RESEARCH PAPER

Chemical Composition, Antibacterial and Antioxidant Potentiel of Achillea ligustica All. Essential Oil Harvested from Bougous Region (Northeast Algeria): Molecular Docking, DFT and ADMET Analyisis

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ABSTRACTS

Achillea ligustica All. (A. ligustica All.) it is a medicinal plant widely used in traditional medicine for therapeutic purposes in the Bougous region (Northeast Algeria). This research aims to investigate the chemical composition, antibacterial, and antioxidant potential of the essential oil extracted from A. ligustica All. from the Bougous region located on the Algerian-Tunisian border. The essential oil from the aerial parts, obtained by hydrodistillation via a Clevenger-type apparatus, was investigated using GC/MS. Thirty-onecompounds were identified, including oxygenated monoterpenes, oxygenated sesquiterpenes, and monoterpene hydrocarbons; the oil was primarily composed of chrysanthenone (17.95%), endo-borneol (17.89%), β-eudesmol (13.47%), camphor (8.83%), p-cymene (8.71%), 4-terpineol (7.62%), and veridiflorol (4.1%). Staphylococcus aureus (S. aureus) ATCC 29213, Staphylococcus epidermidis (S. epidermidis), Listeria spp., Enterococcus faecalis (E. faecalis), Salmonella DRB 560, Serratia marcescens (S. marcescens), Escherichia coli (E. coli) ATCC 25982, Klebsiella pneumoniae (K. pneumoniae) ATCC 104725, and Candida albicans (C. albicans) were the most susceptible bacterial and fungal strains tested. A. ligustica All. essential oil showed significant activity, particularly against C. albicans, Salmonella spp. and K. pneumoniae. The antioxidant activity of A. ligustica All. essential oil, evaluated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical trapping assay, indicated moderate radical scavenging activity when compared to ascorbic acid. To elucidate the antibacterial and antioxidant activity of the main components of the A. ligustica All. essential oil, we applied Density Functional Theory (DFT) and molecular docking methodology. In addition, we utilized ADME and Pro-Tox II evaluations to predict drug-likeness, pharmacokinetic properties, and toxicity. These results position A. ligustica All. essential oil as a promising candidate for natural therapeutic agents targeting microbial infections and oxidative stress.

Keywords: Achillea ligustica All. Bougous region, Essential oil, Chemical composition, Antibacterial activity, Antioxidant activity, DFT, ADME analysis.

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1. INTRODUCTION

Algeria has more than 3,000 plant species, of which around 15-20% are endemic. The richest flora is found in the northeast of the country and in certain areas of the northern Sahara (1-5). Several plants are the subject of ancient ethnobotanical traditions passed down from generation to generation for treating various ailments (6-11). Among the many medicinal plants found in the country, Ligurian Yarrow *A. ligustica* All. (Asteraceae, Anthemideae) was chosen for investigation, given the numerous properties reported both in the literature and in the ethnobotanical surveys that we carried out during our first work (11). This aromatic plant, widely distributed across the Mediterranean region, is used in traditional medicine in several countries, notably Italy, Sicily, and Corsica (12). It is also used to treat haemorrhages, gastric disorders, and skin diseases, as

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well as to relieve sprains and insect bites (13). Several studies have investigated the chemical composition and biological activity of the essential oil extracted from the leaves and the flowers of *A. ligustica* All. particularly in Greece, northern Italy, and Sardinia (14-21).

Previous phytochemical studies have indicated that the plant is rich in sesquiterpenes, particularly of the guaianolide type, as well as flavonoids and essential oils (EOs) predominantly composed of oxygenated monoterpenes and sesquiterpenes (22, 23). Moreover, biological investigations have revealed a broad spectrum of activities, including antioxidant, antimicrobial, and antipsoriatic effects (11, 24). This species exhibits a fairly uniform distribution, occurring from Crete and the western Balkans through Italy, Sicily, and the Tyrrhenian Islands, extending to northwestern Africa. It typically grows in open woodlands and along stream edges (25, 26).

In Algeria, *A. ligustica* All. is found mainly in the northeastern region of the country (Mila, Jijel, and El-Tarf), which is the most wooded and has a semi-humid climate, where it is called “Belkisoum” or “Belkismoun,” and also “Defretkhadem” or “Defretkhatem” in the study area, on the Algerian-Tunisian border (11). Few studies have been devoted to this species; the existing ones have been reported in the literature (11, 27-31).

Our literature review indicates that *A. ligustica* All. from the Bougous region has received little to no scientific attention, particularly regarding its ethnobotanical uses, which remain poorly documented. Despite its presumed traditional medicinal value, both the ethnobotanical knowledge and the pharmacological potential of this species in this zone are largely unexplored. Consequently, the present study represents a first and pioneering investigation of *A. ligustica* All.in this region of Algeria.

In this context, this original work aims to evaluate the biological properties of *A. ligustica* All. essential oil, to determine its chemical composition and predict the potential molecular interactions of its major constituents using molecular docking approaches. By integrating experimental analyses with *in silico* modelling, this study seeks to provide new scientific insights into the therapeutic potential of this plant and to support its valorization as a promising source of bioactive natural compounds of medicinal interest.

MATERIALS AND METHODS

Plant Collection

A. ligustica All. was collected in May 2026 during the flowering period (April-May) from the Bougous region, situated insouth-east of El Kala National Park (Altitude 183 mm – Latitude 36°39′34″ N – Longitude 8°22′10″ E) **Figure 1**. Aerial parts were washed with water, then allowed to air-dry for 2 weeks in the dark, after which they were crushed into small pieces and preserved for later experiments. Plant identification was carried out using standard floras and supported by recognized botanical databases, including the African Plant Database and The Plant List. Freshly collected voucher specimens were prepared and deposited in the herbarium of the Environmental Sciences and Agroecology Research Laboratory at Chadli Bendjedid University, El Tarf, Algeria.

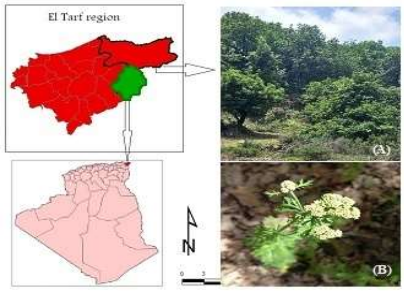


Figure 1: Location of El Tarf region (in red) and the study site (in green) (A): Bougous forest;

(B) *Achillea ligustica* All.

Essential Oil Extraction and Gas Chromatography Analysis

100 g of dried *A. ligustica* All. aerial parts were distilled at 100 °C in a Clevenger-type device for two hours. After the extraction process, the obtained essential oil was collected in a beaker, and residual moisture was removed by adding anhydrous sodium sulfate (Na_2SO_4). The oil was then stored at 4 °C in dark glass bottles for further analysis.

Essential oils chemical analysis was performed by gas chromatography coupled to mass spectrometry (GC-MS) using a SHIMADZU GCMS-QP2020 instrument equipped with a fused Rxi®-5ms capillary column (phase: Crossbond® 5% diphenyl/95% dimethylpolysiloxane). The column dimensions were 30 m × 0.25 mm with a film thickness of 0.25 µm, using helium as the carrier gas at a flow rate of 1.3 mL/min. A total volume of 1.0 µL of an essential oil's 10% solution in hexane was injected onto an injector heated to 250 °C operating in split mode (split ratio 1:50). The oven temperature was ramped from 45 to 250 °C at a heating rate of 5 °C/min. The ionizing energy of MS was 70 eV, the ionization source temperature was 250 °C, and acquisition was achieved by scanning from m/z 40 to 400. The results were expressed as relative area (percent area, %) and linear

retention indices (RT, min) were calculated by injecting an n-hydrocarbon series.

