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Artemisia herba alba Essential Oil: GC/MS analysis, antioxidant activities with molecular docking on S protein of SARS-CoV-2

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ABSTRACT

This study was conceived to work on *Artemisia herba* alba essential oils (EOs) originating from Eastern Morocco. We investigated the chemical properties and determined the antiradical scavenging activity. The GC-MS technique was used to elucidate the chemical composition of the two studied regions. Jerada Eo was distinguished by the existence of 1,6-Dimethylhepta-1,3,5-triene (36.44%), Camphor (22.50%), and Thujone (7.21%). While, Taourirt EO was found to be rich in Camphor (55.31%), Eucalyptol (14.64%), and Camphene (9.95%). Moreover, the free radical scavenging ability (DPPH•), and ferric reducing power assay (FRAP) were conducted. The EOs tested are found to be weakly active and to have important antioxidant potential. The docking study was also carried out by theoretical investigation with molecular docking of four active predominating components (1,6-dimethylhepta-1,3,5-triene; Chrysanthone; Eucalyptol; Alpha-pinene) against S protein of SARS-CoV-2, and all the four ligands were found to bind to the S protein 6CS2 of SARS-CoV-2 differently and that the stable complex formed as a result of these interactions may prevent the binding of ACE2 with the spike S protein of SARS-CoV-2.

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1. INTRODUCTION

Artemisia herba alba is a plant belonging to the Asteraceae family. It is called desert or white "Wormwood" in English, "Armoise" in French, or "Shih" in Morocco (Fakchich and Elachouri, 2021). This plant grows widely in arid and semi-arid climates. Besides, this plant was found to mark the steppes and the desert of the middle east (Bertella *et al*., 2018), North Africa (Aziz *et al*., 2018), and the Northwestern Himalayas (Mighri *et al*., 2010). The Artemisia herba alba leaves are characterized by a small silvery appearance, while the flowers are grouped in clusters (Hudaib and Aburjai, 2006). The presence of components of monoterpenes and sesquiterpenes gives the plant its scents and tastes (Pirbalouti *et al*., 2013; Moussi *et al*., 2017).

Paolini *et al*. (2010) studied the chemical variability compositions of 16 Artemisia herba-alba oil samples harvested in eight East Moroccan locations using Gas Chromatography (GC) and Gas Chromatography – Mass Spectroscope (GC/MS). Detailed analysis of the essential oils led to the identification of 52 components amounting to 80.5–98.6 % of the total oil. According to their major components (camphor, chrysanthenone, and α- and β-thujone), three main groups of essential oils were found. This study also found regional specificity of the major components (Paolini *et al*., 2010). The richness of chemical composition of *Artemisia herba alba* received also several applications as a corrosion inhibitor of metals in aggressive media (Bouyanzer *et al*., 2004; Benabdellah *et al*., 2006; Bouklah *et al*., 2006; Ouachikh *et al*., 2009; Bammou *et al*., 2011; Bouyanzer *et al*., 2017).

Artemisia herba alba is a plant known for its various pharmacological properties such as an anti-inflammatory (Khlifi *et al*., 2013), antifungal (Sami *et al*., 2010), anticancer (Tilaoui *et al*., 2015), antibacterial (Younsi *et al*., 2016), anthelmintic (Ahmed *et al*., 2020), antispasmodic (Amor *et al*., 2019), and antidiabetic (Bouyahya *et al*., 2021). In addition to that, this herb was used in folk medicine for many years against respiratory disorders, colds, abdominal aches, and kidney sand and stones (Abu-Irmaileh and Afifi, 2003), and for its safety, less toxicity, efficacy, and its availability (Asdadi *et al*., 2020). Artemisia herba alba EO has shown a promising antiviral effect against human pathogenic viruses such as the flu and other viral respiratory infections (Hatem and Shamran, 2020).

Saptura *et al*. (2022) demonstrated the value of bibliometric analysis in providing analytical data about a phenomenon. The findings of this study are beneficial for future research to find potential areas of Computational Chemistry that can be studied further, due to the discovery of less-researched areas. The Docking estimation is widely to give more explanation of the chemical activity of several molecules issued from natural plants on COVID-19 (El Hadki *et al*., 2021; Razon, 2020; Saputra *et al*. 2022); Sharma and Kaur, 2021 & 2022). QSAR models were used to explain the relationship between anti-MERS-CoV activity and the structure of 43 peptidomimetic derivatives based on physicochemical descriptors using many statistical methods such as the principal components analysis (PCA), the multiple linear regression (MLR) Y-randomization test and the multiples non-linear regression (MNLR) (Hammoudan *et al*., 2022).

This study aims to elucidate the chemical composition of the two *Artemisia herba alba* EOs originating from Taourirt and Jerada, and to investigate their antioxidant potential using the free radical DPPH• and the ferric reducing power assay. The *in-silico* docking simulation was exhibited to predict computationally the fixation sites of four compounds named, (1,6-dimethylhepta-1,3,5-triene; Chrysanthone; Eucalyptol; α-pinene) for further SARS-CoV-2 drug design. This analysis is important, especially for

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facing pandemic problems that create issue in many aspects from education, economic, to industry (Sukmawati & Maryanti, 2022; Fahrannisa *et al*., 2022; Azzahra *et al*., 2022; Huwaidi *et al*., 2021; Maryanti, 2021; Afifah, 2021; Coyoca *et al*., 2022; Anggraeni *et al*., 2020; Hashim *et al*., 2020; Phanse, 2021; Dirgantari *et al*., 2020; Mulyanti *et al*., 2020; Sangsawang, 2020)

2. METHOD

2.1. Plant Material

The aerial parts of the plant (leaves, stems, and flowers) of *Artemisia herba alba* that grow naturally in two regions in Eastern Morocco (Taourirt and Jerada) (**Figure 1**), were used in this study. The plant material was harvested in June (**Figure 2**).

2.2. Preparation of *Artemisia Herba Alba* Essential Oils

The EOs were extracted in two cooperatives located in Jerada and Taourirt, two cities in Eastern Morocco (**Figure 1**). The plant material was dried naturally in a shady room at a temperature of 25°C for five days until total dryness.

Afterward, the EOs were extracted for about 2h using the steam distillation method which consists first of boiling water in a boiler to obtain steam, this steam is sent into the still (in stainless steel) which previously contains the plant material to be distilled, crossing the plant the steam will burst the aromatic bags of the plant which contain the essences.

The vapor charged with essences will pass through a cooling system (Condenser) to become liquid again which will be collected in the Essencier, and at this level that the EO separates from the Hydrolates which will be recovered and returned to the boiler for a new cycle. Finally, the EO obtained was stored at 4°C in tight vials for further use.

