated with the Laboratory of Environment Biomonitoring (LR01/ES14), Group "Ecological Risk of Pharmaceuticals & Pesticides", Zarzouna 7021, Tunisia. Herbarium vouchers of leaf samples from both species were deposited in the same institution under the codes P.L/LBE 22-004 and P.A/LBE 22-005. The leaves were washed and dried in the shade at room temperature (25 °C) to avoid light oxidation, weighed, and then ground using a RETSCH GM300 grinder (3000 W, 50/60 Hz). The resulting powders were stored in glass containers at 4 °C for later experimental use.

2.3. Extraction and Yield Assessment

The extracts of each plant species were obtained through maceration at room temperature (25 °C) with solvents of increasing polarities, following the method outlined by Ouahabi et al. [37]. These solvents were selected for their complementary polarities (hexane: non-polar, ethyl acetate: medium polarity, methanol: polar), allowing comprehensive and selective extraction of lipophilic to hydrophilic phytochemicals. Ten grams of powdered dried leaves was mixed with 200 mL of n-hexane, ethyl acetate, or methanol, and then subjected to magnetic stirring at room temperature for 2 h with n-hexane, and for 24 h with ethyl acetate and methanol. The extracts were then filtered under vacuum using a Büchner filter funnel with porosity 4. The filtrate was evaporated to dryness under vacuum

using a rotary evaporator (Laborota 4000, Heidolph Instruments, Schwabach, Germany). The dried extracts obtained were weighed (expressed in grams, g), and all assays were performed in triplicate (n = 3). The extraction yield was subsequently determined using the following equation:

$$\text{Yield (\%)} = (\text{mass of dried extract}/\text{mass of dried sample}) \times 100 \quad (1)$$

2.4. Phytochemicals

2.4.1. Quantification of Total Phenolic Constituents

The total polyphenol content in *P. lentiscus* and *P. atlantica* extracts was measured using the Folin–Ciocalteu method which quantifies the total concentration of hydroxyl groups in the sample. The protocol follows the method described by Nea et al. [38] and Singleton and Rossi [39] with slight modifications. Briefly, 200 µL of extract solution (1 mg/mL) diluted in ethyl acetate and methanol were mixed with 1 mL of Folin–Ciocalteu reagent (diluted 10-fold in deionized water), Afterwards, 800 µL of a 7.5% sodium carbonate solution was added to the reaction mixture. The samples were left to react for 1 h at ambient temperature in the dark. The absorbance of each mixture was then recorded at 765 nm using a UV–Visible spectrophotometer (Ultrospec 7000, GE Healthcare, Chalfont St Giles, UK), with the solubilization solvent serving as the blank and distilled water as the control. A calibration curve was generated using gallic acid standards at concentrations ranging from 0 to 1000 µg/mL under identical conditions. All experiments were performed in triplicate and the total phenolic content was expressed as mg of gallic acid equivalents per gram of the extract (mg GAE/g) [40].

2.4.2. Measurement of Total Flavonoid Contents

Flavonoids were quantified using a modified method described by Nair et al. [41] and Kim et al. [42]. A volume of 400 µL of methanol or ethanol acetate extract, standard solution (quercetin), solubilization solvent (blank), or distilled water (control) was mixed with 120 µL of 5% $NaNO_2$. After a 5 min incubation, 120 µL of 10% aluminum chloride ($AlCl_3$) was added, and the mixture was vigorously stirred. After 6 min, 800 µL of 1 M NaOH was added. The absorbance was immediately measured at 510 nm against the control using a UV-Vis spectrophotometer (Ultrospec 7000, GE Healthcare, Chalfont St Giles, UK).

The calibration curve was established using quercetin standards at concentrations ranging from 0 to 0.1 mg/mL under identical conditions. All measurements were performed in triplicate. The total flavonoid content was expressed as mg of quercetin equivalents per gram of the extract (mg QE/g) [40].

2.4.3. Fatty Acid GC-FID Analysis

The fatty acid methyl ester (FAME) profiles were determined by GC-FID following the method of Bourgou et al. [43] and Saha Tchinda et al. [44], with minor modifications. For analysis, 10 mg of *P. lentiscus* and *P. atlantica* extracts were incubated at 70 °C for 90 min in a mixture of n-hexane (0.2 mL) and boron trifluoride (BF_3) reagent (0.5 mL) to induce transesterification. After the reaction, a saturated NaCl solution (0.5 mL, 40%) and sulfuric acid (0.2 mL, 10% v/v) were added, followed by methyl ester extraction with 8 mL of n-hexane under agitation. Analysis was performed using an Agilent HP 6890 GC system equipped with an RT-2560 capillary column (30 m × 0.25 mm × 0.20 µm) and nitrogen carrier gas (1.6 mL/min). The temperature program included an initial hold at 170 °C (2 min), a 3 °C/min ramp to 240 °C, and a 15 min hold. Injector and detector temperatures were set and maintained at 225 °C. Methyl esters were identified by comparing their retention times to those of a certified FAME reference standard. Relative FAME percentages were calculated from peak areas and expressed as % of total fatty acids.

2.4.4. LC-MS/MS Analysis

The identification and semi-quantification of molecules were carried out by LC-MS/MS in the negative ionization mode, using an approach combining LC-QTOF for qualitative structural identification and LC-TQ for quantitative purposes using the multiple reaction monitoring (MRM) mode. Methanolic extract samples were prepared at a concentration of 10 mg/mL. As relative quantification was performed with a standard addition method, each sample was separated in two aliquots of 1 mL and an internal standard solution of flavone (0.5 mg/mL) was added to one aliquot, followed by thorough vortex mixing. The mixture was then filtered through a 0.22 µm PTFE membrane before injection.

For structural identification, exact mass data were recorded using an Agilent 1290 Infinity II LC system coupled to an Agilent 6530 Accurate-Mass Q-TOF LC/MS hybrid quadrupole time-of-flight mass spectrometer (Agilent Technologies, Santa Clara, CA, USA), equipped with an ESI source, operating in negative ionization mode. Ten µL of sample was injected onto an Acquity® BEH C18 column (2.1 × 100 mm; 1.8 µm particle size, Waters Co., Milford, MA, USA) that was used for compound separation. A 16 min LC method was developed according to the method of Wojdylo et al. [45], with modifications. Its flow rate was maintained constant at 0.450 mL/min, with solvents A and B consisting of milliQ water and MS-grade acetonitrile, respectively, both supplemented with 0.1% formic acid. The elution gradient started at 1% solvent B and was held for 1 min. Then, a linear gradient ramp was applied to reach 100% solvent B in 11 min. This was followed by a 1.5 min isocratic wash at 100% B, then a return to 1% B for 2.5 min to re-equilibrate the column. The column and autosampler temperatures were set to 30 °C and 15 °C, respectively. The source parameters were set as follows: gas temperature 300 °C, drying gas flow 8 L/min, nebulizer pressure 35 psi, sheath gas temperature 350 °C, sheath gas flow 11 L/min, capillary voltage 3500 V and nozzle voltage 1000 V. Data were first acquired in full scan mode MS1, with a fragmentor voltage of 175 V and an m/z range from 100 to 1000. Putative polyphenols were identified based on mass errors lower than 16 ppm. Targeted MS2 was then used to break down these precursor ions into their fragments. Collision energy, isolation width, and fragment mass range were set at 35 eV, 1.3 m/z, and 100–650 m/z, respectively. MS/MS fragmentation profiles were thereby obtained for each selected precursor ion, and polyphenol identification was validated after comparison with the MassBank, PubChem databases and scientific literature.

For semi-quantification purposes, MRM transitions were recorded using an Agilent 1290 Infinity II LC system (Agilent Technologies, Santa Clara, CA, USA) coupled to an Agilent 6475 Triple Quadrupole LC-MS mass spectrometer (Agilent Technologies, Santa Clara, CA, USA). The LC method used was the same as for LC-QTOF, to achieve similar retention times. The TQ ion source parameters were set as follows: drying gas temperature 300 °C, drying gas flow 13 L/min, nebulizer pressure 35 psi, sheath gas temperature 250 °C, sheath gas flow 11 L/min, capillary voltage 4000 V.

MRM transitions were recorded in the negative ionization mode, except for flavone (internal standard), with a dwell time of 5 ms while fragmentor voltage and collision energy were set at 150 V and 30 V, respectively. Recorded MRM transitions are presented in Table 1. Relative quantification was performed using the following formula:

$$\text{Polyphenol content (A.U./mg DW)} = [\text{MRM peak area}/(\text{spiked MRM flavone peak area} - \text{non-spiked MRM flavone peak area})]/\text{sample dry weight} \quad (2)$$

With:
A.U. = Arbitrary Units
DW = Dry Weight
MRM = Multiple Reaction Monitoring

All data acquisition and processing were carried out using MassHunter® Workstation software (Version 10.0, Agilent Technologies, Santa Clara, CA, USA).

2.5. Biological Activities

2.5.1. Antioxidant Assays

The antioxidant power of methanolic extracts from *P. lentiscus* and *P. atlantica* was evaluated through DPPH radical scavenging and the ferric reducing antioxidant power (FRAP) assays. These two methods assess the extracts' capacity to scavenge free radicals and to reduce ferric ion (Fe^{3+}) to ferrous ion (Fe^{2+}) [43], in comparison, respectively, with the reference standards: ascorbic acid and Trolox.

- DPPH assay (2,2-diphenyl-1-picrylhydrazyl radical scavenging test)

The ability of the methanolic extracts of *P. lentiscus*, *P. atlantica*, and Trolox to reduce acellular free radicals was assessed by monitoring the discoloration of the DPPH solution in methanol, originally purple, following the method of Brand-Williams et al. [46], with slight modifications.

The samples were analyzed at concentrations of 5, 15, 45, and 135 µg/mL. A volume of 800 µL of each sample diluted in methanol or the standard Trolox at different concentrations was added to 2 mL of DPPH solution (0.001%) in methanol, then manually shaken. After a 30 min incubation in the dark at ambient temperature, the absorbance of each preparation was recorded using a UV/visible double-beam spectrophotometer (Ultrospec 7000, GE Healthcare, UK) at a wavelength of 517 nm. The same procedure was followed for Trolox (Cayman Chemical, Ann Arbor, MI, USA) used as the positive control, while methanol with DPPH (Alfa Aesar, Karlsruhe, Germany) was used as the blank. All experiments were performed in triplicate. The percentage of inhibition was calculated using the following formula:

$$\text{Inhibition\%} = [(\text{Abs}_{\text{Blank}} - \text{Abs}_{\text{Sample}})/\text{Abs}_{\text{Blank}}] \times 100 \quad (3)$$

where "$\text{Abs}_{\text{Blank}}$" refers to the absorbance of the blank and "$\text{Abs}_{\text{Sample}}$" corresponds to the absorbance of the sample (or positive control).

- Ferric reducing antioxidant power (FRAP) assay

The ferric-reducing antioxidant power of the extracts was evaluated according to the method described by Tanoh et al. [47], with some adjustments. Four dilutions of the extracts and ascorbic acid (standard, Sigma Aldrich, Taufkirchen, Germany) were prepared in methanol (12.5 to 100 µg/mL). A volume of 1000 µL of each dilution was mixed with an equal volume of phosphate buffer (200 mM, pH 6.6) and potassium ferricyanide solution (1%). The mixture was incubated at 50 °C for 20 min, then 1000 µL of trichloroacetic acid (10% *v*/*v*) was added. After centrifugation (3000 g, 10 min) at ambient temperature, the supernatant was collected and mixed with 1 mL of distilled water and 150 µL of $FeCl_3$ solution (0.1%).

The absorbance was measured at 700 nm using a double-beam UV/visible spectrophotometer (Ultrospec 7000, GE Healthcare, UK). This measurement relies on the increase in absorbance of the reaction mixture, reflecting the reduction of Fe^{3+} ions to Fe^{2+}. Higher absorbance (compared to the blank containing phosphate buffer, potassium ferricyanide solution, trichloroacetic acid, distilled water, and $FeCl_3$, but without the sample or ascorbic acid) indicates greater reducing power. All samples were performed in triplicate.

2.5.2. Assessment of the Anti-Inflammatory Activities

- Bovine Serum Albumin Denaturation Assay

The anti-inflammatory activity of the methanolic extracts of *P. lentiscus* and *P. atlantica* leaves was assessed using the protein denaturation assay, as described by Kar et al. and Nea et al. [48,49], with minor modifications. Briefly, the reaction mixtures were prepared by combining 1000 µL of the methanolic extract samples with diclofenac (≥98.5 purity, Sigma-Aldrich, Buchs, Switzerland) as the reference standard, at concentrations of 400, 300, 200, and 100 µg/mL. To this, 500 µL of a 2% BSA solution in water, and 2500 µL of phosphate-buffered saline (PBS), adjusted to pH 6.3 with hydrochloric acid (HCl), were added. The tubes were incubated at room temperature for 20 min, then heated to 70 °C for 5 min, and cooled down for 10 min. The extent of BSA denaturation was assessed by measuring absorbance at 660 nm using an UV-Vis spectrophotometer (Ultrospec 7000, GE Healthcare, UK).

The assay was conducted in triplicate, and the percentage of albumin denaturation inhibition was expressed as the mean ± standard deviation (SD) relative to control, according to the following formula:

$$\text{BSA denaturation\%} = [(\text{Abs}_{\text{Blank}} - \text{Abs}_{\text{sample}})/\text{Abs}_{\text{blank}}] \times 100 \quad (4)$$

where "$\text{Abs}_{\text{blank}}$" presents the absorbance (Abs) of the reaction mixture without the methanolic extract, "$\text{Abs}_{\text{sample}}$" corresponds to the absorbance of the reaction mixture containing the methanolic extract, adjusted by subtracting the absorbance of the diluted methanolic extract.

