Essential Oil Content, Chemical Composition, Antioxidant Activity and Antiviral Potential of Four Aromatic and Medicinal Plants

Fatima Taoufik[1], Aicha Hamdouch[2], Salma Zine[1], Bouchra Chebli[3], Miloud EL Hadek[1], Lalla Mina Idrissi Hassani[2]

[1] *Laboratory of Chemical Engineering, Department of Chemistry, Faculty of Science, University IBN ZOHR, Morocco*

[2] *Plant Biotechnology Laboratory, Planta South Team, Department of Biology, Faculty of Science, University IBN ZOHR, Morocco*

[3] *Biotechnology and Environnement Engineering Team, ENSA, University IBN ZOHR, , Morocco*

Abstract

Essential oils of Lavender (*Lavandula dentata* (*L. d.*), *Lavandula stoechas* (*L. s.*)), mint (*Mentha viridis* (*M. v.*)) and *Cistus villosus* (*C. v.*) from the south of Morocco were obtained by hydrodistillation and studied for chemical composition, antioxidant activity and antiviral potential against Covid-19. Gas Chromatography-Mass Spectrometry determines essential oils chemical composition, and the antioxidant activity was determined by measuring the free radical scavenging power of DPPH. The results shown that the essential oil of the leaves of *L. d.* and *L. s.* are as source of camphor. The *C. v.* essential oil consists of different compounds, mainly alloaromadendrene, β-selinene. While *M. v.* is revealed to be a D-carvone mint. Aromatic plants essential oils show high scavenging effect of DPPH.

Results suggest that essential oils have biological activities, namely antioxidant and antiviral activities of at least the predominant compounds. Hence, we are proposing the plants for scientific research as a natural antioxidant and a potential substance for beating COVID-19 virulence and transmission spread.

Key-words: essential oil; antioxidant and antiviral potential; *Cistus villosus;* Covid-19; *Lavandula dentata*; *Lavandula stoechas; Mentha viridis*; Morocco.

(*) Corresponding author : taoufik.fatima@gmail.com

1. Introduction

Chtouka Ait Baha and Tiznit regions are semi-arid zones located in southern Morocco. This area is the best agricultural region in Morocco, characterized by a suitably sloping topography and sandy soils. *Lavandula dentata* (*L. d*.), *Lavandula stoechas* (*L. s*.)), *Mentha viridis* (*M. v*.)), *Cistus villosus* (*C. v*.) are aromatic and medicinal plants growing wildly in this area except for mint, which is a cultivated plant. They contain a various chemical compound with therapeutic properties such as essential oils (EOs), which are volatile extracts containing usually mixtures of terpenoids (mainly monoterpenoids and sesquiterpenoids), aromatic compounds and aliphatic compound.

Lavandula dentata is popularly known as lavender, grows on rocky ground and phrygana of the arid Mediterranean or Saharan regions. It is a medicinal plant used in the traditional medicine as an antidiabetic, antispasmodic, anti-hypertensive against common flu and renal colic. It is also used in the ornamentation and as a melliferous plant. *Lavandula stoechas* is also growing around the Mediterranean basin. In Morocco, this plant grows at high altitudes on calcareous soils, especially in the north of Morocco, in the middle and high Atlas and Rif mountains. It is used throughout the Mediterranean region for its medicinal virtues, for the preparation of traditional meals and herbal teas, and for cosmetic purposes. About *Mentha viridis,* this plant, commonly known as garden or green mint, is a native of the Mediterranean region, and widely distributed in Euroasia, Australia and South Africa. It has been grown in irrigated or wet places. On a daily basis, Moroccans consume mint tea which is an infusion of *M. v*. leaves. This mint is used in the cosmetic, pharmaceutical and food industry. *Cistus villosus,* it is a medicinal plant of perennial shrubs also known as rock rose; holly rose. These shrubs grow wild in the Moroccan and Mediterranean edges. All the Cistus species are frequently used in many traditional medicines for their antimicrobial, antitumor, antiviral and anti-inflammatory properties.

Several studies revealed that EOs have considerable antifungal, antibacterial, antiviral, antioxidant activities (El Bouzidi L. et al., 2013; Gilling D. H. et al., 2014; Hamdouch A.et al. 2022; Rhoades J. et al., 2013 ; Talibi I. et al., 2014; Zakaryan H. at al., 2017), and corrosion inhibition effect (Taoufik F. et al., 2017). Observations from traditional medicine reported that many essential oils can be effective in the prevention and treatment of viral-induced respiratory tract infections (Meghana K. et al., 2017; Salem M. et al., 2021).

