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In silico identification of compounds from *Nigella sativa* seed oil as potential inhibitors of SARS-CoV-2 targets

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Abstract

Background: The growing number of cases, severity and fatality of the COVID-19 pandemic, coupled with the fact that no cure has been found has made infected individuals especially in Africa, to resort to the consumption of different natural products to alleviate their condition. One of such plant materials that have been consumed to remedy the severity of this viral infection is the oil of *Nigella sativa* seed commonly called black seed oil. In this study, we extracted and characterized the oil from this seed using gas chromatography coupled to a mass selective detector to identify the component phytochemicals. Site-directed multiligand docking of the identified compounds was performed on SARS-CoV-2 molecular targets- Replicase polyprotein 1a, RNA binding protein of NSP9, ADP ribose phosphatase of NSP3, 3-chymotrypsin-like protease 3CLpro, and RNA-dependent RNA polymerase RDRP, and ACE2-angiotensin-converting enzyme from the Homo sapiens.

Results: The binding affinity of caryophyllene oxide was the highest on 3CLpro (− 6.0 kcal/mol), NSP3 (− 6.3 kcal/mol), NSP9 (− 6.3 kcal/mol), and RDRP (− 6.9 kcal/mol) targets, while α -bergamotene gave the best binding affinity on RPIA (5.7 kcal/mol) target. The binding affinity of β -bisabolene on the ACE2 target (− 8.0 kcal/mol) was almost the same as Remdesivir (− 8.1 kcal/mol). The ADMET properties of these three phytochemicals showed that they are good drug leads for these SARS-CoV-2 receptors.

Conclusion: The findings from this study strongly indicate that the reported recovery from COVID-19 infection claimed by patients who consumed black seed oil could be linked to the presence of caryophyllene oxide, α -bergamotene, and β -bisabolene in this natural product.

Keywords: *Nigella sativa*, Angiotensin-converting enzyme, SARS-CoV-2, β -bisabolene, Binding affinity

Background

Black cumin, scientifically known as *Nigella sativa* L., is an annual dicotyledonous herb that belongs to the family Ranunculaceae (Datta et al. 2012). It is a small shrub ranging between 20 and 90 cm in height, with tapering green leaves and rosaceous pink, purple, white, yellow, or pale blue flowers with 5–10 petals. Flowering starts in July and the seeds ripen in September. The ripe fruit

is a capsule with 3–7 united follicles containing numerous tiny, pitch-black seeds with an aromatic and slightly bitter taste (Ahmad et al. 2013). It is native to north-eastern Africa, the eastern Mediterranean, and south-western Asia (Vavilov and Dorofeev 1992). The species is grown in many countries like India, Turkey, Middle East, Pakistan, Syria, and Saudi Arabia (Naz 2011). The seeds of *N. sativa* have been widely used as diuretics, anti-diarrheal, analgesic, antibacterial, antidiabetic, anti-cancer, immunomodulator, anti-inflammatory, spasmolytic, bronchodilator, hepatoprotective, renal protective, gastro-protective, antioxidant, etc. (Ahmed et al. 2013; Sultan et al. 2014).

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The chemical composition of seed extracts of *N. sativa* seed varies from one country to another and also from one region in a country to another (Shariq et al. 2015). The major components in *N. sativa* seed are fatty oils and aliphatic hydrocarbons, arachidonic acid, tocopherols, γ -linolenic acid, and essential oil, which contains carvacrol, p -cymene, thymoquinone, α -pinene, and indazole-type alkaloids, isoquinoline alkaloids, as well as dolabellane-type diterpene alkaloids. The food and therapeutic applications of *N. sativa* oil and seed have a long history in many cultures. Islamic medicine also cataloged the numerous benefits of this plant (Sharma et al. 2009). Its compounds have been shown to have various pharmacological effects on different body parts. Empirical studies have reported that the seed oil and seed extracts have antimicrobial activities, which some workers have attributed to the presence of compounds such as thymohydroquinone and melanin (Kalim 2013; Al Yahya 1986). The seed extract contains numerous antioxidants like carvacrol, t -anethole, and 4-terpineol, and their activities have been reported in different studies (Awadalla 2012). Also, available reports have shown the anti-inflammatory, anti-cancer, anti-diabetic, and hepatoprotective activities of its oil and extracts (Umar et al. 2012; Peng et al. 2013; Abdelmeguid et al. 2010).

The Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) began in Wuhan, China, and was reported to the World Health Organization on December 31, 2019 (WHO 2020). The pandemic ravaged the entire globe, claiming hundreds of thousands of lives. Community to community transmission is now evident in many countries, with a daily rise in the number of cases. There are potential drug targets essential for the survival of the coronavirus, which include a 3-chymotrypsin-like protease (3CLpro), Angiotensin-converting enzyme (ACE2), ADP ribose phosphatase of Nonstructured Protein 3 (NSP3), Nonstructured Protein 9 RNA binding protein (NSP9), RNA-dependent RNA polymerase (RdRp), and Replicase Polyprotein 1a (RP1a). To infect the host, the structural spike glycoprotein interacts with the transmembrane protein of the human host cell receptor ACE2 (Guy et al. 2005). The main protease 3CLpro acts in the viral polyprotein large Replicase Polyprotein 1a (RP1a) proteolytic cleavage, cleaving it into functional units to produce non-structural viral constituents like RdRp, NSP3, and NSP9. This makes 3CLpro and ACE2 important drug targets to inhibit Nonstructured Proteins production and terminate viral action. The RP1a and the NSPs (RdRp, NSP3, and NSP9) are important targets involved in the replication and translation process, which lead to a viral proliferation in host cells (Kumar et al. 2020). In vitro and in silico studies of possible cures for this dreaded disease have

become hot topics in current research. Although no drug is currently available to cure this disease, Remdesivir, an antiviral drug has been clinically tested and confirmed useable in the interim (Williamson et al. 2020).

Recently, the governor of Oyo State in Nigeria revealed that the oil from *N. sativa* seed was one of the remedies he consumed to combat the disease, a week after he tested positive for COVID-19 (Punch Newspaper, April 7, 2020). So far, no attempt has been made to investigate the veracity of this claim. In this study, the oil from the seed of *N. sativa* was extracted, and the identified phytochemical components docked on some selected SARS-CoV-2 proteins. The dock scores of these compounds were compared to the values obtained with a standard COVID-19 prescription drug.

Methods

Sample collection and preparation

Mature seeds of *N. sativa* were collected toward the end of rainy season in October 2020 (average temperature 29 °C), from a fallow farmland in Northern Nigeria (N 10° 9' 32.2524", E 8° 8' 1.8816"), and no permissions or licenses were required for the collection and study. They were identified by a professional taxonomist Prof. F.N. Mbagwu of the Department of Plant Science and Biotechnology, Imo State University, Owerri, Nigeria, and the voucher specimen was deposited at the Imo State University Herbarium, with herbarium number IMSUH-468. They were washed with tap water and left to dry on a laminated paper for one week under room conditions. The dried seeds were subjected to preliminary grinding using mortar and pestle, and the particle size was further reduced using an electric blender. The seed powder was transferred in an airtight plastic container and stored in a refrigerator at 4 °C.

Extraction of oil

Oil was extracted from the ground seed powder using a Soxhlet apparatus mounted on a heating mantle (Duru 2020). The seed powder of weight 100 g was encapsulated in a clean white cotton cloth previously degreased in hexane ($\geq 98.5\%$, Sigma-Aldrich, Darmstadt, Germany). The sample was held in the thimble-holder of the extractor which was gradually filled with condensed redistilled hexane from a distillation flask placed on a heating mantle. When the solvent reaches the overflow level in the thimble-holder, it is siphoned back into the distillation flask, carrying the extracted oil with it. The operation was repeated until complete extraction was achieved. The extracted oil was then recovered from the solvent by rotary evaporation.