- Lipoxygenase inhibition assay

The anti-inflammatory activities of methanolic extracts were evaluated according to the method of Nikhila and Sangeetha [50], with slight modifications. To summarize, the reaction mixture, containing methanolic extracts at different concentrations (100, 75, 50, and 25 µg/mL in methanol), was prepared in triplicate, along with 10 mg of lipoxygenase (≥50,000 U/mg) in 100 mL of distilled water to obtain a solution of 5000 U/mL (Sigma, Taufkirchen, Germany) and 35 µL (0.1 mg/mL) of a 0.2 M borate buffer solution (pH = 9.0). The prepared samples were incubated at 25 °C for 15 min. The reaction was initiated by adding 35 µL of a substrate solution (250 µM linoleic acid, ≥98.5 purity, Sigma-Aldrich, St. Louis, MO, USA), and then absorbance was measured at 234 nm using a UV spectrophotometer (Ultrospec 7000, GE Healthcare, UK). Quercetin (Sigma-Aldrich, Taufkirchen, Germany) was used as the positive control and prepared at the same concentration as our methanolic extract. The percentage of lipoxygenase activity inhibition was calculated as follows:

$$\text{Lipoxygenase inhibition\%} = [(\text{Abs}_{\text{blank}} - \text{Abs}_{\text{sample}})/(\text{Abs}_{\text{blank}})] \times 100 \quad (5)$$

"$\text{Abs}_{\text{blank}}$" denotes the absorbance of the reaction mixture without the methanolic extract, while "$\text{Abs}_{\text{sample}}$" represents the absorbance of the mixture containing the extract, corrected by subtracting the intrinsic absorbance of the diluted methanolic extract.

2.5.3. Anti-Tyrosinase Activity Evaluation

The anti-tyrosinase activity of methanolic extracts of *P. lentiscus* and *P. atlantica* obtained by maceration was evaluated following the protocols described by Rangkadilok et al. [51] and Genva et al. [52].

Tyrosinase inhibition was assessed by incubating 100 µL of each sample, the control (1 mM kojic acid solution), or the blank (50 mM phosphate buffer, pH 6.5) with 50 µL of the tyrosinase solution (625 U/mL) and 250 µL of oxygenated buffer. The mixture was incubated at room temperature for 15 min. After incubation, the reaction mixture was

transferred to a quartz cuvette, and 400 µL of substrate solution (1 mM L-DOPA) was added. Absorbance was measured at 475 nm using a spectrophotometer (Ultrospec 7000, GE Healthcare, Cambridge, UK).

Quercetin (Sigma, Germany) was used as a positive control. Each sample was tested in triplicate. The percentage of tyrosinase inhibition was calculated using the following formula:

$$\text{Tyrosinase inhibition } \% = [(\text{Abs}_{\text{blank}} - \text{Abs}_{\text{sample}})/\text{Abs}_{\text{blank}}] \times 100 \quad (6)$$

where "$\text{Abs}_{\text{blank}}$" corresponds to the absorbance of the blank (50 mM phosphate buffer, pH 6.5) representing 0% inhibition, and "$\text{Abs}_{\text{sample}}$" presents the absorbance of the assay reaction mixture containing the extract, kojic acid, or quercetin. The IC_{50} values of the extracts, kojic acid, and quercetin were then calculated.

2.5.4. Data Analysis

Quantitative data were presented as mean ± SD and mean ± SEM. The Student's *t*-test for unpaired series was used to compare the means of *P. lentiscus* and *P. atlantica*. Dunnett's post hoc test was used to evaluate the differences between the pairs of means in the groups. One way and two-way ANOVA followed by the Tukey post hoc test were applied for the multiple comparison using the GraphPad Prism 8 program (San Diego, CA, USA). Additionally, the nonlinear regression feature was used to calculate the IC_{50} values. The threshold for statistical significance was set at a *p*-value of 0.05.

3. Results and Discussion

3.1. Chemical Composition

3.1.1. Extraction Yields, Phenolic and Flavonoid Contents

The extraction of phenolic compounds was carried out using solvents of increasing polarities: methanol, ethyl acetate, and hexane in order to compare the extraction yields of *P. lentiscus* and *P. atlantica* leaves, along with their phenolic and flavonoid contents.

Extraction yields varied significantly depending on the solvent used ($p < 0.001$) (Figure 1). Methanolic extracts exhibited the highest yields, reaching 42.10 ± 1.0% for *P. atlantica* and 35.20 ± 1.1% for *P. lentiscus*, with a significant difference in favor of *P. atlantica* ($p < 0.001$). Extracts obtained with ethyl acetate showed intermediate yields of 11.10 ± 0.5% for *P. atlantica* and 13.90 ± 0.5% for *P. lentiscus*, with the latter species presenting a significantly higher yield ($p < 0.001$). Hexane, an apolar solvent, generated the lowest yields, with 11.20 ± 0.25% for *P. atlantica* and 3.33 ± 0.2% for *P. lentiscus*, with the yield being significantly higher for *P. atlantica* ($p < 0.001$).

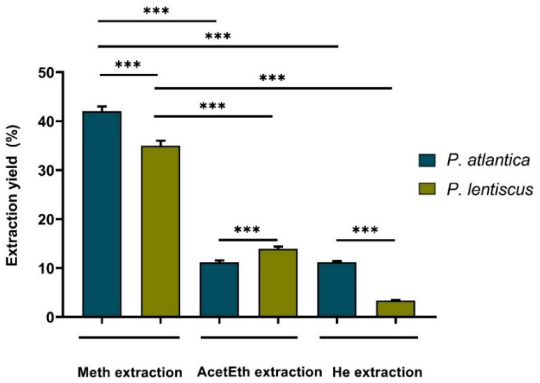


Figure 1. Comparison of extraction yields of *P. lentiscus* and *P. atlantica* using solvents of varying polarity. Methanol yielded the highest extraction efficiency. *** $p < 0.001$. Results were expressed as a mean ± standard deviation (SD) of three independent experiments ($n = 3$).

The methanol yield of *P. atlantica* was considerably higher than that reported by Belyagoubi et al. (36.40%) [53], while for *P. lentiscus*, it was markedly higher than that obtained with ethanol by Remila et al. (6.09%) [25]. These observations indicate that the use of polar solvents, such as methanol, significantly increases yields and highlights that *P. atlantica* provides a higher yield than *P. lentiscus*. These results are coherent with previously reported studies and highlight the importance of solvent polarity in maximizing extraction [53,54]. Based on these extraction yields, the two most efficient and most polar solvents were selected for total polyphenol and flavonoid quantification.

Consistent with the yield obtained, methanol allowed the extraction of the highest concentrations of polyphenols and flavonoids in both species compared to extraction with ethyl acetate ($p < 0.001$) (Figure 2). The polyphenol content of the methanolic extracts reached 343.06 ± 0.02 mg GAE/g for *P. lentiscus* and 430.28 ± 0.01 mg GAE/g for *P. atlantica*, whereas the ethyl acetate extracts contained only 88.6 ± 0.03 mg GAE/g and 90.56 ± 0.56 mg GAE/g, respectively (Figure 2a). The inter-solvent comparison showed that methanol extracted significantly higher amounts of polyphenols than ethyl acetate in both species ($p < 0.001$). Furthermore, inter-species analysis revealed that both methanolic and ethyl acetate extracts of *P. atlantica* exhibited significantly higher polyphenol contents than those of *P. lentiscus* ($p < 0.001$). Concerning flavonoids, the methanolic extracts contained 230.00 ± 0.01 mg QE/g for *P. lentiscus* and 183.00 ± 0.01 mg QE/g for *P. atlantica*, while the ethyl acetate extracts showed markedly lower levels of 86.39 ± 0.03 mg QE/g and 74.3 ± 0.04 mg QE/g, respectively (Figure 2b). The inter-solvent comparison once again demonstrated the superior extraction capacity of methanol over ethyl acetate for flavonoids ($p < 0.001$). Conversely, the inter-species comparison indicated that *P. lentiscus* exhibited significantly higher flavonoid contents than *P. atlantica* in both solvent extracts ($p < 0.001$).

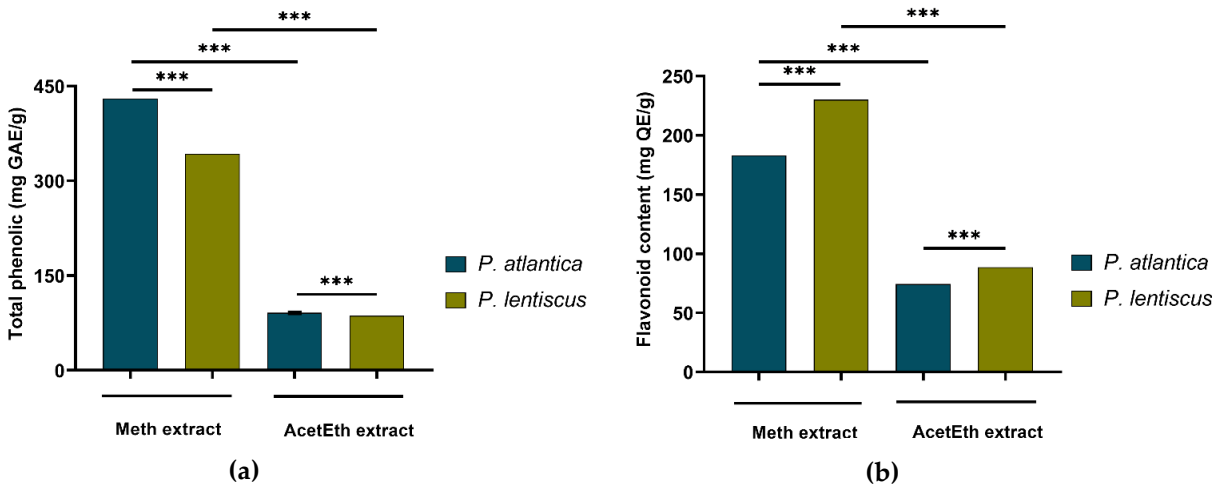


Figure 2. Total phenolic (**a**) and flavonoid content (**b**) of different extracts (Meth and EthAcet) of *P. lentiscus* and *P. atlantica*. Methanolic extracts showed the highest contents *** $p < 0.001$. Results were expressed as a mean ± SD ($n = 3$), GAE: gallic acid equivalents, QE: quercetin equivalents.

The polyphenol content of *P. lentiscus* foliar extract showed moderate variation compared to existing literature, being slightly higher to the findings of Amel et al. [55] (216.29 ± 20.62 mg GAE/g) but approximately 2.3-fold lower than the maximum value of 524.87 ± 1.17 mg GAE/g reported in Morocco [56].

Regarding flavonoids, the content measured in this study was significantly higher than some earlier findings, such as the 19.162 ± 0.436 mg QE/g reported by the same team [55], but remains consistent with the values obtained by Remila et al. [25] and Seddoqi et al. [56], which were around 139.38 ± 3.11 and 147.91 ± 0.04 mg QE/g, respectively.

In *P. atlantica* foliar extract, the flavonoid content was up to four times higher than the 51.77 ± 4.34 mg QE/g reported by Peksel et al. [57] and the range of 100.10 to 110.62 mg QE/g reported by Amri et al. [55]. In contrast, the polyphenol content was lower than the 245.60 ± 6.02 mg GAE/g observed in Turkish extracts obtained by methanol extraction using a Soxhlet apparatus [57].

These differences maybe originate from variations in extraction methods, climatic conditions, and the geographical origin of the plants [58,59]. It is widely recognized that phenolic compounds are key components of plant metabolism and tend to accumulate under stress conditions, such as drought, extreme temperatures, and pollution [60]. Moreover, the solubility of phenolic compounds depends on several factors such as their degree of polymerization, the plant part used, and soil characteristics [61,62].

Our results highlight the richness of the methanolic extract of *P. atlantica* and *P. lentiscus* in polyphenols and flavonoids. To further characterize this promising composition, the methanolic extract was analyzed by LC-MS/MS and GC-FID. Analyses by LC-MS/MS indeed enables precise identification of individual polyphenols to determine the extract's composition and investigate the potential origin of its biological activities, while GC-FID provides information on the fatty acid profile, which may indicate potential moisturizing properties. This combined analytical approach enhances understanding of the extract's functional properties and guides its targeted use for dermo-cosmetic applications.

3.1.2. Fatty Acid Composition

GC-FID analysis was performed to identify and compare the fatty acids present in leaf extracts of *P. lentiscus* and *P. atlantica*, which may influence the dermo-cosmetic properties of our extracts, particularly their moisturizing. As illustrated in Figure 3 and Table A1, both extracts contain much more of unsaturated fatty acids (85.66% in *P. atlantica* and 70.71% in *P. lentiscus*) than saturated fatty acids. The *P. lentiscus* extract was primarily composed of palmitic acid (C16:0, 18.35%), γ-linolenic acid (C18:3γ, 31.54%), and linoleic acid (C18:2, 23.96%). In contrast, *P. atlantica* was characterized by the predominance of *cis*-13,16-docosadienoic acid (C22:2), which accounted for 54.13% of its composition.

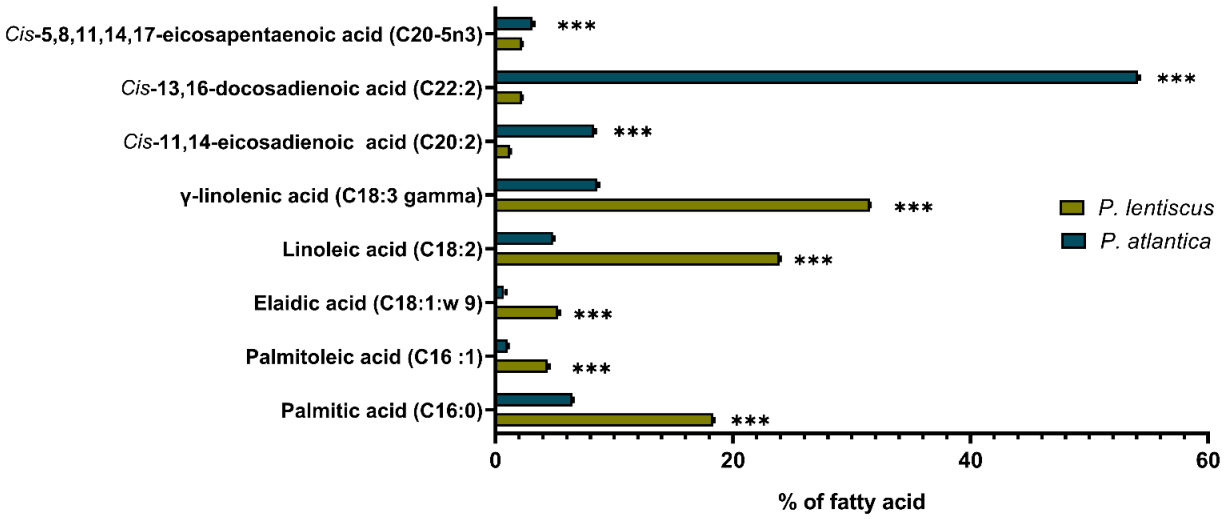


Figure 3. Assessment of the fatty acid composition of *P. lentiscus* and *P. atlantica* methanolic extracts using GC-FID. Both extracts contained higher levels of unsaturated fatty acids. Data were expressed as mean ± SD (n = 3), *** $p < 0.001$.