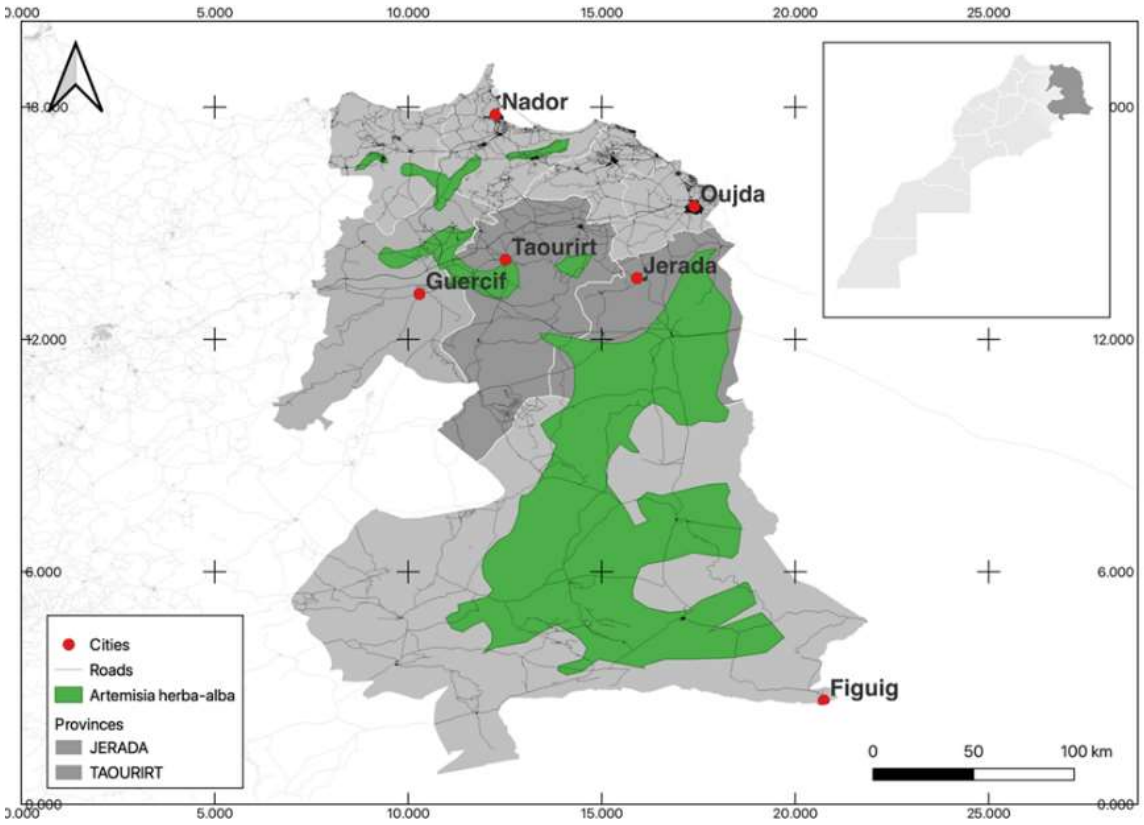

Figure 1. Geographical distribution of Artemisia herba alba in Eastern Morocco.

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Figure 2. A.herba alba of Jerada, Eastern Morocco.

2.3. Qualitative and Semi-quantitative Analysis of *Artemisia Herba Alba* using GC-MS

The obtained EOs were analyzed using gas chromatography (Shimadzu GC-2010) coupled with the Mass spectroscopy GC-MS-QP2010) according to the protocol described by Dalli *et al.* (2021). Helium inert gas was used as a carrier its pressure was adjusted to a pressure of 100 KPa. Further modifications were realized such as the oven temperature that was maintained at 50°C for about 1 min, then a gradient of about 10°C/min was followed to reach an oven temperature of 150°C.

Afterward, a gradient of 20°C/min was set to reach a temperature of 250°C. Concerning the analysis of the samples, a quantity (1 µL) was taken from each EOs and diluted in hexane. After all the samples were prepared an injection using split mode with a ratio of (25:1). For the identification of the different constituents a comparison of the retention time of each compound with its MS data using the National Institute of Standards and Technology (NIST) computer library. Detailed information for the use of GC-MS is reported in elsewhere.

2.4. Antioxidant Potential of *Artemisia Herba Alba* Essential Oils

To demonstrate the antioxidant potential of the extracted *Artemisia herba alba* EOs, the free radical scavenging activity against the DPPH• and the ferric reducing power assay (FRAP) were used.

2.4.1. Free radical scavenging ability against DPPH•

The DPPH assay is the most frequently used assay and the simplest method that offers the first approach for evaluating antioxidant activity (Zhong and Shahidi, 2015). This method aims to evaluate the antioxidant potential of the different extracts of *Artemisia herba alba* EO. From each EO different concentrations were prepared (50, 100, 200, 400, and 600 mg/mL). 200 µl was taken from each concentration and mixed with 1.8 ml of DPPH (0.5mM). The reaction mixture was then incubated in dark conditions for 20 min at room temperature. The absorbance was measured at 517 nm against the blank (Dalli *et al.*, 2021). All measurements were performed in triplicate. The inhibition percentage was calculated according to the Eq. (1) (Elshafie *et al.*, 2020):

$$\%\ \boldsymbol{Radical\ scavenging\ activity} = \frac{(\boldsymbol{Abs_{Control} - Abs_{sample}})}{\boldsymbol{Abs_{Control}}} \times \mathbf{100} \quad (1)$$

2.4.2. Ferric reducing power assay (FRAP)

The ferric reducing antioxidant power (FRAP) assay aims to evaluate the antioxidant potential of the EOs by measuring the increase of absorbance in the reaction mixtures (Alam *et al.*, 2016). For this reason,

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different concentrations were prepared and then a quantity of 0.5 ml of each concentration was taken and mixed with 1.25 ml of phosphate buffer (0.2M, pH 6.6) and 1.25 ml of potassium ferricyanide $K_3Fe(CN)_6$ (1%w/v). This method is mainly based on the reduction of Fe^{3+} found in $K_3Fe(CN)_6$ to Fe^{2+}. then, the reaction mixture was incubated at 50°C for 20 min in a water bath. After cooling the reaction was stopped by adding 1.25 mL of Trichloroacetic acid (10% w/v). The mixture was centrifuged at 3000 rpm for 10 minutes. An aliquot of 1.25 ml was taken from the supernatant and mixed with 1.25 ml of distilled water and 0.25 ml of ferric chloride (0.1% w/v). The absorbance was measured at 700 nm against a blank. Ascorbic acid was used as a positive control. All measures were performed in triplicate (Azizi *et al*., 2021).

2.5. Molecular Docking Study

SARS-CoV2 are mainly classified into four categories viz. α-COV, β-COV, γ-COV, and δ-COV, of which the latest, classified as SARS-CoV-2, belongs to the β-CoV category. It has four different proteins such as spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins (**Figure 3**). Recent studies showed that β-Coronaviruses enter human host cells via the angiotensin 2 converting enzyme receptors (ACE2) in humans, causing severe acute respiratory inflammation (Hattori *et al*., 2021). The spike protein on the surface of SARS-CoV-2 is a major antigen and its adhesion to the human ACE2 receptor plays an essential role in viral entry into host cells (Jungreis *et al*., 2021; Touzani *et al*., 2020).

Four active molecules (1,6-dimethylhepta-1,3,5-triene¬; chrysanthone; eucalyptol; alpha-pinene) presenting in *Artemisia herba alba* essential oil were studied computationally (*in silico*) by evaluating their toxicity, their physicochemical parameters calculated to ensure their suitability with Lipinski's rules. Also, their antiviral activity was assessed by studying their interactions with SARS-CoV-2 Protein S using MOE program (**Figure 4**).

2.5.1. Preparation of the protein structure

The receptor-binding domain (RBD) of protein S of SARS-CoV-2 has been uploaded to the PDB data bank under the code: 7KGJ. The protein is formed by two chains A and B, of which A is the RBD domain of glycoprotein S and B is a synthetic nanobody assembly. The structure was prepared by the Molecular Operating Environment (MOE 2015.10) by removing water, heteroatoms, and the B chain. The A chain was then protonated, its active site determined, and its potential energy fixed to avoid any potential change during docking (**Figure 5**).

2.5.2. Preparation of the ligands

The four ligands were drawn by the ChemDraw 20.1.1 program and then converted into a 3D format. Their energy is then minimized using the dynamic MM2 method and saved in PDB format.

2.5.3. Docking protocol

The calculations of the Docking and the 2D/3D protein-ligand interactions were performed with the MOE program using the triangle matcher method under rigid Docking.

2.6. Statistical Analysis

The statistical tests were applied using GraphPad Prism, version 6.00 (GraphPad Software, San Diego, CA, USA).

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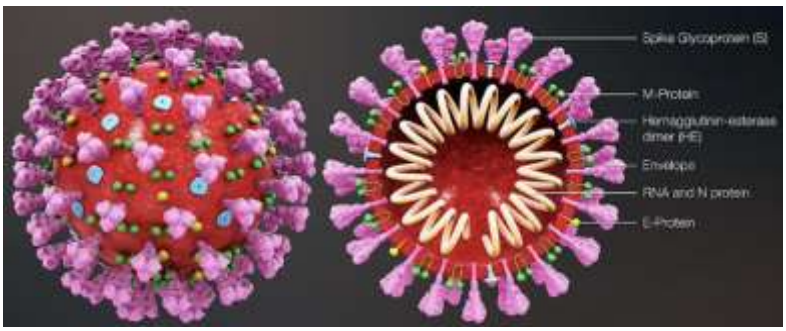

Figure 3. The 3D Coronavirus Structure (Touzani *et al*., 2020).

