Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 03 August 2026
Revised : 10 October 2026
Accepted 12 November 2026

Natural Resources for Human Health 2026, Vol. 6 (6): 715–733

KEYWORDS:
Lavandula dentata L.; aqueous extract; phenolic compounds; antioxidant activity; anti-inflammatory activity; *in silico* studies.

Antioxidant and Anti-Inflammatory Potential of *Aqueous* Extract From Lavandula Dentata L. Collected from Setif Region, Algeria: In Vitro and in Silico Target-Profile Studies

Ayoub Bekka[1], Ahlem Karbab[1*], Noureddine Charef[1*], Imene Zenbout[2], Nuha Sweidan[3], Lekhmici Arrar[1]

[1]Laboratory of Applied Biochemistry, Department of Biochemistry, Faculty of Nature and Life Sciences, Setif-1 University Ferhat Abbas 19000 Algeria
[2]Department of computer sciences, Faculty of sciences, Setif-1 University Ferhat Abbas 19000 Algeria
[3]Department of Chemistry, Faculty of Arts and Sciences, University of Petra, Amman, 961343, Jordan
*Corresponding author:
E-mail: ahlem.karbab@univ-setif.dz, karbabal2@gmail.com, charefnr@univ-setif.dz

ABSTRACT: *Lavandula dentata* L. (*L. dentata*) is a commonly found aromatic and medicinal plant used in Algeria for a long time to treat infections, inflammation, insomnia, anxiety, and digestive problems. This study aimed to evaluate the *in vitro* antioxidant and anti-inflammatory activities and the *in silico* target-profile studies of the aqueous extract from the aerial parts of *L. dentata*, collected in the Setif region, Algeria. Decoction was used for the preparation of the *L. dentata* aqueous extract (LDA). Total phenolic, flavonoid, and tannin contents were determined using spectrophotometric methods. The antioxidant potential was assessed using complementary *in vitro* assays, including DPPH, ABTS radical scavenging, CUPRAC, metal chelating activity, and reducing power assays. Evaluation of anti-inflammatory activity was performed using egg albumin and bovine serum albumin (BSA) denaturation assays. The results showed that the extract contained total phenolic, flavonoid, and tannin contents with values of 87.36 ± 1.2 mg gallic acid equivalent/mg dry extract, 54.72 ± 1.1 µg quercetin equivalent/mg dry extract, and 23.8 ± 0.9 µg tannic acid equivalent/mg dry extract, respectively. In terms of antioxidant activity, the extract showed excellent radical scavenging activity in different methods. The aqueous extract also exhibited significant and dose-dependent inhibitory activity in both bovine serum albumin and egg albumin models with percentages of 89.35 ± 0.09 and 93.49 ± 1.23 % at a concentration of 150 µg/mL, respectively. All three compounds were enriched for both phenotypes, with ferulic acid favouring Nrf2/KEAP1 antioxidant response, caffeic acid NF-κB/cytokine pathways, and ascorbic acid redox-cofactor profile, linked by eleven shared targets: NFE2L2, HMOX1, TNF, IL6 and PTGS2. Overall, the findings indicate that the aqueous extract of *L. dentata* contains appreciable levels of phenolic compounds and exhibits notable *in vitro* antioxidant and anti-inflammatory activities.

1. INTRODUCTION

Medicinal plants play an essential and enduring role in global healthcare systems, particularly in developing countries, where more than 80% of the population relies on traditional remedies as a primary source of healthcare [1]. These plants are not only an invaluable part of cultural heritage and the local economy, but also a significant source of diverse bioactive compounds, including antioxidants, anti-inflammatory molecules, phenolic acids, flavonoids, and terpenoids, which

contribute to the modulation of oxidative stress, inflammation, and cellular damage. These mechanisms are closely associated with the pathophysiology of several chronic diseases, including diabetes, cardiovascular disorders, neurodegenerative diseases, and gastrointestinal and respiratory illnesses [2]. *Lavandula dentata* L. (Lamiaceae) is an aromatic plant widely distributed throughout the Mediterranean basin, particularly in North Africa and Algeria. Its characteristic toothed leaves and violet inflorescences make it easily recognizable. The plant has a long-standing place in Algerian traditional medicine, where it is traditionally used to alleviate anxiety, insomnia, microbial infections, inflammation, digestive disorders, and musculoskeletal pain. Traditional preparations commonly include infusions, decoctions, essential oils, poultices, and aromatic baths [3]. Phytochemical studies have consistently reported that *L. dentata* contains abundant phenolic acids, particularly rosmarinic and caffeic acid derivatives, as well as flavonoids and terpenoids, which are considered important contributors to its biological activities.

Previous investigations have demonstrated that essential oils and methanolic extracts of *L. dentata* exhibit significant antioxidant, antimicrobial, and antifungal properties [4]. Comparative analyses of Algerian *Lavandula* species, including *L. stoechas*, *L. multifida*, and *L. dentata*, have further revealed that *L. dentata* often exhibits marked radical-scavenging and reducing abilities, although the magnitude of these activities may vary according to the plant part used, solvent polarity, and extraction technique [5, 6]. Additionally, environmental factors, such as soil composition and exposure to heavy metals, have been shown to influence the phenolic profile of the plant and, consequently, its antioxidant capacity [7]. Nevertheless, a gap remains in the literature regarding studies that integrate ethnopharmacological surveys with biochemical, antioxidant, and anti-inflammatory profiling of aqueous extracts, which closely reflect some traditional modes of preparation and use. In particular, limited information is available regarding the relationship between the frequency of use, preparation methods, and perceived efficacy reported by local populations and the measurable phytochemical composition and *in vitro* biological activities of *L. dentata* aqueous extracts.

This study aimed to document the ethnopharmacological uses of *L. dentata* in the Setif region, Algeria, and to evaluate the biological properties of its aqueous extract. Antioxidant activity was investigated using complementary *in vitro* assays, including DPPH and ABTS radical-scavenging assays, CUPRAC, metal-chelating activity, and reducing power. In addition, the anti-inflammatory activity of the aqueous extract was evaluated using egg albumin and bovine serum albumin (BSA) denaturation assays. The total phenolic, flavonoid, and tannin contents were also determined to provide further insight into the phytochemical characteristics of the extract. This work also aims to bridge traditional knowledge and scientific validation, contributing to the valorization of *L. dentata* as a potential natural source of bioactive compounds for the prevention or management of oxidative stress- and inflammation-related disorders in Algeria and beyond. The objective of the present study is to record the ethnopharmacological use of *L. dentata* in Setif, Algeria, and to establish the antioxidant activity of its aqueous extract (LDA) by DPPH and Reducing Power assays, and to assess the total phenolic and flavonoid content. We conducted an in silico study to profile the protein targets of ferulic, caffeic, and ascorbic acid and test their antioxidant and anti-inflammatory relevance using gene-set enrichment and STRING network analysis. This work intends to bridge traditional knowledge and scientific validation, contributing to the valorization of *L. dentata* as a potential natural therapeutic agent in the prevention or management of oxidative stress-related disorders in Algeria and beyond.

2. MATERIALS AND METHODS

2.1 Collection and Identification of Plant Material

Aerial parts of fresh *L. dentata* L. were gathered from the Beni Aziz area, in the wilaya of Setif in northeastern Algeria (Latitude: 36.19°N, Longitude: 5.41°E), during the flowering season (April–June, 2023). This region's semi-arid Mediterranean climate supports the natural growth of several therapeutic plants, including *L. dentata.* Dr. Laouar Houcinen, an expert botanist from Setif-1 Ferhat Abbas University's Department of Biology, taxonomically identified the plant at Setif-1. A voucher specimen was placed in the university's herbarium (reference number LAV 2024-001). The aerial parts were harvested, thoroughly cleaned to remove contaminants, and then allowed to air-dry for two weeks at room temperature in a well-ventilated, shaded area. The dried material was ground into a fine powder using an electric grinder and stored in airtight containers until extraction.

2.2 Preparation of Aqueous Extract

The aqueous extract was prepared by decoction [8]. Briefly, 50 g of powdered plant material was boiled in 500 mL of distilled water at 100 °C for 30 min under gentle stirring. After cooling to room temperature, the mixture was filtered through Whatman No. 1 filter paper to remove plant debris. The filtrate was concentrated under reduced pressure at 40 °C using a rotary evaporator and subsequently lyophilized to obtain a dry extract. The extraction yield (%) was calculated relative to the initial dry weight of the plant material. The final extract was stored in airtight containers at 4 °C until further phytochemical and antioxidant analyses. This decoction technique is particularly suited for traditional pharmacological investigations, as it mimics the commonly used method of preparation in folk medicine and allows efficient recovery of water-soluble bioactive compounds.

2.3 Determination of Total Phenolic, Flavonoid, and Tannin Contents

The quantification of phenolic substances, flavonoids, and condensed tannins was conducted using conventional spectrophotometric methods commonly employed in phytochemical research. Singleton and Rossi [9] described how to use the Folin–Ciocalteu colorimetric method, with minor adjustments, to find the total phenolic content (TPC). To put it simply, 0.5 mL of the aqueous extract (1 mg/mL) was mixed with 2.5 mL of 10% Folin–Ciocalteu reagent and 2 mL of a 7.5% sodium carbonate solution. The mixture was held at 45 °C for 30 minutes, and a UV–Vis spectrophotometer measured the absorbance at 765 nm. We used gallic acid to calibrate, and the results were provided in mg GAE/g, which stands for mg gallic acid equivalent per g of dry extract. We employed the aluminum chloride colorimetric approach, which Chang et al. (2002) wrote about, to find out how much flavonoids were in the sample. To sum up, 1.0 mL of extract was mixed with 1 mL of a 2 % $AlCl_3$ solution and 3.0 mL of methanol. After 30 minutes of incubation at room temperature, the absorbance was measured at 415 nm. The reference ingredient was quercetin, and the data were presented in mg QE/g, which means mg quercetin equivalent per g of dry extract. We employed the vanillin–HCl test, which was based on the work of Broadhurst and Jones [10], to determine how much condensed tannins (proanthocyanidins) there were. We combined 0.5 mL of extract, 3.0 mL of 4% vanillin in methanol, and 1.5 mL of concentrated HCl and let it sit at room temperature for 20 minutes. Next, we measured the absorbance at 500 nm. The outcomes were quantified as milligrams of catechin equivalent per gram of dry extract (mg CE/g). These spectrophotometric techniques are dependable, reproducible, and frequently utilized for the chemical characterization of medicinal plants, clarifying the correlation between phenolic composition and biological activity [11].

