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# Ocimum Species as Potential Bioresources against COVID-19: A Review of Their Phytochemistry and Antiviral Activity

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#### Authors' contributions

This work was carried out in collaboration of all authors. Authors CMM, KTNN and PTM wrote the first draft of the manuscript. Authors BZG, JTK, DSTT, CLI, EML, DTM and GNK collected information on plants bioactivity. Authors AM, EMN and DDT collected information on plant phytochemistry. All authors read and approved the final manuscript.

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# ABSTRACT

**Aim:** The aim of this work was to review literature data reported on some species of the *Ocimum* genus regarding their phytochemistry and antiviral potential in order to show how *Ocimum* species might be used in the management of COVID-19.

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**Methodology:** Various databases like PubMed, PubMed Central., Science Direct, SCIELO, DOAJ, Science alert, Semantic scholar and Google scholar were used.

**Results:** Essential oils and extracts of *Ocimum* species possess the compounds involved in antiviral activity. In addition, this plant contains certain nutrients which boost the immune system. *Ocimum* genus displayed antiviral activity against several viruses like Herpes Simplex Virus, Human Immunodeficiency Virus, Infectious Hematopoietic Necrosis Virus, Adenovirus, Enterovirus 71, Parainfluenza virus type 3, Hepatitis C virus, etc. Toxicological data indicated that these plants are safe.

**Conclusion:** Till now, there is no effective treatment of COVID-19. Ethnopharmacology constitutes an alternative approach for the discovery of effective antiviral drugs. The literature survey reveals that *Ocimum* species exhibit high antiviral activity, and thus can be used as potential bioresources against COVID-19. Molecular docking study of the interaction of some compounds derived from *Ocimum* species with SARS-CoV-2 protease is in progress in order to identify the potential inhibitors of the virus.

Keywords: Ocimum sp; COVID-19; antiviral activity; SARS-CoV-2; phytochemistry.

# **1. INTRODUCTION**

The world population is currently being challenged by several viral infections of which the most recent is the one of COVID-19. Coronavirus belongs to the β-coronaviridae family called Severe Acute Respiratory Syndrome (SARS-CoV-2) which causes several thousand deaths around the globe. Reported for the first time in 2019 in the city of Wuhan in China, COVID-19 has been declared a global health emergency by the World Health Organization (WHO) [1]. SARS-CoV-2 is a RNA virus that appears under an electron microscope in the form of a crown due to the spike of glycoproteins that surrounds it. This spike has been reported to be the major part of the SARS-CoV-2 virulence due to its capacity of binding the virus and the host cell. Having being bound, the virus membrane fuses with the host cell and allows the virus genome to enter the human cell and start the multiplication which leads to the infection Having a diameter between 60-140 nm, studies on its mode of action have shown that it attacks the cells of the respiratory system [1,2].

Relying on the genome sequence and modeling of the protease structure of the virus, the scientific community has proposed a list to the Food and Drug Administration (FDA) approved drugs namely Sofosbuvir, Ribavirin, Lopinavir/Ritonavir, Chloroquine, etc., which can be used for the management of COVID-19 patients. Unfortunately, the efficiency of these drugs is still under debate though Chloroquine has been adopted in the treatment of COVID-19 patients [3]. The treatment of viral diseases has always been a major challenge for humans because viruses are capable of continuously producing resistance that can make ineffective the drugs used. Due to the inefficiency of drugs used against this viral pandemic, the globe solely relies on the availability of a COVID-19 vaccine. In the same frame than the new SARS-CoV-2 virus, there are no vaccines available for several viral pathologies though for some viruses like rabies, measles, polio, smallpox, hepatitis, vaccines have shown a real success. Considering this situation, there is an urgent need of searching for new molecules having antiviral potential and which can be accessible at lower cost. In fact, medicinal plants have been used as alternative for the treatment of several ailments, and thus constitute a real factory for the production of secondary metabolites, which have antiviral potential [4-8].

Henceforth, the ethnopharmacology constitutes an alternative approach for the discovery of effective antiviral agents [9,10]. Among the plants that have shown antiviral properties, there is the species of Ocimum genus that belongs to Lamiaceae family. Ocimum is one of the largest genus in the Lamiaceae family, which includes more than 150 aromatic species and is considered as a source of essential oils (EO). Due to their use in food and medicine, the most cultivated species are O. africanum Lour., O. americanum L., O. basilicum L., O. gratissimum L., O. canum, O. minimum L., and O. tenuiflorum L. [11,12]. The aim of this review was to describe the phytochemistry and the antiviral activities of few species of Ocimum genus against some viruses. This antiviral potential may be noted and

needed for the management of SARS-CoV-2 virus.