Characterization of oil

The oil sample was characterized using gas chromatography-mass Spectrometer (GC-MS) instrument (Model: 7890 GC and 5977B MSD, Agilent Technologies, USA). An HP-5 MS capillary standard nonpolar column L × I.D., 30 m × 0.25 mm and film thickness 0.25 μm was used. The flow rate of mobile phase (carrier gas: He) was set at 1.0 mL/min. In the gas chromatography part, the temperature program (oven temperature) was set at 40 °C and raised to 250 °C at 5 °C/min and injection volume 1 μL. The oil sample was dissolved in methanol (≥ 99.8%, Sigma-Aldrich, Darmstadt, Germany) and fully scanned at a range of 40–650 m/z, and the results were compared using NIST mass spectral library search program (El-Sawi et al. 2020).

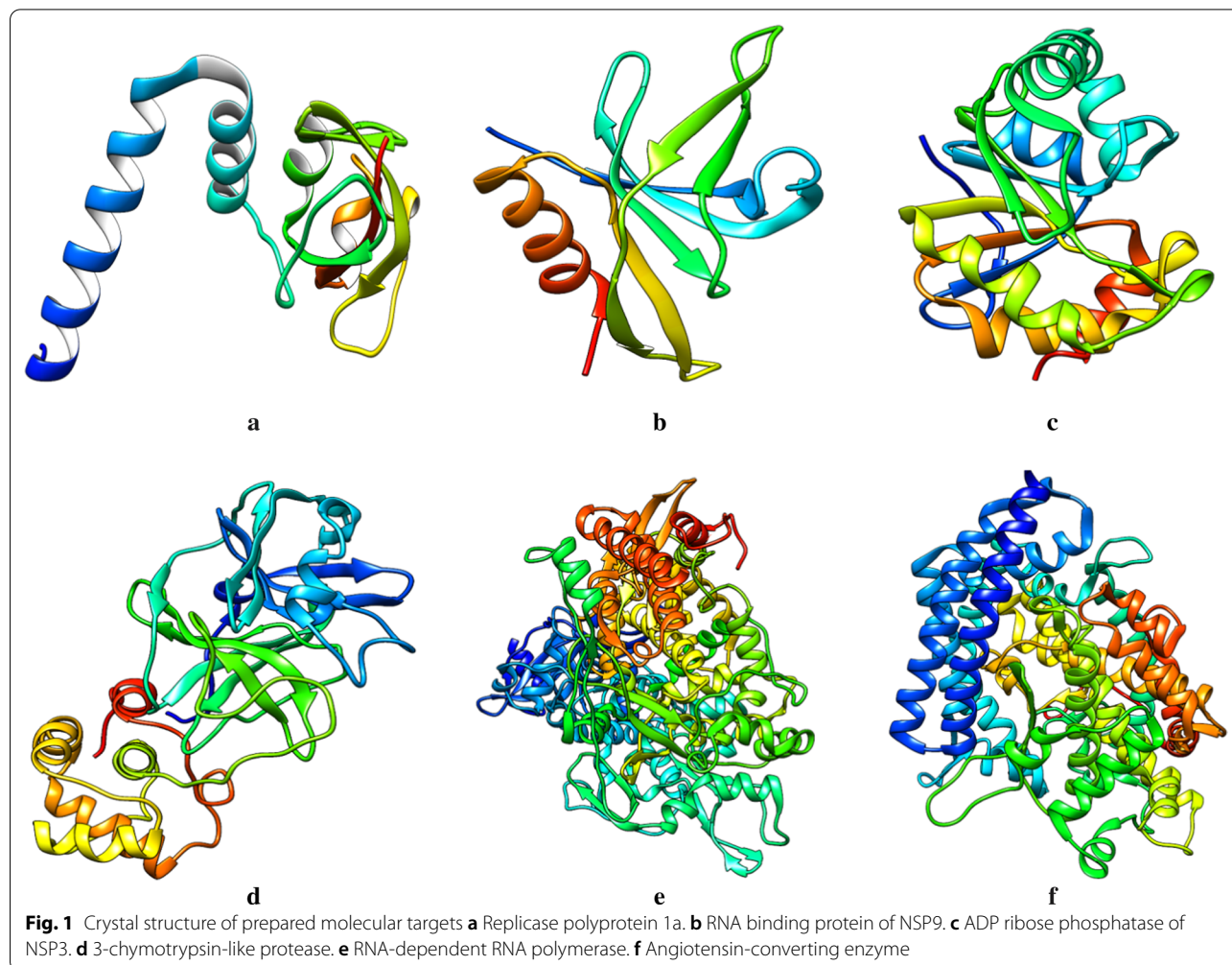
Identification and preparation of ligands