2.4 *In Vitro* Antioxidant Activity

2.4.1 DPPH Radical Scavenging Assay

We used a modified approach based on Brand-Williams et al. [12] to find out how well the aqueous extract worked as an antioxidant by scavenging 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals. One milliliter of the extract at different doses (10–200 µg/mL) was combined with one milliliter of 0.1 mM DPPH dissolved in methanol. The mixture was kept in the dark at room temperature for 30 minutes to achieve equilibrium. A UV–Vis spectrophotometer measured the value at 517 nm. The proportion of radical scavenging activity was calculated using the following equation:

Inhibition (%) = $(A_0 - A_s) / A_0 \times 100$

Where A_0 is the absorbance of the control, and A_s is the absorbance of the sample. The IC_{50} values, the concentration that stops 50% of DPPH radicals from reacting, were found by drawing the dose–response curve. A diminished IC_{50} signifies an augmented radical scavenging capability. Each antioxidant assay was performed in triplicate.

2.4.2 ABTS Radical Cation-Scavenging Assay

The antioxidant activity of the aqueous extract of *L. dentata* was further evaluated using the 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) radical cation ($ABTS^{\bullet+}$) decolorization assay, according to the method originally described by Re et al. [13], with minor modification to the aqueous plant extract. The $ABTS^{\bullet+}$ radical cation was generated by mixing an aqueous ABTS solution (7 mM) with potassium persulfate (2.45 mM). The resulting solution was allowed to stand in the dark at room temperature for 12–16 h to ensure complete radical generation. Prior to the assay, the activated $ABTS^{\bullet+}$ solution was diluted with the appropriate solvent until an absorbance of 0.70 ± 0.02 at 734 nm was obtained. Appropriate concentrations of the aqueous *L. dentata* extract were prepared from the same dried aqueous extract used for the other antioxidant assays. For each measurement, an aliquot of the extract was mixed with the diluted $ABTS^{\bullet+}$ working solution and

thoroughly homogenized. The reaction mixture was allowed to react at room temperature, protected from excessive light, and the decrease in absorbance was measured spectrophotometrically at 734 nm. A reagent blank containing the corresponding solvent instead of the extract was prepared in parallel. The percentage of $ABTS^{\bullet+}$ radical-scavenging activity was calculated using the same formula as the DPPH assay. The concentration of extract required to decrease the initial $ABTS^{\bullet+}$ response by 50% (IC_{50}) was determined from the concentration–response relationship. Lower IC_{50} values were interpreted as an indication of greater radical-scavenging capacity under the experimental conditions.

2.4.3 Cupric Reducing Antioxidant Capacity Assay

The cupric reducing antioxidant capacity (CUPRAC) of the aqueous *L. dentata* extract was determined using the CUPRAC method based on the reduction of Cu (II) to Cu(I) in the presence of neocuproine [14]. The method is based on the formation of a colored Cu(I)-neocuproine complex, which is measured spectrophotometrically at 450 nm. Briefly, the reaction mixture was prepared by combining the aqueous extract with copper (II) chloride solution, neocuproine solution prepared in an appropriate alcoholic solvent, and ammonium acetate buffer adjusted to approximately pH 7.0. The reagents were mixed thoroughly and allowed to react under controlled conditions. After color development, the absorbance of each reaction mixture was measured at 450 nm against an appropriate reagent blank. A concentration series of the aqueous extract was analyzed under identical experimental conditions. The antioxidant capacity was evaluated from the increase in absorbance resulting from the reduction of Cu (II) by antioxidant constituents present in the extract. The concentration corresponding to an absorbance of 0.50 ($A_{0.5}$) was calculated from the concentration–absorbance relationship. The CUPRAC assay was selected as a complementary electron-transfer-based method because it measures the reducing capacity of antioxidants through a copper (II)/copper(I) redox system, providing information complementary to radical-scavenging assays. The CUPRAC response was expressed as $A_{0.5}$ (mg/L) of aqueous *L. dentata* extract.

2.4.4 Ferrous-Ion Chelating Activity

The ability of the aqueous *L. dentata* extract to chelate ferrous ions (Fe^{2+}) was evaluated using the ferrozine-based metal-chelating assay [15]. This method is based on the competition between compounds present in the extract and ferrozine for ferrous ions. The formation of the Fe^{2+}–ferrozine complex produces a colored complex measurable at approximately 562 nm; therefore, a decrease in absorbance indicates greater ferrous-ion chelation. The assay is based on established ferrous-ion chelation methodology. Briefly, aliquots of the aqueous extract at different concentrations were mixed with a ferrous chloride solution. Deionized or distilled water was subsequently added, followed by the addition of ferrozine solution. The reaction mixtures were vortexed thoroughly and incubated at room temperature for the appropriate reaction period. Absorbance was then measured at 562 nm against a reagent control. The percentage of ferrous-ion chelating activity was calculated as: chelating activity (%)=$A_c - A_s / A_c \times 100$.

Where A_c is the absorbance of the control reaction containing all reagents except the plant extract, and A_s is the absorbance obtained in the presence of the aqueous extract. EDTA was used as the reference chelating agent. The concentration of the aqueous extract producing 50% inhibition of the Fe^{2+}–ferrozine complex formation (IC_{50}) was estimated from the concentration response curve.

2.4.5 *Reducing power assay*

We used the potassium ferricyanide reduction method that Oyaizu [16] wrote about to see how well the extract could reduce. We added 1 milliliter of the extract at different doses (10–200 µg/mL) to a mixture of 2.5 milliliters of phosphate buffer solution (0.2 M, pH 6.6) and 2.5 milliliters of 1% potassium ferricyanide solution [$K_3Fe(CN)_6$]. After 20 minutes at 50°C, the reaction mixture was stopped by adding 2.5 mL of 10% trichloroacetic acid. The contents were centrifuged at 3000 rpm for 10 minutes, after which 2.5 mL of the supernatant was combined with an equal volume of distilled water and 0.5 mL of 0.1% ferric chloride solution. We measured absorbance at 700 nm. Increased absorbance signifies enhanced reducing capacity, reflecting the extract's ability to donate an electron pair and to scavenge free radicals.

2.5 *In Vitro* Anti-inflammatory Assays

2.5.1 Egg Albumin Denaturation Assay

The inhibition of heat-induced egg albumin denaturation was evaluated [17]. Fresh hen's egg albumin was used as the protein substrate. The reaction mixture consisted of egg albumin, phosphate-buffered saline (PBS), and the aqueous *L. dentata* extract

at concentrations of 1, 10, 100, and 150 µg/mL. A corresponding control mixture containing the same protein and buffer components without the plant extract was prepared simultaneously. Diclofenac sodium was used as the reference anti-inflammatory drug at concentrations of 50, 100, and 150 µg/mL. The reaction mixtures were initially incubated at approximately 37 °C for 15 min to allow interaction between the extract and the protein. The tubes were subsequently subjected to controlled heating at approximately 70 °C for 5 min to induce heat-mediated protein denaturation. After heating, the samples were allowed to cool to room temperature. The absorbance of the resulting mixtures was measured spectrophotometrically at 660 nm. Similar temperature and spectrophotometric conditions have been described for egg-albumin denaturation assays. The percentage inhibition of albumin denaturation was calculated according to: Inhibition (%)=Ac−As/Ac×100

Where A_c is the absorbance of the control reaction, and A_s is the absorbance of the reaction containing the aqueous extract or diclofenac.

2.5.2 Bovine Serum Albumin Denaturation Assay

The ability of the aqueous *L. dentata* extract to inhibit heat-induced denaturation of bovine serum albumin (BSA) was evaluated using a BSA protein-denaturation model derived from the method of Mizushima and Kobayashi [18] with modifications described in subsequent *in vitro* studies. Bovine serum albumin was prepared as an aqueous protein solution, and the aqueous *L. dentata* extract was evaluated at 1, 10, 100, and 150 µg/mL. For each concentration, the test solution was combined with the BSA solution to obtain the reaction mixture. A negative control containing BSA and distilled water instead of the plant extract was prepared in parallel. Diclofenac sodium at 50, 100 and 150 µg/mL was used as the reference standard. The pH of the reaction mixtures was adjusted to approximately 6.3 using dilute hydrochloric acid where required. The mixtures were incubated at 37 °C for 20 min, followed by controlled heating at approximately 57 °C to induce thermal denaturation. After the heating period, the reaction mixtures were cooled to room temperature, and phosphate buffer was added. The resulting turbidity was determined spectrophotometrically at 660 nm. Similar BSA-denaturation protocols employ BSA, pH adjustment, incubation at 37 °C, subsequent heating at 57 °C, and spectrophotometric measurement of the resulting turbidity. Appropriate sample blanks were prepared where necessary to correct for the intrinsic absorbance or turbidity of the plant extract. The percentage inhibition of BSA denaturation was calculated using: Inhibition (%)=Ac−As/Ac×100

Where A_c represents the absorbance of the untreated control and A_s represents the absorbance of the reaction mixture containing the aqueous extract.

***2.6 In Silico* Target-Profile analysis**

Compound structures were retrieved from PubChem (PUG-REST), [19] and characterised in RDKit (physicochemical descriptors, Lipinski rules, QED, PAINS alerts, antioxidant-relevant substructures and Morgan-fingerprint Tanimoto similarity). Protein targets were collected for each compound from ChEMBL [20] (human targets, pChEMBL ≥ 4, i.e., activity ≤ 100 µM, excluding censored ">" values) and from active outcomes in PubChem BioAssay (gene identifiers converted to symbols with MyGene.info), complemented by a literature-curated set of well-documented redox and inflammatory targets that was tracked as a separate evidence source. Gene-set libraries (GO Biological Process, KEGG, Reactome and WikiPathways) were downloaded through gseapy/Enrichr [21] and "antioxidant", "anti-inflammatory" and an unrelated "control" gene universe were defined by keyword matching on term names (term size 5–500 genes). Phenotype relevance of the complete target sets was tested with one-sided hypergeometric tests against these universes (Benjamini–Hochberg FDR); target genes were then restricted to those annotated in at least two antioxidant and/or anti-inflammatory terms, and the retained genes were analysed by over-representation analysis against each library. Protein-protein interactions among the retained targets were obtained from STRING [22], (human, combined score ≥ 0.4) and analysed in NetworkX (degree, betweenness, greedy-modularity communities). All analyses were run in Python (pandas, SciPy, NetworkX, matplotlib and seaborn) and every intermediate table was exported for reproducibility.