# 2. METHODOLOGY

Data published on EO and extracts of some species of *Ocimum* genus for their phytochemistry and antiviral activity have been collected in the online bibliographic databases, such as: PubMed, PubMed Central, Science Direct, SCIELO, DOAJ, Science alert, Semantic scholar and Google scholar.

## **3. RESULTS AND DISCUSSION**

#### 3.1 Results

#### 3.1.1 Phytochemistry

The biological activities of aromatic plants are due to the chemical compounds that these species contain. Several studies have identified and isolated many EO compounds and extracts from certain *Ocimum* species (Table 1).

The table presents the chemical composition of most used species of the genus *Ocimum*.

Fig. 1 displays chemical structures of some EO compounds and extracts of some species of *Ocimum* species.

#### 3.1.2 Antiviral activity

EO play an important role in inhibiting the multiplication of some viruses as reported in the literature. Compounds such as methyl chavicol, trans-anethole, eugenol, methyl-eugenol, βeudesmole, farnesole,  $\beta$ -caryophyllene and  $\beta$ caryophyllenes oxide, y-terpinen, 4-allylanisole, dihydrocarvone, D-limonene, cuminyl aldehyde, cuminol, camphor, camphene, isoborneol, Lbornvl acetate, 2-decanol, 2-heptanol. methylheptane, nerol, isopulegol, citral are present in EO of certain species of the genus Ocimum, but few have been reported to be responsible for the antiviral activity against HSV-1, HSV-2, parainfluenza type-3 (PI-3), hepatitis C virus (HCV), enterovirus 71 (EV71), adenovirus (ADV), Bovine herpes virus (BHV-1), human rotavirus (RV) [62-65].

Caamal-Herrera et al. reported that the methanol and dichloromethane extracts of *O. americanum*, *O. basilicum* and *O. sanctum* exhibited an anti-HSV activity before, during and after the adsorption [66]. While Tang et al. and Ghoke et al. (2018) demonstrated the antiviral activity of *O. sanctum* methanol extract (terpenoids and polyphenols) against DENV 1 and H9N2 respectively [67].

Table 1. Four major constituents of EO and some molecules of the extracts of most used
plants of <i>Ocimum</i> genus

Plant species	References	
	Major constituents of EO (%)	
O. americanum	Geranial (28.58), neral (20.16), linalool (12.15), nerol (7.15).	[13]
(canum)	Linalool (53.8), limonen (22.2), eugenol (9.5), α-cardinol (2.4).	[14]
	1,8-cineol	[15]
	trans-methylcinnamate (79.7), cis-methylcynnamate (5.8),trans-	[16]
	α-bergamotene (4.8), β-caryophylene (3.8).	
	Macro and micronutrients (g/kg)	
	Carbohydrate (639.6), crude fibers (170.0), crude proteins (0.40),	[17]
	vitamin C (0.05), Ca (50.72), K (18.76), Na (9.58), P (7.59), Mg	
	(4.26), Fe (1.85), Zn (0.13), Mn (0.10), Cd (0.01), Pb (0.02)	
	Other compounds	
	Phenolic acids: rosmarinic acid, lithospermic acid, vanilic acid, p-	[18]
	coumaric acid, hydroxybenzoic acid, syringic acid, caffeic acid,	
	ferulic acid, cinnamic acid, sinapic acid.	
	Dichloromethane extract: oleanolic acid	[19]
	Methanolic extract : rosmarinic acid	
O. basilicum	Major constituents of EO (%)	
	Methyl chavicol (35.72), Linalool (21.25), epi- $\alpha$ -cadinol (8.02), $\alpha$ -	[20]
	bergamotene (6.56)	
	Linalool (55.55), 1,8-cineol (11.67), β-farnescene (7.10), α-	[21]
	Guaiene (6.14)	
	Linalool (28.6), estragol (21.7), (E) methylcinnamate (14.5), α-	[22]