The 3D structure-data files (SDF) of the compounds in the crude oil sample were identified and downloaded from the PubChem database. They were minimized in

PyRx virtual screening tool, using Universal Force Field at 200 steps. They were then converted to AutoDock ligands (pdbqt) and used for the docking analysis.

Identification and preparation of molecular targets

Five SARS-CoV-2 molecular targets (Fig. 1), Replicase polyprotein 1a (6YHU), RNA binding protein of NSP9 (6W4B), ADP ribose phosphatase of NSP3 (6VXS), 3-chymotrypsin-like protease 3CLpro (6LU7) and RNA-dependent RNA polymerase RDRP (7BTF), and one protein of host, ACE2-Angiotensin-converting enzyme (6LZG), were identified from literature (Konkolova et al. 2020; Tan et al. 2020; Michalska et al. 2020; Jin et al. 2020; Gao et al. 2020; Wang et al. 2020) and downloaded from the Protein Data Bank (PDB). The interfering crystallographic water molecules and cocrystallized ligand were removed, and minimization of the energy of the protein was then done using UCSF Chimera 1.14 (Pettersen 2004; Duru et al. 2020). The protein was minimized at 300 steepest descent steps at 0.02 Å. The conjugate gradient



steps were 10 at 0.02 Å and 10 update intervals. Gasteiger charges were added using Dock Prep to get a good structure conformation.

Determination of active sites on SARS-CoV-2 proteins

The active sites of the proteins were determined using CASTp (Computed Atlas for Surface Topography of Proteins).

(Tian et al. 2018; http://sts.bioe.uic.edu/castp/index.html?j_5f45dd381f58d).

Docking procedure and analysis of results

The screening of the phytochemical compounds from the oil was performed by docking them on selected binding pockets of SARS-CoV-2 proteins and ranked based on their binding energies. The multiple docking of the ligands and proteins was done with Autodock Vina in PyRx software (Tsao et al. 2020; Johnson et al. 2020). The molecular docking results were organized on an Excel spreadsheet, and the Heat Map of the data was viewed using the Conditional Formatting function.

Absorption, distribution, metabolism and elimination and toxicity (ADMET) analysis

The compounds with the lowest binding energy for each protein were selected and submitted to the ADMETSar 2 server to examine their drug-like properties, pharmacokinetics, and pharmacodynamics parameters (Yang et al. 2019).

Analysis of protein–ligand interactions

The interactions between the most potent compounds in the oil and amino acid residues of the proteins were visualized using Biovia Discovery studio client 20.1 (BIOVIA 2020) and UCSF Chimera software.