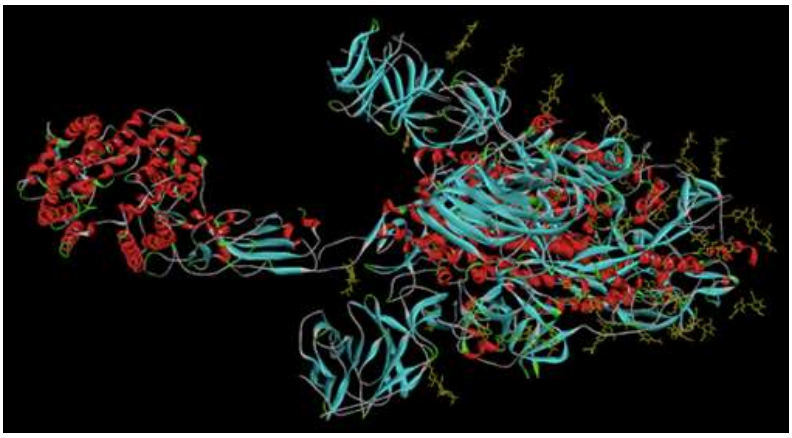

Figure 4. Crystal structure of S protein 6CS2 bound to ACE2**.**

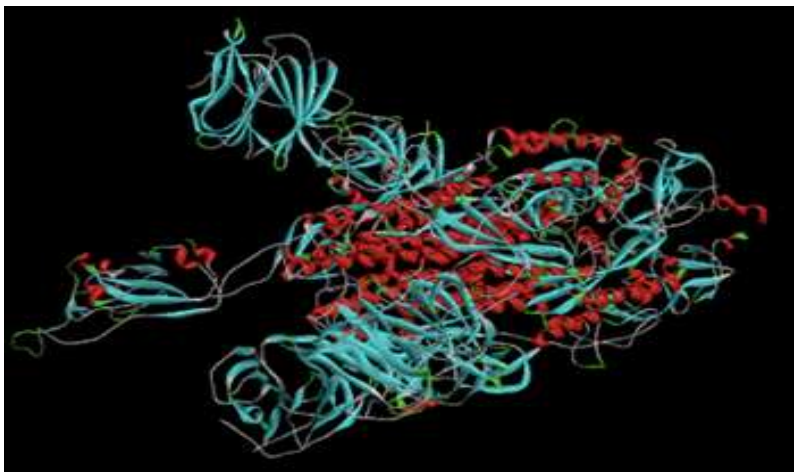

Figure 5. Prepared S protein 6CS2.

3. RESULTS AND DISCUSSION

3.1. Chemical Composition

Analysis of the *Artemisia herba alba* EOs originating from Jerada and Taourirt permitted the identification of 26 and 23 constituents respectively. The results drafted in **Table 1** and **Figure 6** represent respectively the total ion chromatogram and chemical components identified in the EOs using GC-MS. The data show that the major compounds in Jerada EO are found to be 1,6-Dimethylhepta-1,3,5-triene (36.44%), Camphor (22.50%), Thujone (7.21%), Eucalyptol (5.96%), Camphene (4.08%), while Taourirt EO was predominated by Camphor (55.31%), followed by Eucalyptol (14.64%), then Camphene (9.95%), 3-Thujanone (3.07%), and, 3,3,6-Trimethyl-1,4-heptadien-6-ol (2.33%) (**Figure 7**).

These main five constituents comprised more than 76.19% of the total composition of

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Jerada EO and 85.30% of Taourirt EO, and all of the remaining individual constituents in Jerada comprised 23.80% of the concentration, with a total of 99.99% of the volatiles identified, and in Taourirt the individual constituents comprised 14.08% of the concentration, with a total of 99.38% of all constituents. A review by Mohamed *et al.* (2010) indicated that *Artemisia herba alba* Eo was extensively investigated, and is characterized by the existence of monoterpenoids, mainly oxygenated ones, such as 1,8-cineole, chrysanthenone, chrysanthenol, α/β-thujones, and camphor as the major components.

Table 1. Chemical constituents identified in *Artemisia herba alba* essential oils from two regions.

N	Nom	Tr (min)	% Jerada	% Taourirt
1	Santolina triene	4.558	-	0.49
2	Tricyclene	4.800	0.38	0.69
3	Alpha-Pinene	4.975	1.07	0.43
4	**Camphene**	5.217	**4.08**	**9.95**
5	Cis-Pinen-3-ol	5.292	0.16	-
6	Thujene	5.583	0.53	-
7	Beta-Pinene	5.650	0.37	0.34
8	**3,3,6-Trimethyl-1,4-heptadien-6-ol**	5.950	-	**2.33**
9	1,2,4-Trimethylbenzene	5.900	0.13	-
10	(+) -4-Carene	6.250	0.20	-
11	1-Isopropyl-2-methylbenzene	6.375	0.70	-
12	Benzene, 2-ethyl-1,3-dimethyl	6.400	-	1.02
13	D-Limonene	6.442	2.38	0.92
14	**Eucalyptol**	6.500	**5.96**	**14.64**
15	Cyclopentene, 3-isopropenyl-5,5-dimethyl	6.908	0.38	-
16	Ocimene	6.933	-	0.42
17	Cis-3-Hexenyl iso-butyrate	7.092	-	0.41
18	**1,5-Heptadien-4-ol, 3,3,6-trimethyl**	7.292	-	**1.90**
19	3,3-Dimethyl-6-methylenecyclohexene	7.625	2.37	-
20	**Chrysanthone**	7.667	1.24	**3.07**
21	**Thujone**	7.833	**7.21**	0.46
22	**1,6-Dimethylhepta-1,3,5-triene**	7.975	**36.44**	-
23	Trans-Pinocarveol	8.233	-	1.03
24	**Camphor**	8.300	**22.50**	**55.31**
25	P-Mentha-1(7),8(10)-dien-9-ol	8.450	-	1.74
26	Santolina epoxide	8.592	-	1.13
27	Borneol	8.608	1.00	0.98
28	4-Carvomenthenol	8.767	0.62	0.61
29	(1R)-(-)-Myrtenal	9.100	-	0.77
30	2-Isopropylidene-5-methylcyclohexanone	9.683	0.42	-
31	Bicyclo[3.1.1]hept-2-en-4-ol, 2,6,6-trimethyl-, acetate	9.950	1.56	-
32	Trans-alpha-Bergamotene	10.083	-	0.30
33	Bornyl acetate	10.350	-	0.44
34	1,3-Cyclopentadiene, 5,5-dimethyl-2-ethyl	10.842	0.41	-
35	**(1,3-Dimethyl-2-methylene-cyclopentyl)-methanol**	11.000	**6.50**	-
36	3,5-Heptadienal, 2-ethylidene-6-methyl-	11.775	3.38	-
Total identified			99.99	99.38

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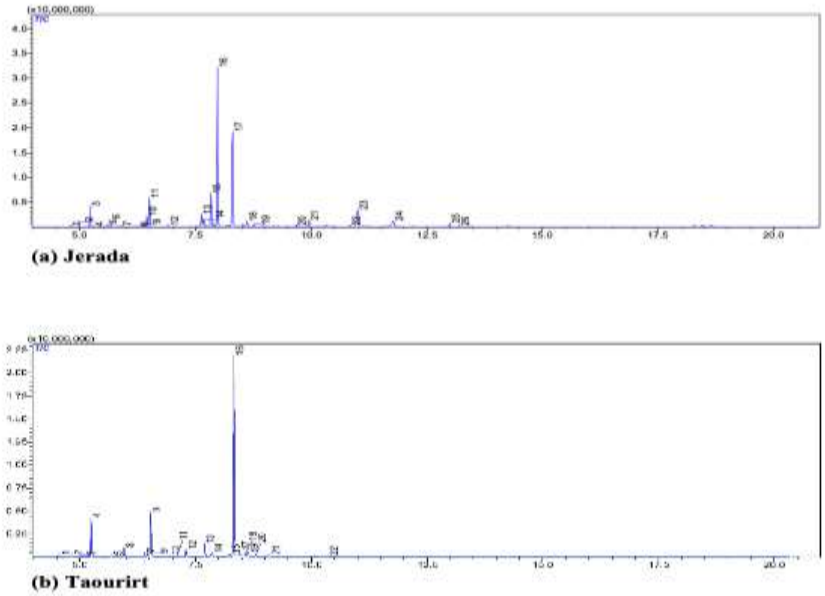

Figure 6. Total ion chromatogram of Artemisia herba alba EOs of (a) Taourirt and (b) Jerada.