Public health and the fight against highly pathogenic and contagious viruses have always been the prime issues because of the continuous emerging of pandemics in last two decades. There were outbreaks of SARS-CoV-1, MERS-CoV, and now the current pandemic Coronavirus disease of 2019 (COVID-19) has become an extreme threat to human life, also has brought about relentless social-economical along with political issues in the infected countries (Indranil C. et al., 2020). The current pandemic of COVID-19 caused by the coronavirus SARS-CoV-2 has as of July 18, 2021, resulted 4 million deaths worldwide (Gupta S.et al., 2021). Although several COVID-19 vaccines, that remains the most effective manner to achieve control of the pandemic, this may not be the final answer to the COVID-19 problem. In one hand, the output of 15.6 billion units is needed to be given two doses of vaccine to distant people all over the world, which is not an easy task. In the other hand, unvaccinated persons, as well as persons with certain immunocompromising conditions (including children aged <12 years who are currently ineligible for vaccination) (CDC, 2021 a) remain at substantial risk for infection, severe illness, and death from infection with the Delta variant and other currently circulating variants of the virus (CDC, 2021 b). Prevention strategies such as staying home when sick, handwashing, and regular cleaning of high-touch surfaces should also be encouraged (Christie A. et al., 2021). Fortunately, a large number of *in silico* studies are going on against various targets of SARS-CoV-2 using phytochemicals, as aromatic and medicinal plants essential oils and computer-designed inhibitors of SARS-CoV-2 (Paul A. et al., 2020). From the above, it can be seen that, EOs may be able to supply at least symptomatic relief if not total cure of COVID-19.

This work contributes to the valorization of medicinal and aromatic species by studing the chemical composition, antioxidant activity and possible antiviral potential against Covid-19 of essential oils obtained by hydrodistillation from the aerial parts of *Lavandula dentata*, *Lavandula stoechas*, *Mentha viridis* and *Cistus villosus* from south of morocco where is no such investigation.

2. Experimental and methods

2.1. ***Aromatic and medicinal plants***

The leaves of the plants were harvested by hand during the full flowering season between April and June 2014, the locations, and the names of the plants are shown in Table1. The extraction of essential oil was by hydrodistillation using Clevenger type apparatus (Clevenger J. F., 1928).

The taxonomic identification of the species of all samples was confirmed by Pr. Msanda (Laboratory of Biotechnology and Valorization of Natural Resources, Faculty of Sciences, Agadir, Morocco).

Table 1. Family, location and utilisation of plantes

Plant	**Mint M. v.**	**Lavender L. d.**	**Lavender L. s.**	**Cistus C. v.**
Family	Lamiaceae			Cistaceae
Place of abundance	Cultivated	Endimic to the Mediterranean region		
Location Latitude / longitude	Tiznit (N29°73/W9°72)	Asgharkiss-Chtouka Ait Baha (N 29°82/W 9°19)	Douar Rabiat-Tiznit (N29°54/W9°33)	Asgharkiss-Chtouka Ait Baha (N 29°77/W 9°17)
Utilisation	Feed and therapy	Therapy and cosmitic		Therapy

2.2. *GC-MS analysis*

GC-MS was carried out with a 5973N Agilent apparatus, equipped with a capillary column (95 dimethylpolysiloxane -5 % diphenyl), Agilent HP-5MS DI (30 m long and 0.25 mm i.d. with 0.25 urn film thickness). The column temperature program was 60°C during 5 min, with 3°C/min increases to 180°C, then 20°C/min increases to 280°C, which was maintained for 10 min. The carrier gas was helium at a flow-rate of 1 mL/min. Split mode injection (ratio 1:30) was employed. Mass spectra were taken over the m/z 30-500 range with an ionizing voltage of 70 eV.

2.3. **Antioxidant activity**

The antioxidant activity in vitro was evaluated by measuring the scavenging power of free radical DPPH by the essential oils (Taoufik F. at al., 2017). Methanolic solution (500µL) of the essential oil tested at different concentrations (1.1 mg/mL, 1mg/mL, 0.5mg/mL, 0.25mg/mL, 0.125mg/mL) was mixed with 500 µL of methanolic solution of DPPH (0.004%). The absorbance is read at 517 nm wavelength after an incubation period of 30 minutes in the dark at ambient temperature. The inhibition of free radical DPPH by BHT and Covi-Ox (references

antioxidants compounds) was also assessed with the same concentrations and the same conditions for comparison. The inhibition of free radical DPPH percentage (I%) is calculated as follows:

$$I\% = 100 \times (A_{control} - A_{test}) / A_{control} \quad (1)$$

Where $A_{control}$ is the absorbance of the control (containing all reagents without the test product) and A_{test} is the absorbance of the test compound (containing all reagents and the test product). All tests were performed in triplicate for each concentration (El Bouzidi L. et al, 2013).