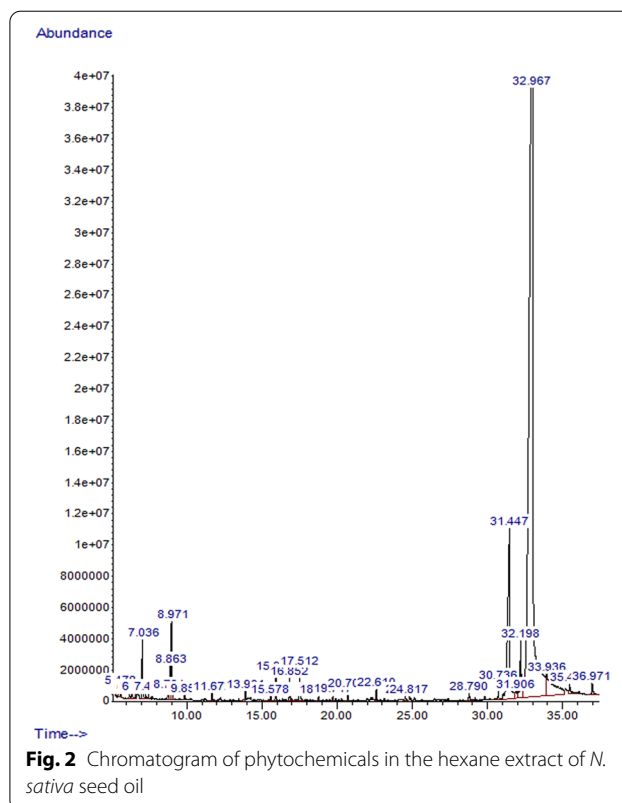
Results

Chemical composition of oil extract

The GC–MS analysis of *N. sativa* seed oil gave 27 peaks for the compounds detected, and the chromatogram is shown in Fig. 2.

The elution information of the compounds and their therapeutic uses are summarized in Table 1.

The phytochemical components were present in the order linoleic acid > palmitic acid > methyl linoleate > D-limonene > 2,4-decadienal, (E,E)- > (Z)-hept-2-enal > m-cymene > 2-decenal, (E)- > 9,17-octadecadienal, (Z)- > methyl palmitate > β-pinene > 1,2-dimethylcyclopentan-1-ol = myristic acid > α-bergamotene = β-bisabolene > α-pinene > trans-4-methoxy thujane > 1-cynaopyrrolidine > terpineol > α-thujene = γ-terpinene > 1,3-dimethylcyclohexanol > caryophyllene oxide > thymoquinone > tetradecane > geranyl-2-methylb-



utyrate > hexadecane (Fig. 3). About 90% of the entire oil was comprised of linoleic acid (79.61%) and palmitic acid (10%).

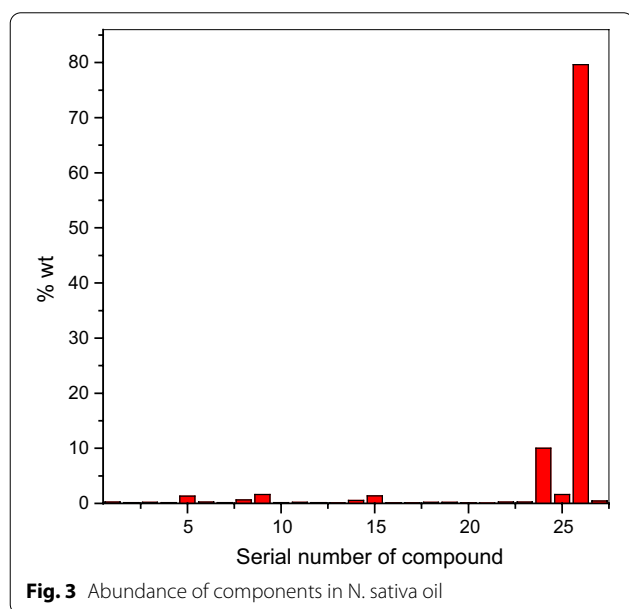
The binding affinities of the compounds from the oil extract to the SARS-CoV-2 receptors are shown in Table 2.