2.7 Statistical Analysis

All antioxidant and anti-inflammatory measurements were conducted in triplicate under identical experimental conditions. Values are expressed as mean ± standard deviation (SD) for the antioxidant assays and mean ± standard error (SE) for the anti-inflammatory assays, in line with the original data sources. Statistical evaluation was performed using GraphPad Prism 9.0. Comparisons between treatments were made using one-way ANOVA, and a p-value < 0.05 was considered significant.

3. RESULTS AND DISCUSSION

3.1 Extraction Yield

Using the decoction method, the mean yield obtained from the aqueous extract of *L. dentata* collected in Beni Aziz (Sétif, Algeria) was 17.8 ± 1.3 % (n = 3). This yield is considerably higher than those reported for essential oil extraction via hydrodistillation, which typically range from 0.4–3.5 % w/w [4, 23]. The elevated yield reflects the high efficiency of decoction in recovering polar constituents such as phenolic acids, flavonoids, and tannins, key contributors to the observed antioxidant activity. Comparable findings have been reported in other Lamiaceae species, where aqueous decoction or infusion yielded between 15–20 % dry extract, confirming its relevance for ethnopharmacological studies [24]. Decoction is also widely recognized for mirroring traditional preparation methods, thereby ensuring that the bioactive profile is close to what is consumed by local populations. Overall, these results validate the use of decoction as a suitable and reproducible extraction method for *L. dentata*, providing sufficient material for *in vitro* antioxidant and phytochemical investigations while maintaining ethnopharmacological relevance.

3.2 Total Phenolic, Flavonoids and Tannins Contents

The total phenolic, flavonoid, and tannin contents were determined using spectrophotometric assays. The aqueous extract of *L. dentata* demonstrated elevated concentrations of phenolic chemicals and flavonoids, which are essential for its biological action. Our results showed that the total phenolic, flavonoids and tannins contents, with values of 87.4 ± 1.2 mg gallic acid equivalent, 54.7 ± 1.1 mg quercetin equivalent, and 23.8 ± 0.9 mg tannic acid equivalent/g dry extract) is similar to or a little greater than what has been found for *Lavandula stoechas* and *Lavandula angustifolia* (70–85 mg GAE/g). This shows that *L. dentata* is a good source of antioxidant phenolics. The flavonoid concentration (54.7 mg QE/g) corresponds with levels previously reported in North African Lavandula species, corroborating their function as free radical scavengers and metal chelators [25]. The tannin concentration (23.8 mg TAE/g) also suggests that there are many hydrolyzable and condensed tannins, which are known to have antibacterial, antioxidant, and anti-inflammatory actions. These results indicate that the aqueous extract retains a broad array of polar bioactive chemicals, hence elucidating the significant antioxidant ability demonstrated in later experiments. Similar results in other Lamiaceae species indicate that aqueous and hydroethanolic extracts produce elevated concentrations of phenolics and flavonoids, hence affirming the therapeutic efficacy of traditional herbal formulations [24, 26].

3.3 *In Vitro* Antioxidant Activity

3.3.1 DPPH Radical Scavenging Activity

The DPPH assay is widely used to evaluate the free-radical-scavenging capacity of plant extracts. This method is based on the reduction of the stable 2,2-diphenyl-1-picrylhydrazyl (DPPH•) radical by antioxidant molecules capable of donating hydrogen atoms and/or electrons, resulting in a decrease in absorbance at 517 nm. The IC_{50} value represents the concentration of extract required to achieve 50 % scavenging of the DPPH radical; consequently, lower IC_{50} values indicate stronger radical-scavenging activity [27]. In the present study, the aqueous extract of *L. dentata* exhibited a marked DPPH radical-scavenging activity, with an IC_{50} value of 44.18 ± 1.08 µg/mL (Table 1). This result indicates that the aqueous extract was able to efficiently neutralize the DPPH radical at relatively low concentrations under the experimental conditions employed. The observed activity reflects the capacity of the constituents present in the aqueous extract to participate in hydrogen-atom and/or electron-transfer reactions, thereby reducing the stable DPPH radical to its non-radical form [28]. Thus, the aqueous extract displayed a stronger DPPH-scavenging activity than BHT under the conditions of the present assay, while its activity remained lower than that of BHA and α-tocopherol.

The strong DPPH-scavenging capacity observed in the present study may be related to the presence of phenolic and flavonoid constituents in *L. dentata*. Phenolic compounds are recognized as important contributors to plant antioxidant activity because their hydroxyl groups can donate hydrogen atoms or electrons to reactive species, while the resulting phenoxyl radicals can be stabilized through resonance and other structural effects.

Table1. Antioxidant activity of *L. dentate* aqueous extract (LDA)

Extract/ standards	IC_{50} (µg/mL)				$A_{0.5}$(µg/mL)
	DPPH	**ABTS**	**Metal chelating**	**Reducing power**	**CUPRAC**
LDA	44.18 ± 1.08^{ns}	71.18 ± 4.45***	243.54 ± 4.06***	329.9 ± 2.3** µM Fe(II)/g	6.03 ± 0.2***
BHT	60.35 ± 1.93***	19.91 ± 0.65***	ND	ND	37.31 ± 0.17***
BHA	15.20 ± 0.40***	5.96 ± 0.05***	ND	450 ± 5 µM Fe(II)/g (BHT)	22.51 ± 0.59***
α-Toc	36.83 ± 1.21	27.68 ± 0.12	ND	ND	107.62 ± 2.18
EDTA	ND	ND	26.85 ± 1.50	ND	ND

Previous phytochemical investigations of *L. dentata* have reported phenolic acids, flavonoids and other secondary metabolites with recognized antioxidant properties. Rosmarinic acid is an important phenolic constituent of *L. dentata*, and its occurrence has been associated with the antioxidant potential of extracts from this species [29]. The authors reported promising DPPH-scavenging activity for *L. dentata* and related the antioxidant properties of the extract to its phenolic composition. The present IC_{50} value agrees with previous studies reporting substantial DPPH-scavenging activity for *L. dentata*. Pereira et al. [29] reported DPPH EC_{50} values ranging approximately from 48.7 to 71.1 µg/mL for *L. dentata* extracts investigated in their study. The value obtained in the present work, 44.18 mg/L, equivalent to 44.18 µg/mL, is therefore within the same order of magnitude and slightly lower than the range reported previously. This close agreement provides further evidence that *L. dentata* contains constituents capable of efficiently scavenging free radicals. Nevertheless, comparisons among studies should be interpreted cautiously because DPPH values are influenced by several experimental factors, including extraction procedure, plant material, geographic origin, solvent composition, extract concentration, DPPH concentration, reaction time and the mathematical procedure used to calculate IC_{50} or EC_{50} [27].

Evidence from Algerian *Lavandula* research further supports the antioxidant potential of *L. dentata*. Haddouchi et al. [6] investigated the phytochemical composition and antioxidant activity of several *Lavandula* species collected in the Tlemcen region of Algeria using hydro-methanolic extracts. The observed activity should also be considered in relation to the broader antioxidant behavior reported for *L. dentata*. El Abdali et al. [4] demonstrated that *L. dentata* possesses measurable antioxidant activity in DPPH, FRAP and total antioxidant capacity assays. Although their investigation concerned the essential oil rather than the aqueous extract studied here, it confirms that *L. dentata* contains chemically diverse constituents capable of interacting with free radicals and participating in antioxidant mechanisms. Their DPPH assay yielded an IC_{50} of 12.95 ± 1.30 mg/mL for the essential oil, illustrating the considerable influence of the chemical nature of the tested plant preparation on the magnitude of the measured DPPH response. Foti et al. [27] emphasized that DPPH-based IC_{50} values should be compared only when methodological conditions are sufficiently similar.

3.3.2 ABTS Radical-Scavenging Activity

The ABTS radical-scavenging activity of the aqueous extract of *L. dentata* was evaluated and expressed as the concentration required to inhibit 50% of the $ABTS^{\bullet+}$ radical (IC_{50}). The aqueous extract exhibited an IC_{50} value of 71.18 ± 4.45 mg/L (Table 1). Thus, the aqueous extract showed measurable and substantial ABTS radical-scavenging activity, although its activity was lower than that of the three reference antioxidants under the experimental conditions employed. The ABTS assay provides complementary information to the DPPH assay because the $ABTS^{\bullet+}$ radical cation can react with antioxidants through electron-transfer and hydrogen-atom-transfer processes. An important advantage of the ABTS system is its applicability to both hydrophilic and lipophilic antioxidant compounds, which makes it particularly useful for complex plant extracts [30]. Recent methodological reviews have nevertheless emphasized that ABTS results are influenced by reaction time,

radical concentration, solvent conditions and the antioxidant standard employed; consequently, IC_{50} values should preferably be compared only between studies using sufficiently similar experimental conditions.

The observed ABTS activity may also be associated with the presence of phenolic compounds in *L. dentata*. Previous phytochemical studies have demonstrated that this species contains phenolic acids and flavonoid derivatives, including rosmarinic-acid-related compounds, which may contribute to its antioxidant activity [29]. The contribution of these compounds is particularly plausible in the present aqueous extract because many phenolic compounds are sufficiently polar to be recovered by water-based extraction. Recent research further supports the importance of extraction conditions in determining antioxidant responses in *L. dentata*. Ortega-Vargas et al. [31] evaluated extracts obtained using solvents of different polarities and demonstrated substantial differences in antioxidant responses among the resulting extracts. In their CUPRAC and FRAP analyses, the water extract displayed measurable reducing activity, although its response differed from that of the other solvent fractions. These observations reinforce the interpretation that the antioxidant profile of *L. dentata* is strongly dependent on the chemical fraction recovered during extraction.