Antibacterial Activity

The antibacterial activity of *A. ligustica* All. essential oil was evaluated against a panel of microorganisms, including four Gram-positive bacteria (*S. aureus* ATCC 29213, *S. epidermidis*, *Listeria* spp., *E. faecalis*), four Gram-negative bacteria (*Salmonella* DRB 560, *S. marcescens*, *E. coli* ATCC 25982, *K. pneumoniae* ATCC 104725), and one fungal strain, *C. albicans*. All microbial strains were obtained from the Microbiology Laboratory, Department of Biology, Faculty of Natural and Life Sciences, Chadli Bendjedid University, El-Tarf (Algeria).

The antibacterial activity was assessed using the agar disc diffusion method (32-36). Firstly, the essential oil was dissolved in 10% aqueous dimethyl sulfoxide (DMSO); subsequently, 10 µL of each dilution was applied to sterile paper discs (6 mm diameter). These discs were then placed on Mueller-Hinton agar plates previously inoculated with bacterial cultures. A negative control was performed using paper discs loaded with 10 µL of 10% DMSO alone to verify any potential antimicrobial effect of the solvent. The plates were kept under aerobic incubation at 37 °C for 24 hours, after which the diameters of the inhibition zones were calculated to determine the antimicrobial activity. The minimum inhibitory concentration (MIC) and minimum lethal concentration (MBC) values of the essential oil against the tested microorganisms were determined.

Antioxidant Activity Assessment

A. ligustica All. essential oil antioxidant activity was estimated employing the DPPH radical scavenging assay, following previously established protocols (37-40). Serial dilutions of the essential oil were prepared in DMSO at concentrations of 6.25, 12.5, 25, 50, 100, 250, and 500 µg/mL. Ascorbic acid was used as a positive control. For each sample, 1 mL of 0.1 mM DPPH solution in methanol was added. The mixtures were maintained in the dark at room temperature for 30 minutes; subsequently, the absorbance was measured at 517 nm by means of a UV-Vis spectrophotometer (Shimadzu UV-1240, Kyoto, Japan). The radical scavenging activity (% RSC) was calculated using the following formula:

$$\%\ \mathrm{RSC} = \left(\frac{\mathrm{A_{blank}} - \mathrm{A_{Sample}}}{\mathrm{A_{blank}}}\right) * 100$$

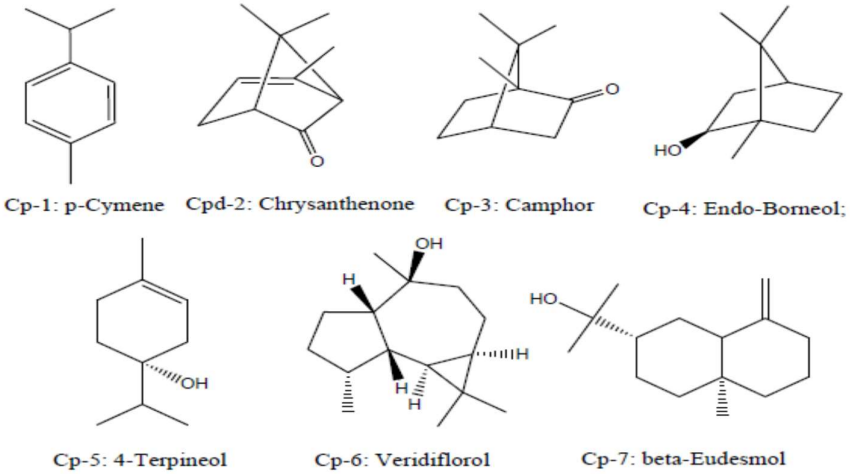
Where:

- $A_{blank}$is the DPPH solutionabsorbance without the sample
- A_{sample} is the DPPH solutionabsorbance in the presence of essential oil

The IC50 value, defined as the sample concentration necessary to inhibit 50% of DPPH radicals, was determined from the dose–response curve. The results are presented as percentage inhibition at each concentration, along with the corresponding IC50 value for the essential oil.

Density Functional Theorycalculation

The features of the *A. ligustica* All. essential oil's major constituents were predicted using the Density Functional Theory (DFT) approach **Figure 2**. Molecular geometries were optimized using the B3LYP functional and the 6-31G+(d,p) basis set. All computations were carried out using the Gaussian 16 software package (41).



Cp-1: p-Cymene Cpd-2: Chrysanthenone Cp-3: Camphor Cp-4: Endo-Borneol;

Cp-5: 4-Terpineol Cp-6: Veridiflorol Cp-7: beta-Eudesmol

Figure 2: The molecular structure of the major constituent of *Achillea ligustica* All. essential oil

Following the geometry optimization, the resulting structures were used to analyze the frontier molecular orbitals, and calculate their corresponding energies. The energy gap, along with global reactivity parameters, was determined using Koopmans' theorem (42).

Molecular Docking Study

Molecular docking predictions were performed to explore the interaction between the major chemical

constituents of *A. ligustica* All. essential oil and the active site of *Escherichia coli* DNA (*E. coli* DNA) gyrase B. The docking process was carried out using AutoDock Tools, following standard molecular docking protocols. The three-dimensional crystal structure of the target protein (PDB ID: 7P2N, resolution 1.16 Å) was obtained from the RCSB Protein Data Bank. The protein preparation was conducted using MGLTools 1.5.7 (43). The chemical structures of the essential oils's dominant chemical components were docked within a grid box of 30 × 30 × 30 Å³, centred on the enzyme active site at coordinates X = –19.073 Å, Y = –8.474 Å, and Z = 12.152 Å

In addition to the isolated compounds, the co-crystallized ligand *2-[[3,4-bis(chloranyl)-5-methyl-1H-pyrrol-2-yl]carbonylamino]-5-hydroxy-1,3-benzothiazole-6-carboxylic* acid was also docked as a reference. The most favorable binding conformations were chosen relying on the minimum binding energy value; on the other hand, protein–ligand interactions were visualized and analyzed using MGL Tools.

In silico Drug-Likeness and Toxicity Prediction

The drug-likeness of *A. ligustica* All. essential oil's major constituents were evaluated relying on the concept proven by Lipinski C. A. (1997) (44). The separated compounds'molecular structures (Cp1–Cp7) were analyzed through the Swiss ADMEweb tool. The key pharmacokinetic parameters, such as total polar surface area (TPSA), were evaluated. To complement these predictions, toxicological properties were examined via the ProTox-II platform, which provides insights into potential organ toxicities and other toxicological endpoints. Each compound was evaluated for its like lihood to serve as a viable drug candidate based on multiple criteria, with particular emphasis on the LD50 value, a higher LD50 indicating lower predicted toxicity and thus a more favorable safety profile.

2. RESULTS AND DISCUSSION

Essential oil of A. *Ligustica* All.'s Chemical components

The essential oil yield obtained from *A. Ligustica* All. was 0.94%; it was expressed as millilitres of oil per 100 g of dried plant material. This oil was characterized by a yellow color and a pleasant odor, reminiscent of an essential oil obtained from Lipari (Italy) (45). GC-MS characterization identified 31 compounds, representing 99.77% of the total oil composition **Figure 3**.

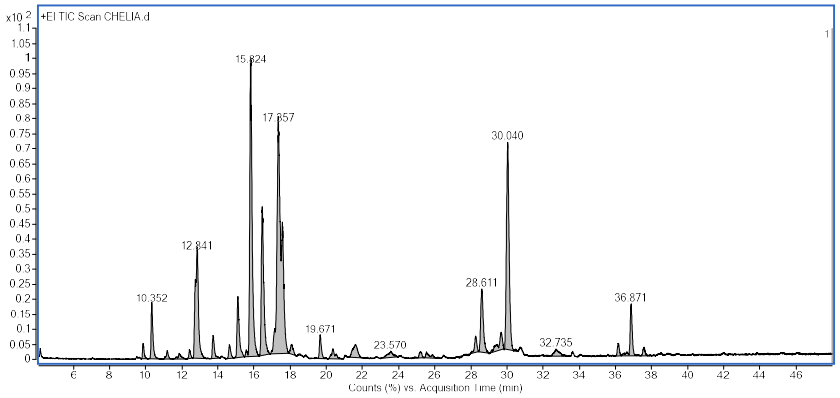


Figure 3: GC-MS profile of *Achillea ligustica* All. essential oil from the Bougous region

All identified constituents and their percentages are presented in **Table 1**.