Discussion

Most of the identified phytochemicals in *N. sativa* seed oil have previously been reported to show antidiabetic, anti-inflammatory, antioxidant, anticancer, antimicrobial, anti-arthritic, anticonvulsant, antiulcer, antihypertensive, anti-nociceptive, hepatoprotective, cytotoxic, antimycomicrobial, antiparasitic, and analgesic activities (Marques et al. 2019; Caboni et al. 2012; Begum et al. 2016; Lang and Buchbauer 2012; Balamurugan et al. 2013; Muniyan and Gurunathan 2016; Saeed et al. 2012; Zhao et al. 2018; Adeoye-Isijola et al. 2018; Wu et al. 2017; Chavan et al. 2009; Yimer et al. 2019; Hadi et al. 2016; Engels and Brinkmann 2017). These compounds showed varying degrees of binding on the SARS-CoV-2 protein targets (Table 2), as revealed by the change in Gibb's free energy values (ΔG) (Duru and Duru 2020). The FDA emergency approved drug Remdesivir (Williamson et al. 2020), administered on adults and children with suspected or confirmed cases of COVID-19,

Table 1 Phytochemical compounds identified in *N. sativa* seed oil

Peak	% wt	Name of compound	PubMed CID	Therapeutic uses
1	0.22	1,2-dimethylcyclopentan-1-ol	551296	Still unknown
2	0.14	α -thujene	17868	Anti-inflammatory; anti-arthritic; antimicrobial
3	0.19	α -pinene	6654	Anti-inflammatory; antioxidant; anticancer; antimicrobial
4	0.13	1,3-dimethylcyclohexanol	558957	Still unknown
5	1.30	(Z)-hept-2-enal	5362616	Still unknown
6	0.23	β -pinene	14896	Antimicrobial
7	0.17	1-cynaopyrrolidine	73737	Still unknown
8	0.63	m-cymene	10812	Anti-inflammatory
9	1.61	D-Limonene	440917	Anti-inflammatory; anticancer; antimicrobial
10	0.14	γ -Terpinene	7461	Anti-inflammatory; antioxidant; antimicrobial
11	0.18	Trans-4-methoxy thujane	–	Antimicrobial
12	0.15	Terpineol	17100	Antioxidant; anticancer; anticonvulsant; antiulcer; anti-hypertensive; anti-nociceptive
13	0.11	Thymoquinone	10281	Anti-inflammatory; hepatoprotective; antioxidant; anticancer; cytotoxic
14	0.52	2-decenal, (E)-	5283345	Antinematocidal
15	1.39	2,4-decadienal, (E,E)-	5283349	Antinematocidal
16	0.08	Geranyl-2-methylbutyrate	6437648	Still unknown
17	0.09	Tetradecane	12389	Antimicrobial
18	0.20	α -bergamotene	86608	Antimicrobial
19	0.20	β -bisabolene	10104370	Antimicrobial; Anti-ulcer
20	0.12	Caryophyllene oxide	1742210	Anti-inflammatory; antimicrobial; antiparasitic; analgesic
21	0.06	Hexadecane	11006	Antibacterial
22	0.22	Myristic acid	11005	Antimycobacterial
23	0.25	Methyl palmitate	8181	Anti-inflammatory
24	10.00	Palmitic acid	985	Antioxidant; antibacterial; anti-inflammatory; antitumor
25	1.62	Methyl linoleate	5284421	Antioxidant
26	79.61	Linoleic acid	5280450	Antidiabetic
27	0.44	9,17-Octadecadienal, (Z)-	5365667	Anti-inflammatory; antioxidant



was used as a control to identify compounds with good binding affinities for the studied COVID-19 proteins. Caryophyllene oxide had the best binding affinities on 3CLpro (– 6.0 kcal/mol), NSP3 (– 6.3 kcal/mol), NSP9 (– 6.3 kcal/mol), and RDRP (– 6.9 kcal/mol) targets. The compound α -bergamotene gave the best binding affinity on RPIA (5.7 kcal/mol), while β -bisabolene displayed an excellent binding affinity on the ACE2 protein target. These values were very close to those obtained using the antiviral control drug. The binding affinity of β -bisabolene (– 8.0 kcal/mol) was almost similar to Remdesivir (– 8.1 kcal/mol) on the ACE2 target. This observation is an indication that β -bisabolene could prevent the interaction of the spike glycoprotein of the virus with the ACE2 protein of the human host cell, thereby preventing infection of the host.