3.3.3 Ferrous-Ion Metal-Chelating Activity

The ability of the aqueous *L. dentata* extract to chelate ferrous ions was evaluated using the metal-chelating assay and expressed as the IC_{50} value. The aqueous extract exhibited an IC_{50} of 243.54 ± 4.06 mg/L. In comparison, the reference chelating agent EDTA exhibited an IC_{50} of 26.85 ± 1.50 mg/L (Table 1). Since lower IC_{50} values indicate a higher metal-chelating capacity, the aqueous *L. dentata* extract displayed a moderate Fe^{2+}-chelating capacity than EDTA under the conditions of the present assay. Metal chelation represents a distinct antioxidant mechanism from direct radical scavenging and electron-transfer reduction. Transition metals such as Fe^{2+} can participate in reactions leading to the formation of highly reactive oxygen species, particularly through Fenton-type chemistry. By binding Fe^{2+}, chelating agents can decrease the availability of free metal ions and thereby limit their participation in pro-oxidant reactions. The ferrous-ion chelation assay therefore provides complementary information that cannot be obtained from DPPH, ABTS or CUPRAC measurements alone [32]. This difference suggests that the antioxidant behavior of LDA is more strongly associated with electron donation and radical neutralization than with sequestration of ferrous ions. Such assay-dependent differences are common in plant extracts because the structural requirements for efficient metal coordination differ from those required for electron transfer or radical scavenging. The ability of phenolic compounds to chelate metal ions depends strongly on their molecular structure. Functional groups such as ortho-dihydroxyl arrangements and carbonyl/hydroxyl combinations can provide favorable coordination sites for transition metals. However, not all phenolic compounds are equally effective chelators, and the total phenolic content of an extract does not necessarily predict its metal-chelating capacity. The chemical composition and relative abundance of individual constituents are therefore important determinants of the chelation response [32].

3.3.4 Reducing Power Activity

In reducing power activity, the extract showed a value of 329.9 ± 2.3 μM Fe(II)/g, indicating good ability to donate electrons, though lower compared to BHT (450 ± 5 μM Fe(II)/g) (Table 1). The value in the reducing power test indicates the extract's ability to reduce ferric ions ($Fe^{3+} \rightarrow Fe^{2+}$), a significant function in antioxidant protection. Similar reducing power values have been noted in hydromethanolic extracts of various Lamiaceae species, evidencing how, in particular, polar fractions are strongly effective in accepting electrons and scavenging pro-oxidant species [24]. These findings are in accordance with previous studies on *L. dentata* and similar species, in which phenolic acids and flavonoids were noted as main contributors to the antioxidant activity [7]. The concomitance between effective radical scavengers DPPH and high indices of FRAP points towards synergistic bioactive molecules, among which are rosmarinic acid, caffeic acid derivatives, and flavonoids typical of the Lamiaceae family. This verifies the ethnopharmacological use of *L. dentata* to prevent oxidative stress–related ailments and its prospective role as a source of antioxidants.

3.3.5 Cupric Ion Reducing Antioxidant Capacity (CUPRAC)

The cupric ion reducing antioxidant capacity of the aqueous *L. dentata* extract was evaluated using the CUPRAC assay and expressed as the concentration required to reach an absorbance of 0.5 ($A_{0.5}$). The aqueous extract exhibited an $A_{0.5}$ value of 6.03 ± 0.20 mg/L (Table 1). The reference antioxidants showed $A_{0.5}$ values of 37.31 ± 0.17 mg/L for BHT, 22.51 ± 0.59 mg/L for BHA, and 107.62 ± 2.18 mg/L for α-tocopherol. Since a lower $A_{0.5}$ value indicates that a lower concentration of the sample is required to produce the defined reducing response, the aqueous *L. dentata* extract exhibited a pronounced

cupric-ion-reducing capacity under the conditions of the present assay. The CUPRAC assay evaluates antioxidant capacity through the reduction of Cu^{2+} to Cu^{+} in the presence of neocuproine, producing a colored Cu(I)-neocuproine complex measured spectrophotometrically. The method is primarily an electron-transfer assay and is particularly useful for evaluating compounds capable of donating electrons to an oxidizing species [14]. This result is especially interesting when compared with the DPPH and ABTS findings. The present result is also compatible with recent observations for *Lavandula* species. Gadouche et al. [33] reported substantial ferric-reducing activity for aqueous *L. dentata* preparations, with the aqueous extract reaching 99.21 ± 0.06 mM Fe^{2+}/g extract in their reducing-power assay. Although their assay and units differ from the CUPRAC procedure used here and direct numerical comparison is therefore inappropriate, the study independently supports the presence of strong electron-donating constituents in aqueous *L. dentata* extracts. Similarly, Ortega-Vargas et al. [31] found that the water extract of *L. dentata* displayed measurable CUPRAC activity, reported as 351.0 mg gallic acid equivalents/kg plant material. Their results demonstrated that water was capable of recovering compounds contributing to Cu^{2+}-reducing activity, although the response differed substantially from that of other solvent fractions. Because their results were expressed in a different unit and based on a different extraction and analytical protocol, the numerical values should not be directly compared with the present $A_{0.5}$ value. Nevertheless, the qualitative agreement is noteworthy and supports the presence of water-soluble reducing constituents in *L. dentata*. Consequently, the complementary results obtained here provide a strong chemical characterization of the antioxidant potential of the aqueous extract, while further biological studies would be required to establish its physiological relevance.

3.4 Anti-inflammatory Activity

3.4.1 Inhibition of Egg Albumin Denaturation

The anti-inflammatory potential of the aqueous extract of *Lavandula dentata* was first evaluated using the heat-induced egg albumin denaturation assay. The extract demonstrated a clear concentration-dependent protective effect against protein denaturation. At concentrations of 1, 10, 100 and 150 µg/mL, the aqueous extract inhibited egg albumin denaturation by 37.63 ± 1.39%, 50.45 ± 2.01%, 87.27 ± 1.14% and 93.49 ± 1.23%, respectively (Table 2). Diclofenac sodium, used as the reference anti-inflammatory drug, produced inhibition values of 66.55 ± 1.47%, 70.81 ± 1.33% and 89.72 ± 2.15% at 50, 100 and 150 µg/mL, respectively. The observed progressive increase in inhibition with increasing concentrations of the aqueous extract indicates a concentration-dependent ability of *L. dentata* constituents to protect egg albumin against heat-induced denaturation.

Table 2. *In vitro* anti-inflammatory activity (%) of the *L. dentata* aqueous extract (LDA) at different concentrations using the egg albumin denaturation method.

Treatments	Concentration (µg/mL)	Denaturation (%)	Inhibition of denaturation (%)
Control	—	**100**	**0**
LDA	1	62.37 ± 1.62	37.63 ± 1.39***
	10	49.63 ± 0.18	50.45 ± 2.01***
	100	12.72 ± 0.98	87.27 ± 1.14ns
	150	6.54 ± 0.24	93.49 ± 1.23 ns
Diclofenac	50	33.45 ± 1.82	66.55 ± 1.47***
	100	29.18 ± 1.22	70.81 ± 1.33**
	150	10.27 ± 1.09	89.72 ± 2.15

Values are expressed as mean ± SE. $p < 0.05$ was considered statistically significant compared with the control according to ANOVA.

Interestingly, at 100 µg/mL, the aqueous extract produced 87.27 ± 1.14% inhibition, compared with 70.81 ± 1.33% for diclofenac at the same concentration. At 150 µg/mL, the extract reached 93.49 ± 1.23% inhibition, compared with 89.72 ±

2.15% for diclofenac at 150 µg/mL. Thus, under the experimental conditions employed, the aqueous extract produced a strong protein-stabilizing response at the two highest concentrations tested.

Protein denaturation involves structural changes of proteins and can contribute to inflammatory processes. Consequently, inhibiting heat-induced protein denaturation is widely used as a preliminary *in vitro* model for evaluating the anti-inflammatory potential of natural products. This assay tests a substance's ability to protect protein structures against thermal destabilization, with less denaturation corresponding to greater protein-stabilizing activity. Recent studies continue to employ egg albumin denaturation as a convenient preliminary model for screening plant-derived anti-inflammatory activity. These observations demonstrate that, within the concentration range investigated, the aqueous *L. dentata* extract produced a strong protein-stabilizing response. However, this should be interpreted as an *in vitro* protein-denaturation inhibitory effect rather than evidence that the plant extract is pharmacologically equivalent to diclofenac. These findings are particularly interesting in relation to recent research on *L. dentata*. Labhar et al. [34] investigated the anti-inflammatory activity of *L. dentata* essential oils using a BSA denaturation model and demonstrated significant inhibition of albumin denaturation. Additionally, their findings indicated that activity varied according to the seasonal origin of the essential oil, which was linked to variations in its chemical constitution. The authors specifically discussed compounds such as eucalyptol, L-trans-pinocarveol and β-eudesmol as possible contributors to the observed anti-inflammatory activity.

Recent studies on other medicinal plants provide further support for the concentration-dependent response observed here. For example, Boussebaa et al. [35] reported increasing inhibition of egg albumin denaturation by an aqueous extract of *Paronychia arabica*, with inhibition increasing from 52.47% to 71.69% as the concentration increased. Their results were interpreted as evidence of concentration-dependent protein-stabilizing and anti-inflammatory potential. Similarly, a recent study of *Moringa oleifera* and *Moringa stenopetala* extracts demonstrated increasing inhibition of egg albumin denaturation with increasing extract concentration, with the highest concentration producing 74.08% and 85.02% inhibition, respectively. The strong protein-stabilizing effect of LDA may be related to the interaction of its phytochemical constituents with albumin. Phenolic compounds and flavonoids can interact with proteins through hydrogen bonding, hydrophobic interactions and other non-covalent forces, potentially modifying protein stability and limiting thermally induced structural changes.

3.4.2 Inhibition of Bovine Serum Albumin Denaturation

The anti-inflammatory activity of the aqueous *L. dentata* extract was further investigated using the heat-induced bovine serum albumin (BSA) denaturation assay. The extract exhibited a concentration-dependent inhibitory effect, although the magnitude of the response differed from that observed with egg albumin (Table 3). At concentration of 150 µg/mL, the aqueous extract inhibited BSA denaturation by 89.35 ± 0.09%. Diclofenac sodium showed inhibition values of 99.27 ± 0.72% at 150 µg/mL. The results therefore demonstrate a progressive increase in BSA protection with increasing extract concentration.

Table 3. Effect of the aqueous extract on *in vitro* anti-inflammatory activity using the bovine serum albumin denaturation method.