3. Results and discussion

3.1. *Essential oil content*

The essential oil content of studied plants leaves is given inTable 2. The results are the means of three extractions.

Table 2: Yields of the extraction of essential oils by hydrodistillation

Aromatic plant	**Yield (% v/w dry material)**
Lavender *(Lavandula dentata)*	2.6 ± 0.7
Lavender *(Lavandula stoechas)*	1.9 ± 0.5
Cistus *(Cistus villosus)*	1.25 ± 0.5
Mint *(Mentha viridis)*	5 ± 0.2

The hydrodistillation gave a yield of 2.6 ± 0.7 % (v/w) for *Lavandula dentata*. This rate is relatively higher than that of the EOs extracted from the same species collected in different sites in Algeria : 0.24% to 1.18% (Bousmaha L. et al., 2006 ; Dris D. et al., 2017), in Yemen with a value of 0.8 % (Gamez M.J. et al., 1990) and 0.58 % (Mothana R.A. et al., 2012), in Tunisia ; 1.96 % (Msaada K. et al., 2012) and also in Morocco 1.41% (Imelouane B. et al., 2010) and 2.18% (Soro N. K. et al., 2014). This difference in essential oil contents of lavender yield from different

regions depends on several factors like the geographical origin, harvest period, location and duration of drying, temperature and extraction technique (Smallfield B., 2001; Svoboda K. P. & Hampson J. B. 1999).

The average yield for essential oils extracted from *Lavandula stoechas* plant studied is around 1,9% ± 0,5 (v/w). This result is higher than those reported by La Bella et al., 2015 from south Italy. Previous studies reported yields of (1.46 % and 1.63 %) from Algerian plants (Baali F. et al., 2019; Benabdelkader T., 2012).

Cistus villosus EO shows a yeild of 1.25 ± 0.5% (v/w). The contents of essential oils in Cistus, depending on the species, on average range from 0.09% in *Cistus creticus* to 0.12% in *Cistus villosus*, as calculated in dry matter (Loizzo M.R. et al., 2013).

The yield of *Mentha viridis* essential oil was 5 ± 0.2% (v/w). This rate is relatively higher than that of the EOs obtaind from the same species collected in the region of Lavras, in southern Minas Gerais state, Brazil (1.52 %) (Silva L. F. et al., 2015) and from Ouezzane province, Morocco (2.5%) (Bouyahya A., 2017).

3.2. ***CG-MS analyses***

After the analysis of the different chromatograms of CG-MS and CG-FID, the main components of essential oils and their percentages were determined. The percentages of the predominant compounds of the four essential oils are given in Table 3.

For *Lavandula stoechas*, and *Lavandula dentata*, the oxygenated monoterpenes represent the predominant fraction of the essential oils (Camphor 76.10% and 61.23% respectively). For the remaining components, the contents of D-Carvone, Eucalyptol, D-Limonene, endo-Borneol and L-pincarveol, were significantly higher. Several works have revealed the dominance of camphor, fenchone and cineole in lavender essential oils of different origins from Morocco (Zrira S. et al., 2003) Algeria (Baali F. et al., 2019) Turkey (Gören A.C. et al., 2002), Italy (La Bella S. et al., 2015) and from Pakistan (Zaheer U. K. et al., 2002). Compared to published data, the chemical profile obtained presents differences, but also some similarities, Soro et al. (2014) found camphor (49.75 %) and 1,8-cineole (39.84%) as major components of *Lavandula dentata*'s essential oil. Other camphor chimotype were found in Yemen and Turkey species (Al-Sarar A.S. et al., 2014; Mothana R. A. et al., 2012). In Morocco, Imelouane et al. (2010)

showed β-pinene (27.08 %) as the chemotype of eastern Morocco species and 1,8-cineol (41.28 %) as the chemotype of the population from Taforalt, Talazart (Morocco).

The major compounds of *Cistus villosus* essential oil are: alloaromadendrene (20.03%), β-selinene (18.12%), α-copaene (9.89%), (-) -α-bourbonene (6.97%), γ-muurolene (6.59%) and α-muurolene (4.88%). In a study conducted on Mediterranean *Cistus albidus* (Ormeño E. et al., 2007), alloaromadendrene constituted one of the highest contents of volatil compounds.