	codinal (7.1)	
	cadinol (7.1). Linalool (46), eugenol (16), 1,8-cineol (6.2), trans-α-	[23]
	beragamotene (3.6).	[20]
	Linalool (36 ±2.6), eugenol (14.2±3.4), eucalyptol (11.4±2.2),	[24]
	trans-α-bergamotene (9.0±0),	
	Linalool (52.4a et 72.3b), methyl chavicol (19.5a et 3.1b), T-	[25]
	cadinol (4.9a et 8.6), (Z)-β-Farnesene (2.3 b).	10.01
	Linalool (35.1), eugenol (20.5), epi-α-Cadinol (5.6), 1,8-cineole (9.9).	[26]
	Macro and micronutrients (ppm)	
	Ca (17.46), Mg (2.66), Na (289.13), K (28.77).	[27]
	K (397.57), Ca (1133.4), Na (85.9), Fe (59.53), Carbohydrates,	[28]
	proteins, amino acids.	
	Mg (0.42), Ca (195.02), P (196.05), Na (81.34), thiamin,	[29]
	riboflavin, niacin.	
	Other compounds	
	Methanolic extract: ursolic acid 0.27% to 0.38	[30]
	Methanolic extract: rosmarinic acid	[31]
	Methanolic extract: rosmarinic acid, lithospermic acid, vanillic acid, <i>p</i> -coumaric acid.	[32]
	Flavonoids (kampferol), malic acid, tartaric acid, caffeic acid,	[33]
	Chicoric acid, caftaric acid.	
O. campechianun	Constituents of essential oils (%)	
	Eugenol (46.5), methyl eugenol (12), trans- $\beta$ -cayophylene (11.9), germacrene D (10.2).	[34]
	Methyl eugenol (53.9), trans- $\beta$ -caryophylene (13.0), $\alpha$ -bulnecene	[35]
	(5.4), germacren D (3.4).	[]
	Methyl eugenol (60.6 to 69.5), eugenol (32.2 to 60.6), elemicine	[36]
	(0.2 to 65.9), 1,8-cineol (0.9 to 19.7).	
	1,8-cineole (20.3), β-caryophylene (14.0), β-elemene (11.1),	[13]
	caryo phylene oxide (8.2).	
	Other compounds	
	Aqueous extracts: 5-dimethyl nobiletin, 5-dimethyl sinensetin,	[37]
<b>0</b>	luteolin, methyl rosmarinate, rosmarinic acid.	
O. gratissimum	Major Constituents of EO (%)	[0.4]
	Eugenol (43.2), 1,8-cineol (12.8), $\beta$ -selinene (9.0), trans- $\beta$ -caryo	[34]
	phylene (6.4). Thymae (4.8.1), n cymana (12.5), y tarninan (5.8), ß hiszbalana	[16]
	Thymol (48.1), p-cymene (12.5), $\gamma$ -terpinen (5.8), $\beta$ -bisabolene (4.0).	[16]
	Thymol (53.2), γ-terpinen (25.7), eugenol (12.7), p-cymene (7.3).	[38]
	Eugenol (68.81), methyl eugenol (13.21), cis-ocimene (7.47),	[39]
	germacrene D (4.25).	[]
	Macro and micronutrients (g/kg)	
	K (5.56), Ca (4.25), P (0.39), Carbohydrates (0.04), crude fibers	[40]
	(0.04), crude proteins (0.03), crude fat (0.009).	
	K (0.30), Ca (0.15), Mg (0.14), Na (0.11), Mn (0.05), Zn (0.03),	[41]
	Fe (0.003), Cu (0.003), ascorbic acid (0.36), niacin (0.0027),	
	thiamin $(0.0018)$ , riboflavin $(0.0014)$ , carbohydrates (649.8),	
	crude fibers (95.2), crude fat (85.0), crude proteins (33.3).	[40]
	K (14.79), Na (0.75), Fe (0.13), Zn (0.12), Mn (0.07), Ca (0.05),	[42]
	P (0.04), Cu (0.01), Mg (0.0053). Zn (0.17), Fe (0.04), Cu (0.03), Pb (0.0009), Cd (0.00018),	[43]
	Carbohydrate (503.5), proteins (91.0).	[40]
	Carbohydrate (42.3), crude fibers (39.2), crude proteins (31.4),	[44]
	Crude fat (9.2)	