Table 1: Chemicalcomposition of *A. Ligustica* All. essential oil obtained from the Bougous region (Algeria)

N°	RT[a] (min)	RI[b]	RI[c]	Area[d] (%)	Compound Name
01	4.17	912	909	tr	11-Dodecen-1-al
02	9.86	940	942	0.63	α-Pinene
03	10.34	955	959	2.51	Camphene
04	11.19	987	973	0.43	Sabinene
05	11.85	992	979	0.47	Cumene
06	12.42	1020	1008	0.41	α-Terpinene
07	12.84	1027	1025	**8.71**	*p*-Cymene
08	13.73	1041	1045	1.19	α-Pinene (-)
09	14.63	1063	1059	0.69	Eucarvone
10	15.11	1083	1093	0.10	Filifolone
11	15.57	1092	1108	tr	Vertonal
12	16.44	1124	1123	**8.83**	Camphor
13	17.35	1140	1147	**17.89**	Endo-Borneol
14	17.56	1180	1174	**7.62**	4-Terpineol

15	18.08	1182	1179	0.64	*p*-Menth-1-en-8-ol
16	19.67	1216	1225	1.14	*Z*-Chrysanthenylacetate
17	20.37	1248	1242	0.89	Myrcenylacetate
18	21.61	1283	1206	1.62	Verbenone
19	23.57	1504	1124	**17.95**	Chrysanthenone
20	25.22	1523	1420	0.37	trans-Caryophyllene
21	25.53	1581	1578	0.28	1-Isopropenyl-2,4-dimethyl-1-cyclohexene
22	28.26	1586	1580	0.99	1,3-Bis-(2-cyclopropyl,2-methylcyclopropyl)-but-2-en-1-one
23	28.61	1591	1590	**4.10**	Veridiflorol
24	29.67	1618	1620	1.23	Aromadendrene
25	30.04	1652	1650	**13.47**	β-Eudesmol
26	30.73	1682	1675	0.37	1,3-Bis-(2-cyclopropyl,2-methylcyclopropyl)-but-2-en-1-one
27	32.73	1741	1747	0.91	α-Pinene oxide
28	33.63	1771	1768	3.00	1-Tetradecyne
29	36.14	1801	1802	0.56	Filipendulal
30	36.87	1827	1819	2.38	3-Methylenecyclopentane carboxylic acid 2-bornyl ester
31	37.58	1838	1838	0.44	3,4,5,6-Tetramethyl-2,5-octadiene
					Total Identified compounds (%) 99.77
					Monoterpenes hydrocarbons 13.88
					Oxygenated monoterpenes 56.76
					Sesquiterpenes hydrocarbons 01.60
					Oxygenated Sesquiterpenes 17.57
					Others 09.96

[a]**RT :** Retention time (min),[b]**RI:** Retention index calculated in relation to n-alkanes, [c]**RI:** Retention index reported in the literature (NIST 2020 and Wiley, 9th edition), [d]**Area (%):** Percentage of the total oil composition in the *A. ligustica* All., **tr:** traces < 0.1%.

According to table 1, *A. ligustica* All. essential oils are made up of oxygenated monoterpenes (56.76%), oxygenated sesquiterpenes (17.57%), monoterpene hydrocarbons (13.88%) as major components and by the presence of low sesquiterpenes hydrocarbons (01.60 %). The main components identified in the studied oil were: chrysanthenone (17.95%), endo-borneol (17.89%), β-eudesmol (13.47%), camphor (8.83%), p-cymene (8.71%), 4-terpineol (7.62%), and veridiflorol (4.10%).

Antibacterial Activity

The *A. Ligustica* All. essential oil was evaluated for its antibacterial activity against various microorganisms, including one fungal strain and a panel of Gram-positive and Gram-negative bacteria **Figure 4**.

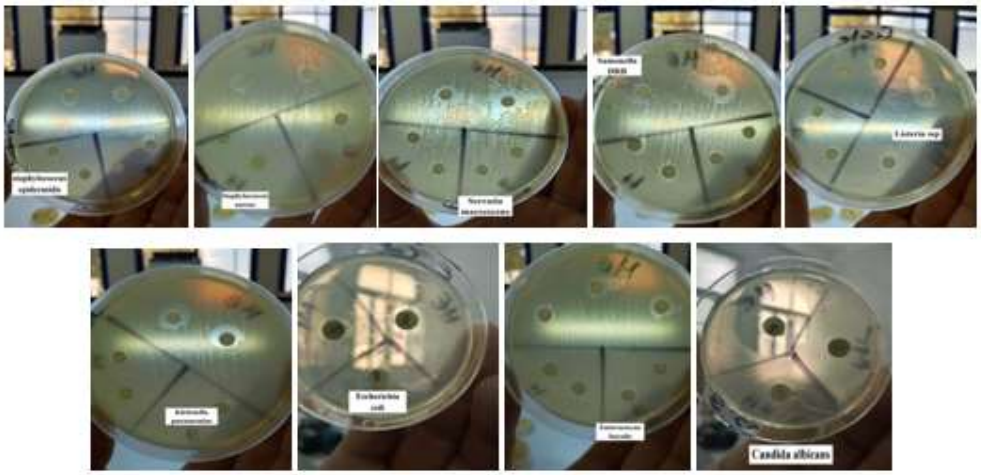


Figure 4: Antimicrobial Effect of *A. ligustica* essential Oil Against Various Microbial Strains: Inhibition Zone Observations

The results, presented in Table 2, demonstrate that the diameter of inhibition zones varied according to both the concentration of the essential oil and the susceptibility of each microbial strain. The inhibition zone diameters varied significantly according to the concentration of the testedessential oil. A one-way ANOVA revealed a statistically significant effect of concentration on antimicrobial activity ($F = 8.70$, $p < 0.001$), confirming a clear dose-dependent response. The pure oil exhibited the highest inhibition values, while progressive dilutions (1/2, 1/4, and 1/8) resulted in a marked reduction of antibacterial efficacy.

Table 2: Evaluation of the minimum inhibitory concentration and the bactericidal concentrations of *A. ligustica* All. essential oil.

Bactirial Strains	Inhibition Zone (mm)				MIC (mg/ml)	MBC (mg/ml)	MBC /MIC
	Pure Oil	Dilution (1/2)	Dilution (1/4)	Dilution (1/8)			
*Listeria*spp.	11.0	8.3	6.0	6.0	0.25	0.30	1.2
Staphylococcus aureus (29213)	8.5	6.0	6.0	6.0	0. 5	0.6	1.2
Enterococcus faecalis	10.0	6.5	6.0	6.0	0.25	0.5	2
Staphylococcus epidermidis	9.0	6.0	6.0	6.0	0.50	0.55	1.1
Salmonella DRB (560)	14.5	10.2	7.0	6.0	0.125	0.165	1.32
Serratia marcescens	11.0	7.5	6.0	6.0	0.25	0.30	1.2
Escherichia coli (25982)	12.0	8.5	6.0	6.0	0.25	0.35	1.4
Klebsiella pneumoniae (104725)	12.5	8.5	6.0	6.0	0.25	0.35	1.4
Candida albicans	23.0	16.5	11.5	7.0	0.0625	0.085	1.3

The essential oil exhibited broad-spectrum antibacterial activity, with the most pronounced effect observed against *C. albicans*, which showed a 23.0 mm zone of inhibition when tested with the undiluted (pure) oil. **It is note worthy that** the antifungal activity remained notably strong even at higher dilutions, suggesting a strong and sustained antimicrobial effect.