Previous studies have indicated that climatic variations can influence fatty acid desaturation, thereby altering the balance between saturated and polyunsaturated fatty acids [63]. This may explain the differences observed between the two species in our study. The higher

levels of γ-linolenic acid and linoleic acid in *P. lentiscus* suggest a greater desaturation activity of C18 fatty acids, while the strong predominance of *cis*-13,16-docosadienoic acid in *P. atlantica* reflects a distinct elongation pathway leading to the synthesis of very-long-chain polyunsaturated fatty acids. In addition to environmental influences, species-specific genetic factors also contribute to determining lipid metabolism and composition [64]. Therefore, the higher proportion of polyunsaturated fatty acids in *P. atlantica* (85.66%) compared with *P. lentiscus* (70.71%) is likely the result of combined effects of genetic regulation and ecological adaptation.

The leaves of *P. lentiscus* and *P. atlantica* remain widely unexplored compared to other parts of the plant, such as *P. lentiscus* seed oil, which is predominantly composed of oleic acid [65–68]. Hexane extracts from *P. lentiscus* leaves reveal a predominance of palmitic and oleic acids [69]. Yet the fatty acid composition of *P. atlantica* leaves had not yet been evaluated, thus justifying its investigation in the present study and the evaluation of its potential value as a source of fatty acids.

These lipidic compounds, particularly unsaturated fatty acids, have moisturizing and emollient properties, promoting skin suppleness, maintaining the skin barrier, and stabilizing cell membranes [70–72]. Topical application of linoleic and linolenic acids has been shown to restore the skin barrier and improve the overall appearance of the skin [71,73], suggesting that extracts of *P. lentiscus* and *P. atlantica* are promising dermo-cosmetic ingredients for enhancing hydration, softness, and barrier function in innovative formulations.

3.1.3. LC-MS/MS Screening and Identification of Polyphenolic Compounds

A total of thirteen phenolic compounds, mainly flavonoids, have been identified by LC-QTOF based on their characteristic fragmentation profiles (Figure 4, Table 1). Seven compounds were detected in *P. lentiscus*: isoquercitrin, myricitrin, methyl gallate, myricetin-3-*O*-hexoside, gallocatechin, epigallocatechin gallate, and pistafolin A. In *P. atlantica*, ten compounds were identified: isoquercitrin, chlorogenic acid, myricitrin, methyl gallate, myricetin-3-*O*-hexoside, rutin, luteolin, quercetin-3-*O*-rhamnoside, kaempferol-3-*O*-galactoside (Trifolin), and quercetin-3-*O*-arabinoside. Among these compounds, four are common to both species and their relative abundances, show significant variations between the two species.

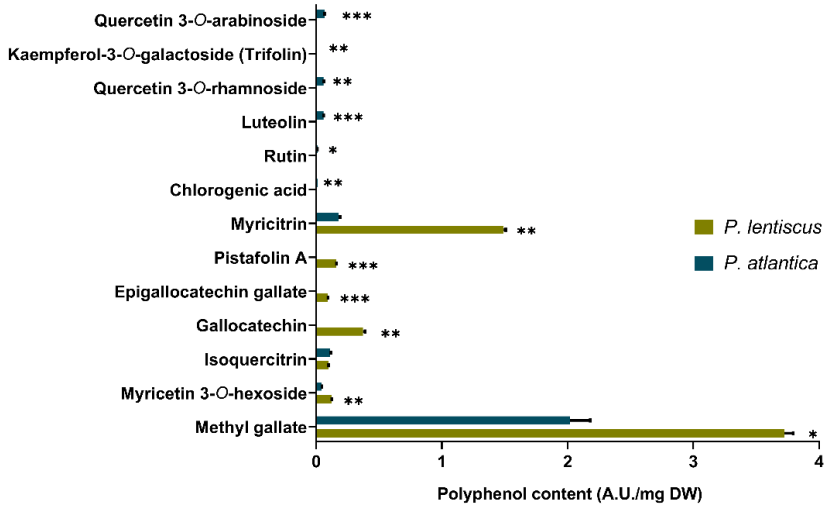


Figure 4. Assessment of polyphenol profile of *P. lentiscus* and *P. atlantica* extracts using LC-TQ. Methyl gallate and myricitrin were the major compounds, with *P. lentiscus* showing higher proportions expressed as mean ± SD (n = 3), * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$.

Table 1. Phytochemical characterization of methanolic extracts of *P. lentiscus* and of *P. atlantica* by LC-MS/MS (negative mode).

N°	Compound	Formula	MRM (*m*/*z*)	MM	Predicted M-H	M-H Obs	Mass Error (ppm)	RT	Observed Fragments	Samples	References
1	Isoquercetin	$C_{21}H_{20}O_{12}$	463 → 301	464.0954	463.0876	463.0840	7.77	3.9	300.0290, 271.0265, 301.0370, 255.0320	PL, PA	[74], PubChem
2	Chlorogenic acid	$C_{16}H_{18}O_9$	353 → 191	354.0950	353.0872	353.0846	7.49	3.1	191.0561	PA	[75], PubChem
3	Myricitrin	$C_{21}H_{20}O_{12}$	463 → 317	464.0954	463.0876	463.0840	7.77	3.9	301.0357, 317.0309, 300.0280, 271.0262	PL, PA	[76], MassBank
4	Methyl gallate	$C_8H_8O_5$	183 → 124	184.0371	183.0293	183.0282	6.31	3.1	124.0163, 123.0089, 106.0057	PL, PA	[77]
5	Myricetin 3-*O*-hexoside	$C_{21}H_{20}O_{13}$	479 → 317	480.0903	479.0825	479.0784	8.59	3.6	316.0223, 271.0262, 287.0190, 317.0298, 179.0006, 151.0004	PL, PA	[78]
6	Gallocatechin	$C_{15}H_{14}O_7$	305 → 125	306.0739	305.0661	305.0661	7.72	2.6	125.0243, 137.0246, 109.0288, 139.0371, 167.0330	PL	PubChem, MassBank
7	Epigallocatechin gallate	$C_{22}H_{18}O_{11}$	457 → 169	458.0849	457.0771	457.0737	7.36	3.4	125.0248, 137.0247, 179.0355, 219.0669, 305.0671	PL	[79], MassBank
8	Pistafolin A	$C_{28}H_{24}O_{18}$	647 → 495	648.0962	647.0884	647.0828	8.72	3.5	343.0688, 169.0149, 495.0788	PL	[80,81]
9	Rutin	$C_{27}H_{30}O_{16}$	609 → 300	610.1533	609.1455	609.1551	−15.73	3.8	300.0275, 301.0380, 272.0316, 178.3373, 151.0027	PA	[82]
10	Luteolin	$C_{15}H_{10}O_6$	285 → 133	286.0477	285.0399	285.0399	−0.06	4.5	133.0399, 151.006, 270.2072, 107.0168, 175.0380, 121.0269	PA	[83]
11	Quercetin 3-*O*-rhamnoside	$C_{21}H_{20}O_{11}$	447 → 301	448.1005	447.0927	447.0959	−7.15	4.2	300.0285, 301.0346, 271.0266, 255.0302, 178.9992	PA	[84]
12	Kaempferol-3-*O*-galactoside (Trifolin)	$C_{21}H_{20}O_{11}$	447 → 284	448.1005	447.0927	447.0959	−7.15	4.2	325.0602, 285.0419, 284.0280, 255.0302	PA	[85], PubChem
13	Quercetin 3-*O*-arabinoside	$C_{20}H_{18}O_{11}$	433 → 301	434.0849	433.0771	433.0772	−0.27	4.1	300.0268, 271.0256, 301.0344, 255.0271	PA	[84]

MRM: Multiple reaction monitoring, MM: Monoisotopic mass, Predicted M-H: Predicted $[M-H]^-$ ion, M-H obs: Observed $[M-H]^-$ ion, Mass error (ppm): Mass error (parts per million), RT: Retention time, PL: *P. lentiscus* L., PA: *P. atlantica* Desf.

Our results show that these Mediterranean species possess a high phenolic content, characterized by a flavonoid-dominated composition. The chemical composition of both extracts was dominated by methyl gallate (3.72 ± 0.07 and 1.97 ± 0.12 for *P. lentiscus* and *P. atlantica*, respectively), a compound rarely reported as a major constituent in previous studies on the genus *Pistacia*. This composition is followed by myricitrin (1.49 ± 0.02 and 0.15 ± 0.01), myricetin-3-*O*-hexoside (0.12 ± 0.02 and 0.04 ± 0.02), and isoquercitrin (0.10 ± 0.02 and 0.10 ± 0.01) in *P. lentiscus* and *P. atlantica*, respectively. The high content of hydrophilic phenolic compounds detected in this extract is mainly linked to the extraction solvent. Methanol, owing to its strong polarity, preferentially dissolves polyphenols that possess multiple hydroxyl groups and therefore exhibit a polar character [86]. This solvent-driven selectivity accounts for the predominance of methyl gallate and myricetin derivatives, both of which are highly polar phenolics, in the LC-MS/MS profile of the methanolic leaf extract.

This composition partially contrasts with that reported in the literature. Numerous previous studies on the phenolic compounds of *P. lentiscus* and *P. atlantica* have revealed significant variability in their composition, influenced by the extraction and analytical methods employed, as well as by geographical factors such as climate, soil characteristics, altitude, and sun exposure.

For instance, Seddoqi et al. [56] reported, for *P. lentiscus* leaves collected in Morocco and analyzed by LC-MS/MS in positive mode, that epigallocatechin was the most abundant compound, whereas Rodriguez et al. [80] identified, for leaves of the same species collected in Algeria and analyzed by HPLC-ESI-QTOF in negative mode, catechin, β-glucogallin, and quercitrin gallate as the main constituents. Moreover, in another study, methyl gallate, gallic acid, rutin, and quercetin-3-*O*-glucoside were identified by RP-HPLC as the major constituents in the methanolic leaf extract of *P. atlantica* from Turkey obtained by maceration [87]. These differences highlight the uniqueness of our finding regarding methyl gallate as the major component.

Beyond methodological aspects, geo-environmental conditions may also shape phytochemical variability between samples. Phenolic biosynthesis is known to increase in response to abiotic stresses such as water deficit, intense sunlight, salinity, and thermal fluctuations, as well as seasonal variations, in addition to biotic pressures [88–90]. These adaptive defense mechanisms can therefore contribute to interspecific differences in phenolic profiles, reflecting the influence of the ecological conditions prevailing at the sampling sites.

The abundant presence of methyl gallate and myricetin derivatives is of particular interest given their multiple biological effects. Flavonoids are well known for their antimicrobial, anti-inflammatory, and strong antioxidant properties [91,92]. Methyl gallate, in particular, exerts various promising anti-inflammatory and dermatological effects, such as the inhibition of Cyclooxygenase-2 (COX-2) and leukotriene C4 (LTC4) production [42], an anti-aging mechanism via the inhibition of protein glycation [93], and a depigmenting effect through modulation of the Glycogen Synthase Kinase 3 beta (GSK3β/β) catenin pathway [94]. Similarly, myricetin (the aglycone of myricitrin and myricetin-3-*O*-hexoside) exhibits cutaneous anti-inflammatory properties and remarkable antioxidant activity, attributed to the presence of three hydroxyl groups on its B ring [95]. The richness of these extracts in such compounds therefore offers up promising application prospects in the field of skin care. Accordingly, we investigated the biological activities of these extracts.

Taken together, our findings show that the methanolic extract of *P. atlantica* exhibited the highest total polyphenol content, whereas *P. lentiscus* contained the highest flavonoid levels. Both extracts were dominated by methyl gallate and myricitrin, and displayed a high proportion of unsaturated fatty acids.

3.2. Biological Activities

Based on the chemical composition of *P. lentiscus* and *P. atlantica* leaf extracts and their traditional use in folk medicine for skin care, biological assays were conducted to evaluate their potential for dermo-cosmetic applications. Antioxidant, anti-inflammatory, and anti-tyrosinase activities were assessed to determine the suitability of these extracts as multifunctional active ingredients in innovative cosmetic formulations targeting skin protection, soothing, and brightening effects

3.2.1. Antioxidant Activities

The results of the DPPH and FRAP tests confirmed the strong antioxidant activity of the extracts from both plant species. The results of the DPPH assay (Figure 5a, Table 2) revealed the dose-dependent antioxidant activity of both extracts, with a slightly higher efficacy ($p < 0.001$) for *P. lentiscus* (IC_{50} = 5.19 ± 0.01 µg/mL, ~11% more active) compared to *P. atlantica* (IC_{50} = 5.61 ± 0.04 µg/mL, ~4% more active) relative to ascorbic acid. Both extracts demonstrated significant antioxidant activity when compared to ascorbic acid (IC_{50} = 5.84 ± 0.05 µg/mL), with highly significant differences for *P. lentiscus* ($p < 0.001$) and significant to highly significant differences for *P. atlantica* ($p < 0.05$ to $p < 0.001$).