	Other compounds	
	Methanolic extract: ursolic acid (1.04%)	[30]
	Aqueous extract: L-caftaric acid, L-chicoric acid, eugenyl-β-d-	[41]
	gluco pyranoside and vicenin-2	
	Methanolic extract: Rosmarinic acid, cafeic acid	[31]
	Ethyl acetate extract: ursolic acid	[20]
O. citriodorum	Major constituents of EO (%)	• •
	Geranial (31.21), neral (21.80), nerol (14.58), linalool (7.20)	[13]
	Nerol (23.1), geranial (15.77), methyl chavicol (9.45), linalool	[45]
	(9.42).	[+0]
	Macro and micronutrients (ppm)	
	Mg (0.35), K (149.85), Ca (188.3), P (80.44), Na (90.34), thiamin,	[20]
	riboflavin, niacin	[29]
	Other compounds	5 4 63
	Rosmarinic acid, lithospermic acid, vanilic acid, p-coumaric acid,	[46]
	hydroxybenzoic acid, syringic acid, caffeic acid, ferulic acid,	
	cinnamic acid, dihydroxyphenyllactic acid, sinapic acid.	
O. kilimands	Major constituents of EO (%)	
charicum	Camphor (56.97), 1,8-cineol (14.63), limomen (9.46), terpinen-4-	[13]
guerke	ol (6.59).	
	Linalool (41), camphor (17), 1,8-cineol (10), limonen (5).	[47]
	Camphor (56.07), D-L-limonene (13.56), camphene (7.32), 4-	[48]
	terpineol (3.50).	
	Camphor (45.9), 1,8-cineol (14.6), limonene (8.1), (Ε)-β-	[49]
	Ocimene (4.2).	
	Other compounds	
	Betulinic acid.	[50]
	Rosmarinic acid, lithospermic acid, vanilic acid, p-coumaric acid,	[46]
	hydroxybenzoic acid, syringic acid, caffeic acid, Ferulic acid,	
	cinnamic acid, Dihydroxyphenyllactic acid, Sinapic acid.	
O mieronthum		[64]
O. micranthum	Eugenol (46.55), β-elemene (9.06), 1,8-cineole (5.08), cis-	[51]
	ocimene (2.69).	1501
	Eugenol (64.8), (E)- $\beta$ -caryophylene (14.3), bicyclogermacrene	[52]
	(8.1), α-humilene (2.3).	
	β-caryophyllene (19.26), eugenol (20.50), 1,8-cineole (20.02), γ-	[43]
	elemene (14.44).	
	Eugenol (64.8), (E)-β-caryophyllene (14.3), bicyclogermacrene	[52]
	(8.1), elemicin (2.0).	
	Other compounds (%)	
	Methanol extract: Ursolic acid (1.05)	[30]
	Ethanolic extract: Eugenol (59%), 2-methoxy-4-vinylphenol (8%),	[38]
	2-hydroxy-1,8-cineole (6%), 4-vinylphenol (5%)	
O. selloi	Major constituents of EO (%)	
	Methyl chavicol (55.3), trans-anethole (34.2), cis-anethole (3.9),	[25]
	caryophyllene (2.1).	[=0]
	Methyl chavicol (93.3), β-caryophylene (2.2), germacrene D	[31]
	(1.3), spatulenol (1.3).	[51]
		[52]
	Anethole (64.6), linalool (20.6), 1,8-cineole (7.4), tetracontane (2.2).	[52]
		[40]
	Anethol (52.2), linalool (16.8), 1,8-cineole (7.4), p-Methoxy-	[42]
	Cinnamaldehyde (2.9).	
	Cinnamaldehyde (2.9). Other compounds	
	Cinnamaldehyde (2.9). Other compounds Methanolic extract: Ursolic acid (0.45%).	[30]
	Cinnamaldehyde (2.9). Other compounds Methanolic extract: Ursolic acid (0.45%). Rosmarinic acid, lithospermic acid, vanilic acid, p-coumaric acid,	[30] [46]
	Cinnamaldehyde (2.9). Other compounds Methanolic extract: Ursolic acid (0.45%).	