Among the tested bacterial strains, the essential oil of *A. ligustica* All. exhibited notable inhibitory effects against Gram-negative bacteria, particularly *Salmonella* DRB (560) (14.5 mm), *K. pneumoniae* (12.5 mm), and *E. coli* (12.0 mm) when applied in its pure form. These findings suggest a pronounced efficacy against certain Gram-negative pathogens. In contrast, Gram-positive strains such as *Listeria* spp. (11.0 mm), *E. faecalis* (10.0 mm), and *S. epidermidis* (9.0 mm) exhibited moderate sensitivity, while *S. aureus* showed the lowest susceptibility among Gram-positive bacteria (8.5 mm inhibition zone). Across all tested strains, a clear concentration-dependent response was observed: zones of inhibition decreased significantly at 1/2, 1/4, and 1/8 dilutions, highlighting the essential oil's dose-dependent antimicrobial potential. The results of the MIC and MBC tests confirmed the high efficacy of the essential oil as an antimicrobial agent against the tested microorganisms. MIC values ranged from 0.0625 to 0.25 mg/ml, with the highest sensitivity observed against Candida albicans. MBC values ranged from 0.085 to 0.165 mg/ml, while the MBC/MIC ratio (1.1–2.0) demonstrated that the essential oil possesses a potent lethal effect against the studied strains.

Overall, these results indicate that *A. ligustica* All. essential oil demonstrate extensive antimicrobial activity, with especially high antifungal potency against *C.albicans.* Its effectiveness at higher concentrations suggests potential applications as a natural antibacterial and antifungal agent, with promising uses in phytotherapy, cosmetics, and natural food preservation systems.

Antioxidant Activity

The antioxidant activity of *A. ligustica* All. essential oil was determined through the DPPH radical scavenging assay and compared to ascorbic acid as a standard. As shown in **Table 3**, the essential oil demonstrated a concentration dependent antioxidative potential. At the highest tested concentration (500 µg/mL), it achieved 86.81% radical scavenging activity, which was comparable to the 90.85% observed for ascorbic acid. Notably, the essential oil maintained considerable antioxidant activity at moderate concentrations, although its efficacy significantly declined at levels below 25 µg/mL.

Table 3: Radical scavengings activities of the essential oilof *A. ligustica* All. and ascorbic acid.

Concentration (µg/mL)	Essential Oil (%)	Ascorbic Acid (%)
500	86.81	90.85
250	82.19	90.51
100	81.85	90.42
50	81.71	90.28
25	76.71	90.12
12.5	47.57	86.23
6.25	27.28	85.14
IC_{50} (µg/mL)	11.7 ± 1.21	6.7 ± 1.12

IC50 represents the concentration necessary to achieve an inhibition 50% of DPPH radicals, and was obtained at 11.7 ± 1.21 µg/mL for the essential oil, compared to 6.7 ± 1.12 µg/mL for ascorbic acid. The one-way ANOVA revealed a statistically significant difference in antioxidant activity between the essential oil and ascorbic acid across the tested concentrations ($F = 5.358$, $p = 0.039$). Overall, ascorbic acid exhibited a

higher percentage of activity than the essential oil, indicating stronger antioxidant effectiveness under the experimental conditions.

This result is consistent with the well-established role of ascorbic acid as a potent reference antioxidant. The agreement between ANOVA results and IC50 comparison strengthens the finding's reliability and supports the interpretation that the essential oil has moderate antioxidant capacity relative to ascorbic acid.

DFT Calculation

The molecular geometry of the major constituents (Cp1–Cp7), identified in *A. ligustica* All. were optimized using DFT methods to obtain the most stable structure. The resulting 3D optimized structures are illustrated in **Figure 5**.

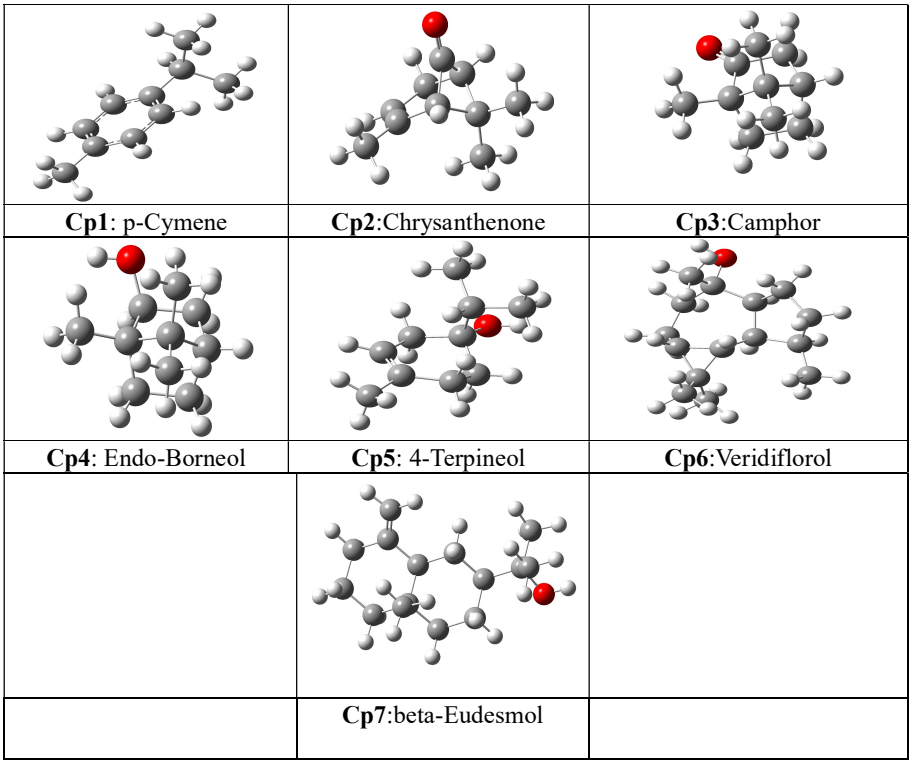


Figure 5: Optimized molecular geometries of investigated components (Cp1–Cp7)

Molecular Orbital Analysis

Molecular orbital analysis was conducted to learn more about the investigated compounds (Cp1–Cp7)'s chemical reactivity. (DFT) Calculations were employed with the aim of determining the frontier molecular orbitals (HOMO and LUMO) energies, which are illustrated in **Figure 6**. These frontier orbitals provide valuable information regarding each molecule's ability to donate or accept electrons. A key parameter derived from this analysis is the frontier molecular orbitals (FMO) gap energy, which represents an index of a compound's kinetic stability and chemical reactivity. A smaller energy gap typically correlates with greater reactivity, whereas a larger gap suggests increased electronic stability and lower chemical reactivity (46).

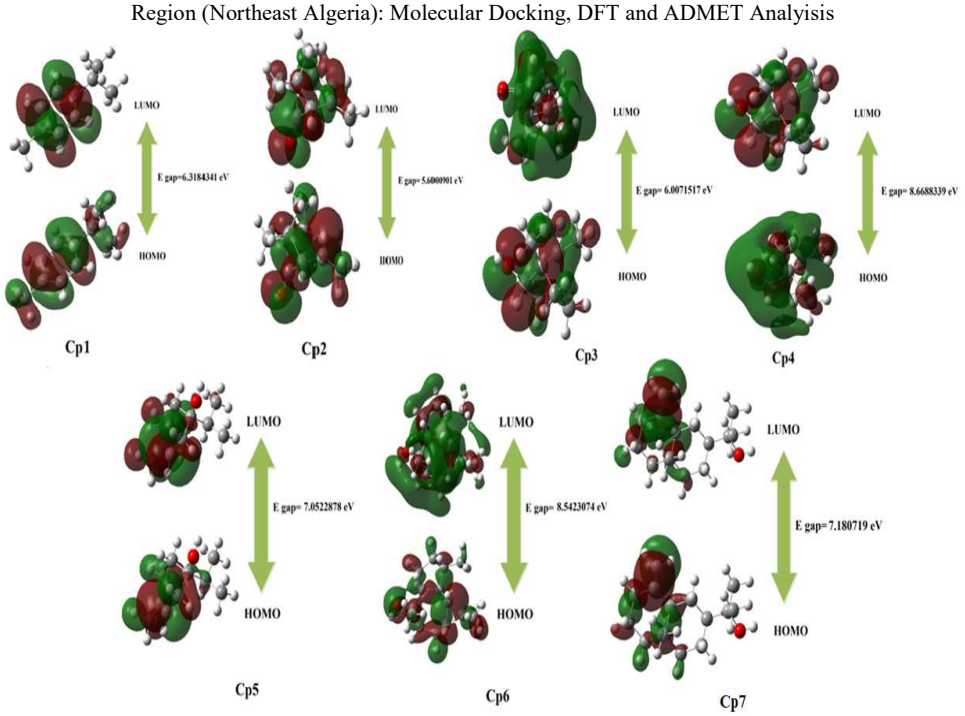


Figure 6: Compounds (Cp1–Cp7)'s FMO orbitals and energy gaps (Egap)

Among the studied compounds, Cp2 (chrysanthenone) and Cp3 (camphor) exhibited the narrowest energy gaps, measured at 5.60 eV and 6.00 eV, respectively, implying a higher chemical reactivity and greater potential for interaction with biological targets. In contrast, Cp4 (endo-borneol) and Cp6 (veridiflorol) displayed the widest energy gaps (8.67 eV and 8.54 eV, respectively), indicating greater electronic stability.