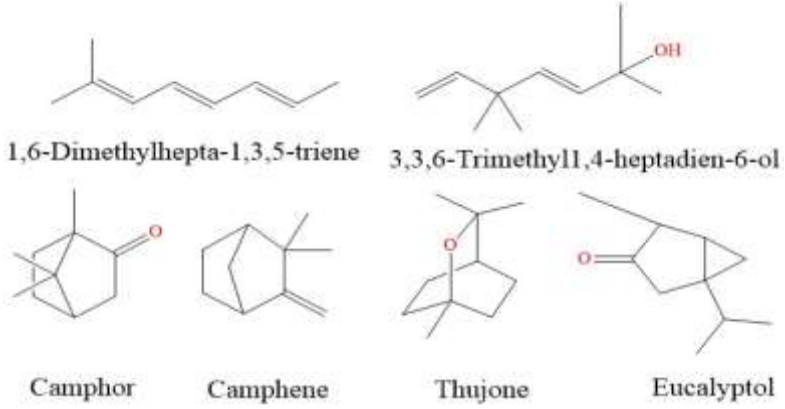

Figure 7. Main identified chemical compounds.

According to Mighri et al. it was reported the existence of some EOs that are dominated by major compounds such as (camphor, α or ß-thujone, chrysanthenone, chrysanthenyl acetate, or davanone), and other EOs that are distinguished with the presence of two or more of these compounds at appreciable levels. Ed-Dra, and Filali (Ed-Dra *et al*., 2021) have reported that the most abundant compounds of the *A.herba alba* EO from the East of Morocco (Talsint) were Davanone (38.25% ± 1.25%), Davana Ether Isomer 1 and 2 (9.91 ± 0.47% and 8.25 ± 0.25%, respectively), 1,2 Dehydro-3-hydroxyisodavanone (6.33 ± 0.67%) and Camphor (6.31 ± 0.16%).

Davanone was identified for the first time as the major component of *Artemisia herba alba* EO, harvested from Morocco. β-thujone (24.34%), camphor (22.23%), α-thujone (14.56%), and 1,8-cineole (10.3%) were also observed as well as main components in *Artemisia herba alba* from Agadir region (Moussii *et al*., 2020). A study performed by Sami *et al*. (2010) on the aerial parts of Tunisian *Artemisia herba alba* has shown the existence of a multitude of chemical compounds among them we cite the presence of Oxygenated monoterpenoids with an amount of 78.6%, such as camphor (39.1%), chrysanthenone (15%) and cis-thujone (7.8%). While the total oxygenated sesquiterpenes amount was 13.9% (9.5% (E)-patchenol, 3.1% (Z)-patchenol, 0.8% spathulenol and 0.5% ar-turmerone).

In another study conducted on *Artemisia herba alba* originating from south Jordan, it was demonstrated a great richness with

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Oxygen-containing monoterpenes mainly 1,8-cineole (20.1%), β-thujone (25.1%), α-thujone (22.9%), and camphor (10.5%) (Abu-Darwish *et al*., 2015). While in the EO of Bechar, Southwestern Algeria is was noted to be constituted by 80.3% of oxygenated monoterpenes, followed by 10.8% of monoterpene hydrocarbons (10.8%), and a very low quantity of oxygenated sesquiterpenes (0.2 %). Of all the identified compounds, α-thujone (48.0%), β-thujone (13.4%), and camphor (13.1%) were the main major compounds, while other components found in a small amount are camphene (3.6%), γ-terpinene (1.4%), borneol (1.3%), and p-cymene (1.0%) (Ouguirti *et al*., 2021).

The difference between the two studied sites could mainly be attributed to the different climatic and edaphic conditions (Dalli *et al*., 2021). For example, the climate of Jerada is arid, while Taourirt's climate is considered semi-arid. This stress caused by the lack of water could play a crucial role in the EO accumulation via a higher density of oil glands due to the reduction in leaf area. These different mentioned effects could be helpful for the plant to assure better growth, which leads to high EOs accumulation in the aerial parts. Following a bibliographic study, our results are comparable to certain research results, but different compared to others. The variability in EO chemical composition from plants grown in different geographical locations has led to many EOs dependent chemotypes assigned to the plant which suggests differences in the volatile composition of the plant material that could be attributed to several factors such as the geographic origin of the plant and chemotype.

3.2. Antioxidant Activities

The antioxidant activity was performed using an antiradical scavenging activity assay against the DPPH• and the ferric reducing power assay (FRAP). The results obtained indicated that the antioxidant activity increases with the increase of the EOs concentrations. The recorded IC_{50} of *Artemisia herba alba* EOs from Jerada and Taourirt are respectively, 115.08 ± 2.58 mg/ml and 380.27 ± 30.28 mg/ml. While the ascorbic acid used as control gave an IC_{50} of 0.029 ± 0.49 mg/ml ($p<0.001$) (**Table 2**). However, based on previous studies, the efficiency of phenolic compounds as anti-radicals and antioxidants depends on many factors. One main factor is the number of hydroxyl groups directly bonded to the aromatic rings (Sroka and Cisowski, 2003; Mohammed *et al*., 2021). Another antioxidant activity test used in this study was the ferric reducing antioxidant power (FRAP) assay. The results showed also that the antioxidant activity increases with the increase of the EOs concentrations. The IC_{50} value of the Os of Jerada and Taourirt are respectively, 13.39 ± 0.058 mg/ml ($p>0.05$) and 161.75 ± 16.20 mg/ml ($p<0.001$). The ascorbic acid used as positive control has an IC_{50} of 0.87 ± 0.058 mg/ml (**Table 3**). As shown in **Table 2**, *Artemisia herba alba* EO of Jerada exhibited a high antioxidant ability against DPPH• compared to *Artemisia herba alba* EO of Taourirt. The results tabulated in **Table 3** indicated that the *Artemisia herba alba* EO originating from Jerada had the strongest ferric reducing power, while the EO originating from Taourirt exhibited relatively weak ferric reducing antioxidant effects compared with that of Jerada region and with the ascorbic acid used as control. A study from Algeria showed that the EO of *Artemisia herba alba* exhibited a distinct antioxidant activity (Amina *et al*., 2022). Indeed, in another research exhibited by (Kadri and Goubi, 2022), it was mentioned that *Artemisia herba alba* EO had similar free radical scavenging activity compared to standard ascorbic acid which means a higher antioxidant potential in comparing to our findings.

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Table 2. The IC_{50} of the different extracts for DPPH and FRAP methods.

	Jerada EO	Taourirt EO	Ascorbic acid
IC_{50} (mg/ml) DPPH	115.082 ± 2.58****	380.27 ± 30.28****	0.74 ± 0.029
IC_{50} (mg/ml) FRAP	13.39 ± 0.058^{ns}	161.75 ± 16.2****	0.87 ± 0.05

Table 3. Toxicity risk of *Artemisia herba alba* molecules calculated by Osiris.

RISK OF TOXICITY					
COMPOUNDS	**MW(g/mol)**	**MUT**	**TUM**	**IRRI**	**REP**
a	136.238	+++	+++	+++	+++
b	122.237	+++	+++	+++	+++
c	276.28	+++	+++	+++	+++
d	154.25	+++	+++	+	+++

The difference in the chemical composition of each EO may be strongly related to the antioxidant effect noted. The statistical analysis showed a highly significant difference between the studied EOs and the ascorbic acid used as a control for the DPPH and the FRAP assays, which made it clear that these EOs are less effective than the synthetic ones. These obtained results were in accordance with those obtained by Lopes-Lutz *et al.*, (2008) which indicated that the EOs predominated by non-phenolic compounds have shown a low antioxidant activity in some Artemisia species.