The structures of the compounds with the highest docking scores for the studied proteins are shown in Fig. 4. The absorption, distribution, metabolism,

Table 2 Binding affinities of compounds in the oil of *N. sativa* seed for SARS-CoV-2 proteins

Compound	ΔG Energy (Kcal/mol)					
	3CLpro	ACE2	NSP3	NSP9	RDRP	RP1A
1,2-dimethylcyclopentan-1-ol	-4.2	-5.0	-3.9	-4.2	-4.5	-3.5
α -thujene	-4.7	-6.6	-4.8	-5.0	-5.8	-4.4
α -pinene	-4.7	-5.2	-4.8	-4.7	-5.8	-4.4
1,3-dimethylcyclohexanol	-4.5	-5.0	-4.4	-4.4	-5.1	-3.8
(Z)-hept-2-enal	-3.8	-5.0	-3.8	-4.0	-4.3	-3.4
β -pinene	-4.8	-5.2	-4.8	-4.7	-5.7	-4.4
1-cynaopyrrolidine	-3.8	-4.7	-3.4	-3.4	-4.3	-3.0
m-cymene	-5.0	-6.9	-4.9	-5.4	-5.8	-4.8
D-Limonene	-5.0	-6.8	-4.8	-5.1	-5.6	-4.6
γ -Terpinene	-5.0	-7.0	-4.7	-5.2	-5.7	-4.9
Trans-4-methoxy thujane	-5.0	-5.4	-4.9	-5.0	-5.3	-4.4
Terpineol	-5.3	-6.8	-5.1	-5.3	-6.2	-4.7
Thymoquinone	-4.9	-7.0	-5.2	-5	-5.7	-5.0
2-decenal, (E)-	-3.7	-5.6	-4.2	-4.2	-4.5	-4.0
2,4-decadienal, (E,E)-	-4.2	-5.7	-4.5	-4.8	-5.0	-4.2
Geranyl-2-methylbutyrate	-5.1	-6.4	-5.7	-5.3	-5.6	-5.1
Tetradecane	-3.8	-5.7	-4.2	-4.1	-4.2	-4.3
α -bergamotene	-5.4	-6.2	-6.1	-5.7	-6.2	-5.7
β -bisabolene	-5.5	-8.0	-5.7	-6.2	-6.0	-5.1
Caryophyllene oxide	-6.0	-5.9	-6.3	-6.3	-6.9	-5.5
Hexadecane	-3.9	-4.7	-4.4	-4.0	-4.6	-3.8
Myristic acid	-4.6	-4.9	-4.6	-4.5	-5.1	-4.2
Methyl palmitate	-3.8	-5.1	-4.9	-5.0	-4.9	-4.6
Palmitic acid	-4.4	-5.2	-4.7	-4.4	-5.1	-4.2
Methyl linoleate	-4.2	-4.9	-4.7	-5.4	-5.3	-4.8
Linoleic acid	-5.0	-5.7	-5.2	-4.9	-5.5	-5.1
9,17-Octadecadienal, (Z)-	-4.2	-6.0	-4.6	-4.3	-4.8	-4.2
Remdesivir (Control drug)	-7.8	-8.1	-7.2	-6.8	-8.0	-6.0

Key: ■ Good ■ Fair ■ Poor

excretion, and toxicity (ADMET) properties which show their pharmacokinetics and pharmacodynamics properties are summarized in Table 3. Lipinski's rule of

five, which is determined by a complex balance of various molecular properties and structural features such as lipophilicity, electronic distribution, hydrogen bonding