Treatments	Concentration (µg/mL)	Denaturation (%)	Inhibition of denaturation (%)
Control	—	100	0
LDA	1	35.45 ± 0.18	64.52 ± 0.16***
	10	22.72 ± 0.98	77.23 ± 1.05***
	100	12.36 ± 0.94	87.64 ± 1.02ns
	150	10.63 ± 0.24	89.35 ± 0.09 ns
Diclofenac	50	3.18 ± 1.08	96.81 ± 1.21 ns
	100	1.18 ± 1.51	98.18 ± 1.68 ns
	150	0.72 ± 1.22	99.27 ± 0.72

Values are expressed as mean ± SE. $p < 0.05$ was considered statistically significant compared with the control according to the ANOVA test.

The BSA denaturation model provides a complementary approach to the egg albumin assay for evaluating the ability of natural products to stabilize proteins under thermal stress. Bovine serum albumin is frequently used as a model protein because thermal denaturation induces structural changes and aggregation that can be monitored spectrophotometrically. The inhibition of this process by a plant extract is therefore interpreted as an indication of protein-stabilizing activity and, consequently, as preliminary evidence of anti-inflammatory potential. Recent studies continue to use BSA denaturation as an established *in vitro* screening model for plant-derived anti-inflammatory agents. The increase in inhibition demonstrates that higher concentrations of the extract were associated with greater stabilization of BSA against thermal denaturation. The response was already substantial at the lowest concentration tested, suggesting that the aqueous extract contains constituents capable of interacting efficiently with the protein even at relatively low concentrations.

This pattern is consistent with recent research using plant extracts. For example, a study of *Ehretia rigida* leaf extract using a thermally induced BSA-denaturation model reported a concentration-dependent increase in inhibition, with the extract reaching approximately 78% inhibition at 400 µg/mL, while diclofenac reached approximately 99% [36]. The magnitude of inhibition observed for LDA at only 150 µg/mL is therefore noteworthy, although direct comparisons must be avoided because the extracts, concentration ranges and assay protocols were different.

The results also provide an interesting link with previous investigations of *L. dentata*. Labhar et al. [34] demonstrated anti-inflammatory activity of *L. dentata* essential oils using albumin denaturation and observed seasonal differences related to variations in essential-oil composition. The present results extend this observation by demonstrating substantial protein-denaturation inhibition for a water-based extract, suggesting that the anti-inflammatory potential of *L. dentata* is not restricted to its volatile fraction.

Taken together, the egg albumin and BSA results indicate that the aqueous extract of *L. dentata* has a strong *in vitro* protein-stabilizing potential, with the most pronounced response observed at 100–150 µg/mL. These findings, combined with the strong antioxidant activity demonstrated by DPPH, ABTS and CUPRAC assays, support the biological interest of the aqueous extract. Nevertheless, these results should be regarded as preliminary *in vitro* evidence. Further studies using cellular models, inflammatory mediators, COX/LOX inhibition, cytokine assays and ultimately *in vivo* models would be necessary to confirm the mechanisms underlying the observed anti-inflammatory activity.

3.5 *In Silico* Profiling

3.5.1 Target Profiles And Focus Filtering

The combined search returned 42 target genes for ferulic acid, 84 for caffeic acid and 34 for ascorbic acid. After the focus filter, 26 (62%), 43 (51%) and 18 (53%) genes were retained, respectively (Figure 1). Most retained genes were annotated to both categories (14, 16 and 9 genes), indicating that antioxidant and inflammatory biology are strongly intertwined in these target profiles. Roughly half of each profile (38–49%) mapped to neither category and was removed from the downstream analysis.

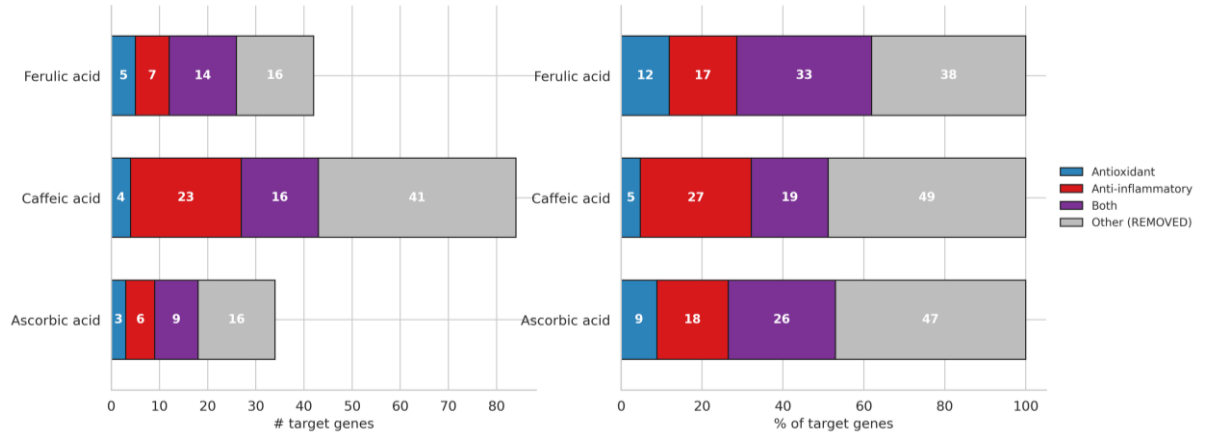


Figure 1. Target genes retained by the antioxidant/anti-inflammatory focus filter for each compound (left, gene counts; right, percentage of each target profile; grey, genes removed).

3.5.2 Specificity of The Antioxidant And Anti-Inflammatory Signal

Tested on the complete target sets, all three compounds were significantly enriched in both phenotype universes, while the unrelated control universe remained below the FDR 0.05 threshold (Figure 2, Table 4). Ferulic acid had the strongest antioxidant enrichment (≈ 13.6-fold, −log10 FDR ≈ 23), caffeic acid had the strongest anti-inflammatory enrichment (−log10 FDR ≈ 17) and an almost balanced profile, and ascorbic acid was enriched in both categories but more weakly, particularly for inflammation (≈ 2.6-fold, −log10 FDR ≈ 4).

Table 4. Phenotype enrichment of the complete target sets

Compounds	Raw targets	Retained	Antioxidant (fold; −log10 FDR)	Anti-inflammatory (fold; −log10 FDR)	Control
Ferulic acid	42	26	≈ 13.6; ≈ 23	≈ 3.6; ≈ 10	n.s.
Caffeic acid	84	43	≈ 7.5; ≈ 18	≈ 3.3; ≈ 17	n.s.
Ascorbic acid	34	18	≈ 9.3; ≈ 11.5	≈ 2.6; ≈ 4	n.s.

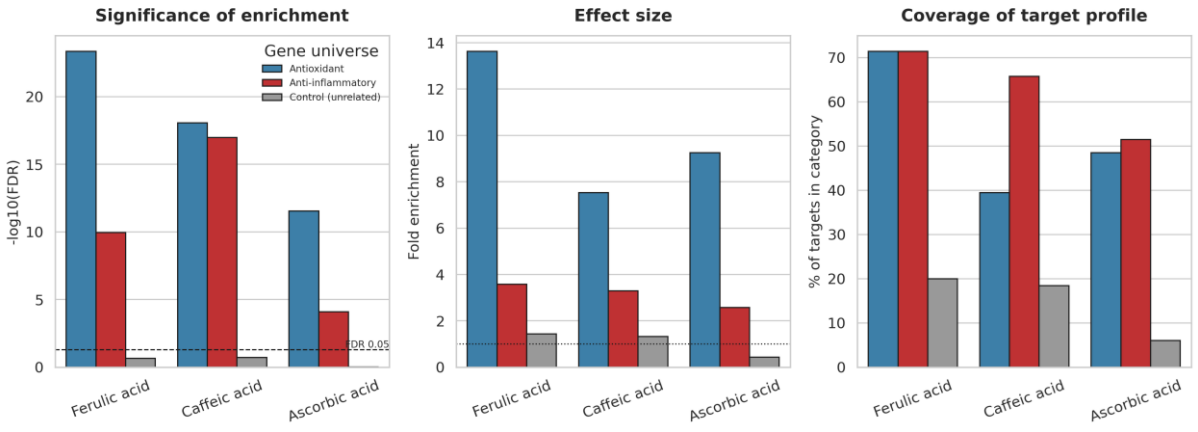
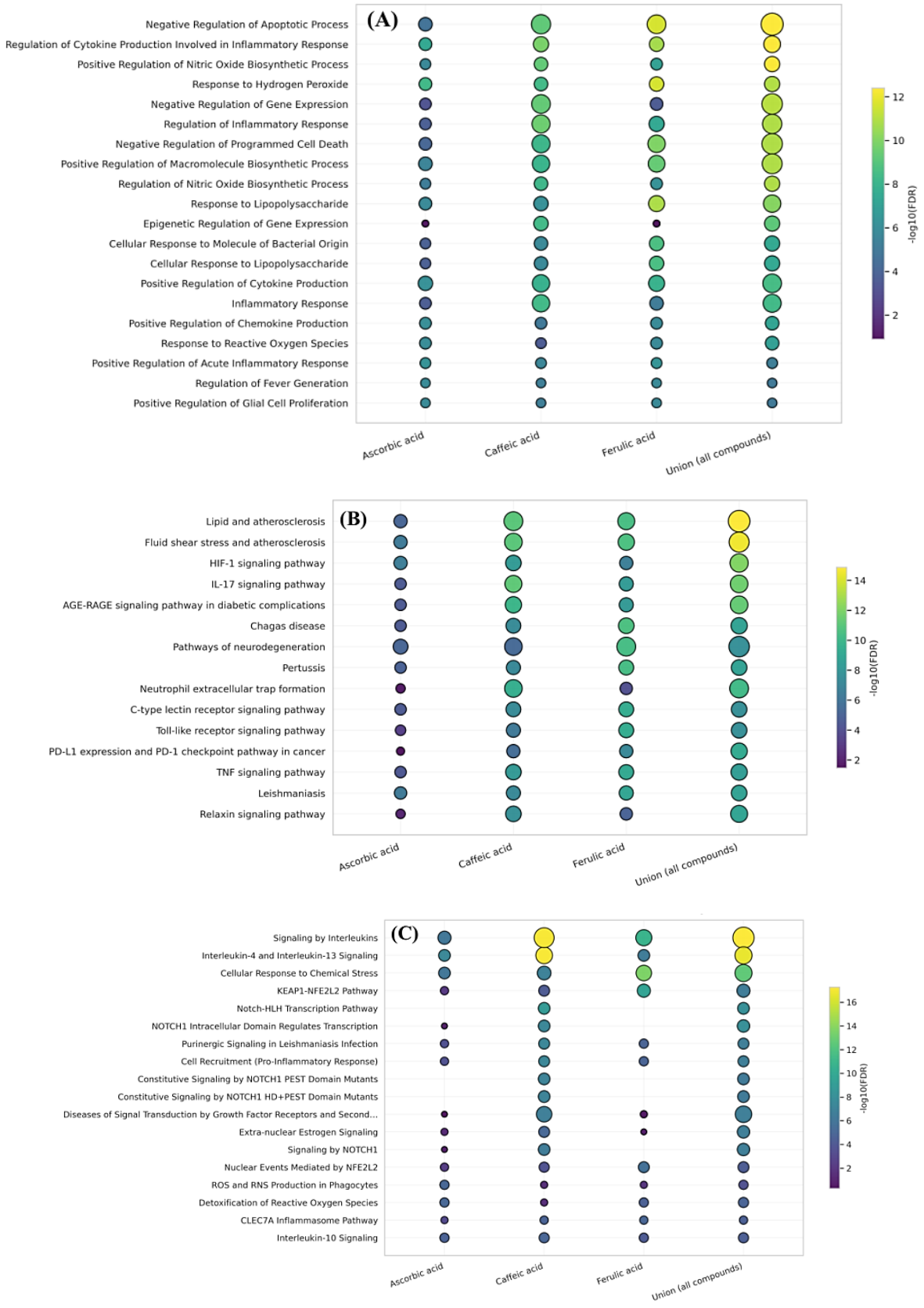