3.3. Molecular Docking Study

3.3.1. Risk of toxicity

During the research phase of drug candidates, their toxicity is one of the most important and feared parameters for developers (Marchant, Briggs, and Long, 2008). Therefore, it is essential for us to predict the toxicity of our four molecules (1,6-dimethylhepta-1,3,5-triene [a] ; Chrysanthone [b] (**Figure 8**); Eucalyptol [c]; α-pinene [d] (**Table 3**), before any other study attempt. The results presented in (**Table 4**) show that only α-pinene could present a slight irritation risk. Below are the data reported by the Osiris toxicity risk study.

3.3.2. Lipinski's rule

Several methods, most of them based on physicochemical parameters, have been proposed to study the similarity to a drug. Lipinski's rule is based on the search for properties common to 2245 molecules extracted from the WDI (World Drug Index) which have at least reached phase II of clinical trials and therefore present a priori good values of solubility and intestinal permeability (Lipinski *et al.*, 1996). The "Lipinski rule" thus proposes threshold values for molecular weight (PM<500), the number of hydrogen bond acceptors and donors (ALH< 10 and DLH< 5), the number of rotational bonds (N-rot< 10), and the water/octanol partition coefficient (logP<5). According to this rule, a compound is more susceptible to poor oral bioavailability when it has more than one violation of this rule. The Lipinski criteria (**Table 5**) for all four molecules show no violations.

3.3.3. Post Docking Results

The results of molecular docking of the four molecules (a, b, c, d) with the receptor-binding domain (RBD) of SARS-CoV-2 protein S encoded 7kgj have been reported (**Figure 9**). The 2D/3D interactions of the complex formed by the four ligands are shown in **Figures 10,11, and 12**. Among the four drug-candidate molecules, Chrysanthone has the lowest binding energy (S= -4.90; E= 8.298kJ/mol) (**Figure 10**), followed by Eucalyptol (S=-4. 370; E= -5.772 kJ/mol) (**Figure 10**) then comes 1,6-dimethylhepta-1,3,5-triene (S= 3.751; E= -6.045 kJ/mol)

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(**Figure 8**) finally alpha-pinene (S=-3.551; E= -5.699 kJ/mol) (**Figure 12**). Based on the S-score (**Figure 9**) which considers all the docking parameters, we see that Chrysanthone (S = -4.90) is the most binding conformation of chrysanthone and therefore the most likely to form a more stable and anchored complex with Protein 7kgj.

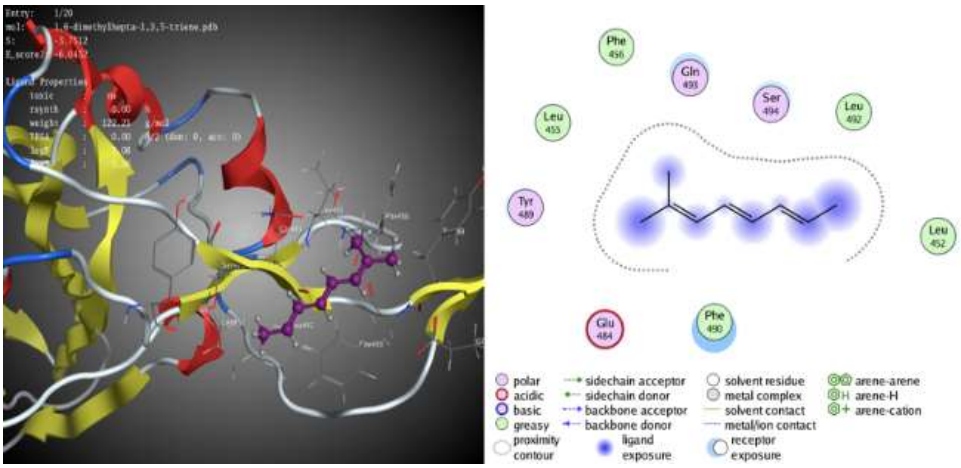


Figure 8. 2D/3D interaction of 1,6-dimethylhepta-1,3,5-triene with 7kgj protein.

Table 4. Osiris analysis of compounds 1–4.

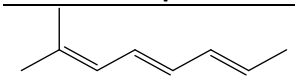
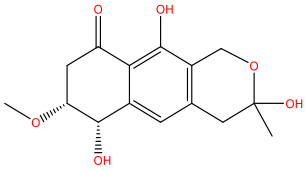
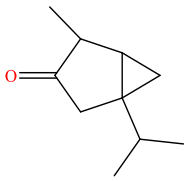
Compound	Toxicity Risks	Solubility	Drug-Score
a 	Toxicity Risks mutagenic tumorigenic irritant reproductive effective	cLogP 3.55 Solubility -2.04 Molweight 122.0	TPSA 0.0 Druglikeness -3.89 Drug-Score 0.45
b 	Toxicity Risks mutagenic tumorigenic irritant reproductive effective	cLogP 0.89 Solubility -2.98 Molweight 276.0	TPSA 75.99 Druglikeness -1.3 Drug-Score 0.55
c 	Toxicity Risks mutagenic tumorigenic irritant reproductive effective	cLogP 2.14 Solubility -2.55 Molweight 154.0	TPSA 9.23 Druglikeness -3.64 Drug-Score 0.48

Table 5. Lipinski's rule as assessed by the MOE

	Lipinski Rule					
Compound	**MW(g/mol)**	**Log P**	**NHBA**	**NHBD**	**N-rotB**	**LR-app**
a	136.238	4.056	0	0	2	None
b	122.237	1.525	5	2	1	None
c	276.28	2.948	1	0	0	None
d	154.25	3.994	0	0	0	None

MW: molecular weight, NHBA: number hydrogen bond acceptor, NHBD: number hydrogen bond donners, N-rotB: number rotative bond, LR-app: Lipinski rule appreciation.

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This is due to the formation of intramolecular hydrogen bonds between the carbonyl groups -CO and -OH, acceptor Oxygen bonds with Arg346, tyr351 but also π- π bonds between the arena and Asn450 (**Figure 10**). Lightly toxic: (+), Not toxic (+++). MW: molecular weight, MUT: Mutagenic, TUM: Tumorigenic, IRRI: Irritant, RE: Reproductive effective.The post-docking results performed by MOE showed strong interactions towards the four molecules, which confirms the previous evaluation shown by Osiris, especially Chrysanthone (b) which showed the formation of oxygen acceptor bonds with Arg346, tyr351, π- π- bonds of arena-H and Asn450 but also the formation of intramolecular hydrogen bonds. Thus, it can be concluded that Chrysanthone can form an anchored and stable complex with the receptor-binding domain (RBD) of SARS-CoV-2 Protein S.

	mol	mseq	S	E_score1	rmsd_refine	E_conf	E_place	E_refine	E_score2
1	chrysanthone.pd	3	-4.4387	-9.1735	1.7626	6.6306	-50.1907	-23.3112	-4.4387
2	chrysanthone.pd	3	-4.5588	-9.1307	1.1770	2.1385	-43.7115	-19.6595	-4.5588
3	chrysanthone.pd	3	-4.2826	-8.8132	1.5885	7.1028	-51.9256	-16.0889	-4.2826
4	chrysanthone.pd	3	-4.5676	-8.6350	1.7393	4.2156	-46.7588	-20.7698	-4.5676
5	chrysanthone.pd	3	-4.9003	-8.2988	1.2945	4.3345	-52.5851	-21.8643	-4.9003
6	eucalyptol.pdb	4	-3.5601	-6.5303	1.9017	-29.7939	-20.2879	-10.4645	-3.5601
7	eucalyptol.pdb	4	-3.7759	-6.1923	0.9996	-29.9329	-22.8687	-11.4965	-3.7759
8	eucalyptol.pdb	4	-3.9821	-6.0697	2.5920	-29.8785	-17.5939	-11.0595	-3.9821
9	1,6-dimethylhep	1	-3.7512	-6.0452	1.1850	0.3802	-18.4733	-11.9215	-3.7512
10	eucalyptol.pdb	4	-3.8850	-5.9244	1.2164	-29.8849	-17.6657	-12.6296	-3.8850
11	eucalyptol.pdb	4	-4.3701	-5.7728	1.9072	-29.7899	-13.7104	-18.5375	-4.3701
12	alpha-pinène.pd	2	-3.5513	-5.6994	1.4333	31.4813	-22.1687	-9.7797	-3.5513
13	1,6-dimethylhep	1	-3.6054	-5.6914	0.9254	0.5191	-34.2878	-9.6617	-3.6054
14	alpha-pinène.pd	2	-3.3830	-5.6687	0.7402	31.5160	-21.4812	-9.8651	-3.3830
15	1,6-dimethylhep	1	-3.6288	-5.6510	1.1326	0.1937	-36.4157	-11.4379	-3.6288
16	alpha-pinène.pd	2	-3.5629	-5.5842	2.5261	31.4799	-21.5649	-10.0850	-3.5629
17	alpha-pinène.pd	2	-3.4906	-5.5544	1.5829	31.5703	-30.2214	-10.5664	-3.4906
18	alpha-pinène.pd	2	-3.3822	-5.5034	1.3602	31.4294	-32.3366	-9.6106	-3.3822
19	1,6-dimethylhep	1	-3.6707	-5.4348	1.3326	0.2079	-19.4715	-11.0659	-3.6707
20	1,6-dimethylhep	1	-3.5627	-5.2621	1.0112	0.1769	-24.8853	-10.5271	-3.5627

Figure 9. Docking result of the four molecules with the SARS-CoV-2 protein S receptor binding domain.