O. Tenuiflorum	Major constituents of EO (%)	
(Sanctum)	β-Bisabolen (20.99), 1,8-cineole (20.78), eugenol (15.70), γ- elemene (10.47).	[53]
	Camphor (31.52), eucalyptol (18.85), eugenol (13.77), ocimene (7.12).	[54]
	Eugenol (22.0), β-elemene (19.2), β- caryophylene (19.1), germacrene D (5.03).	[55]
	Eugenol (58.20), germacrene D (11.68), cis-β-ocimene (10.79), β-caryophyllene (4.31)	[56]
	Macro and micronutrients (ppm)	
	Mn (61.75), Zn (32.38), Cu (14.48), Ni (5.67).	[57]
	Mg (1.8 to 4.8), K (49.8 to 3969.4), Ca (35.98 to 1950.2), P	[29]
	(1005.4 to 1960.5), Na (269.4 to 813.4), Fe (2.2 to 161.8), Zn	
	(0.8 to 1), protein (33), carbohydrate (45), thiamin (4.8), riboflavin (2.4), niacin (2.7).	
	K (52.60), Na (680), Zn (81.66), Mn (51.35), Cu (12.31), P (10.90), Mg (1.05), Ca (1.00), crude fibers (90.900), crude proteins (174.500).	[58]
	Other compounds	
	Methanolic extract: Ursolic acid (2.02%).	[30]
	Oleanolic acid, rosmarinic acid, ursolic acid, luteoline.	[59]
	Apigenin, myrcetine, vicenine, kaempferol.	[43]
	Methanolic extract: orientine, vicenine and luteoline.	[28,60]
	Ethanolic extract: Luteoline, orientine, ursolic acid, apigenin-7-	[61]
	oglucuronide, luteolin-7-O-glucuronide, isorientine, aesculine,	
	triacontanolferulate, vallinin acid, gallic acid, circineol,	
	stigmasterol, caffeic acid, 4-hydroxybenzoic acid, chlorogenic acid, procatechic acid, phenylpropaneglucoside, β-stigmasterol.	

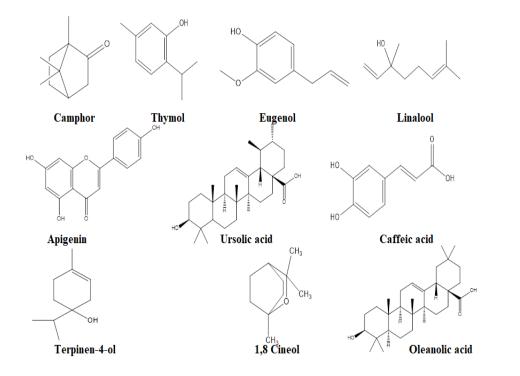


Fig. 1. Chemical structures of some molecules identified in EO and isolated from extracts of some species of *Ocimum* genus

Aqueous and ethanol extracts of *O. basilicum* demonstrated an antiviral activity against ADV-3 (174.1  $\mu$ g/mL and >1000  $\mu$ g/mL respectively), ADV-8 (129.6  $\mu$ g/mL and > 200  $\mu$ g/mL respectively) and ADV-11 (129.1  $\mu$ g/mL and 91.9  $\mu$ g/mL respectively). While the ursolic acid isolated from *O. basilicum* displayed an

antiviral activity against ADV-8 with 50% of inhibition with a concentration of 4.2  $\mu$ g/mL [68].

Table 2 summarizes some *Ocimum* species that have demonstrated antiviral effect against several DNA and RNA viruses.

Plants species	Chemical components	Mode of action	Type of virus	References
O. basilicum	1,8-cineole Camphor, Thymol.	Destruction of the viral envelope preventing entry of the virus into the host cell.	HSV 1 et 2(DNA enveloped virus)	[69]
	Eugenol, Eugenol epoxide	Inhibition of virus replication	HIV-1(RNA non- enveloped virus	[70]
	Apigenine	Inhibition of virus replication	HSV, ADV-3,8, 11 (DNA non- enveloped virus), HBV (DNA enveloped virus), EV (RNA non- enveloped virus), CVB1 (RNA non- enveloped virus)	[71]
	Linalool	-	ADV-3,8,11, HBV,	-
	Ursolic acid		ADV-8,11, HSV, HBV, EV, CVB1	
O. sanctum	Ursolic acid, Eugenol, 1,8- cineole	Inhibition of virus replication	HSV-1,2	[66]
	Rosmarinic acid	Inhibition of replication and protease.	HSV-1,2	[71]
O. gratissimum	Eugenol	Inhibition of virus replication	HSV-1,2	[34,72]
	Thymol	Direct destruction of the virion	HSV-1	[16,73]
O. campechianum	β-caryophyllene	Inhibition of virus replication	HSV-1,2	[13,74]
	1,8-cineole	Nucleocapsid (N) protein destruction of the virus	IBV	[36,75]
O. americanum	Rosmarinic acid	inhibit viral IRES	EV71	[46,76]
(canum)	Oleanolic acid	inhibits the HIV-1 protease	HIV-1	[19]
O. citriodorum	Caffeic acid	Inhibit the multiplication	HSV-1	[46,77]
	Linalool	Not determined	AVD-II	[21]
O. kilimands	1,8-cineole	Inhibit the multiplication	IBV	[47]
charicum guerke	Terpinen-4-ol		HSV-1	[74]
O. micranthum	Ursolic acid	Inhibit the multiplication	HCV (RNA)	[30]
O. selloi	Trans-Anethole	Inhibit the multiplication	HSV-1,2	[74]