Figure 2. Phenotype relevance of all retrieved targets (before focusing) for the antioxidant, anti-inflammatory and unrelated control gene universes: significance (−log10 FDR; dashed line, FDR 0.05), fold enrichment and coverage of each target profile. Values are read from Figure 2; n.s., not significant.

3.5.3 Pathway-Level Enrichment

The retained genes were enriched in coherent antioxidant and inflammatory pathways across all four libraries (Figures 3 and 4). Anti-inflammatory terms were dominated by interleukin signalling (Reactome "Signaling by Interleukins", −log10 FDR ≈ 17; IL-4/IL-13 signalling), cytokine production and inflammatory response (GO), TNF, IL-17 and Toll-like receptor signalling (KEGG) and neutrophil extracellular trap formation. Antioxidant terms included hydrogen peroxide response and reactive oxygen species (GO), the KEAP1–NFE2L2 pathway and nuclear events mediated by NFE2L2 (Reactome), and the oxidative stress response and Nrf2 pathways (WikiPathways). Compound-specific differences were apparent: ferulic acid showed the strongest enrichment for the KEAP1–NFE2L2 pathway and the WikiPathways oxidative stress response, caffeic acid for interleukin signalling, and ascorbic acid for the selenium micronutrient network and detoxification of reactive oxygen species. Several high-ranking terms, such as negative regulation of apoptosis, AGE–RAGE signalling and atherosclerosis, reflect the pleiotropy of the shared hub genes rather than a distinct activity.

Natural Resources for Human Health
eISSN: 2583-1194



Natural Resources for Human Health
eISSN: 2583-1194

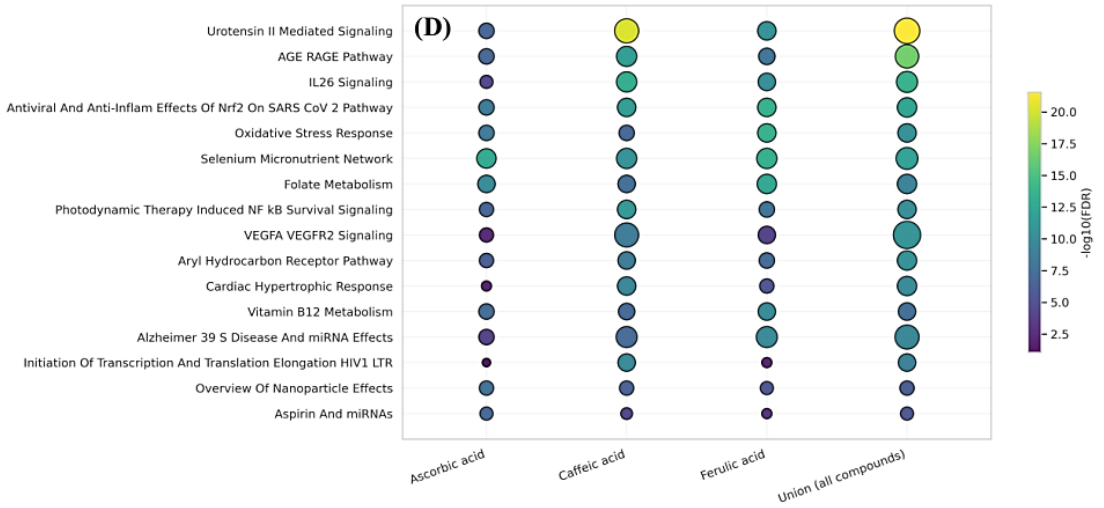


Figure 3. Top enriched terms per compound and for the union of targets: **(A)** GO Biological Process, **(B)** KEGG, **(C)** Reactome, **(D)** WikiPathways. Black outline, FDR < 0.05; point size, number of overlapping genes; colour, −log10 FDR.

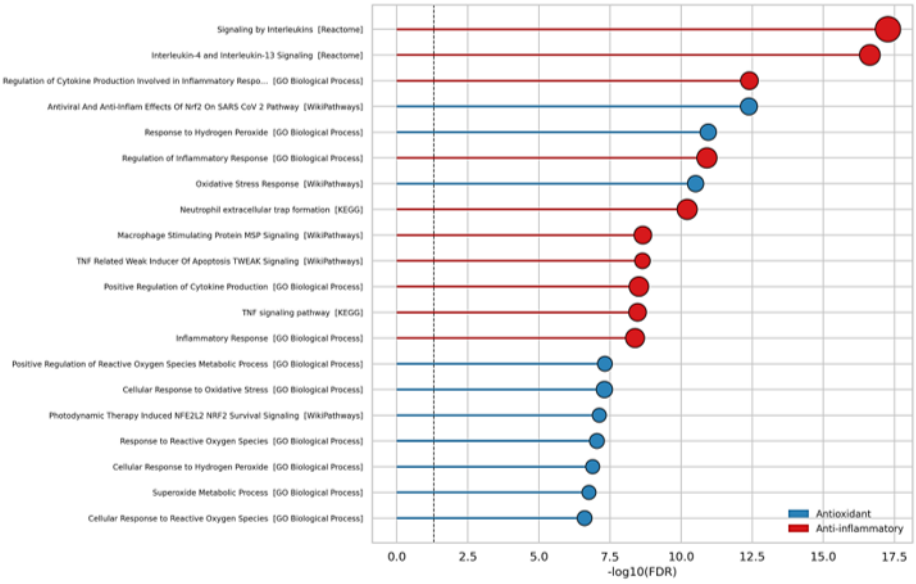


Figure 4. Top antioxidant (blue) and anti-inflammatory (red) terms enriched in the combined target set (dashed line, FDR 0.05).

3.5.4 Network and Gene-Level Analysis

The STRING network of retained targets separated into two large communities and one minor module (Figure 5). The first (n = 30; NFKB1, TNF, IL6, IL1B, PTGS2, NOS2, TLR4) combined cytokine and redox-enzyme genes (SOD1/2, HMOX1, MPO, NFE2L2). The second (n = 23; AKT1, HSP90AA1, HIF1A, EGFR, STAT3, MAPKs) contained signalling and stress-response regulators. The highest-degree hubs were AKT1, NFKB1, TNF, GAPDH, IL6, PPARG, IL1B and PTGS2. Eleven genes were hit by all three compounds (IL6, IL1B, TNF, NFKB1, NFE2L2, HMOX1, SOD1, PTGS2, NOS2, CAT, MPO), and the gene-by-pathway map (Figure 6) showed that these shared genes underlie most of the antioxidant (NFE2L2, HMOX1, SOD1, CAT) and anti-inflammatory (IL6, IL1B, TNF, NFKB1) terms. Caffeic acid contributed the largest number of additional genes, including several HDAC isoforms, ALOX5/ALOX15 and MMP9. The integrated profile (Figure 7) summarises these differences: ferulic acid ranked highest for antioxidant enrichment and coverage, caffeic acid for anti-

Natural Resources for Human Health
eISSN: 2583-1194

inflammatory enrichment and number of targets, and ascorbic acid for mean network connectivity of a small target set.

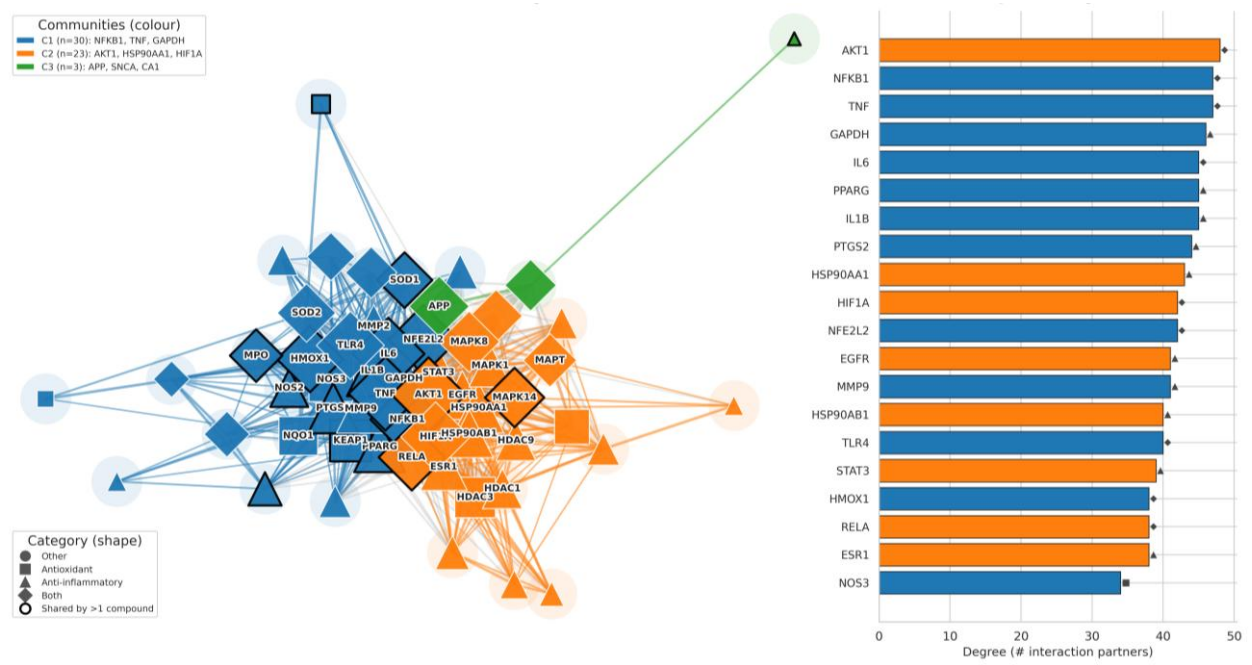


Figure 5. STRING protein-protein interaction network of the retained targets. Colour, network community; shape, functional category; black ring, gene shared by more than one compound; right, top 20 hub genes by degree.