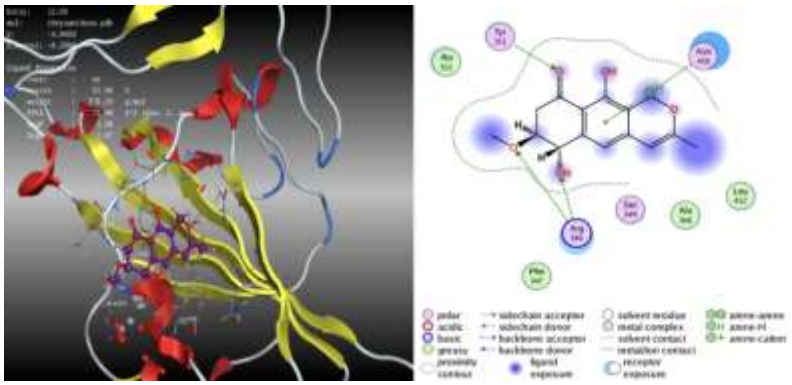

Figure 10. 2D/3D interaction of Eucalyptol with the 7kgj protein.

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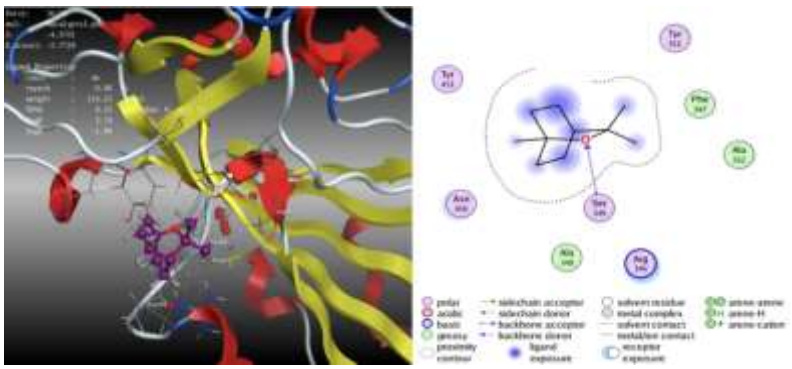

Figure 11. 2D/3D interaction of Chrysanthone with the 7kgj protein.

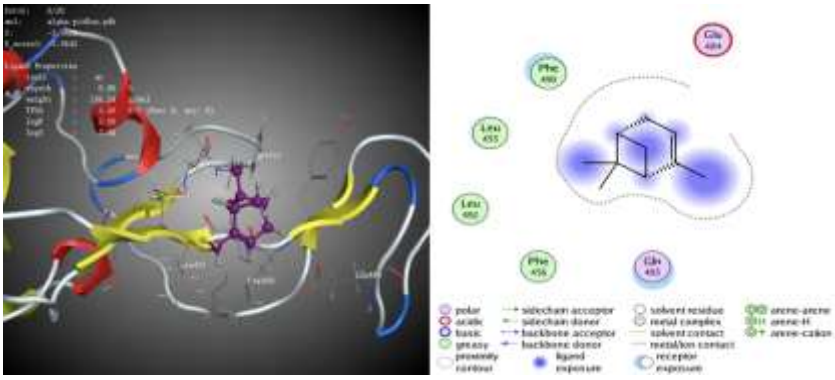

Figure 12. 2D/3D interactions of alpha-pinene with the 7kgj protein.

4. CONCLUSION

The present work showed that *Artemisia herba alba* EO of Jerada was marked by codominance of three main components such 1,6-Dimethylhepta-1,3,5-triene, Camphor, and Thujone, which are not described in the literature, and seems characteristic of Eastern Morocco. While Taourirt EO was found to be rich with Camphor, Eucalyptol, and Camphene. The obtained results demonstrated that the Jerada EOs possesses a low antioxidant activity compared to Vitamin C, and it was found to be more active compared to the EO of Taourirt. The four molecules have been evaluated computationally for toxicity by Osiris test, none of them showed toxic effects except α-pinene which presents a very low risk of irritation. Their similarity to a drug is estimated for 1,6-dimethylhepta-1,3,5-triene (a) at 54%; Chrysanthone (b) 55%; Eucalyptol(c) 48% and alpha-pinene 31%. All molecules showed high respect for Lipinski's rule. Our findings suggest that chrysanthone could play a potential role in preventing further binding of the virus to ACE2 which is the gateway of SARS-CoV-2 into the human body. Indeed, further *in vitro* and then *in vivo* studies are needed to confirm the obtained results.

5. AUTHORS' NOTE

The authors declare that there is no conflict of interest regarding the publication of this article. The authors confirmed that the paper was free of plagiarism.

6. REFERENCES

Abed, E. H., Shamran, D. J., and Al-Bakri, S. A. A. Decreasing COVID-19 effect by inhalation of some medical plants vapor. *Journal of Wasit*, *97*, 9–13.

DOI: https://doi.org/10.17509/ijost.v8i1.50737
p- ISSN 2528-1410 e- ISSN 2527-8045

Abu-Darwish, M. S., Cabral, C., Gonçalves, M. J., Cavaleiro, C., Cruz, M. T., Efferth, T., and Salgueiro, L. (2015). Artemisia herba-alba essential oil from Buseirah (South Jordan): Chemical characterization and assessment of safe antifungal and anti-inflammatory doses. *Journal of Ethnopharmacology*, *174*, 153-160.

Abu-Irmaileh, B. E., and Afifi, F. U. (2003). Herbal medicine in Jordan with special emphasis on commonly used herbs. *Journal of Ethnopharmacology*, *89*(2-3), 193-197.

Afifah, Q. A. (2021). Analysis of the impact of the covid-19 pandemic on family harmony: case studies on family with and without people with special needs. *Indonesian Journal of Community and Special Needs Education, 1*(2), 87-92

Ahmed, A. H., Ejo, M., Feyera, T., Regassa, D., Mummed, B., and Huluka, S. A. (2020). In vitro anthelmintic activity of crude extracts of Artemisia herba-alba and Punica granatum against Haemonchus contortus. *Journal of Parasitology Research*, *2020*, 1-7.

Alam, M. N., Bristi, N. J., and Rafiquzzaman, M. (2013). Review on in vivo and in vitro methods evaluation of antioxidant activity. *Saudi Pharmaceutical Journal*, *21*(2), 143-152.

Alshehri, M. A., Panneerselvam, C., Murugan, K., Trivedi, S., Mahyoub, J. A., Maggi, F., and Benelli, G. (2018). The desert wormwood (Artemisia herba-alba)–From Arabian folk medicine to a source of green and effective nanoinsecticides against mosquito vectors. *Journal of Photochemistry and Photobiology B: Biology*, *180*, 225-234.

Amina, B., Soumeya, B., Salim, B., Mahieddine, B., Sakina, B., Chawki, B., and Carmine, N. (2022). Chemical profiling, antioxidant, enzyme inhibitory and in silico modeling of Rosmarinus officinalis L. and Artemisia herba alba Asso. essential oils from Algeria. *South African Journal of Botany*, *147*, 501-510.