Essential oil analysis of *Mentha viridis* revealed that D-carvone, Eucalyptol, Limonene, 8-p-Menthen-2-yl, acetate, trans, Dihydrocarvone are the predominant compounds, this agrees with references (Abdalla O. A. E., 2020 ; Mkaddem M. et al., 2009 ; Silva L. F. et al., 2019). Mentha viridis is also known for its low menthol content compared to other mint varieties (Mkaddem M. et al., 2009).

Comparison of these results with those found in previous works showed some differences. This can be attributed to ecological factors, genetic differences, stage of plant development (Chalchat J. C. & M.M. Özcan 2008 ; Zeković Z.P. et al, 2009).

Table 3: Predominant components of the essential oils

Plant	Predominant components
Lavender (*Lavandula dentata*)	Camphor (61.23%); D-Carvone (7.99%); Eucalyptol (5.08 %); D-Limonene (3.18%); L-pincarveol (2.04%)
Lavender (*Lavandula stoechas*)	Camphor (76.10%); D-Carvone (3.90%); endo-Borneol (2.95%); Eucalyptol (1.51%)
Cistus (*Cistus villosus*)	Alloaromadendrene (20.03%); β-Selinene (18.12%); α-Copaene (9.89%); (−)-α-Bourbonene (6.97%); γ-Muurolene (6.59%); α-Muurolene (4.88%)
Mint (*Mentha viridis*)	D-Carvone (63.61%); Eucalyptol (5.81%); Limonene (5.51%); 8-p-Menthen-2-yl, acetate, trans (4.34%); Dihydrocarvone (3.14%)

3.3 Study of antioxidant activity

The inhibition percentage of free radicals for the essential oils studied is ragher lower than that of BHT and Covi-Ox for all the concentrations used, except for *Lavandula dentata* EO wich reach the maximum inhibition value (60%) obtained by the controls at a concentration of 1 mg/ml (Figure 1).

The concentration corresponding to 50% inhibition of DPPH (IC_{50}) was determined graphically, it characterizes the antioxidant activity of the essential oils studied. *Lavandula stoechas* EOs for example has a value of IC_{50} = 0.37 mg / ml and for the reference compounds BHT and Covi-Ox, the value of IC_{50} was 0.11 mg / ml (Table 3), that means references have 3 time more antioxidant capacity than *Lavandula stoechas* EOs.

Indeed, the essential oil, which has a minimum IC_{50} value is considered to have the highest antioxidant activity. We deduce that the *Lavandula stoechas* (0.37 mg / ml) shows the highest antioxidant capacity, followed by the other oils: *Lavandula dentata*, *Cistus villosus* and *Mentha viridis* (IC_{50} at between 0.72 mg/ml and 1.1 mg/ml).

Camphor, which is an oxygenated monoterpene, is the major component of *Lavandula stoechas* and *Lavandula dentata* essential oils, it represents more than 60%. These essential oils showed the highest antioxidant activity that could be ascribed to the high percentage of oxygenated monoterpenes (camphor) or to their synergy (Ruberto G. & Baratta M.T., 2000). It is well-known that antioxidant activity of EOs depends on their chemical composition with particular emphasis for oxygenated compounds content. For exemple, *Lavandula dentata* 1,8-cineole-camphor chymotype specie showed IC_{50}=14.03±0.16 mg/ml (Dammak I., 2019), *Lavandula dentata* β-eudesmol-myrtenol-sabinol chymotype specie has a value of IC_{50}=113.29± 0.012 mg/ml (Imen D. et al, 2021).