The FMO orbitals distribution over different molecular regions provides clues into the compound's potential reactive sites. For Cp2 (chrysanthenone) and Cp3 (camphor), the HOMO was primarily localized over the hydrocarbon chainand the carbonyl oxygen atoms, suggesting these regions may serve as electron-donating centers during molecular interactions. In contrast, the LUMO was predominantly concentrated around electrophilic regions, especially the carbon atom of the carbonyl group (C=O), identifying this site as a likely target for nucleophilic attack.

Regarding Cp4–Cp7, the HOMO orbitals were mainly distributed over the hydrocarbon skeletons, with additional localization around the hydroxyl oxygen atoms in Cp4 (endo-borneol) and Cp6 (veridiflorol), and over the carbon–carbon double bond in Cp7, suggesting that these regions are probable electron-donating sites. Conversely, the LUMO orbitals were predominantly concentrated around the oxygen atoms and adjacent carbon centers in compounds Cp4, Cp5, and Cp6, and over the double bond in compound Cp7, highlighting them as the main potential sites for nucleophilic attack.

A carbonyl functional group (C=O), which is present in both Cp2 (chrysanthenone) and Cp3 (camphor), is known to have a major impact on a molecule's electrical characteristics. As seen with Cp2 (5.60 eV) and Cp3 (6.00 eV), the presence of this strongly electronegative group helps to reduce the energy gap. Their potential interactions with biological targets may be improved by this decrease in the energy gap, which indicates greater chemical reactivity.

Global Reactivity Parameters

(DFT) evaluations provided a set of quantum chemical descriptors, namely the FMO orbitals (E_{HOMO} and E_{LUMO}), their gap energy (Egap), electronegativity, chemical potential and hardness, softness and electrophilicity index, which are respectively abbreviated as (χ, μ, η, S and ω) as well as the maximum number of electrons that can be accepted (ΔNmax), which collectively offer valuable informationsaboutinvestigated compoundschemical reactivity (Table 4).

Table 4: Quantum chemical parameters of major compounds identified in *A. ligustica* All. essential Oil.

Compound	Code	E_{HOMO}	E_{LUMO}	E_{gap}	χ	μ	η	S	Ω	ΔNmax
p-Cymene	Cp1	-6.158	0.160	6.318	2.998	2.998	3.159	0.158	1.423	0.949
Chrysanthenone	Cp2	-6.017	-0.417	5.600	3.217	3.217	2.800	0.179	1.848	1.149
Camphor	Cp3	-6.234	-0.227	6.007	3.231	3.231	3.004	0.166	1.738	1.076
Endo-Borneol	Cp4	-6.812	1.857	8.669	2.478	2.478	4.334	0.115	0.708	0.572
4-Terpineol	Cp5	-6.198	0.854	7.052	2.672	2.672	3.526	0.142	1.013	0.758

Veridiflorol	Cp6	-6.714	1.829	8.542	2.443	2.443	4.271	0.117	0.698	0.572
β-Eudesmol	Cp7	-6.422	0.759	7.181	2.832	2.832	3.590	0.139	1.117	0.789

Among the analyzed compounds, chrysanthenone (Cp2) exhibited the lowest energy gap (5.60 eV), followed by camphor (Cp3) with 6.007 eV. These two compounds also displayed relatively high electrophilicity indices (ω = 1.848 for Cp2 and 1.738 for Cp3) and the highest maximum number of electrons accepted (ΔNmax =1.149 and 1.076, respectively), indicating a strong tendency to accept electrons. Their low chemical hardness values (2.800 for Cp2 and 3.004 for Cp3) further corroborate their high reactivity profiles. This theoretical analysis provides meaningful insights into the essential oil constituents'electronic behavior, contributing to a better understanding and prediction of their potential bioactivity. Notably, Cp2 (chrysanthenone) and Cp3 (camphor) emerged as the most chemically reactive compounds among those investigated.

Molecular Docking

Molecular docking analysis was conducted to predict the major constituents of *A. ligustica* All. essential oil's binding affinities toward *Escherichia coli* DNA gyrase B. The results, summarized in **Figure 7**, revealed variable binding affinities between -4.2 and -6.8 kcal/mol. Co-crystallized ligand demonstrated the most favorable binding affinity (-7.4 kcal/mol), forming interactions with key residues including Val43, Asn46, Ile94, Glu80, Asp73, Thr185, Val71, Val167, and Met166.

Among the essential oil constituents, chrysanthenone (Cp2) and camphor (Cp3) demonstrated the most promising binding affinities, showing docking scores respectively -6.8 and -6.71 kcal/mol. These compounds formed interactions with critical residues such as Asp73, Thr165, Asn46, Glu50, and Ile78, several of which are also involved in the binding of the reference ligand, suggesting a good fit within *E. coli* DNA gyrase B's active site. Veridiflorol (Cp6) and *p*-cymene (Cp1) exhibited moderate binding energies (-5.6 and -5.4 kcal/mol, respectively), where as endo-borneol (Cp4), 4-terpineol (Cp5), and β-eudesmol (Cp7) showed the lowest interactions, with binding energies between -4.13 and -4.32 kcal/mol. Cp2 and Cp3 were identified as the most promising compounds, potentially responsible for the antimicrobial activity of A. ligustica essential oil. The docking method was validated by re-docking the co-crystallized ligand 2-[[3,4-bis(chloranyl)-5-methyl-1H-pyrrol-2-yl]carbonylamino]-5-hydroxy-1,3-benzothiazole-6-carboxylic acid,, with an RMSD lower than 1 Å, demonstrating the reliability of the protocol **Figure 8**.

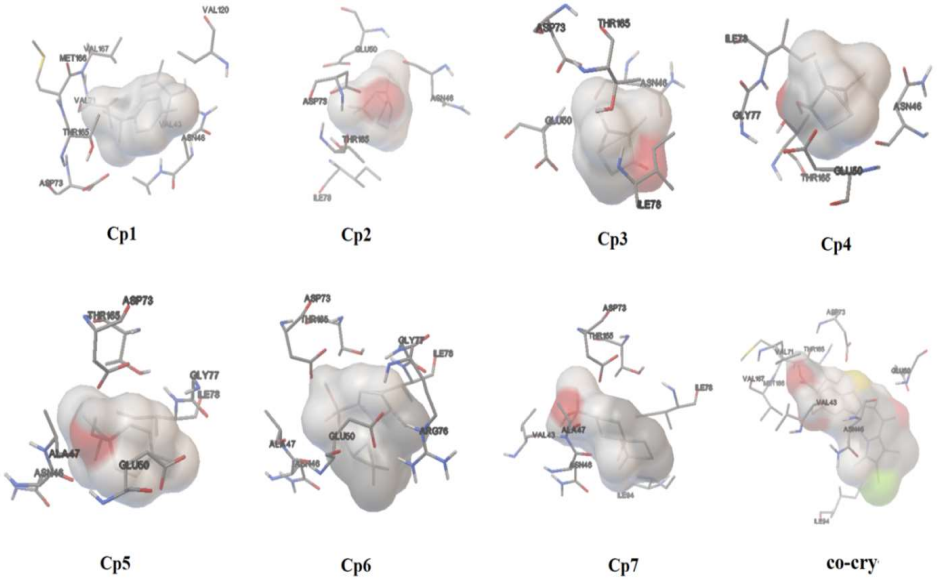


Figure 7: 3D Molecular docking interactions of cp1–cp7 and co-crystallized ligand (co-crys) within the active site of E. coli DNA gyrase B.