Amor, G., Caputo, L., La Storia, A., De Feo, V., Mauriello, G., and Fechtali, T. (2019). Chemical composition and antimicrobial activity of Artemisia herba-alba and Origanum majorana essential oils from Morocco. *Molecules*, *24*(22), 4021.

Anggraeni, S., Maulidina, A., Dewi, M. W., Rahmadianti, S., Rizky, Y. P. C., Arinalhaq, Z. F., and Al-Obaidi, A. S. (2020). The deployment of drones in sending drugs and patient blood samples COVID-19. *Indonesian Journal of Science and Technology*, 5(2), 193-200.

Asdadi, A., Hamdouch, A., Gharby, S., and Hassani, L. M. I. (2020). Chemical characterization of essential oil of Artemisia herba-alba asso and his possible potential against covid-19. *Journal of Analytical Sciences and Applied Biotechnology*, *2*(2), 2-2.

Azizi, S., Dalli, M., Berrichi, A., and Gseyra, N. (2021). Quantification of secondary metabolites and the evaluation of the in vitro antioxidant activity of the Argan tree of eastern Morocco. *Materials Today: Proceedings*, *45*, 7314-7320.

Azzahra, S., Maryanti, R., Wulandary, V. (2022). Problems faced by elementary school students in the online learning process during the Covid-19 pandemic. *Indonesian Journal of Multidiciplinary Research, 2*(2), 245-256.

Bakchiche, B., Gören, A. C., Aydoğmuş, Z., Mataracikara, E., and Ghareeb, M. A. (2022). Artemisia campestris and Artemisia herbaalba: LC-HRESI-MS Profile Alongside Their Antioxidant and Antimicrobial Evaluation. *ACTA Pharmaceutica Sciencia*, *60*(2), 101-152.

DOI: https://doi.org/10.17509/ijost.v8i1.50737
p- ISSN 2528-1410 e- ISSN 2527-8045

Bammou, L., Mihit, M., Salghi, R., Bouyanzer, A., Al-Deyab, S., Bazzi, L., and Hammouti, B. (2011). Inhibition effect of natural Artemisia oils towards tinplate corrosion in HCL solution: chemical characterization and electrochemical study. *International Journal of Electrochemistry Science*, *6*(5), 1454-1467.

Benabdellah, M., Benkaddour, M., Hammouti, B., Bendahhou, M., and Aouniti, A. (2006). Inhibition of steel corrosion in 2 M H3PO4 by artemisia oil. *Applied surface science*, *252*(18), 6212-6217.

Bertella, A., Benlahcen, K., Abouamama, S., Pinto, D. C., Maamar, K., Kihal, M., and Silva, A. M. (2018). Artemisia herba-alba Asso. essential oil antibacterial activity and acute toxicity. *Industrial Crops and Products*, *116*, 137-143.

Bouklah, M., and Hammouti, B. (2006). Thermodynamic characterisation of steel corrosion for the corrosion inhibition of steel in sulphuric acid solutions by Artemisia. *Portugaliae Electrochimica Acta*, *24*(4), 457.

Bouyahya, A., El Omari, N., Elmenyiy, N., Guaouguaou, F. E., Balahbib, A., Belmehdi, O., and Bakri, Y. (2021). Moroccan antidiabetic medicinal plants: Ethnobotanical studies, phytochemical bioactive compounds, preclinical investigations, toxicological validations and clinical evidences; challenges, guidance and perspectives for future management of diabetes worldwide. *Trends in Food Science and Technology*, *115*, 147-254.

Bouyanzer, A., and Hammouti, B. (2004). A study of anti-corrosive effects of Artemisia oil on steel. *Pigment and Resin Technology*, *33*(5), 287-292.

Bouyanzer, A., Bouklah, M., Chetouani, A., Majidi, L., Hammouti, B., and Aouniti, A. (2017). Valorization of essential oil and extracts of Artemisia herba alba in the inhibition of corrosion and antibacterial and other effects-Review. *Arabian Journal of Chemical and Environmental Research*, *4*(1), 31-45.

Coyoca, M. B. P., Del Rosario, M. A. B., Lazo, J. R. L., Calixtro Jr, V. L., and Edaño, L. B. (2022). Impact of gardening on physical and mental health in the midst of Covid-19 pandemic. *Indonesian Journal of Community and Special Needs Education*, *2*(2), 99-102.

Dalli, M., Azizi, S. E., Benouda, H., Azghar, A., Tahri, M., Bouammali, B., and Gseyra, N. (2021). Molecular composition and antibacterial effect of five essential oils extracted from Nigella sativa L. seeds against multidrug-resistant bacteria: A comparative study. *Evidence-Based Complementary and Alternative Medicine*, *2021*, 1-9.

Dalli, M., Azizi, S. E., Kandsi, F., and Gseyra, N. (2021). Evaluation of the in vitro antioxidant activity of different extracts of Nigella sativa L. seeds, and the quantification of their bioactive compounds. *Materials Today: Proceedings*, *45*, 7259-7263.

Dirgantari, P. D., Hidayat, Y. M., Mahphoth, M. H., and Nugraheni, R. (2020). Level of use and satisfaction of e-commerce customers in covid-19 pandemic period: An information system success model (ISSM) approach. *Indonesian Journal of Science and Technology*, *5*(2), 261-270.

Ed-Dra, A., Filali, F. R., Presti, V. L., Zekkori, B., Nalbone, L., Elsharkawy, E. R., and Giarratana, F. (2021). Effectiveness of essential oil from the Artemisia herba-alba aerial parts against multidrug-resistant bacteria isolated from food and hospitalized patients. *Biodiversitas*

DOI: https://doi.org/10.17509/ijost.v8i1.50737
p- ISSN 2528-1410 e- ISSN 2527-8045

Journal of Biological Diversity, *22*(7), 2995–3005.

El Hadki, A., El Hadki, H., Tazi, R., Komiha, N., Zrineh, A., El Hajjaji, S., Kabbaj O.K. (2021) DFT and molecular docking study of natural molecules proposed for Covid-19 treatment. *Moroccan Journal of Chemistry, 9*, 198-209.

Elshafie, H. S., Caputo, L., De Martino, L., Gruľová, D., Zheljazkov, V. Z., De Feo, V., and Camele, I. (2020). Biological investigations of essential oils extracted from three Juniperus species and evaluation of their antimicrobial, antioxidant and cytotoxic activities. *Journal of Applied Microbiology*, *129*(5), 1261-1271.

Fahrannisa, A. L., Muktiarni, M., Mupita, J. (2022). The use of short stories as learning media for character education for elementary school students during the Covid-19 pandemic. *Indonesian Journal of Multidiciplinary Research, 2*(2), 237-244.

Fakchich, J., and Elachouri, M. (2021). An overview on ethnobotanico-pharmacological studies carried out in Morocco, from 1991 to 2015: Systematic review (part 1). *Journal of Ethnopharmacology*, *267*, 113200.

Hammoudan, I., Chtita, S., Bakhouch, M., and Temsamani, D. R. (2022). QSAR study of a series of peptidomimetic derivatives towards MERS-CoV inhibitors. *Moroccan Journal of Chemistry*, *10*(4), 405-416.

Hashim, S., Masek, A., Abdullah, N. S., Paimin, A. N., and Muda, W. H. N. W. (2020). Students' intention to share information via social media: A case study of COVID-19 pandemic. *Indonesian Journal of Science and Technology*, *5*(2), 236-245.

Hattori, T., Koide, A., Noval, M. G., Panchenko, T., Romero, L. A., Teng, K. W., and Koide, S. (2021). The ACE2-binding interface of SARS-CoV-2 Spike inherently deflects immune recognition. *Journal of Molecular Biology*, *433*(3), 166748.

Hudaib, M. M., and Aburjai, T. A. (2006). Composition of the essential oil from Artemisia herba-alba grown in Jordan. *Journal of Essential Oil Research*, *18*(3), 301-304.

Huwaidi, F., Nandiyanto, A. B. D., Muhammad, N. (2021). The urgency of online learning media during the Covid-19 pandemic at the vocational school in Indonesia. *Indonesian Journal of Educational Research and Technology, 1*(2), 35-40.

Jungreis, I., Sealfon, R., and Kellis, M. (2021). SARS-CoV-2 gene content and COVID-19 mutation impact by comparing 44 Sarbecovirus genomes. *Nature Communications*, *12*(1), 1-20.