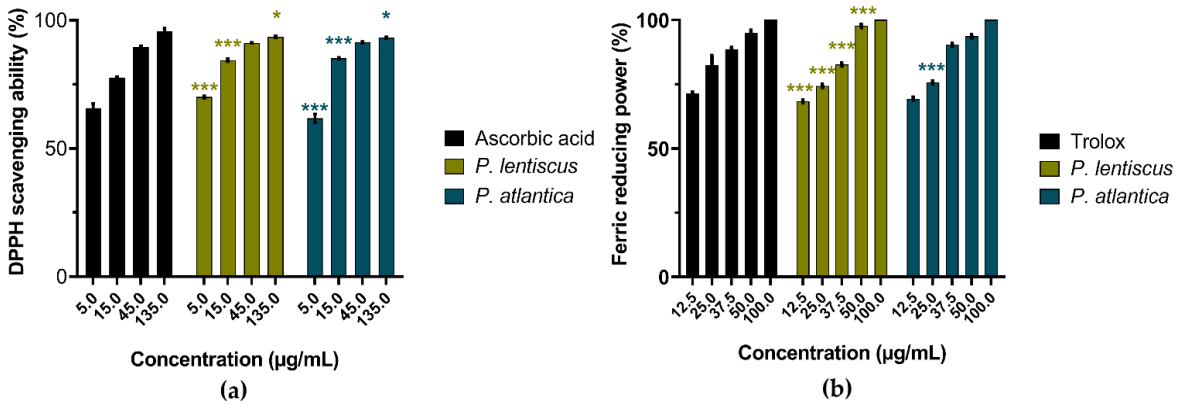


Figure 5. Determination of the antioxidant capacities of *P. lentiscus* and *P. atlantica* methanolic extracts using the DPPH scavenging ability (**a**) and FRAP ferric reducing power (**b**). Both extracts showed strong antioxidant activity, with *P. lentiscus* being slightly more effective. Data analysis was presented as mean ± SD (n = 3), * $p < 0.05$, *** $p < 0.001$.

Table 2. Antioxidant, anti-inflammatory and anti-tyrosinase activities of methanolic extracts of *P. lentiscus* and *P. atlantica*.

Samples and Standards	Biological Activities IC_{50} (µg/mL) [a]			
	DPPH	BSA Denaturation	LOX Denaturation	Anti-Tyrosinase
P. lentiscus	5.19 ± 0.01 ***	143.00 ± 0.70 ***	22.53 ± 0.05 ***	39.80 ± 0.08 ***
P. atlantica	5.61 ± 0.04 *$^{\#\#\#}$	139.10 ± 0.55 ***$^{\#\#}$	22.67 ± 0.04 ***^{ns}	38.25 ± 0.02 ***$^{\#\#\#}$
Ascorbic acid	5.84 ± 0.05	-	-	-
Diclofenac	-	60.88 ± 0.03	-	-
Quercetin	-	-	17.91 ± 0.03	
Kojic acid	-	-	-	34.28 ± 0.07

[a] IC_{50} value defined as half-maximal inhibitory concentration and expressed as mean ± SD (n = 3). DPPH: 2,2-diphenyl-1-picrylhydrazyl, LOX: lipoxygenase, BSA: bovine serum albumin and anti-tyrosinase. * denotes p-value < 0.05, *** p-value < 0.001, extracts vs. to standard; $^{\#\#}$ denotes p-value < 0.01, *P. lentiscus* vs. *P. atlantica*; $^{\#\#\#}$ denotes p-value < 0.001, *P. lentiscus* vs. *P. atlantica*; ^{ns}: no significant, comparison between *P. lentiscus* and *P. atlantica*.

To further evaluate their antioxidant properties, the FRAP assay was performed to assess the reducing power of the extracts. The results (Figure 5b, Table 2) revealed a concentration-dependent increase in reducing activity for both extracts. *P. lentiscus* exhibited significantly higher FRAP values ($p < 0.001$) than *P. atlantica* at the same concentrations. At 100 µg/mL, *P. lentiscus* showed a reducing capacity close to that of Trolox, highlighting its strong antioxidant potential.

The strong antioxidant activity of both extracts, linked to their richness in phenolic compounds [61,96], was confirmed by our results using the DPPH assay. Therefore, the redox potential of phenolic compounds plays a crucial role in assessing the antioxidant potential of the extracts [97].

The observed variations can be largely attributed to the flavonoid richness of both extracts, known for their redox properties and their ability to donate electrons or hydrogen atoms, which is strongly associated with improved radical-scavenging and reducing capacities [98]. The higher content of these compounds in the *P. lentiscus* extract explains its greater DPPH·radical-scavenging activity [99]. These differences may also be reinforced by the specific predominance in *P. lentiscus* of other major antioxidants such as methyl gallate and myricitrin, two compounds well known for their strong antioxidant effects [95,100,101], due to their ability to neutralize the DPPH· radical and chelate iron ions [102–104] whose concentrations are higher in this extract.

Our findings are consistent with a previous study reporting that the methanolic extract of *P. lentiscus* displayed strong antioxidant activity, with an IC_{50} value of 8 µg/mL, which is fairly close to our results (5.19 µg/mL). However, our results and those of Amessis-Ouchemoukh et al. [105] show significantly higher activity than those reported by Bourroubey et al. [106] and Hemma et al. [107], who obtained IC_{50} of 0.06 mg/mL and 0.4 mg/mL, respectively. Furthermore, a study conducted in Morocco in 2022 [108] revealed lower activity (IC_{50} of 27.22 µg/mL) compared to our findings. Similarly, in Algeria, Benabdellah et al. [109] reported that the 80% methanolic extract of *P. atlantica* showed high antioxidant capacity with an IC_{50} of 5.61 µg/mL. These differences can be attributed to various exogenous factors, such as geographical origin, climatic conditions, harvesting period, extraction methods, and phytochemical composition of the extracts [110].

An important reducing capacity of Fe^{3+} to Fe^{2+} was also observed in both extracts. These results are consistent with previous studies carried out in Morocco and Greece, where leaf extracts from these species demonstrated, using the same method, a significantly higher iron-reducing capacity than reference standards [108,111]. This reducing power is due to their richness in polar compounds acting as hydrogen donors or electron transfer agents [112]. Moreover, the solubility of phenolic compounds, influenced by their degree of polymerization, the part of the plant used, and climatic conditions, also plays a role in this activity [61,62]. Since the two assays rely on different chemical principles, the variations observed in antioxidant activities can be explained by the nature of the reagents used: the DPPH method primarily assesses free radical scavenging ability, whereas the FRAP method evaluates reducing power [113].

The results of both antioxidant assays indicate that the leaf extracts of *P. lentiscus* and *P. atlantica* exhibit significant antioxidant activity, highlighting their promising potential as natural ingredients in anti-aging cosmetic formulations and as formulation-stabilizing agents.

3.2.2. Anti-Inflammatory Activities

Given the traditional use of *Pistacia* spp. to treat inflammatory skin conditions [114], the anti-inflammatory potential of *P. lentiscus* and *P. atlantica* was assessed through their ability to inhibit bovine serum albumin (BSA) denaturation and the activity of the lipoxygenase (LOX) enzyme activity, two key mechanisms involved in inflammatory processes. Both

extracts demonstrated high to moderate anti-inflammatory activity, with similar overall efficacy; *P. atlantica* stood out for slightly greater inhibition in the BSA denaturation test, while *P. lentiscus* was more effective in inhibiting LOX (Figure 6). The results indicate that the protective effect against BSA denaturation was dose-dependent, with IC_{50} values of 143.0 ± 0.70 µg/mL for *P. lentiscus* and 139.1 ± 0.55 µg/mL for *P. atlantica*. For comparison, diclofenac, used as a positive control, exhibited a stronger effect with an IC_{50} of 60.88 ± 0.03 µg/mL. At higher concentrations (300 µg/mL), *P. atlantica* shows a slightly stronger inhibition than *P. lentiscus* ($p < 0.01$) (Figure 6a, Table 2). The anti-LOX activity of both extracts was strong, with IC_{50} values of 22.53 ± 0.05 µg/mL for *P. lentiscus* and 22.67 ± 0.04 µg/mL for *P. atlantica*, with IC_{50} values slightly higher than that of quercetin used as a standard (17.91 ± 0.03 µg/mL, ~26% less potent). The lipoxygenase inhibition curve (Figure 6b, Table 2) shows a concentration-dependent increase for both species, with values close to each other. Both extracts reached inhibition levels comparable to quercetin at 100 µg/mL. Statistical analysis revealed highly significant differences ($p < 0.001$) between the extracts and the positive control.

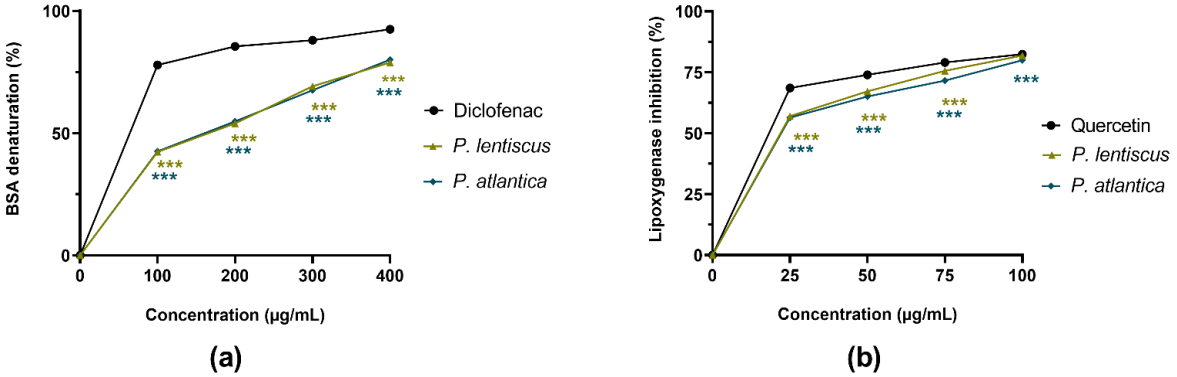


Figure 6. Determination of the anti-inflammatory properties of *P. lentiscus* and *P. atlantica* methanolic extracts using the BSA denaturation method (**a**) and lipoxygenase enzymatic activity (**b**). Both extracts showed moderate to high anti-inflammatory activity. Results were presented as mean ± SD ($n = 3$), *** $p < 0.001$.

The results regarding the capacity to inhibit BSA denaturation surpass those reported by Bourroubey et al. [115]. Indeed, our extract achieved 75% inhibition at a concentration of only 400 µg/mL, while their study reported a maximum inhibition of 66.53% at a fivefold higher concentration (2000 µg/mL). Extending the comparison to other studies conducted on the same species but using different extraction solvents, Bakka et al. [116] reported that an ethyl acetate extract of *P. atlantica* exhibited a maximum inhibition of 97% at 10 mg/mL. In comparison, sodium diclofenac, used as the reference drug, achieved only 55.56% inhibition at the same concentration (10 mg/mL). Similarly, the ethanolic extract of *P. lentiscus* from southern Algeria inhibited protein denaturation by 92.65 ± 0.67% at 1000 µg/mL [117].

This enhanced potency could be attributed to the distinct climatic conditions of our collection sites, which may influence the composition and concentration of bioactive compounds. The observed anti-inflammatory effect appears to be related to the ability of the extracts to prevent the formation of autoantigens through the inhibition of protein denaturation [115]. This mechanism is thought to be attributable to the presence of bioactive compounds, especially flavonoids and tannins, which exert their effects not only through antioxidant activity but also by inhibiting pro-inflammatory enzymes, but may also modulate the expression of genes involved in the inflammatory response, representing an interesting avenue for future studies [118,119]. The inhibition of protein denaturation may

also reflect a potential membrane-stabilizing effect, attenuating the amplification of the inflammatory process [120]. A similar mechanism is observed with certain nonsteroidal anti-inflammatory drugs, such as diclofenac, which bind to specific sites to prevent protein denaturation and the subsequent activation of the inflammatory cascade [121]. It should be noted that this inhibitory effect may decline at higher concentrations, likely due to the saturation of active sites or antagonistic interactions among certain polyphenols [56].

In parallel, the strong anti-inflammatory activity observed in both species may be closely linked to their phenolic profile, particularly the abundance of myricetin (the aglycone of myricitrin and myricetin-3-*O*-hexoside) and methyl gallate, known to act through the prevention of protein denaturation and the inhibition of LOX activity [95,122]. The anti-lipoxygenase potential of the extracts could also be attributed to other phenolic constituents, including isoquercitrin, gallic acid derivatives, and precursors of condensed tannins [114,123]. Isoquercitrin, a quercetin glycoside identified in the analyzed samples, is well known for its inhibitory affinity toward lipoxygenase [123,124]. The inhibition of this enzyme leads to a reduction in leukotriene synthesis, key mediators of inflammation, thereby limiting cell recruitment and the intensification of the inflammatory response [125]. Additionally, the antioxidant properties of the extracts, allowing the neutralization of reactive oxygen species (ROS) generated during inflammation, further support and strengthen their overall anti-inflammatory effect [106,123].

These results pave the way for improved valorization of these two extracts as natural sources of bioactive compounds, with potential applications in dermatological or cosmetic formulations aimed at reducing skin inflammation and its associated effects.

3.2.3. Anti-Tyrosinase Activity

The last aim of this study was to investigate the phenomenon of cutaneous hyperpigmentation, which manifests as the appearance of dark spots, mainly due to prolonged exposure to ultraviolet radiation or skin aging [32]. This pigmentary imbalance results from the excessive production of melanin, a pigment synthesized from L-tyrosine via a series of enzymatic reactions that are primarily regulated by three enzymes: tyrosinase, along with two associated proteins, Tyrosinase-Related Protein 1 (TRP-1) and Tyrosinase-Related Protein 2 (TRP-2) [126]. Since *P. atlantica* and *P. lentiscus* are traditionally employed in folk medicine for skin disorders, we aimed to evaluate their potential in inhibiting tyrosinase [13,14].

Methanolic extracts of the leaves of these two plant species showed dose-dependent inhibitory profiles against tyrosinase activity (Figure 7). Comparative analysis of IC_{50} values indicated that *P. atlantica* exhibited slightly higher inhibitory potency (38.25 $\pm$ 0.02 µg/mL) than *P. lentiscus* (39.80 $\pm$ 0.08 µg/mL), although this difference was not statistically significant (Table 2). Remarkably, both extracts demonstrated comparable activity to kojic acid, the reference compound (IC_{50} = 34.28 $\pm$ 0.07 µg/mL), with *P. atlantica* being only 11.58% less potent and *P. lentiscus* only 16.10% less potent than the reference standard ($p < 0.001$).