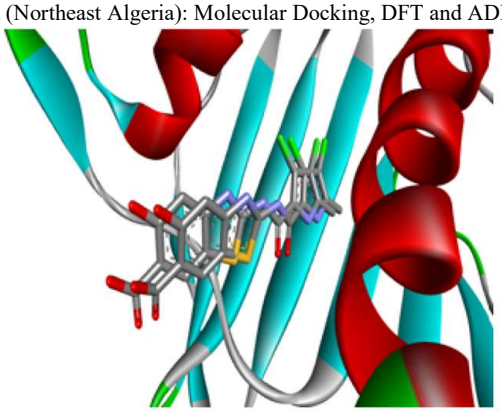


Figure 8: Re-docking of the co-crystallized ligand 2-[[3,4-bis(chloranyl)-5-methyl-1h-pyrrol-2-yl]carbonylamino]-5-oxidanyl-1,3-benzothiazole-6-carboxylic acid into the active site of E. coli DNA gyrase B.

ADMET Prediction

Swiss ADME served to estimate the absorption, distribution, metabolism, excretion, (ADME) profiles of the main components (Cp1–Cp7) of *A. ligustica* All**.** essential oil. The skin permeation value (Kp) reflects the compound's ability to penetrate the skin barrier. For all compounds, the *in silico* skin permeability values (log Kp) ranged from -4.21 to -6.00 cm/s, indicating relatively weak skin permeability. In terms of blood–brain barrier (BBB) penetration and gastrointestinal (GI) absorption, Cp2–Cp7 demonstrated strong GI absorption, while Cp1 showed low GI absorption. Curiously, every molecule showed the capacity to traverse the (BBB), which is a crucial feature for medications that target the central nervous system.

The interaction with permeability glycoprotein (P-gp) and cytochrome P450 (CYP) enzymes is crucial for predicting drug metabolism and potential drug interactions. None of the compounds wasregarded assubstrates for P-gp, showing a low risk of efflux-related bioavailability issues. Regarding CYP inhibition profiles, only Cp6 (Veridiflorol) was predicted to inhibit CYP1A2, while none of the other major CYP enzymes (CYP2C19, CYP2C9, CYP2D6, CYP3A4) were inhibited by the targetmolecules, **Table 5**.

Table 5: ADME observations and Pharmacokinetic properties of major compounds from *A. ligustica* All. essential oil.

ADME observations							
Compounds	Cp1	Cp2	Cp3	Cp4	Cp5	Cp6	Cp7
Mol.Wt. (g/mol)	134.22	150.22	152.23	154.25	154.25	222.37	222.37
NRB	1	0	0	0	1	0	1
NHA	0	1	1	1	1	1	1
NHD	0	0	0	1	1	1	1
TPSA (Å²)	0.00	17.07	17.07	20.23	20.23	20.23	20.23
LogP (cLogP)	3.12	2.18	2.40	2.38	2.60	3.43	3.61
Lipinski Violation	0	0	0	0	0	0	0
Pharmacokinetic properties							
Skin Permeation Value (log Kp) cm/s	–4.21	–6.00	–5.67	–5.31	–4.93	–5.00	–5.00
GI Absorption	Low	High	High	High	High	High	High
BBB Permeability	Yes	Yes	Yes	Yes	Yes	Yes	Yes
P-gp Substrate	No	No	No	No	No	No	No
CYP1A2 Inhibitor	No	No	No	No	No	No	No
CYP2C19 Inhibitor	No	No	No	No	No	Yes	No
CYP2C9 Inhibitor	No	No	No	No	No	No	No
CYP2D6 Inhibitor	No	No	No	No	No	No	No
CYP3A4 Inhibitor	No	No	No	No	No	No	No

According to Lipinski's rule of five, which predicts good oral bioavailability based on criteria like molecular weight, lipophilicity, hydrogen bond donors, and acceptors, the SwissADME prediction parameters suggest favorable ADME profiles for the main constituents of *A. Ligustica* All. essential oil. Additionally, the substances generally show good gastrointestinal absorption and a low risk of major cytochrome-mediated drug interactions. These results call for further experimental validation and support the studied molecules' promising pharmaceutical applications.

Figure 9 represents the under study compounds bioavailability radar According to this figure, it can be observed that, for all compounds, the five characteristic parameters of this radar belong to the favorable zone for bioavailability (pink zone).

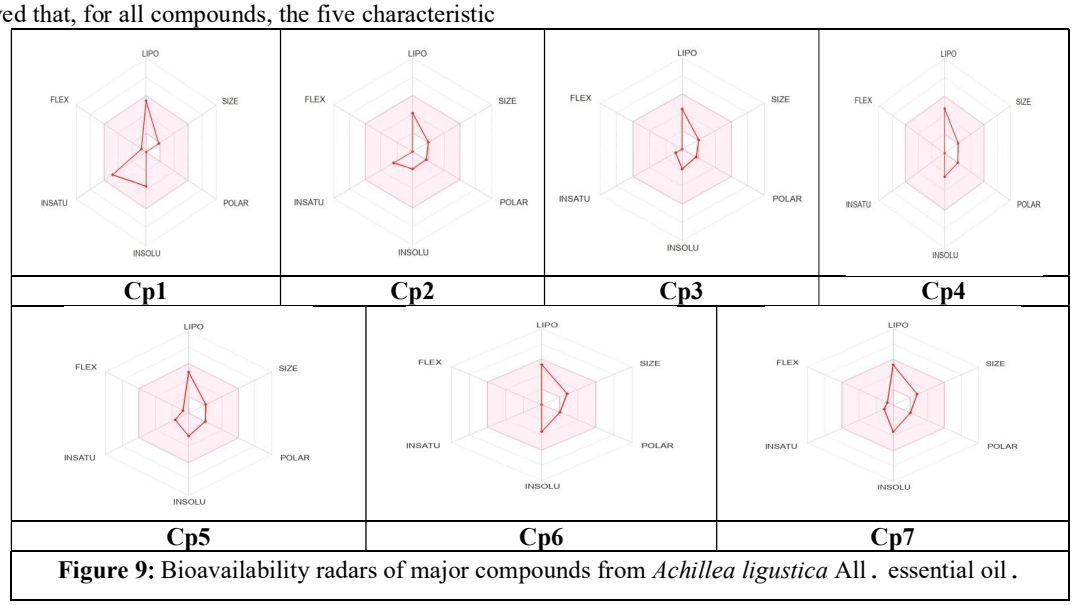


Figure 9: Bioavailability radars of major compounds from *Achillea ligustica* All. essential oil.

In silico toxicity predictions, obtained through ProTox-II property explorer, are regrouped in **Table 6**. The predicted toxicity observations, including LD50 measurements and toxicity category, suggest that the major constituents of *A. ligustica* All. essential oil exhibit low acute toxicity. Most compounds fall into toxicity classes 4 and 5, indicating a relatively low risk upon exposure, except for p-Cymene (Cp1), which is classified in class 1 due to its very low IC_{50} value (3 mg/kg). According to the toxicological endpoints analyzed (hepatotoxicity, carcinogenicity, immunotoxicity, mutagenicity, and cytotoxicity) the majority of compounds were expectedto be non-toxicdrugs, especially non-mutagenic, safe for cellsand none showed hepatotoxic potential except for camphor Cp3, which displayed possible hepatotoxicity and immunotoxicity.

Table 6: Predicted toxicological properties of major compounds from *A. ligustica* All. essential oil.