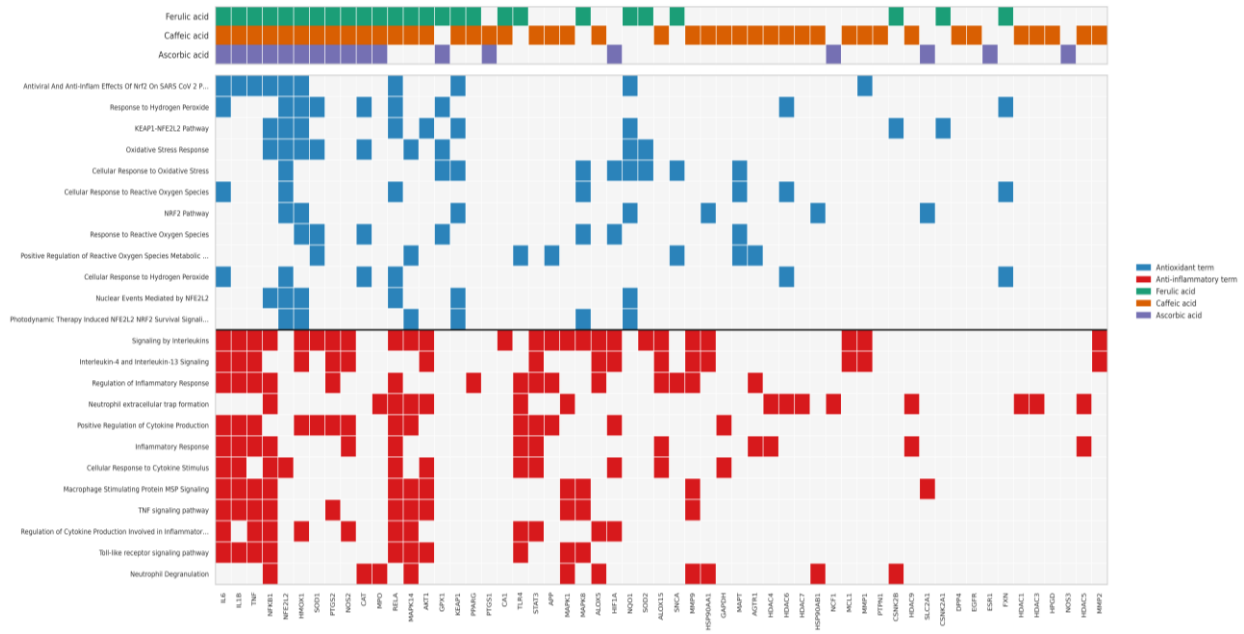


Figure 6. Gene-by-pathway membership map. The top strip shows which compound hits each gene; the heatmap shows the antioxidant (blue) and anti-inflammatory (red) terms each gene belongs to.

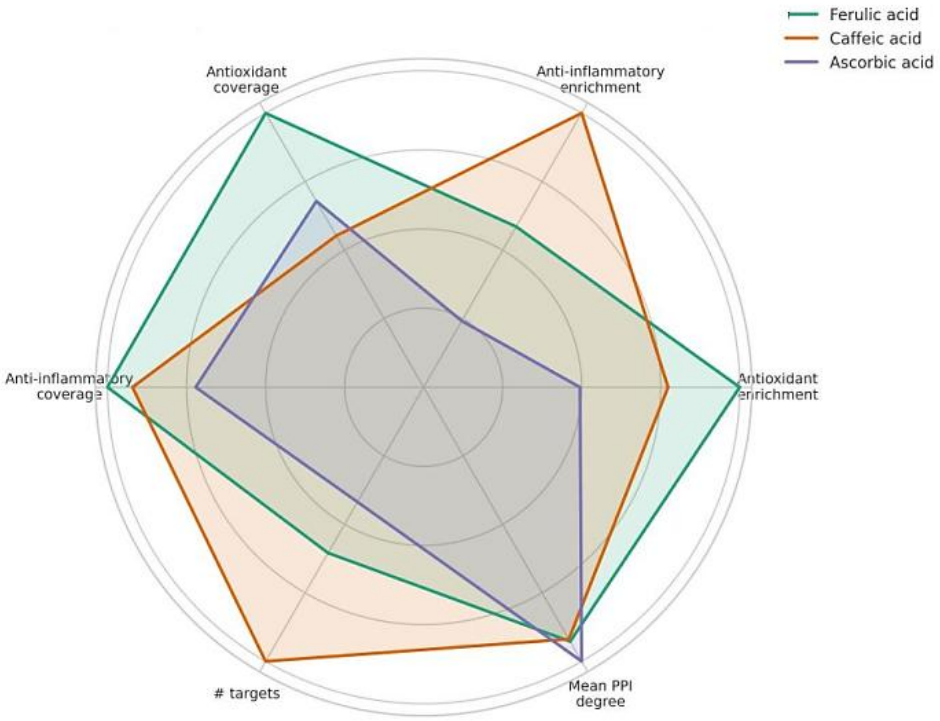


Figure 7. Integrated profile of the three compounds; each axis is scaled to the best-performing compound.

The analysis supports the working hypothesis that the target profiles of ferulic, caffeic and ascorbic acid converge on two connected axes: the Nrf2/KEAP1–HMOX1/NQO1 antioxidant-response axis and the NF-κB–TNF/IL-6/IL-1β–PTGS2/NOS2 inflammatory axis. The lack of enrichment in the control universe indicates that the signal is not an artefact of generic gene-set size or of the background used. The two hydroxycinnamic acids behaved similarly, consistent with their structural similarity (shared conjugated C=C–C=O motif and phenolic hydroxyls), but with a different emphasis: ferulic acid, with a methoxylated phenol, leaned towards the Nrf2 response, whereas caffeic acid, with a catechol, leaned towards cytokine and arachidonate-pathway targets. Ascorbic acid, a small enediol lactone structurally unrelated to the two phenolic acids, showed a profile closer to a redox cofactor, with enrichment for selenium, folate and vitamin B12 metabolism, which fits its physiological role better than that of a classical ligand of signalling proteins. The overall picture is in line with the literature describing phenolic acids both as direct radical scavengers and as indirect antioxidants that activate Nrf2 and suppress NF-κB signaling [37].

These findings are computational associations and carry three caveats. The antioxidant and inflammatory gene universes are keyword-defined on well-studied pathways, and the target sources are biased towards well-characterised genes, so inference rests on the unfiltered test (Figure 2), while enrichment after filtering is descriptive. P-values grow with the number of targets, so caffeic acid (the largest set) should be compared mainly through fold enrichment and coverage, and catechol-related assay interference may inflate some hits. Direct radical scavenging cannot be captured by a target-based analysis; docking (KEAP1, PTGS2, MAPK14), DPPH/ABTS assays and LPS-stimulated macrophage assays (NO, TNF, IL-6, HMOX1 induction) are the logical next validation steps.

3.6 Conclusion

The results obtained from complementary antioxidant assays revealed a multifaceted antioxidant profile, encompassing radical-scavenging, electron-donating and reducing activities, although the intensity of the response varied according to the experimental model. The aqueous extract also exhibited a marked capacity to inhibit heat-induced protein denaturation in both egg albumin and bovine serum albumin models, supporting its preliminary *in vitro* anti-inflammatory potential. These findings are consistent with the growing body of evidence indicating that *L. dentata* contains phenolic compounds, flavonoids and other secondary metabolites that may contribute to its biological activities. The *in silico* analysis reveals intriguing

investigational outcomes, indicating that the target profiles of ferulic, caffeic, and ascorbic acid converge on an interconnected Nrf2/KEAP1–HMOX1 antioxidant axis and an NF-κB–TNF/IL-6/IL-1β–PTGS2 inflammatory axis, with compound-specific focus aligned with their structures; these findings require further validation. This study provides further evidence of the biological potential of *Lavandula dentata L.* and, more specifically, of its aqueous extract as a source of naturally occurring bioactive compounds.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the Algerian Ministry (MESRS) and the Directorate of Scientific Research (DGRSDT) for their financial support.

AUTHOR CONTRIBUTIONS

Bekka A. methodology, validation, writing–original draft.

Karbab A. conceptualization, data curation, supervision, formal analysis, investigation, writing – review & editing, methodology, resources, validation, software.

Charef N. conceptualization, data curation, supervision, writing – review & editing, methodology, resources, validation.

Zembout I. data curation, formal analysis, validation.

Sweidan N. data curation, formal analysis, validation.

Arrar L. methodology, validation, resources.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

[1] World Health Organization, 2012. WHO Traditional Medicine Strategy: 2014–2023. World Health Organization, Geneva, Switzerland.

[2] Chaouchi, O., Fernane, F. 2024. 'Antimicrobial and antioxidant activities of Algerian Lavandula stoechas essential oil'. *The Eurasia Proceedings of Science, Technology, Engineering & Mathematics*, 29, 16–21.

[3] Hendel, N., Sarri, M., Sarri, D., Seghiour, S., Napoli, E., Selloum, M., Ruberto, G., 2024. Phytochemical analysis, antibacterial and antifungal effect of *Lavandula dentata* L. essential oil and methanol extract. *Natural Product Research* 38(20), 3498–3507.

[4] El Abdali, Y., Agour, A., Allali, A., Bourhia, M., El Moussaoui, A., Eloutassi, N., Salamatullah, A.M., Alzahrani, A., Ouahmane, L., Aboul-Soud, M.A.M., Giesy, J.P., Bouia, A. 2022 "*Lavandula dentata* L.: phytochemical analysis, antioxidant, antifungal and insecticidal activities of its essential oil". *Plants*, 11(3), 311.