The dose–response curves revealed a notable convergence in maximal inhibitory efficacy between the tested extracts and the standard. At saturating concentrations (≈200 µg/mL), tyrosinase inhibition reached approximately 90% for all samples, suggesting a similar inhibition mechanism and a comparable efficacy plateau. These findings indicate that despite differences in potency (IC_{50}), *Pistacia* extracts retain a maximal inhibitory potential equivalent to that of kojic acid, a well-established pharmacological reference for this enzymatic activity.

To our knowledge, no previous studies have reported the anti-tyrosinase activity of methanolic extracts of *P. lentiscus* and *P. atlantica*. However, several studies have described this activity using other types of extracts. The 80% hydro-methanolic extract of *P. atlantica*

leaves obtained by maceration exhibited an IC_{50} of 153.07 ± 2.63 µg/mL [109]. Higher levels of activity were observed in other plant organs: the hydro-methanolic extract of leaf buds showed an EC_{50} of 0.098 ± 0.00 mg/mL [19], while that of unripe fruits presented an EC_{50} of 0.70 mg/mL [36].

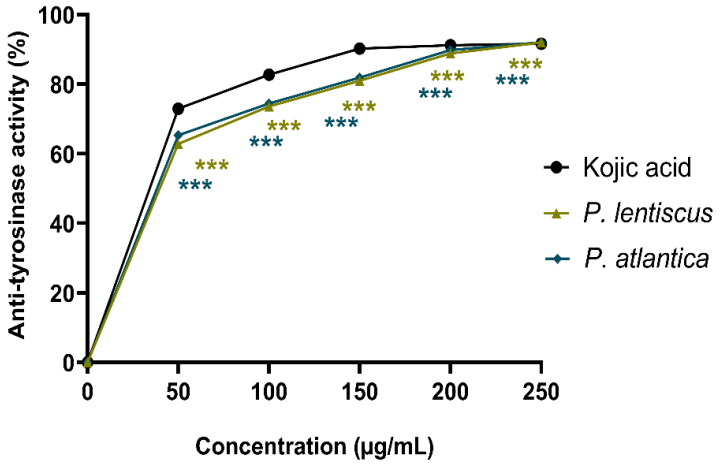


Figure 7. Effect of *P. lentiscus* and *P. atlantica* methanolic extracts on the anti-tyrosinase enzymatic activity. Both extracts showed strong. Results were presented as mean ± SD (n = 3), *** $p < 0.001$.

Extracts obtained with different solvents have also demonstrated tyrosinase inhibitory activity, showing variability in their inhibitory potential. The ethyl acetate extract of *P. lentiscus* obtained by SPE exhibited an IC_{50} of 123 µg/mL [32], while a hydro-methanolic extract achieved 78% inhibition with an IC_{50} of 40 µg/mL, values comparable to those observed in the present study. For *P. atlantica*, Ghafari et al. [127] reported 59.07% inhibition, whereas Eghbali et al. [128] observed a reduction in cellular tyrosinase activity and melanin content, suggesting a potential intracellular effect.

The observed activity may be attributed to the presence of phenolic compounds and flavonoids that can interact with the active site of tyrosinase [129]. As reported by Lee et al. [130], polyphenols and flavonoids exhibit a strong inhibitory potential against tyrosinase and its related proteins (TRP-1 and TRP-2), and certain toxic and mutagenic compounds [131]. To date, polyphenols also represent the largest group of tyrosinase inhibitors [132]. It can also be assumed that the tannin content in *P. lentiscus* and *P. atlantica* may precipitate the tyrosinase enzyme, thereby inhibiting its enzymatic activity in the reaction medium. These constituents are readily soluble in methanol and have shown strong tyrosinase inhibitory activity in different plants [133,134]. Kishore et al. [135] also reported that flavonol glycosides have significant anti-tyrosinase activity.

Beyond the properties already highlighted in our study, the leaf extracts of *P. lentiscus* and *P. atlantica* also demonstrate a notable ability to modulate the mechanisms involved in skin pigmentation. This natural activity makes them promising candidates for the development of innovative, safe, and effective products aimed at evening out skin tone and preventing pigmentation disorders. with a lower risk of adverse effects compared to conventional agents such as kojic acid.

In summary, the methanolic leaf extracts of *P. lentiscus* exhibited stronger radical scavenging capacity, reducing power, and anti-inflammatory activity through albumin denaturation inhibition. In contrast, *P. atlantica* showed slightly higher anti-tyrosinase activity. Moreover, both extracts demonstrated strong LOX inhibition, further supporting their potential as natural bioactive agents for managing skin inflammation and hyperpigmentation.

4. Conclusions

This study demonstrates for the first time the complementary bioactivities of *P. lentiscus* and *P. atlantica* leaf extracts, providing a solid scientific rationale for their incorporation into cosmeceutical formulations targeting oxidative stress, inflammation, and hyperpigmentation. The LC-MS/MS profiling highlighted phytochemical richness dominated by methyl gallate and myricetin derivatives, which supports the observed antioxidant, anti-inflammatory and anti-tyrosinase effects.

P. lentiscus exhibited a stronger capacity to counteract oxidative stress and inhibit melanogenesis, while *P. atlantica* showed superior anti-inflammatory potential, suggesting distinct and complementary dermoprotective applications. These findings validate their traditional use and position both species as promising natural alternatives to synthetic skin-care agents, in line with the current interest in plant-derived cosmetic agents.

Future investigations should focus on comparative evaluation of methanolic versus ethyl acetate extracts to assess polarity-dependent cosmeceutical efficacy, cytotoxicity assessments to confirm safety profiles, and in silico evaluations to predict molecular interactions and biological targets. These approaches would contribute to the scientific understanding and potential utilization of these Mediterranean species by supporting the development of value-added formulations, while encouraging responsible management practices to preserve natural populations.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/pr13113712/s1, Figure S1: GC-FID chromatograms of the fatty acid profiles in methanolic leaves extracts of (a) P. atlantica and (b) P. lentiscus; Figure S2: LC/MS-MS spectra of the polyphenol profile in methanolic leaf extracts of P. lentiscus; Figure S3: LC/MS-MS spectra of the polyphenol profile in methanolic leaf extracts of P. atlantica; Table S1: Chemical and reagents.

Author Contributions: Conceptualization, M.B., M.B.-A. and M.-L.F.; methodology, M.B., M.G., LV., M.M. and P.L.K.T.T.; software, M.A.-A.; validation, M.G., M.A.-A., S.E.-B., M.B.-A. and M.-L.F.; formal analysis, M.B., M.G., A.K., L.V., M.A.-A., S.E.-B., M.B.-A. and M.-L.F.; investigation, M.B.; data curation, M.B.; writing—original draft preparation, M.B.; writing—review and editing, M.G., A.K., L.V., M.M., P.L.K.T.T., S.E.-B., M.B.-A. and M.-L.F.; visualization, A.K.; supervision, M.B.-A. and M.-L.F. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by Carthage University and by the Laboratory of Chemistry of Natural Molecules, Gembloux Agro-Bio Tech, University of Liège.

Institutional Review Board Statement: The leaves of *Pistacia lentiscus* and *Pistacia atlantica* were used in this study. The leaves of *P. lentiscus* and *P. atlantica* used in this study were kindly provided by the Directorate General of Forests, Wilaya of Bouira, Algeria. No other plant or animal sources were used in this study.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

Acknowledgments: The authors gratefully thank Thomas Bertrand, Franck Michels, Adrien Francis, Maxime Grégoire and Mohamed Dridi for their technical help.

Conflicts of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

The following abbreviations are used in this manuscript:

DPPH	2,2-Diphenyl-1-picrylhydrazyl
FRAP	Ferric-reducing antioxidant power
LOX	Lipoxygenase

BSA	Bovine serum albumin
LC-MS/MS	Liquid Chromatography–Tandem Mass Spectrometry
GC-FID	Gas Chromatography–Flame Ionization Detection
LC-QTOF	Liquid Chromatography–Quadrupole Time-of-Flight
LC-TQ	Liquid Chromatography–Triple Quadrupole

Appendix A

Table A1. Assessment of the fatty acid composition of *P. lentiscus* and *P. atlantica* methanolic extracts using Gas Chromatography coupled to Flame Ionization Detector.

	Fatty Acid	Rt (min)	*P. lentiscus* (%)	*P. atlantica* (%)	*p*-Value
1	Caproic acid (C6:0)	3.59	0.13 ± 0.02	0.10 ± 0.06	0.54
2	Undecanoic acid (C11:0)	5.50	0.19 ± 0.07	0.15 ± 0.01	0.47
3	Lauric acid (C12:0)	7.81	0.38 ± 0.11	0.55 ± 0.31	0.42
4	Tridecanoic acid (C13:0)	8.96	0.40 ± 0.01	1.07 ± 0.13	<0.001
5	Myristic acid (C14:0)	10.31	3.63 ± 0.07	1.52 ± 0.09	<0.001
6	Pentadecanoic acid (C15:0)	11.74	nd	0.54 ± 0.23	-
7	Palmitic acid (C16:0)	13.34	18.35 ± 0.06	6.51 ± 0.02	<0.001
8	Palmitoleic acid (C16:1)	13.72	4.42 ± 0.09	1.02 ±0.05	<0.001
9	Margaric acid (C17:0)	14.88	nd	nd	-
10	Stearic acid (C18:0)	16.49	1.36 ± 0.04	0.91 ± 0.01	<0.001
11	Oleic acid (C18:1)	16.50	1.36 ± 0.03	nd	-
12	Elaidic acid (C18:1: ω9)	16.83	5.30 ± 0.11	0.72 ± 0.17	<0.001
13	Vaccenic acid (C18:1: ω7)	16.92	0.65 ± 0.01	nd	-
14	Linoleic acid (C18:2)	17.56	23.96 ± 0.04	4.86 ± 0.06	<0.001
15	γ-linolenic acid (C18:3 γ)	18.60	31.54 ± 0.01	8.60 ± 0.09	<0.001
16	Arachidic acid (C20:0)	19.63	0.61 ± 0.16	0.48 ± 0.01	0.21
17	*Cis*-11,14-eicosadienoic acid (C20:2)	20.76	1.24 ± 0.02	8.31 ± 0.11	<0.001
18	*Cis*-5,8,11,14,17-eicosapentaenoic acid (C20-5n3)	22.22	nd	3.12 ± 0.12	-
19	Behenic acid (C22:0)	22.64	1.18 ± 0.05	0.45 ± 0.02	<0.001
20	*Cis*-13,16-docosadienoic acid (C22:2)	23.73	2.24 ± 0.02	54.13 ± 0.09	<0.001
21	Lignoceric acid (C24:0)	25.75	2.17 ± 0.02	0.63 ± 0.13	<0.001
22	Nervonic acid (C24:1n9)	26.10	nd	4.90 ± 0.07	-
	Saturated fatty acids (SFA) [a]		29.29	14.34	
	Unsaturated fatty acids (UFA) [b]		70.71	85.66	
	Unsaturation ratio = UFA/SFA [c]		2.41	5.97	

Rt: retention time. nd: not detected. [a]: saturated fatty acids (SFA). [b]: unsaturated fatty acids (UFA). [c]: unsaturation ratio = UFA/SFA. Data were determined as a mean ± SEM retention time of each phenolic composition in three independent experiments. SEM: standard error of the mean.

References

1. Papaccio, F.; D'Arino, A.; Caputo, S.; Bellei, B. Focus on the contribution of oxidative stress in skin aging. *Antioxidants* **2022**, *11*, 1121. [CrossRef]
2. Davids, L.M.; Van Wyk, J.; Khumalo, N.P.; Jablonski, N.G. Phenomenon of skin lightening: Is it right to be light? *S. Afr. J. Sci.* **2016**, *112*, 5. [CrossRef]
3. Villareal, M.O.; Kume, S.; Bourhim, T.; Bakhtaoui, F.Z.; Kashiwagi, K.; Han, J.; Gadhi, C.; Isoda, H. Activation of MITF by argan oil leads to the inhibition of the tyrosinase and dopachrome tautomerase expressions in B16 murine melanoma cells. *Evid.-Based Complement. Altern. Med.* **2013**, *2013*, 340107. [CrossRef] [PubMed]
4. Mulholland, D.A.; Mwangi, E.M.; Dlova, N.C.; Plant, N.; Crouch, N.R.; Coombes, P.H. Non-toxic melanin production inhibitors from *Garcinia livingstonei* (Clusiaceae). *J. Ethnopharmacol.* **2013**, *149*, 570–575. [CrossRef] [PubMed]
5. Opperman, L.; De Kock, M.; Klaasen, J.; Rahiman, F. Tyrosinase and melanogenesis inhibition by indigenous african plants: A review. *Cosmetics* **2020**, *7*, 60. [CrossRef]
6. Chiocchio, I.; Mandrone, M.; Sanna, C.; Maxia, A.; Tacchini, M.; Poli, F. Screening of a hundred plant extracts as tyrosinase and elastase inhibitors, two enzymatic targets of cosmetic interest. *Ind. Crops Prod.* **2018**, *122*, 498–505. [CrossRef]
7. Tian, L.; Zhao, Y.; Guo, C.; Yang, X. A comparative study on the antioxidant activities of an acidic polysaccharide and various solvent extracts derived from herbal *Houttuynia cordata*. *Carbohydr. Polym.* **2011**, *83*, 537–544. [CrossRef]
8. Wang, Z.; Jiang, Y.; Ge, C.; Wang, Y.; He, J.; Chen, J.; Hou, X. Anti-inflammatory activity evaluation and molecular docking analysis of four new compounds isolated from *M. oleifera* seeds. *J. Mol. Struct.* **2024**, *1318*, 139269. [CrossRef]