Compounds	**LD_{50} (mg/kg)**	**Toxicity Class**	**OrganToxicity**				
			Hepatotoxicity	Carcinogenicity	Immunotoxicity	Mutagenicity	Cytotoxicity
Cp1	3	1	Inactive	Active	Inactive	Inactive	Inactive
Cp2	5000	5	Inactive	Inactive	Inactive	Inactive	Inactive
Cp3	1190	4	Active	Inactive	Active	Inactive	Inactive
Cp4	500	4	Inactive	Inactive	Inactive	Inactive	Inactive
Cp5	1016	4	Inactive	Inactive	Inactive	Inactive	Inactive
Cp6	2000	4	Inactive	Inactive	Inactive	Inactive	Inactive
Cp7	2000	4	Inactive	Inactive	Inactive	Inactive	Inactive

The results suggest that most compounds may represent safe and promising candidates for pharmacological applications, except for Cp3, which warrants further investigation due to its predicted organ-specific toxicities.

CONCLUSION

The present investigationrevealed that the essential oil extracted from *A. ligustica* All., is rich in oxygenated monoterpenes, oxygenated sesquiterpenes and monoterpenes hydrocarbons, with chrysanthenone, endo-borneol, β-eudesmol, camphor, p-cymene, 4-terpineol and veridiflorol as the predominant components. The experimental results demonstrated the potential of *A. ligustica* All. essential oil to possess a potent antibacterial effect on bacteria *Salmonella spp.*, *K. pneumoniae* and good antifungal potency against *C. albicans*. In addition, the studied essential oil exhibita moderateantioxidant activity, which was confirmedusing the DPPH assay. The molecular docking study of the major oil constituents using the *E. coli* DNA gyrase B macromolecule revealed favorable binding affinities. Among the major compounds, chrysanthenone and camphor displayed the most favorable binding energies, suggesting strong affinity binding to the enzyme's active site. Moreover,

DFT simulations provided insights into the principal compoundselectronic and structural properties, while ADMET analyses indicated favorable drug-likeness profiles. To sum up, it can be inferred that the *A. ligustica* All. essential oil examined in this study holds promise as a natural source of antibacterial and antioxidant for use in food and therapeutic products.

REFERENCES

1. Chehma, A.; Djebar, M. Les Espèces Médicinales Spontanées de Sahara Septentrional Spatio-Temporelle et Étude Ethnobotanique. Rev. Synt. 2008, 17, 36–45.
2. El-Bouhissi, M.; Mehdadi, Z.; El Zerey, W. Contribution à l'étude de la biodiversité floristique dansun écosystème montagneux Cas de versant sud demonts de Tessala (Algérie occidentale). J. Med. Est. Biol.2014, 25, 53-89.
3. Aouadj, S.A.; Nasrallah, Y.; Hasnaoui, O.; Khatir, H. Ethnobotanical Approach and Floristic Inventory of Medicinal Plants in the Doui Thabet Region (Saida-Western Algeria). J. PhytChem. BioSub 2020, 14 (1), 92-104.
4. Larbi, R.;Sahar Meddour, O.;Bouxin, G.; Meddour, R. Diversité floristique et phytogéographie de la cédraie du massif forestier d'Ait Ouabane (versant nord-oriental du parc national du Djurdjura, Algérie). Lejeunia 2021, 204, 1-15.
5. Saidi, A.; Kefifa, A. Floristicdiversity of vascular plants in the MimounaForest (north-western Algeria). Biod. Res. Cons 2024, 73, 13-22.
6. Lakhdari, W.;Dehliz, A.;Acheuk, F.;Mlik, R.;Hammi, H.;Doumandji, M.B.;Gheriani, S.;Berrekbia, M.;Guermit, K.;Chergui, S.Ethnobotanicalstudy of some plants used in traditionalmedicine in the region of Oued Righ (Algerian Sahara).J. Med. Plants. Stud 2016, 4(2), 204-211.
7. Bendif, H.;Miara, M.D.; Harir, M.; Merabti, K.; Souilah, N.; Guerrouj, S.Ethnobotany of medicinal plants of El Mansourah (West of Bordj Bou Arreridj, Algeria).J. Soil. Plant. Biol 2018, 1, 24-39.
8. Lazli, A.;Beldi, M.;Ghouri, L.; Nouri, N. Etude ethnobotanique et inventaire des plantes médicinales dans la région de Bougous (Parc National d'El Kala, Nord-est algérien). **Bull. Soc. r. sci. Liège** 2019, 88, 22-43.
9. Miara, M.D.; Teixidor-Toneu, I.; Sahnoun, T.; Bendif, H.; Ait Hammou, M. Herbal Remedies and Traditional Knowledge of the Tuareg Community in the Region of Illizi (Algerian Sahara). J. Arid. Env 2019, 167, 65–73.
10. Beldi, M.;Merzougui, H.;Lazli A. Etude ethnobotanique du Pistachier lentisque *Pistacialentiscus* L. dans la wilaya d'El Tarf (Nord-est algérien). Ethnob. Res. Appl 2021, 21(09), 1-17.
11. Gherib, I.; Lazli, A.; Guenadil, F.; Seraoui, H.Ethnobotanicalknowledge of AchillealigusticaAll. in El Tarfregion (Northeastern Algeria). *Ethnobot. Res. Appl* 2024, 29-73.
12. Quézel, P.; Santa, S. Nouvelle Flore de l'Algérie et des régions désertiques méridionales. C.N.R.S 1962,1, 1-565.
13. Bader, A.; AlQathama, A.; Cioni, P.L.;Ceccarini, L.;Abdelhady, M.; AlShareef, W.;Ascrizzi, R.;Flamini, G. Essential OilBiodiversity of *Achillealigustica*All. Obtainedfrom Mainland and Island Populations. Plants 2022, 11(8), 1054.
14. Ahmed, A.A.; Gáti, T.; Hussein, T.A.; Ali, A.T.; Tzakou, O.A.; Couladis, M.A.; Mabry, T.J.; Tóth, G. Ligustolide A and B, two novel sesquiterpenes with rare skeletons and three 1,10-seco-guaianolide derivatives from *Achillea ligustica*. Tetrahedron 2003, 59, 3729–3735.
15. Conforti, F.; Loizzo, M.R.; Statti, G.A.; Menichini, F. Comparative Radical Scavenging and Antidiabetic Activities of Methanolic Extract and Fractions from *Achillea ligustica*. Biol. Pharm. Bull 2005, 28, 1791–1794.
16. Tuberoso, C.I.G.; Kowalczyk, A.; Coroneo, V.; Russo, M.T.; Dessì, S.; Cabras, P. Chemical Composition and Antioxidant, Antimicrobial, and Antifungal Activities of the Essential Oil of *Achillea ligustica* All. J. Agric. Food. Chem 2005, 53, 10148–10153.
17. Filippi, J.-J.; Lanfranchi, D.-A.; Prado, S.; Baldovini, N.; Meierhenrich, U.J. Composition, Enantiomeric Distribution, and Antibacterial Activity of the Essential Oil of *Achillea ligustica* All. from Corsica. J. Agric. Food Chem 2006, 54, 6308–6313.
18. Maggi, F.; Bramucci, M.; Cecchini, C.; Coman, M.M.; Cresci, A.; Cristalli, G.; Lupidi, G.; Papa, F.; Quassinti, L.; Sagratini, G.; et al. Composition and biological activity of essential oil of *Achillea ligustica* All. (Asteraceae) naturalized in central Italy: Ideal candidate for anti-cariogenic formulations. Fitoterapia 2009, 80, 313–319.
19. Tuberoso, C.I.G.; Montoro, P.; Piacente, S.; Corona, G.; Deiana, M.; Dessì, M.A.; Pizza, C.; Cabras, P. Flavonoid characterization and antioxidant activity of hydroalcoholic extracts from *Achillea ligustica* All. J. Pharm. Biomed. Anal. 2009, 50, 440–448.
20. Muselli, A.; Pau, M.; Desjobert, J.-M.; Foddai, M.; Usai, M.; Costa, J. Volatile Constituents of Achillea ligustica All. by HS-SPME/GC/GC-MS.