Kadri, M., Yahia, A., Goubi, S., Mekhedmi, N. E., Selmane, M., and Chemsa, A. E. (2022). Chromatography analysis, in vitro antioxidant and antibacterial activities of essential oil of Artemisia herba-alba Asso of Boussaâda, Algeria. *Biodiversitas Journal of Biological Diversity*, *23*(9), 4424-4431.

Khlifi, D., Sghaier, R. M., Amouri, S., Laouini, D., Hamdi, M., and Bouajila, J. (2013). Composition and anti-oxidant, anti-cancer and anti-inflammatory activities of Artemisia herba-alba, Ruta chalpensis L. and Peganum harmala L. *Food and Chemical Toxicology*, *55*, 202-208.

Lipinski, C. a., Lombardo, F., Dominy, BW, and Feeney, PJ (2012). Experimental and computational approaches to estimate solubility and permeability in drug discovery and

DOI: https://doi.org/10.17509/ijost.v8i1.50737
p- ISSN 2528-1410 e- ISSN 2527-8045

development settings. *Advanced Drug Delivery Reviews*, *64*, 4-17.

Lopes-Lutz, D., Alviano, D. S., Alviano, C. S., and Kolodziejczyk, P. P. (2008). Screening of chemical composition, antimicrobial and antioxidant activities of Artemisia essential oils. *Phytochemistry*, *69*(8), 1732-1738.

Marchant, C. A., Briggs, K. A., and Long, A. (2008). In silico tools for sharing data and knowledge on toxicity and metabolism: Derek for windows, meteor, and vitic. *Toxicology Mechanisms and Methods*, *18*(2-3), 177-187.

Maryanti, R. (2021). Assessment of mathematical abilities of students with intellectual disabilities during the covid-19 pandemic. *Indonesian Journal of Community and Special Needs Education, 1*(2), 47-52.

Mighri, H., Hajlaoui, H., Akrout, A., Najjaa, H., and Neffati, M. (2010). Antimicrobial and antioxidant activities of artemisia herba-alba essential oil cultivated in tunisian arid zone. *Comptes Rendus Chimie*, *13*(3), 380-386.

Mohamed, A. E. H. H., El-Sayed, M., Hegazy, M. E., Helaly, S. E., Esmail, A. M., and Mohamed, N. S. (2010). Chemical constituents and biological activities of artemisia herba-alba. *Records of Natural Products*, *4*(1), 1–25.

Mohammed, M. J., Anand, U., Altemimi, A. B., Tripathi, V., Guo, Y., and Pratap-Singh, A. (2021). Phenolic composition, antioxidant capacity and antibacterial activity of white wormwood (Artemisia herba-alba). *Plants*, *10*(1), 164.

Moussi Imane, M., Houda, F., Said Amal, A. H., Kaotar, N., Mohammed, T., Imane, R., and Farid, H. (2017). Phytochemical composition and antibacterial activity of moroccan lavandula angustifolia mill. *Journal of Essential Oil-Bearing Plants*, *20*(4), 1074-1082.

Moussi, I. M., Nayme, K., Timinouni, M., Jamaleddine, J., Filali, H., and Hakkou, F. (2020). Synergistic antibacterial effects of Moroccan Artemisia herba alba, Lavandula angustifolia and Rosmarinus officinalis essential oils. *Synergy*, *10*, 100057.

Mulyanti, B., Purnama, W., and Pawinanto, R. E. (2020). Distance learning in vocational high schools during the covid-19 pandemic in West Java province, Indonesia. *Indonesian Journal of Science and Technology*, *5*(2), 271-282.

Ouachikh, O., Bouyanzer, A., Bouklah, M., Desjobert, J. M., Costa, J., Hammouti, B., and Majidi, L. (2009). Application of essential oil of Artemisia herba alba as green corrosion inhibitor for steel in 0.5 MH 2 SO 4. *Surface Review and Letters*, *16*(01), 49-54.

Ouguirti, N., Bahri, F., Bouyahyaoui, A., and Wanner, J. (2021). Chemical characterization and bioactivities assessment of Artemisia herba-alba Asso essential oil from South-western Algeria. *Natural Volatiles and Essential Oils*, *8*(2), 27-36.

Paolini, J., Ouariachi, E., Bouyanzer, A., Hammouti, B., Desjobert, J. M., Costa, J., and Muselli, A. (2010). Chemical variability of Artemisia herba-alba Asso essential oils from East Morocco. *Chemical Papers*, *64*(5), 550-556.

Phanse, S. (2021). The online education impact on students during covid- 19 pandemic. *Indonesian Journal of Teaching in Science*, *1*(2), 137-140.

DOI: https://doi.org/10.17509/ijost.v8i1.50737
p- ISSN 2528-1410 e- ISSN 2527-8045

Pirbalouti, A. G., Firoznezhad, M., Craker, L., and Akbarzadeh, M. (2013). Essential oil compositions, antibacterial and antioxidant activities of various populations of Artemisia chamaemelifolia at two phenological stages. *Revista Brasileira de Farmacognosia*, *23*(6), 861-869.

Razon, B. C. (2020). Covid-19: Impetus for community spirits among Filipinos. *Indonesian Journal of Science and Technology*, *5*(2), 201-208.

Sami, Z., Nacim, Z., Nahed, F., Ali, B., and Mohamed, N. (2010). Chemical composition and biological activities of a new essential oil chemotype of Tunisian Artemisia herba alba Asso. *Journal of Medicinal Plants Research*, *4*(10), 871-880.

Sangsawang, T. (2020). An instructional design for online learning in vocational education according to a self-regulated learning framework for problem solving during the COVID-19 crisis. *Indonesian Journal of Science and Technology*, *5*(2), 283-198.

Saputra, H., Albar, C. N., and Soegoto, D. S. (2022). Bibliometric Analysis of Computational Chemistry Research and Its Correlation with Covid-19 Pandemic. *Moroccan Journal of Chemistry*, *10*(1), 10-1.

Sharma, A.D., and Kaur, I. (2021). Homology modeling and molecular docking of natural metabolites from eucalyptus essential oil against SARS-COV-2 spike protein. *Arabian Journal of Medicinal and Aromatic Plants, 7*(3), 282-300.

Sharma, A.D., and Kaur, I. (2022). GC-FID based aromatic profiling and molecular docking studies of lemon grass (Cymbopogon citratusL.) essential oil as novel therapeutic for SARS-Cov2 spike protein, *Arabian Journal of Medicinal and Aromatic Plants*, *8*(1), 1-20.

Sroka, Z. and Cisowski, W. (2003). Hydrogen peroxide scavenging, antioxidant and anti-radical activity of some phenolic acids. *Food and Chemical Toxicology*, *41*(6), 753–758.

Sukmawati, D., Maryanti, R. (2022). Development of education and economic circulation in supporting local potential as community empowerment efforts amid the Covid-19 pandemic. *Indonesian Journal of Multidiciplinary Research, 1*(2), 235-250.

Tilaoui, M., Ait Mouse, H., Jaafari, A., and Zyad, A. (2015). Comparative phytochemical analysis of essential oils from different biological parts of Artemisia herba alba and their cytotoxic effect on cancer cells. *PloS One*, *10*(7), e0131799.

Touzani, R., Hammouti, B., El Malki, F., and Benhadda, T. (2020). Coronavirus, covid19, covid-19 and sars-cov-2: A global pandemic, a short review. *Journal of Materials and Environmental Science*, *11*(5), 736.

Younsi, F., Trimech, R., Boulila, A., Ezzine, O., Dhahri, S., Boussaid, M., and Messaoud, C. (2016). Essential oil and phenolic compounds of Artemisia herba-alba (Asso.): Composition, antioxidant, antiacetylcholinesterase, and antibacterial activities. *International Journal of Food Properties*, *19*(7), 1425-1438.

Zhong, Y., and Shahidi, F. (2015). 12–methods for the assessment of antioxidant activity in foods, handbook of antioxidants for food preservation a volume in woodhead publishing series in food science. *Technology Nutrition*, *2015*, 287-333.

DOI: https://doi.org/10.17509/ijost.v8i1.50737
p- ISSN 2528-1410 e- ISSN 2527-8045