9. Shi, S.; Li, K.; Peng, J.; Li, J.; Luo, L.; Liu, M.; Chen, Y.; Xiang, Z.; Xiong, P.; Liu, L.; et al. Chemical characterization of extracts of leaves of *Kadsua coccinea* (Lem.) A.C. Sm. by UHPLC-Q-Exactive Orbitrap Mass spectrometry and assessment of their antioxidant and anti-inflammatory activities. *Biomed. Pharmacother.* **2022**, *149*, 112828. [CrossRef]
10. Othman, S.O.K.; El-Hashash, M.A.; Hussein, S.; El-Mesallamy, A.M.D.; Rizk, S.A.; Elabbar, F.A. Phenolic content as antioxidant and antimicrobial activities *Pistacia atlantica* Desf. (Anacardiaceae) Extract from Libya. *Egypt. J. Chem.* **2018**, *62*, 21–28. [CrossRef]
11. Yousfi, M.; Nedjmi, B.; Bellal, R.; Ben Bertal, D.; Palla, G. Fatty acids and sterols of *Pistacia atlantica* fruit oil. *J. Am. Oil. Chem. Soc.* **2002**, *79*, 1049–1050. [CrossRef]
12. Benhassaini, H.; Benabderrahmane, M.; Chikhi, K. Contribution à l'évaluation de l'activité antiseptique de l'oléorésine et des huiles essentielles du Pistachier de l'Atlas sur certaines sources microbiennes: *Candida albicans* (ATC 20027), *Candida albicans* (ATCC 20032) et *Saccharomyces cerevisiae*. *Ethnopharmacologia* **2003**, *30*, 38–46.
13. Farahpour, M.R.; Mirzakhani, N.; Doostmohammadi, J.; Ebrahimzadeh, M. Hydroethanolic *Pistacia atlantica* hulls extract improved wound healing process; evidence for mast cells infiltration, angiogenesis and RNA stability. *Int. J. Surg.* **2015**, *17*, 88–98. [CrossRef] [PubMed]
14. Pachi, V.K.; Mikropoulou, E.V.; Gkiouvetidis, P.; Siafakas, K.; Argyropoulou, A.; Angelis, A.; Mitakou, S.; Halabalaki, M. Traditional Uses, Phytochemistry and pharmacology of chios mastic gum (*Pistacia lentiscus* var. Chia, Anacardiaceae): A review. *J. Ethnopharmacol.* **2020**, *254*, 112485. [CrossRef] [PubMed]
15. Mahjoub, F.; Rezayat, K.A.; Yousefi, M.; Mohebbi, M.; Salari, R. *Pistacia atlantica* Desf. A review of its traditional uses, phytochemicals and pharmacology. *J. Med. Life* **2018**, *11*, 180. [CrossRef] [PubMed]
16. Bahmani, M.; Zargaran, A.; Rafieian-Kopaei, M.; Saki, K. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus in the Urmia, Northwest Iran. *Asian Pac. J. Trop. Med.* **2014**, *7*, S348–S354. [CrossRef]
17. Ellahi, H.; Khalili Sadrabad, E.; Hekmatimoghaddam, S.; Jebali, A.; Sarmast, E.; Akrami Mohajeri, F. Application of essential oil of *Pistacia atlantica* gum, polypropylene and silica nanoparticles as a new milk packaging. *Food Sci. Nutr.* **2020**, *8*, 4037–4043. [CrossRef]
18. Belkessam, M.; Genva, M.; Souissi, N.; Dridi, M.; Dennemont, I.; Loiseau, P.M.; Fauconnier, M.-L.; Ben-Attia, M. Dioecy impacts the chemical profile and biological activities of essential oils from leaves of *Pistacia lentiscus* L. *J. Essent. Oil Bear. Plants* **2025**, *28*, 158–175. [CrossRef]
19. Benmahieddine, A.; Belyagoubi-Benhammou, N.; Belyagoubi, L.; Amari, N.O.; Zerey-Belaskri, A.E.; Gismondi, A.; Di Marco, G.; Canini, A.; Habi, S.; Atik Bekkara, F. Leaf-buds of *Pistacia atlantica*: A novel source of bioactive molecules with high anti-inflammatory, antioxidant, anti-tyrosinase and antimicrobial properties. *Physiol. Mol. Biol. Plants* **2023**, *29*, 209–219. [CrossRef]
20. Bullitta, S.; Piluzza, G.; Manunta, M.D.I. Cell-based and chemical assays of the ability to modulate the production of intracellular reactive oxygen species of eleven mediterranean plant species related to ethnobotanic traditions. *Genet. Resour. Crop Evol.* **2013**, *60*, 403–412. [CrossRef]
21. Hashemnia, M.; Nikousefat, Z.; Yazdani-Rostam, M. Antidiabetic Effect of Pistacia Atlantica and Amygdalus Scoparia in Streptozotocin-Induced Diabetic Mice. *Comp. Clin. Pathol.* **2015**, *24*, 1301–1306. [CrossRef]
22. Floris, S.; Di Petrillo, A.; Pintus, F.; Delogu, G.L. Pistacia Lentiscus: Phytochemistry and Antidiabetic Properties. *Nutrients* **2024**, *16*, 1638. [CrossRef]
23. Benmohamed, M.; Guenane, H.; Messaoudi, M.; Zahnit, W.; Egbuna, C.; Sharifi-Rad, M.; Chouh, A.; Seghir, B.B.; Rebiai, A.; Boubekeur, S.; et al. Mineral Profile, Antioxidant, Anti-Inflammatory, Antibacterial, Anti-Urease and Anti-α-Amylase Activities of the Unripe Fruit Extracts of Pistacia Atlantica. *Molecules* **2023**, *28*, 349. [CrossRef]
24. Quartu, M.; Serra, M.P.; Boi, M.; Pillolla, G.; Melis, T.; Poddighe, L.; Del Fiacco, M.; Falconieri, D.; Carta, G.; Murru, E. Effect of acute administration of *Pistacia lentiscus* L. essential oil on rat cerebral cortex following transient bilateral common carotid artery occlusion. *Lipids Health Dis.* **2012**, *11*, 8. [CrossRef] [PubMed]
25. Remila, S.; Atmani-Kilani, D.; Delemasure, S.; Connat, J.-L.; Azib, L.; Richard, T.; Atmani, D. Antioxidant, cytoprotective, anti-inflammatory and anticancer activities of *Pistacia lentiscus* (Anacardiaceae) leaf and fruit extracts. *Eur. J. Integr. Med.* **2015**, *7*, 274–286. [CrossRef]
26. Albalawi, A.E.; Althobaiti, N.A.; Alhasani, R.H.; Alnomasy, S.F. Anti-tumor effects and cellular mechanisms of *Pistacia atlantica* methanolic extract against Ehrlich solid tumor in mice. *Asian Pac. J. Trop. Biomed.* **2022**, *12*, 69–77. [CrossRef]
27. Hosseini, S.; Nili-Ahmadabadi, A.; Nachvak, S.M.; Dastan, D.; Moradi, S.; Abdollahzad, H.; Mostafai, R. Antihyperlipidemic and antioxidative properties of *Pistacia atlantica* subsp. Kurdica in streptozotocin-induced diabetic mice. *Diabetes Metab. Synd. Obes.* **2020**, *13*, 1231–1236. [CrossRef] [PubMed]
28. Moussaoui, S.; Mokrani, E.H.; Kabouche, Z.; Guendouze, A.; Laribi, A.; Bradai, N.; Bensouici, C.; Yilmaz, M.A.; Cakir, O.; Tarhan, A. Evaluation of polyphenolic profile, antioxidant, anti-cholinesterase, and anti-alpha-amylase activities of *Pistacia lentiscus* L. Leaves. *Nat. Prod. Res.* **2025**, *39*, 1–14. [CrossRef]

29. Achili, I.; Amrani, A.; Bensouici, C.; Gül, F.; Altun, M.; Demirtas, I.; Zama, D.; Benayache, F.; Benayache, S. Chemical constituents, antioxidant, anticholinesterase and antiproliferative effects of Algerian *Pistacia atlantica* Desf. extracts. *Recent Pat. Food Nutr. Agric.* **2020**, *11*, 249–256. [CrossRef]
30. Mehenni, C.; Atmani-Kilani, D.; Dumarçay, S.; Perrin, D.; Gérardin, P.; Atmani, D. Hepatoprotective and antidiabetic effects of *Pistacia lentiscus* leaf and fruit extracts. *J. Food Drug Anal.* **2016**, *24*, 653–669. [CrossRef]
31. Hussein, S.A.A.; El-Mesallamy, A.; Othman, S.O.K.; Soliman, A.E.-M.M. Identification of novel polyphenolic secondary metabolites from *Pistacia atlantica* Desf. and demonstration of their cytotoxicity and CCL4 induced hepatotoxicity in rat. *Egypt. J. Chem.* **2020**, *63*, 117–130. [CrossRef]
32. Elloumi, W.; Maalej, A.; Ortiz, S.; Michel, S.; Chamkha, M.; Boutefnouchet, S.; Sayadi, S. *Pistacia lentiscus* L. distilled leaves as a potential cosmeceutical ingredient: Phytochemical characterization, transdermal diffusion, and anti-elastase and anti-tyrosinase activities. *Molecules* **2022**, *27*, 855. [CrossRef] [PubMed]
33. Tohidi, M.; Khayami, M.; Nejati, V.; Meftahizade, H. Evaluation of antibacterial activity and wound healing of *Pistacia atlantica* and *Pistacia khinjuk*. *J. Med. Plants Res.* **2011**, *5*, 4310–4314.
34. Guerine, L.; Hadjadj, K. Ecodendrometric characterization of Atlas pistachio (*Pistacia atlantica* desf.) stands in the Ain Ben Khelil region (southwestern Algeria). *Indian Four* **2019**, *145*, 1053–1061.
35. Hamelian, M.; Hemmati, S.; Varmira, K.; Veisi, H. Green synthesis, antibacterial, antioxidant and cytotoxic effect of gold nanoparticles using *Pistacia atlantica* extract. *J. Taiwan Inst. Chem. Eng.* **2018**, *93*, 21–30. [CrossRef]
36. Belyagoubi-Benhammou, N.; Belyagoubi, L.; Benmahieddine, A.; El Zerey-Belaskri, A.; Di Marco, G.; D'Agostino, A.; Canini, A.; Gismondi, A. Nutraceutical content and biological properties of lipophilic and hydrophilic fractions of the phytocomplex from *Pistacia atlantica* Desf. buds, roots, and fruits. *Plants* **2024**, *13*, 611. [CrossRef]
37. Ouahabi, S.; Loukili, E.H.; Daoudi, N.E.; Chebaibi, M.; Ramdani, M.; Rahhou, I.; Bnouham, M.; Fauconnier, M.-L.; Hammouti, B.; Rhazi, L. Study of the phytochemical composition, antioxidant properties, and in-vitro anti-diabetic efficacy of *Gracilaria bursa-pastoris* extracts. *Mar. Drugs* **2023**, *21*, 372. [CrossRef]
38. Nea, F.; Bitchi, M.B.; Genva, M.; Ledoux, A.; Tchinda, A.T.; Damblon, C.; Frederich, M.; Tonzibo, Z.F.; Fauconnier, M.-L. Phytochemical investigation and biological activities of *Lantana rhodesiensis*. *Molecules* **2021**, *26*, 846. [CrossRef]
39. Singleton, V.L.; Rossi, J.A. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. *Am. J. Enol. Vitic.* **1965**, *16*, 144–158. [CrossRef]
40. Hbika, A.; Daoudi, N.E.; Bouyanzer, A.; Bouhrim, M.; Mohti, H.; Loukili, E.H.; Mechchate, H.; Al-Salahi, R.; Nasr, F.A.; Bnouham, M. *Artemisia absinthium* L. aqueous and ethyl acetate extracts: Antioxidant effect and potential activity in vitro and in-vivo against pancreatic α-amylase and intestinal α-glucosidase. *Pharmaceutics* **2022**, *14*, 481. [CrossRef]
41. Nair, S.S.; Kavrekar, V.; Mishra, A. In-vitro studies on alpha amylase and alpha glucosidase inhibitory activities of selected plant extracts. *Eur. J. Exp. Biol.* **2013**, *3*, 128–132.
42. Kim, J.-H.; Park, S.-M.; Ha, H.-J.; Moon, C.-J.; Shin, T.-K.; Kim, J.-M.; Lee, N.-H.; Kim, H.-C.; Jang, K.-J.; Wie, M.-B. *Opuntia ficus-indica* attenuates neuronal injury in in-vitro and in-vivo models of cerebral ischemia. *J. Ethnopharmacol.* **2006**, *104*, 257–262. [CrossRef] [PubMed]
43. Bourgou, S.; Bettaieb Rebey, I.; Ben Kaab, S.; Hammami, M.; Dakhlaoui, S.; Sawsen, S.; Msaada, K.; Isoda, H.; Ksouri, R.; Fauconnier, M.-L. Green solvent to substitute hexane for bioactive lipids extraction from black cumin and basil seeds. *Foods* **2021**, *10*, 1493. [CrossRef] [PubMed]
44. Saha Tchinda, J.; Mbitnkeu Fetngna Tchebe, T.; Tchoukoua, A.; Cheumani Yona, A.M.; Fauconnier, M.L.; Ndikontar Kor, M.; Richel, A. Fatty acid profiles, antioxidant, and phenolic contents of oils extracted from *Acacia polyacantha* and *Azadirachta indica* (neem) seeds using green solvents. *J. Food Process. Preserv.* **2021**, *45*, e15115. [CrossRef]
45. Wojdyło, A.; Jáuregui, P.N.N.; Carbonell-Barrachina, Á.A.; Oszmiański, J.; Golis, T. Variability of phytochemical properties and content of bioactive compounds in *Lonicera caerulea* L. var. *Kamtschatica* Berries. *J. Agric. Food Chem.* **2013**, *61*, 12072–12084. [CrossRef]
46. Brand-Williams, W.; Cuvelier, M.E.; Berset, C. Use of a free radical method to evaluate antioxidant activity. *LWT—Food Sci. Technol.* **1995**, *28*, 25–30. [CrossRef]
47. Tanoh, A.E.; Blanchard Boué, G.; Nea, F.; Genva, M.; Wognin, E.L.; Ledoux, A.; Martin, H.; Tonzibo, Z.F.; Frederich, M.; Fauconnier, M.-L. Seasonal effect on the chemical composition, insecticidal properties and other biological activities of *Zanthoxylum leprieurii* Guill. & Perr. essential oils. *Foods* **2020**, *9*, 550. [CrossRef]
48. Kar, B.; Kumar, R.B.S.; Karmakar, I.; Dola, N.; Bala, A.; Mazumder, U.K.; Hadar, P.K. Antioxidant and in-vitro anti-inflammatory activities of *Mimusops elengi* leaves. *Asian Pac. J. Trop. Biomed.* **2012**, *2*, S976–S980. [CrossRef]
49. Nea, F.; Tanoh, E.A.; Wognin, E.L.; Kemene, T.K.; Genva, M.; Saive, M.; Tonzibo, Z.F.; Fauconnier, M.-L. A new chemotype of *Lantana rhodesiensis* Moldenke essential oil from Côte d'Ivoire: Chemical composition and biological activities. *Ind. Crops Prod.* **2019**, *141*, 111766. [CrossRef]