[5] Rahmani, M., Dif, M.M., Benyahia, M., Toumi Benali, F., Bouazza, S. 2016. "Phenolic content and antioxidant activity of three Algerian species of lavenders". *Phytothérapie*, 15(6), 367–372.

[6] Haddouchi, F., Chaouche, T. M., Saker, M., Ghellai, I., Boudjemai, O. 2021. "Phytochemical screening, phenolic content and antioxidant activity of *Lavandula* species extracts from Algeria". *İstanbul Journal of Pharmacy*, 51(1), 111–117.

[7] Terfi, S., Djerrad, Z., Krimat, S., Sadi, F., 2022. Phytochemical composition, cytotoxicity, antioxidant and antimicrobial responses of *Lavandula dentata* L. grown under different levels of heavy metals stress condition. *Drug and Chemical Toxicology* 46(5), 864–878.

[8] Karbab, A., Charef, N., Jaber, A.M., Siedat, A.M., Kharchi, M., Nini, R., Sanabrah, A., 2025. Antioxidant, anti-inflammatory effects of *Centaurium erythraea* Rafn. aerial part extracts and identification of its bioactive constituents by LC-MS/MS analysis. *International Journal of Computational and Experimental Science and Engineering* 11(3), 4237–4245.

[9] Singleton, V.L., Rossi, J.A. 1965. "Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents". *American Journal of Enology and Viticulture*, 16(3), 144–158.

[10] Broadhurst, R.B., Jones, W.T. 1978. 'Analysis of condensed tannins using acidified vanillin'. *Journal of the Science of Food and Agriculture*, 29(9), 788–794.

[11] Amari, S., Karbab, K., Charef, N., Arrar, L., Mubarak, M.S. 2023. Anti-urolithiatic, antibacterial, anti-inflammatory and analgesic effects of *Erica arborea* flowers and leaves hydromethanolic extracts: An ethnopharmacological study. *Saudi Journal of biological Sciences.* 30, 103785.

[12] Brand-Williams, W., Cuvelier, M. E., Berset, C. 1995. "Use of a free radical method to evaluate antioxidant activity". *LWT – Food Science and Technology*, 28(1), 25–30.

[13] Re, R., Pellegrini, N., Proteggente, A., Pannala, A., Yang, M., Rice-Evans, C. 1999. "Antioxidant activity applying an improved ABTS radical cation decolorization assay". *Free Radical Biology and Medicine*, 26(9–10), 1231–1237.

[14] Apak, R., Güçlü, K., Özyürek, M., Karademir, S.E. 2004. Novel total antioxidant capacity index for dietary polyphenols and vitamins C and E, using their cupric ion reducing capability in the presence of neocuproine: CUPRAC method. *Journal of Agricultural and Food Chemistry* 52(26), 7970–7981.

[15] Dinis, T.C.P., Madeira, V.M.C., Almeida, L.M., 1994. Action of phenolic derivatives (acetoaminophen, salicylate, and 5-aminosalicylate) as inhibitors of membrane lipid peroxidation and as peroxyl radical scavengers. *Archives of Biochemistry and Biophysics* 315(1), 161–169.

[16] Oyaizu, M. 1986 "Studies on products of browning reaction: antioxidative activities of products of browning reaction prepared from glucosamine". *The Japanese Journal of Nutrition and Dietetics*, 44(6), 307–315.

[17] Karbab, A., Charef, N., Zarga, M.H.A., Qadri, M.I., Mubarak, M.S. 2021. Ethnomedicinal documentation and anti-inflammatory effects of n-butanol extract and of four compounds isolated from the stems of *Pituranthos scoparius*: An in vitro and in vivo investigation. *Journal of Ethnopharmacology.* 267, 113488.

[18] Mizushima, Y., Kobayashi, M. 1968. "Interaction of anti-inflammatory drugs with serum proteins, especially with some biologically active proteins". *Journal of Pharmacy and Pharmacology*, 20(3), 169–173.

[19] Kim, S., Chen, J., Cheng, T., Gindulyte, A., He, J., He, S., Li, Q., Shoemaker, B.A., Thiessen, P.A., Yu, B., Zaslavsky, L., Zhang, J., Bolton, E.E. 2023. "PubChem 2023 update". *Nucleic Acids Research*, 51(D1), D1373–D1380.

[20] Zdrazil, B., Felix, E., Hunter, F., Manners, E.J., Blackshaw, J., Corbett, S., de Veij, M., Ioannidis, H., Mendez Lopez, D., Mosquera, J.F., Magarinos, M.P., Bosc, N., Arcila, R., Kizilören, T., Gaulton, A., Bento, A.P., Adasme, M.F., Monecke, P., Landrum, G.A., Leach, A.R. 2024. "The ChEMBL Database in 2023: a drug discovery platform spanning multiple bioactivity data types and time periods". *Nucleic Acids Research*, 52(D1), D1180–D1192.

[21] Kuleshov, M.V., Jones, M.R., Rouillard, A.D., Fernandez, N.F., Duan, Q., Wang, Z., Koplev, S., Jenkins, S.L., Jagodnik, K.M., Lachmann, A., McDermott, M.G., Monteiro, C.D., Gundersen, G.W., Ma'ayan, A. 2016. "Enrichr: a comprehensive gene set enrichment analysis web server 2016 update". *Nucleic Acids Research*, 44(W1), W90–W97.

[22] Szklarczyk, D., Kirsch, R., Koutrouli, M., Nastou, K., Mehryary, F., Hachilif, R., Gable, A.L., Fang, T., Doncheva, N.T., Pyysalo, S., Bork, P., Jensen, L.J., von Mering, C. 2023. "The STRING database in 2023: protein-protein association networks and functional enrichment analyses for any sequenced genome of interest". *Nucleic Acids Research*, 51(D1), D638–D646.

[23] Kara Ali, M., Kara Ali, W., Ait Kaki, A., Berrabah, H., Rechachi, A., Kacem Chaouche, N. 2023. "*In vitro* characterization of the essential oil extracted from *Lavandula dentata* and its application in the field of biotherapy". *Pakistan Journal of Biological Sciences*, 26(6), 300–310.

[24] Dobros, N., Zawada, K., Paradowska, K. 2022. "Phytochemical profile and antioxidant activity of Lavandula angustifolia and Lavandula × intermedia cultivars extracted with different methods". *Antioxidants*, 11(4), 711.

[25] Dobros, N., Zawada, K.D., Paradowska, K. 2023. "Phytochemical profiling, antioxidant and anti-inflammatory activity of plants belonging to the Lavandula genus". Molecules, 28(1), 256.

[26] Gerique, A. 2006. "An introduction to ethnoecology and ethnobotany: Theory and methods". *Integrative Assessment and Planning Methods for Sustainable Agroforestry in Humid and Semiarid Regions*, Advanced Scientific Training, Universidad Técnica Particular de Loja (UTPL) & Dresden International University (DIU), Loja, Ecuador, 20 pp.

[27] Foti, M.C. 2015. Use and abuse of the DPPH• radical. *Journal of Agricultural and Food Chemistry* 63(40), 8765–8776.

[28] Karbab, A., Charef, N., Wardana, A.P., Abdjan, M.I., Shakya, A.K., Aminah, N.S. 2026. Antidiabetic, antioxidant, and anti-inflammatory activities of *Paronychia capitata* L. and *Paronychia argentea* L. from Algerian medicinal plants and identification of its bioactive compounds by LC-MS/MS phytochemical analysis. *Kuwait Journal of Science* 53(1), 100509.

[29] Pereira, O. R., Macias, R. I. R., Domingues, M. R. M., Marin, J. J. G., Cardoso, S. M. 2019. "Hepatoprotection of *Mentha aquatica* L., *Lavandula dentata* L. and *Leonurus cardiaca* L." *Antioxidants*, 8(8), Article 267.

[30] Re, R., Pellegrini, N., Proteggente, A., Pannala, A., Yang, M., Rice-Evans, C. 1999. 'Antioxidant activity applying an improved ABTS radical cation decolorization assay'. *Free Radical Biology and Medicine*. 26(9–10), 1231–1237.

[31] Ortega-Vargas, N.G., Galicia-Cortés, J.E., Hernandez-Rivera, J.A., Mena Muñoz, G., Marin-Torres, J.L., Carrasco-Carballo, A. 2026. 'Antioxidant properties by differential extraction of *Lavandula dentata*'. GSC Biological and Pharmaceutical Sciences, 34(3), 042–048.

[32] Gülçin, İ., & Alwasel, S. H. (2022). "Metal ions, metal chelators and metal chelating assay as antioxidant method". *Processes*, 10(1), Article 132.

[33] Gadouche, L., Riati, S., Mekraf, S., Bahraoui, S. E., Rekmouche, K. 2025. Antioxidant and antimicrobial activities of *Lavandula dentata* extracts: A comparative study of solvent efficacy. *Notulae Scientia Biologicae*, 17(4), 12748.

[34] Labhar, A., El-Mernissi, Y., Ahidar, N., Zouhri, A., Benamari, O., Siddique, F., Bashir, M., Salhi, A., Ahari, M., Ibenmoussa, S., Bourhia, M., Salamatullah, A. M., ELyoussfi, A., Amhamdi, H. 2024. "Seasonal variations in the essential oil composition and biological activities of wild *Lavandula dentata* L." *Natural Product Communications*, 19(2).

[35] Boussebaa, W., Rahmani, Z., Mokhtar, S., Ben Amor, S., Khaldoun, B., Henni, A., Abdellattif, M. H., Atoki, A. V., Zahnit, W., Messaoudi, M. 2025. Phenolic compounds analysis and in vitro biological activities of aqueous extract from leaves of Paronychia arabica collected in South Algeria. *Food Science & Nutrition*, 13(9), e70912.

[36] Oselusi, S.O., Sibuyi, N.R.S., Meyer, M., Madiehe, A.M. 2025. Anti-inflammatory, cytotoxic, and potential wound healing effects of phytofabricated *Ehretia rigida* leaf aqueous extract-synthesized silver nanoparticles. *Scientific Reports*, 15, Article 40301.

[37] Kumar, N., Goel, N. 2019. "Phenolic acids: natural versatile molecules with promising therapeutic applications". *Biotechnology Reports*, 24, e00370.