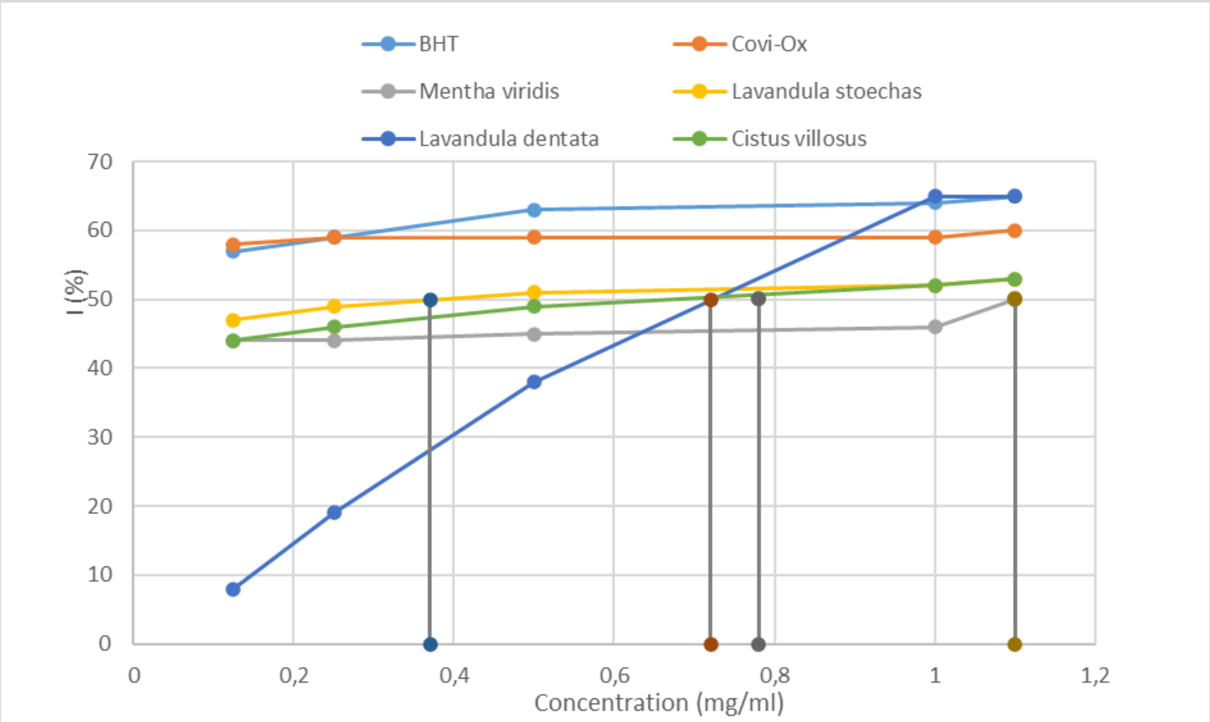

Figure 1: DPPH oxidation inhibition of essential oils, Covi-Ox and BHT

Table 3. Activity of DPPH (IC_{50}). [a] Values are means of (n = 3).

Sample	IC_{50} (mg/ml)[a]
BHT	0.11
Covi-Ox	0.11
Lavandula stoechas EOs	0.37
Lavandula dentata EOs	0.72
Cistus villosus EOs	0.78
Mentha viridis EOs	1.1

The essential oils of plants: *Cistus villosus* indicate an interesting inhibition power (I%> 44%) at low concentrations, but it remains below 52% at high concentrations (1 mg / ml). Indeed, some authors have demonstrated that, a tronger antioxidant activity was IC_{50} =0.055 mg/mL for *Cistus arabicus* (Sabinene, β-pinene, myrcene, and α-pinene) chymotype spiece from Ourika,

Morocco (Aghraz A. et al., 2017). Otherwise, a lower antioxidant activity was IC_{50}=2.53 mg/mL for Cistus *Creticus* leaves of Tafraout, Morocco (Lahcen S. A. et al., 2020).

The antioxidant results show that *Mentha viridis* Eos has the ability to scavenge DPPH radicals. Their IC_{50} Values of 1.1 mg/mL propose their anatioxidant capacity compared to reference compounds IC_{50} value (IC_{50}=0.11 mg/mL for BHT and Covi-Ox)). Therefore, the observed antioxidant activity of our oils may be due to the presence of monoterpenes: D-carvon, Eucalyptol (=1,8 cineol) and limonene. Our results are similar to those reported by previous studies (Bouyahya A. et al., 2017 ; Mkaddem M. et al., 2009 ; Silva L. F. et al., 2015). All these references confirm the role of Mentha viridis essential oils as natural antioxidants.

All essential oils have shown interesting antioxidant activity, this activity is attributed to the different constituents of the essential oils thanks to their synergistic or antagonistic effect, as essential oil contains several classes of compounds.

Essential oils and some of their components have always been at the head of antiviral studies; the same is true in the case of COVID-19 (Asif M. et al., 2020 ; da Silva J. K. R. et al., 2020 ; Hughes L. J. et al., 2018 ; Paul A. et al., 2020).