50. Nikhila, G.S.; Sangeetha, G. Anti inflammatory properties of the root tubers of *Gloriosa superba* and its conservation through micropropagation. *J. Med. Plants Res.* **2015**, *9*, 1–7. [CrossRef]
51. Rangkadilok, N.; Sitthimonchai, S.; Worasuttayangkurn, L.; Mahidol, C.; Ruchirawat, M.; Satayavivad, J. Evaluation of free radical scavenging and antityrosinase activities of standardized longan fruit extract. *Food Chem. Toxicol.* **2007**, *45*, 328–336. [CrossRef] [PubMed]
52. Genva, M.; Lheureux, L.; Saive, M.; Maes, C.; Fauconnier, M.-L. Study of the cosmetic potential uses of plants from Mayotte as skin care agents through the screening of their biological activities. *Nutraceuticals* **2022**, *2*, 420–440. [CrossRef]
53. Belyagoubi, L.; Belyagoubi-Benhammou, N.; Atik-Bekkara, F.; Coustard, J.M. Effects of extraction solvents on phenolic content and antioxidant properties of *Pistacia atlantica* Desf fruits from Algeria. *Int. Food Res. J.* **2016**, *23*, 948.
54. Chaabani, E.; Abert Vian, M.; Bott, R.; Ginies, C.; Defoort, C.; Ksouri, R.; Chemat, F. Extraction of aromas from *Pistacia lentiscus* L. leaves using alternative solvents: COSMO-RS-Assisted solvent screening and GC-MS metabolites profiling. *Sep. Sci. Technol.* **2020**, *55*, 716–727. [CrossRef]
55. Amel, Z.; Nabila, B.-B.; Nacéra, G.; Fethi, T.; Fawzia, A.-B. Assessment of phytochemical composition and antioxidant properties of extracts from the leaf, stem, fruit and root of *Pistacia lentiscus* L. *Int. J. Pharmacogn. Phytochem. Res.* **2016**, *8*, 627–633.
56. Seddoqi, S.; Aouinti, F.; Fatnassi, H.; Nouioura, G.; Conte, R.; Abdullah Alsahli, A.; Bourhia, M.; Mahamat, O.B.; Kandsi, F.; Gseyra, N. phytochemical composition analysis, antioxidant, antimitotic, and anti-inflammatory effects of leaf and stem extracts of *Pistacia lentiscus* L. *Int. J. Food Prop.* **2024**, *27*, 1415–1433. [CrossRef]
57. Peksel, A.; Arisan-Atac, I.; Yanardag, R. Evaluation of antioxidant and antiacetylcholinesterase activities of the extracts of *Pistacia atlantica* Desf. Leaves. *J. Food Biochem.* **2010**, *34*, 451–476. [CrossRef]
58. Terouzi, W.; Yacine, Z.A.; Hanine, H.; Boulli, A.; Oussama, A. Comparative study of physical and chemical propriety of the oil of some varieties of olive trees. *Int. J. Innov. Appl. Stud.* **2014**, *6*, 1096.
59. Brahmi, F.; Haddad, S.; Bouamara, K.; Yalaoui-Guellal, D.; Prost-Camus, E.; De Barros, J.-P.P.; Prost, M.; Atanasov, A.G.; Madani, K.; Boulekbache-Makhlouf, L. Comparison of chemical composition and biological activities of algerian seed oils of *Pistacia lentiscus* L., *Opuntia ficus indica* (L.) Mill. and *Argania spinosa* L. skeels. *Ind. Crops Prod.* **2020**, *151*, 112456. [CrossRef]
60. Šamec, D.; Karalija, E.; Šola, I.; Vujčić Bok, V.; Salopek-Sondi, B. The role of polyphenols in abiotic stress response: The influence of molecular structure. *Plants* **2021**, *10*, 118. [CrossRef]
61. Kähkönen, M.P.; Hopia, A.I.; Vuorela, H.; Rauha, J.P.; Pihlaja, K.; Kujala, T.S.; Heinonen, M. Antioxidant activity of plant extracts containing phenolic compounds. *J. Agric. Food Chem.* **1999**, *47*, 3954–3962. [CrossRef]
62. Naczk, M.; Shahidi, F. Extraction and analysis of phenolics in food. *J. Chromatogr. A* **2004**, *1054*, 95–111. [CrossRef]
63. Boschin, G.; D'Agostina, A.; Annicchiarico, P.; Arnoldi, A. The fatty acid composition of the oil from *Lupinus albus* cv. luxe as affected by environmental and agricultural factors. *Eur. Food Res. Technol.* **2007**, *225*, 769–776. [CrossRef]
64. Akremi, I.; Kabtni, S.; Ammar, H.B.; Genva, M.; Hejazi, S.; Elbok, S.; Rouz, S.; Marghali, S.; Fauconnier, M.-L. Comparative highlights of morphological, phytochemical and nutritional key characteristics of mediterranean Lupinus species. *Food Chem.* **2025**, *480*, 143962. [CrossRef]
65. Nejib, M. GC/MS chemical analysis of *Pistacia lentiscus* fatty oil from the north of Tunisia. *Int. J. Pharm. Tech Res.* **2011**, *3*, 2245–2248.
66. Trabelsi, H.; Cherif, O.A.; Sakouhi, F.; Villeneuve, P.; Renaud, J.; Barouh, N.; Boukhchina, S.; Mayer, P. Total lipid content, fatty acids and 4-desmethylsterols accumulation in developing fruit of *Pistacia lentiscus* L. growing wild in Tunisia. *Food Chem.* **2012**, *131*, 434–440. [CrossRef]
67. Mezni, F.; Khaldi, A.; Maaroufi, A.; Hamrouni, L.; Msallem, M.; Boussaid, M.; Khouja, M.L. Fatty acid composition and biological properties of the fixed oil fruits of *Pistacia lentiscus* L. *Acta Hortic.* **2013**, *997*, 219–224. [CrossRef]
68. Haouli, A.; Seridi, R.; Djemli, S.; Bourdjiba, O.; Frih, H. Contribution to the analysis of *Pistacia lentiscus* extracted oil. *Am.-Eur. J. Agric. Environ. Sci.* **2015**, *15*, 1075–1081.
69. Boke Sarikahya, N.; Sumer Okkali, G.; Coven, F.O.; Isen, F.; Goren, A.C.; Nalbantsoy, A. Chemical characteristics and biological activity screening of *Pistacia lentiscus* mastic gum and leaves from Türkiye. *J. Sci. Food Agric.* **2024**, *104*, 1691–1701. [CrossRef]
70. Kohl, E.; Steinbauer, J.; Landthaler, M.; Szeimies, R. Skin Ageing. *J. Eur. Acad. Dermatol. Venereol.* **2011**, *25*, 873–884. [CrossRef]
71. Ashawat, M.; Banchhor, M.; Saraf, S.; Saraf, S. Herbal cosmetics:" Trends in skin care formulation". *Pharmacogn. Rev.* **2009**, *3*, 82.
72. Ahmed, I.A.; Mikail, M.A. Anti-aging skincare: The natural and organic way. In *Anti-Aging. Pharmacology*; Academic Press: New York, NY, USA, 2023; pp. 269–284. [CrossRef]
73. Soimee, W.; Nakyai, W.; Charoensit, P.; Grandmottet, F.; Worasakwutiphong, S.; Phimnuan, P.; Viyoch, J. Evaluation of moisturizing and irritation potential of *Sacha inchi* oil. *J. Cosmet. Dermatol.* **2020**, *19*, 915–924. [CrossRef]
74. Lim, D.J.; Song, J.-S.; Lee, B.-H.; Son, Y.K.; Kim, Y. Qualitative and quantitative analysis of the major bioactive components of *Juniperus chinensis* L. using LC-QTOF-MS and LC-MSMS and investigation of antibacterial activity against pathogenic bacteria. *Molecules* **2023**, *28*, 3937. [CrossRef]

75. Pearson, J.L.; Lee, S.; Suresh, H.; Low, M.; Nang, M.; Singh, S.; Lamin, F.; Kazzem, M.; Sullivan, S.; Khoo, C.S. The liquid chromatographic determination of chlorogenic and caffeic acids in Xu duan (*Dipsacus asperoides*) raw herb. *Int. Sch. Res. Not.* **2014**, *2014*, 968314. [CrossRef]
76. Zhang, C.; Ma, Y.; Zhao, Y.; Hong, Y.; Cai, S.; Pang, M. Phenolic composition, antioxidant and pancreatic lipase inhibitory activities of Chinese sumac (*Rhus chinensis* Mill.) fruits extracted by different solvents and interaction between myricetin-3-o-rhamnoside and quercetin-3-o-rhamnoside. *Int. J. Food Sci. Technol.* **2018**, *53*, 1045–1053. [CrossRef]
77. Shahzad, M.N.; Ahmad, S.; Tousif, M.I.; Ahmad, I.; Rao, H.; Ahmad, B.; Basit, A. Profiling of phytochemicals from aerial parts of *Terminalia neotaliala* using LC-ESI-MS2 and determination of antioxidant and enzyme inhibition activities. *PLoS ONE* **2022**, *17*, e0266094. [CrossRef]
78. Wojdyło, A.; Nowicka, P.; Grimalt, M.; Legua, P.; Almansa, M.S.; Amorós, A.; Carbonell-Barrachina, Á.A.; Hernández, F. Polyphenol compounds and biological activity of Caper (*Capparis spinosa* L.) flowers buds. *Plants* **2019**, *8*, 539. [CrossRef]
79. Aissat, A.K.; Chaher-Bazizi, N.; Richard, T.; Kilani-Atmani, D.; Pedrot, E.; Renouf, E.; Atmani, D.; Fonayet, J.V. Analysis of individual anthocyanins, flavanols, flavonols and other polyphenols in *Pistacia lentiscus* L. fruits during ripening. *J. Food Compos. Anal.* **2022**, *106*, 104286. [CrossRef]
80. Rodríguez-Pérez, C.; Quirantes-Piné, R.; Amessis-Ouchemoukh, N.; Madani, K.; Segura-Carretero, A.; Fernández-Gutierrez, A. A metabolite-profiling approach allows the identification of new compounds from *Pistacia lentiscus* leaves. *J. Pharm. Biomed. Anal.* **2013**, *77*, 167–174. [CrossRef]
81. Boucheffa, S.; Sobhi, W.; Attoui, A.; Selli, S.; Kelebek, H.; Semmeq, A.; Benguerba, Y. Effect of the main constituents of *Pistacia lentiscus* leaves against the DPPH radical and xanthine oxidase: Experimental and theoretical study. *J. Biomol. Struct. Dyn.* **2022**, *40*, 9870–9884. [CrossRef]
82. Mashitoa, F.M.; Shoko, T.; Shai, J.L.; Slabbert, R.M.; Sivakumar, D. Changes in phenolic metabolites and biological activities of Pumpkin Leaves (*Cucurbita moschata* Duchesne ex Poir.) during Blanching. *Front. Nutr.* **2021**, *8*, 641939. [CrossRef]
83. Abdl Aziz, F.T.; Temraz, A.S.; Hassan, M.A. Metabolites profiling by LC-ESI-MS/MS technique and in-vitro antioxidant activity of *Bauhinia madagascariensis* Desv. and *Bauhinia purpurea* L. aerial parts cultivated in Egypt: A comparative study. *Azhar Int. J. Pharm. Med. Sci.* **2024**, *4*, 169–188. [CrossRef]
84. Li, A.; Hou, X.; Wei, Y. Fast screening of flavonoids from switchgrass and *Mikania micrantha* by liquid chromatography hybrid-ion trap time-of-flight mass spectrometry. *Anal. Methods* **2018**, *10*, 109–122. [CrossRef]
85. An, H.; Wang, H.; Lan, Y.; Hashi, Y.; Chen, S. Simultaneous qualitative and quantitative analysis of phenolic acids and flavonoids for the quality control of *Apocynum venetum* L. leaves by HPLC–DAD–ESI–IT–TOF–MS and HPLC–DAD. *J. Pharm. Biomed. Anal.* **2013**, *85*, 295–304. [CrossRef]
86. Lee, J.-E.; Jayakody, J.; Kim, J.-I.; Jeong, J.-W.; Choi, K.-M.; Kim, T.-S.; Seo, C.; Azimi, I.; Hyun, J.; Ryu, B. The influence of solvent choice on the extraction of bioactive compounds from Asteraceae: A comparative review. *Foods* **2024**, *13*, 3151. [CrossRef]
87. Pekacar, S.; Deliorman Orhan, D. Investigation of antidiabetic effect of *Pistacia atlantica* leaves by activity-guided fractionation and phytochemical content analysis by LC-QTOF-MS. *Front. Pharmacol.* **2022**, *13*, 826261. [CrossRef]
88. Huang, W.-Y.; Cai, Y.-Z.; Zhang, Y. Natural phenolic compounds from medicinal herbs and dietary plants: Potential use for cancer prevention. *Nutr. Cancer* **2009**, *62*, 1–20. [CrossRef]
89. Achakzai, A.K.K.; Achakzai, P.; Masood, A.; Kayani, S.A.; Tareen, R.B. Response of plant parts and age on the distribution of secondary metabolites on plants found in Quetta. *Pak. J. Bot.* **2009**, *41*, 2129–2135.
90. Naghiloo, S.; Movafeghi, A.; Delazar, A.; Nazemiyeh, H.; Asnaashari, S.; Dadpour, M.R. Ontogenetic variation of total phenolics and antioxidant activity in roots, leaves and flowers of *Astragalus compactus* Lam. (Fabaceae). *Bioimpacts* **2012**, *2*, 105. [CrossRef]
91. Harborne, J.B.; Williams, C.A. Advances in flavonoid research since 1992. *Phytochemistry* **2000**, *55*, 481–504. [CrossRef]
92. Havsteen, B.H. The biochemistry and medical significance of the flavonoids. *Pharmacol. Ther.* **2002**, *96*, 67–202. [CrossRef] [PubMed]
93. Shin, S.; Lee, J.; Yoon, S.H.; Park, D.; Hwang, J.S.; Jung, E. Anti-glycation activities of methyl gallate in-vitro and in human explants. *J. Cosmet. Dermatol.* **2022**, *21*, 2602–2609. [CrossRef] [PubMed]
94. Kim, I.W.; Jeong, H.S.; Kim, J.K.; Lee, J.K.; Kim, H.R.; Yun, H.Y.; Baek, K.J.; Kwon, N.S.; Park, K.C.; Kim, D.S. Methyl gallate from Acer barbinerve decreases melanin synthesis in Mel-Ab cells. *Pharmazie* **2015**, *70*, 55–59. [CrossRef] [PubMed]
95. Imran, M.; Saeed, F.; Hussain, G.; Imran, A.; Mehmood, Z.; Gondal, T.A.; El-Ghorab, A.; Ahmad, I.; Pezzani, R.; Arshad, M.U. Myricetin: A comprehensive review on its biological potentials. *Food Sci. Nutr.* **2021**, *9*, 5854–5868. [CrossRef]
96. Irshad, M.; Zafaryab, M.D.; Singh, M.; Rizvi, M.M.A. Comparative analysis of the antioxidant activity of *Cassia fistula* extracts. *Int. J. Med. Chem.* **2012**, *2012*, 157125. [CrossRef]
97. Rice-Evans, C.; Miller, N.; Paganga, G. Antioxidant properties of phenolic compounds. *Trends Plant Sci.* **1997**, *2*, 152–159. [CrossRef]
98. Leopoldini, M.; Marino, T.; Russo, N.; Toscano, M. Antioxidant properties of phenolic compounds: H-atom versus electron transfer mechanism. *J. Phys. Chem. A* **2004**, *108*, 4916–4922. [CrossRef]