# Table 2. Antiviral activity of some Ocimum species

HHV: Human Herpes Virus, VACV: Vaccinia Virus, IHNV: Infectious Hematopoietic Necrosis Virus, OMV: Oncorhynchus Masou Virus, BHV-1: Bovine Herpes Virus-1

#### 3.1.3 Toxicological activities

*Ocimum* species have been in different traditional recipes to prevent and cure many diseases. Most plants belonging to this family are generally edible. Given their phytochemical composition rich in secondary metabolites and nutrients, all these molecules can at a certain degree of concentration, have a certain intrinsic toxicity towards animals. Few studies reported that the species of the genus *Ocimum* may or may not present a slight toxicity, which depends on geographical parameters [78,79].

## 3.2 Discussion

Knowing that most species of the genus *Ocimum* are responsible for several biological activities, this review confirms their antiviral activity which is due to their varied chemical composition and which depends on the geographical distribution and ecological conditions.

Several pure compounds isolated and identified from EO extracts (eugenol, methyleugenol, carvacrol, linalool, 1,8-cineole, apigenin, ursolic acid, oleanolic acid, luteoline, quercetin) and from certain species of the *Ocimum* genus have showed activity against certain DNA and RNA viruses like HSV, HIV, NDV, DENV, CMV, CVB, HPAI (H5N1), EV71, HBV, etc., some of which cause respiratory and gastrointestinal disorders [68].

Others compounds such as kampferol, quercetin, apigenin, catechin and ursolic acid generally found in *Ocimum* species are potential inhibitors of SARS-CoV-2 protease, which would suggest that these species have an anti SARS-CoV-2 effect [80,81].

Molecular docking is an important tool that explores non covalent interactions mainly hydrogen bonds,  $\pi/\pi$  and van der Waals interactions that are established between proteins and ligands [82,83]. Kumar et al. have carried out molecular docking calculations on some compounds derived from *O. sanctum* (methyl eugenol, rosmarinic acid, oleanolic acid and ursolic acid) and found that these compounds bind to the spike glycoproteins of the SARS-CoV-2, thus preventing attachment of the virus to the host cell and viral replication [84].

It should be noted that, despite the variable chemical composition depending on geographic

parameters, most species of the genus *Ocimum* are used for their innumerable biological activities including antiviral activity. In addition, at least two majority molecules found respectively in EO and in the extracts of some species cited in this study, have been reported to have antiviral activity, which would indicate that all these species could be used against viral diseases including COVID-19.

# 4. CONCLUSION

The main objective of this study was to collect information on phytochemistry and the ability of a few species of the *Ocimum* genus to treat certain viral diseases.

Confronting this new coronavirus, the lack of effective therapy and vaccine, the urgency is imperative to find alternatives. Beside the barrier measures recommended by WHO and which are of strict and compulsory application for limiting the spread of SARS-CoV-2, scientific work is directed towards medicinal plants for their capacity to strengthen the immune system and to search for the antiviral potential.

The involvement of certain molecules contained in essential oils and extracts of species of the *Ocimum* genus in the inhibition of the attachment of glycoproteins on the surface of SARS-CoV-2 allows the prevention of viral replication and thus strengthens the immune system. *Ocimum* species may be considered as potential candidates in the management of COVID-19.

# CONSENT

It is not applicable.

# ETHICAL APPROVAL

It is not applicable.

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# **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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