Indeed, bioactive major compounds present in *Lavandula stoechas* and *Lavandula dentata* are camphor and eucalyptol known for thier antifungal and antibacterial activity (Martins, R. D. P. et al., 2019 ; Mourey A. et al., 2002). In silico studies have evaluate the effect of bioactive compounds found in Eucalyptus and *Corymbia* species essential oil on main protease (Mpro) by docking analysis. The calculated parameters such as binding energy, hydrophobic interactions, and hydrogen bond interactions of 6LU7 (Mpro) with Eucalyptus and *Corymbia* volatile secondary metabolites represented its scope as an effective therapy option against covid-19. Among the docked compounds, **eucalyptol** shows the least binding energy without toxicity (Panikar S. et al., 2021). En addition, privious studies revealed EOs components such as **Limonene** and **pinocarveol** to be good inhibitors of the angiotensin converting enzyme 2 and the S1 glycoprotein of coronavirus by in silico methods (Ang L. et al., 2020 ; da Silva J. K. R. et al., 2020 ; Yadalam P. K. et al., 2021). Hence our proposal for *Lavandula stoechas*, *Lavandula dentata* and *Mentha viridis* as nature source of high potential activity substances against SARS-COV-2.

Through previous studies, several components of leaves of the plant *Tasmannia lanceolata*, including **alloaromadendrene**, showed promising binding affinities to the main protease in molecular docking studies *in silico,* with binding energies at or below-6.3 kcal/mol (Paul A. et al., 2020). Hence **alloaromadendrene** EOs extracted from Cistus villosus can be used in further studies through the synthesis of various derivatives and evaluation of its potential as possible anti-COVID-19 drugs.

Some authors have demonstrated that**, D-Carvone** is a terpenoid found in many medicinal and aromatic plants that are endued with many biological activities (Abirami S. G. & Nirmala P., 2014). **D-carvone** has been found to reduce forestomach tumour formation and pulmonary adenoma formation induced by Nnitrosodimethylamine in mice (Zhiying Y. et al., 2008). Carvone has several therapeutic effects including the treatment of coughs, bronchitis, and bronchial asthma. (Abdalla O. A. E., 2020). Hence **D-Carvone** EOs merit further investigation for any SARS-CoV-2 virucidal activity in wet lab tests.

Since EOs extracted from *plants studied* are not expensive and readily available, they will be of great value if they are used against SARS-CoV-2. Further studies through the synthesis of an antiviral drug or a potentiator of another conventional antiviral drug based on EOs are needed. EOs can also be used as a dietary supplement to relieve symptoms or strengthen the immune system of affected patients, or least as an adjuvant in hydro-alcoholic solutions and gels to increase their effectiveness in the external fight against COVID-19 (Asdadi A. et al., 2020).

4. Conclusion

Chemical analysis shows that the major constituent of *Lavandula dentata* and *Lavandula stoechas* essential oils is Camphor. The *Cistus villosus* essential oil contains different compounds (alloaromadendrene, β-selinene, α-copaene. However, *Mentha viridis* is a D-carvone mint. These results contribute to the determination of the aromatic plants chemotype.

The antioxidant activity detected in studied plants essential oils by DPPH essay is the product of additive, synergic and/or antagonistic effects, as these essential oils contain several classes of compounds. Results obtained demonstrate that all essential oils studied can be used as bionatural antioxidants.

Studied plants may provide low yields of essential oil, but it is a rich source for antioxydant compounds. In addition, according to recent studies, molecular docking analyses indicate that several major components of EOs studied may be suitable candidates for further structural modifications and future preclinical studies related to the development of therapeutics for COVID-19.

Abbreviations

ACE2	Angiotensin-Converting Enzyme 2	**IC50**	Concentration at 50% of DPPH Inhibition
BHT	Butylhydroxytoluene	***L. d.***	*Lavandula dentata*
C. v.	*Cistus villosus*	***L. s.***	*Lavandula stoechas*
CG-FID	Gas Chromatography with Flame Ionization Detection	***M. v.***	*Mentha viridis*
COVID-19	Coronavirus Disease 2019	**MERS-CoV**	Middle East respiratory syndrome coronavirus
DPPH	2,2- diphenyl-1-picryhydrazyl	**Mpro**	Main protease
EOs	Essential oils	**SARS-CoV-1**	Severe AcuteRrespiratory Syndrome Coronavirus 1
GC-MS	Gas Chromatography-Mass Spectrometry	**SARS-CoV-2**	Severe AcuteRrespiratory Syndrome Coronavirus 2

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Arabian Journal of Medicinal and Aromatic Plants
www.ajmap.info ISSN 2458-5920