99. Huang, D.; Ou, B.; Prior, R.L. The chemistry behind antioxidant capacity assays. *J. Agric. Food Chem.* **2005**, *53*, 1841–1856. [CrossRef]
100. Ekaprasada, M.T.; Nurdin, H.; Ibrahim, S.; Dachriyanus, D. Antioxidant activity of methyl gallate isolated from the leaves of *Toona sureni*. *Indones. J. Chem.* **2009**, *9*, 457–460. [CrossRef]
101. Liang, H.; Huang, Q.; Zou, L.; Wei, P.; Lu, J.; Zhang, Y. Methyl gallate: Review of pharmacological activity. *Pharmacol. Res.* **2023**, *194*, 106849. [CrossRef]
102. Milenković, D.; Đorović, J.; Petrović, V.; Avdović, E.; Marković, Z. Hydrogen Atom Transfer versus Proton Coupled Electron Transfer Mechanism of Gallic Acid with Different Peroxy Radicals. *React. Kinet. Mech. Catal.* **2018**, *123*, 215–230. [CrossRef]
103. Shojaee, M.S.; Moeenfard, M.; Farhoosh, R. Kinetics and stoichiometry of gallic acid and methyl gallate in scavenging dpph radical as affected by the reaction solvent. *Sci. Rep.* **2022**, *12*, 8765. [CrossRef]
104. Li, X.; Mai, W.; Chen, D. Chemical study on protective effect against hydroxyl-induced DNA damage and antioxidant mechanism of myricitrin. *J. Chin. Chem. Soc.* **2014**, *61*, 383–390. [CrossRef]
105. Amessis-Ouchemoukh, N.; Madani, K.; Falé, P.L.V.; Serralheiro, M.L.; Araújo, M.E.M. Antioxidant capacity and phenolic contents of some mediterranean medicinal plants and their potential role in the inhibition of cyclooxygenase-1 and acetylcholinesterase activities. *Ind. Crops Prod.* **2014**, *53*, 6–15. [CrossRef]
106. Bourroubey, B.; Chelli, N.; Touil, A.T.; Meddah, B. Ethnobotanical survey, phytochemical screening and antioxidant activity of methanolic extracts of *Pistacia lentiscus* L. growing in northwestern Algeria. *Fr.-Ukr. J. Chem.* **2023**, *11*, 1–16. [CrossRef]
107. Hemma, R.; Belhadj, S.; Ouahchia, C.; Saidi, F. Antioxidant activity of *Pistacia lentiscus* methanolic extracts. *Agrobiologia* **2018**, *8*, 845–852.
108. Zerkani, H.; Tagnaout, I.; Khiya, Z.; Boutahiri, S.; Amalich, S.; Fadili, K.; Cherrat, A.; Mouradi, A.; Benhlima, N.; Zair, T. Comparative study of the antioxidant power of polyphenols of leaves, fruits, and bark of *Pistacia atlantica* Desf. from Morocco. *J. Chem.* **2022**, *2022*, 7432169. [CrossRef]
109. Benabdallah, F.Z.; Zellagui, A. HPLC/UV analysis and in vitro, promising antioxidant, antidiabetic, anti-alzheimer, and anti-tyrosinase potentials of the Algerian *Pistacia atlantica* Desf. methanolic extract. *Phytothérapie* **2023**, *21*, 214–224. [CrossRef]
110. Rawat, P.; Dasila, K.; Singh, M.; Kuniyal, J.C. Influence of environmental factors on phytochemical compositions and antioxidant activity of *Juniperus communis* L. *Discov. Environ.* **2025**, *3*, 1–17. [CrossRef]
111. Gardeli, A.; Papageorgiou, V.; Mallouchos, A.; Kibouris, T.; Komaitis, M. Essential Oil Composition of *Pistacia lentiscus* L. and *Myrtus communis* L.: Evaluation of antioxidant capacity of methanolic extracts. *Food Chem.* **2008**, *107*, 1120–1130. [CrossRef]
112. Salhi, A.; Bellaouchi, R.; El Barkany, S.; Rokni, Y.; Bouyanzer, A.; Asehraou, A.; Amhamdi, H.; Zarrouk, A.; Hammouti, B. Total phenolic content, antioxidant and antimicrobial activities of extracts from *Pistacia lentiscus* leaves. *Caspian J. Environ. Sci.* **2019**, *17*, 189–198. [CrossRef]
113. Ouedraogo, R.A.; Koala, M.; Dabire, C.; Hema, A.; Bazie, V.; Outtara, L.P.; Gnoula, C.; Pale, E.; Nebie, R.H.C. Teneur en phénols totaux et activité antioxydante des extraits des trois principales variétés d'oignons (*Allium cepa* L.) cultivées dans la région du centre-nord du Burkina Faso. *Int. J. Biol. Chem. Sci.* **2015**, *9*, 281–291. [CrossRef]
114. Bozorgi, M.; Memariani, Z.; Mobli, M.; Salehi Surmaghi, M.H.; Shams-Ardekani, M.R.; Rahimi, R. Five *Pistacia* species (*P. vera*, *P. atlantica*, *P. terebinthus*, *P. khinjuk* and *P. lentiscus*): A review of their traditional uses, phytochemistry, and pharmacology. *Sci. World J.* **2013**, *2013*, 219815. [CrossRef]
115. Bourroubey, B.; Chelli, N.; Touil, A.T.; Meddah, B.; Bettouati, A.; Berkane, I. Evaluation of the in-vitro toxicity and anti-inflammatory activity of the methanolic extract of the leaves of *Pistacia lentiscus* L. harvested from northwestern Algeria. *Acta. Biol. Slov.* **2024**, *67*, 50–60. [CrossRef]
116. Bakka, C.; Smara, O.; Hadjadj, M.; Dendougui, H.; Mahdjar, S.; Benzid, A. In vitro anti-inflammatory activity of *Pistacia atlantica* Desf. extracts. *Asian J. Res. Chem.* **2019**, *12*, 322. [CrossRef]
117. Labhar, A.; Benamari, O.; El-Mernissi, Y.; Salhi, A.; Ahari, M.; El Barkany, S.; Amhamdi, H. Phytochemical, anti-inflammatory and antioxidant activities of *Pistacia lentiscus* L. leaves from Ajdir, Al Hoceima province, Morocco. *Ecol. Eng. Environ. Technol.* **2023**, *24*, 172–177. [CrossRef]
118. Zam, W.; Ali, A.; Hasan, R. Determination of phenolic compounds' extraction conditions from *Pistacia palaestina* leaves at two different stages of maturity. *Curr. Nutr. Food Sci.* **2020**, *16*, 808–814. [CrossRef]
119. Tebbi, S.O.; Trapali, M.; Letsiou, S. Exploring the anti-diabetic, antioxidant and anti-microbial properties of *Clematis flammula* L. leaves and *Pistacia lentiscus* L. fruits using choline chloride-based deep eutectic solvent. *Waste Biomass Valoriz.* **2024**, *15*, 2869–2879. [CrossRef]
120. Michalak, M.; Zagórska-Dziok, M.; Klimek-Szczykutowicz, M.; Szopa, A. Phenolic profile and comparison of the antioxidant, anti-ageing, anti-inflammatory, and protective activities of *Borago officinalis* extracts on skin cells. *Molecules* **2023**, *28*, 868. [CrossRef]
121. Bakhouche, I.; Aliat, T.; Boubellouta, T.; Gali, L.; Şen, A.; Bellik, Y. Phenolic contents and in vitro antioxidant, anti-tyrosinase, and anti-inflammatory effects of leaves and roots extracts of the halophyte *Limonium delicatulum*. *S. Afr. J. Bot.* **2021**, *139*, 42–49. [CrossRef]

122. Kim, S.J.; Jin, M.; Lee, E.; Moon, T.C.; Quan, Z.; Yang, J.H.; Son, K.H.; Kim, K.-U.; Son, J.K.; Chang, H.W. Effects of methyl gallate on arachidonic acid metabolizing enzymes: Cyclooxygenase-2 and 5-lipoxygenase in mouse bone marrow-derived mast cells. *Arch. Pharm. Res.* **2006**, *29*, 874–878. [CrossRef]
123. Kutil, Z.; Temml, V.; Maghradze, D.; Pribylova, M.; Dvorakova, M.; Schuster, D.; Vanek, T.; Landa, P. Impact of wines and wine constituents on cyclooxygenase-1, cyclooxygenase-2, and 5-lipoxygenase catalytic activity. *Mediat. Inflamm.* **2014**, *2014*, 406–413. [CrossRef]
124. Sadik, C.D.; Sies, H.; Schewe, T. Inhibition of 15-Lipoxygenases by flavonoids: Structure–activity relations and mode of action. *Biochem. Pharmacol.* **2003**, *65*, 773–781. [CrossRef]
125. Hu, C.; Ma, S. Recent development of lipoxygenase inhibitors as anti-inflammatory agents. *Med. Chem. Commun.* **2018**, *9*, 212–225. [CrossRef] [PubMed]
126. Ijaz, S.; Shoaib Khan, H.M.; Anwar, Z.; Talbot, B.; Walsh, J.J. HPLC profiling of *Mimosa pudica* polyphenols and their non-invasive biophysical investigations for anti-dermatoheliotic and skin reinstating potential. *Biomed. Pharmacother.* **2019**, *109*, 865–875. [CrossRef] [PubMed]
127. Ghafari, S.; Sahranavard, S.; Sarkhail, P.; Keramatian, B. Tyrosinase inhibitory activity of selected plants based on iranian traditional medicine: Detection of mushroom tyrosinase inhibitors based on ITM. *Int. Pharm. Acta* **2022**, *5*, e4. [CrossRef]
128. Eghbali-Feriz, S.; Taleghani, A.; Al-Najjar, H.; Emami, S.A.; Rahimi, H.; Asili, J.; Hasanzadeh, S.; Tayarani-Najaran, Z. Anti-melanogenesis and anti-tyrosinase properties of *Pistacia atlantica* subsp. *mutica* extracts on B16F10 murine melanoma cells. *Res. Pharm. Sci.* **2018**, *13*, 533–545. [CrossRef]
129. Espín, J.C.; Wichers, H.J. Effect of captopril on mushroom tyrosinase activity in vitro. *Biochim. Biophys. Acta BBA* **2001**, *1544*, 289–300. [CrossRef]
130. Lee, O.-S.; Kim, E.-J. Skin Lightening: A review of melamin formation and the isolation of a new ingredient for products that minimize skin discolorations due to excessive melamin production. *Cosmet. Toilet.* **1995**, *110*, 51–56.
131. Slominski, A.; Zbytek, B.; Slominski, R. Inhibitors of melanogenesis increase toxicity of cyclophosphamide and lymphocytes against melanoma cells. *Int. J. Cancer* **2009**, *124*, 1470–1477. [CrossRef]
132. Chuang, S.-Y.; Lin, Y.-K.; Lin, C.-F.; Wang, P.-W.; Chen, E.-L.; Fang, J.-Y. Elucidating the skin delivery of aglycone and glycoside flavonoids: How the structures affect cutaneous absorption. *Nutrients* **2017**, *9*, 1304. [CrossRef] [PubMed]
133. Kubo, I.; Kinst-Hori, I.; Kubo, Y.; Yamagiwa, Y.; Kamikawa, T.; Haraguchi, H. Molecular design of antibrowning agents. *J. Agric. Food Chem.* **2000**, *48*, 1393–1399. [CrossRef]
134. Meda, A.; Lamien, C.E.; Romito, M.; Millogo, J.; Nacoulma, O.G. Determination of the total phenolic, flavonoid and proline contents in Burkina Fasan honey, as well as their radical scavenging activity. *Food Chem.* **2005**, *91*, 571–577. [CrossRef]
135. Kishore, N.; Twilley, D.; Blom van Staden, A.; Verma, P.; Singh, B.; Cardinali, G.; Kovacs, D.; Picardo, M.; Kumar, V.; Lall, N. Isolation of flavonoids and flavonoid glycosides from *Myrsine africana* and their inhibitory activities against mushroom tyrosinase. *J. Nat. Prod.* **2018**, *81*, 49–56. [CrossRef]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.