Comparison with Essential Oils Obtained by Hydrodistillation from Corsica and Sardinia. Chromatographia 2009, 69, 575–585.

21. Abdalla, A.N.; Shaheen, U.; Abdallah, Q.; Flamini, G.; Bkhaitan, M.M.; Abdelhady, M.I.; Ascrizzi, R.; Bader, A. Proapoptotic activity of Achillea membranacea essential oil and its major constituent 1, 8-cineole against A2780 ovarian cancer cells. Molecules 2020, 25, 1582.
22. Tuberoso, C.; Montoro, P.; Piacente, S.; Corona, G.; Deiana, M.; Dessi, M.A.; Pizza, C.; Cabras, P. Flavonoid characterization and antioxidant activity of hydroalcoholic extracts from *Achillea ligustica* All. J. Pharm. Biomed. Anal 2009, 50, 440-448.
23. Bader, A.; Martini, F.;Schinella, G.R.; Rios, J.L.;Prieto, J.M. Modulation of Cox-1, 5-,12- and 15-Lox by popular herbal remedies used in southern Italy against psoriasis and other skin diseases. Phyt. Res 2015, 29(1), 108-113.
24. Bouteche, A.; Touil, A.; Segueni, N. *Achillea ligustica* All. Phytochemical composition, ethnomedicinal uses and pharmacologicalproperties: A review. J. Res. Pharm 2024, 28, 313-325.
25. Quézel, P.; Santa, S. Nouvelle flore de l'Algérie et des régions désertiques méridionales. *C.N.R.S* 1963, 1, 1-158.
26. Conforti, F.; Loizzo, M.R.; Statti, G.A.; Menichini, F. Comparative Radical Scavenging and Antidiabetic Activities of Methanolic Extract and Fractions from *Achillea ligustica* All. Biol. Pharm. Bull 2005, 28, 1791–1794.
27. Boudjerda, A.;Zaiter, H.;Benayache, S.;Chalchat, J.C.; Gonzalez-Platas, J.; Leon, F.; Brouard, I.; Bermejo, J.;Benayache, F. A new guaianolide and other constituents from *Achillea ligustica*. **Biochem. Syst. Ecol** 2008, 36(5-6), 461-466.
28. Méradji, B.;Tebbakh, R. Contribution à l'étude des composés phénoliques des extraits de Rutachalepensis et Achillea ligustica et évaluation in vitro de leurs activités biologiques. MSc Thesis, Mohamed Seddik Benyahia University, Jijel, Algeria, 2016.
29. Bourouis, N.;Merazka, F. Etudes des huiles essentielles de Rutachalepensis et Achillealigusticaet évaluation de leur activité biologique. MSc Thesis, Mohamed Seddik Benyahia University, Jijel, Algeria, 2018.
30. Habitouche, M.; Maamar, H. Composition chimique et activité biologique des huiles essentielles de quelques plantes de la région de Jijel. MSc Thesis, Mohamed Seddik Benyahia University, Jijel, Algeria, 2021.
31. Boubertakh, H.;Kabouche, Z.;Boudechicha, A.; Madi, A.;Khalfallah, A.; Kabouche, A. RP-UHPLC-ESI-QTOF-MS analyses, antioxidant, antimicrobial, analgesic activities and toxicity of *Achillea ligustica*. **Nat. Prod. Res** 2024,1-6.
32. Fillippi, J.J.; Lanfranchi, D.A.; Prado, S.; Baldovini, N.; Mereierhenrich, U.J. Composition, enantiomeric distribution, and antibacterial activity of the Essential Oil of *Achillea ligustica* All. from corsica. **J. Agric. Food. Chem** 2006**,** 54, 6308-6313.
33. Boutabia, L.;Telailia, S.; Bouguetof, I.;Guenadil, Faouzi.; Chefrour, A. Composition chimique et activité antibactérienne des huiles essentielles de *Rosmarinus officinalis* L. de la région de Hammamet (Tébessa-Algérie). **Bull. Soc. r. sci. Liège** 2016, 85, 174–189.
34. Boutabia, L.; Telailia, S.; Guenadil, Faouzi.; Chefrour, A. Chemical composition and antibacterial activity of essentiel oils from *Mentha pulegium* L. and *Mentha suaveolens* Ehrh. Growing in north-east of Algeria. **An. Univ. Oradea, Fasc. Biol** 2020, 2, 143-148.
35. Alijalli, S.H.; El Hachlafi, N.; Abdallah, E.M.; Jeddi, M.; Assaggaf, H.; Qasem, A.; Alnasser, S.M.; Attar, A.; Naem, M.A.; Lee, L.H. Exploring the Antibacterial Mechanisms of Chemically Characterized Essential Oils from Leaves and Buds of Syzygium Aromaticum (L.) Merr. Et Perry Against Staphylococcus Aureus and Pseudomonas aeruginosa. **Ind. Crop. Prod** 2023, 205, 117561. 36. Khanzad, M. A.; Layla, J.N. ; Atallah, M.S. synthesis, antibacterial activity, and DFT of metal complexes with hydra**z**on ligand. Bull. Chem. Soc. Ethiop 2025, 39(11), 2359-2370.
37. Ridaoui, K.; Guenaou, I.; Taouam, I.; Cherki, M.; Bourhim, N.; Elamrani, A.; Kabine, M. Comparative study of the antioxidant activity of the essential oils of five plants against the H_2O_2 induced stress in Saccharomyces cerevisiae. **Saudi J. Biol. Sci** 2022, 29(3), 1842-1852.
38. Maggi, F.; Bramucci, M.; Cecchini, C.; Coman, M. M.; Cresci, A.;Cristalli, G.; Vittori, S. Composition and biological activity of essential oil of Achillea ligustica All. (Asteraceae) naturalized in central Italy: Ideal candidate for anti-cariogenic formulations. Fitoterapia 2009, 80(6), 313-319.
39. Noor Nazar, A.A.; Khansaa, S.A.N.; Shaymaa, H.A. De**s**ign, **synthesis**, antioxidant potential, antibacterial and molecular dokingin**sicht of Schiff base complexes**. Bull. Chem. Soc. Ethiop 2025, 39(11), 2157-2171.
40. Carvalho, R.S.; Carollo, C.A.; De Magalhães, J.C.; Palumbo, J.M.C.;Boaretto, A.G.;E Sá,

I.N.Ferreira, J.M.S. Antibacterial and antifungal activities of phenolic compound-enriched ethyl acetate fraction from Cochlospermum regium (mart. Et. Schr) Pilger roots: Mechanisms of action and synergism with tannin and gallic acid. ***S.*** **Afr. J. Bot** 2018, 114, 181-187.

41. Nessaibia, H.; Guenadil, F.; Khaoua, O. Synthesis, in vitro antibacterial and antioxidant evaluation, DFT calculation, molecular docking, and ADMET studies of novel N-Acyl-6-chloro-2 (3H)-benzoxazolone derivatives. **J. Mol. Struct** 2025, 1322, 140308.
42. Morris, G.M.;Ruth, H.;Lindstrom, W.;Sanner, M.F.;Belew, R.K.;Goodsell, D.S.;Olson, A.J. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. J. Comput. Chem 2009, 30(16), 2785-2791.
44. Lipinski, C. A,; Franco, L.; Dominy, B. W. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug. Deliv. Rev 1997, 23, 3–25.
45. Ben Jemia, M.;Rouis, Z.; Maggio, A.; Venditti, A.; Bruno, M.; Senatore, F. Chemical composition and free radical scavenging activity of the essential oil of *Achillea ligustica*growing wild in Lipari (Aeolian Islands, Sicily). Nat. Prod Commun 2013; 8(11), 1629-1632.
46. Anza, M.; Endale, M.; Cardona, L.; Cortes, D.; Eswaramoorthy, R.; Zueco, J.; Abarca, B. Antimicrobial activity, *in silico* molecular docking, ADMET and DFT analysis of secondary metabolites from roots of three Ethiopian medicinal plants. **Adv. appl. bioinfo.chem** 2021. 117-132.