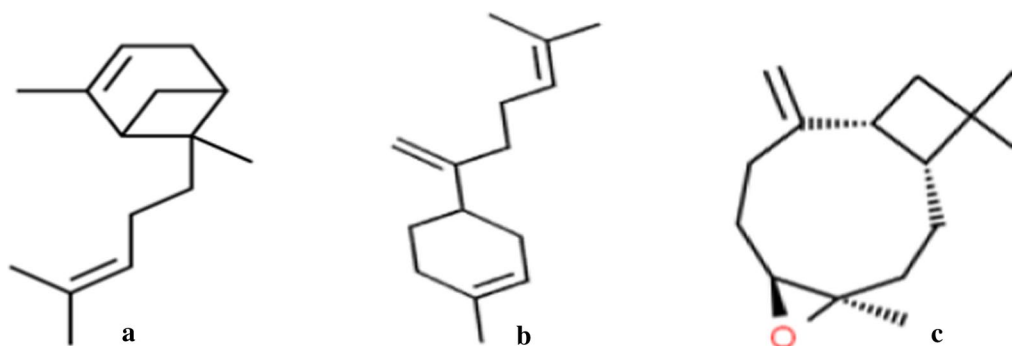


Fig. 4 Structures of **a** α -bergamotene, **b** β -bisabolene, **c** Caryophyllene oxide

Table 3 ADMET properties of α -bergamotene, β -bisabolene, and Caryophyllene oxide relative to Remdesivir

ADMET properties	α -bergamotene	β -bisabolene	Caryophyllene oxide	Remdesivir
Molecular weight	204.36	204.36	220.36	602.56
WlogP	4.7	5.0	3.9	2.2
H-bond acceptor	0	0	1	13
H-bond donor	0	0	0	4
Rotatable bonds	3	3	0	13
Blood–brain barrier	+	+	+	+
Carcinogenicity (binary)	–	–	–	–
Human intestinal absorption	+	+	+	+
Acute oral toxicity	2.32	2.05	2.24	3.43
Water solubility	– 4.97	– 4.89	– 3.45	– 4.12

characteristics, molecule size, and flexibility, as well as the presence of various pharmacophores that influence the behavior of a molecule in a living organism, were used to predict the drug likeliness of the compounds. A good drug candidate should not violate more than one of the rules (Lipinski 2016).

The molecular weights of the compounds were < 500, and their hydrophobicity (log P) did not exceed 5. The hydrogen bond donor (≤ 5 hydrogens) and hydrogen bond acceptor (not more than 10 hydrogens) of the compounds were in line with the rule. The rotatable bonds (not more than 3) were in line with the rule of three, and their acute oral toxicity values were well below 5 mg/kg. Caryophyllene oxide is soluble in water, while α -bergamotene and β -bisabolene are moderately soluble. The human intestinal adsorption and blood–brain barrier of the compounds were very high, and the compounds were not carcinogenic. These results are indications that α -bergamotene, β -bisabolene, and caryophyllene oxide are excellent drug candidates (Zhong 2017).

The 3D and 2D protein–ligand interaction images for α -bergamotene, β -bisabolene, and caryophyllene oxide are shown in Fig. 5. The amino acid residues involved

in the interactions with the compounds and the control drug Remdesivir are depicted in Table 4.

The hydrogen bond, pi-sigma, pi-alkyl, and alkyl type interactions were the main forces that held the compounds in the protein pockets. At least two hydrogen bonds were observed in all the protein–Remdesivir interactions, and one was found only in the RDRP–caryophyllene oxide interaction. The protein–Remdesivir interactions in all the protein pockets had at least two hydrogen bonds and the other interacting forces, in the pockets of the studied proteins. Caryophyllene oxide and Remdesivir interacted with ASN 209 by hydrogen bonding in RDRP, while α -bergamotene and Remdesivir interacted by alkyl forces with ILE 120, ALA 150, and ALA 102. These suggested that the mechanism of inhibition of the proteins at these sites by caryophyllene oxide and α -bergamotene was similar to the action of Remdesivir at those sites.

Conclusions

The phytochemical composition and binding affinity of compounds in the oil extract from *Nigella sativa* seed on SARS-CoV-2 molecular targets were investigated. The

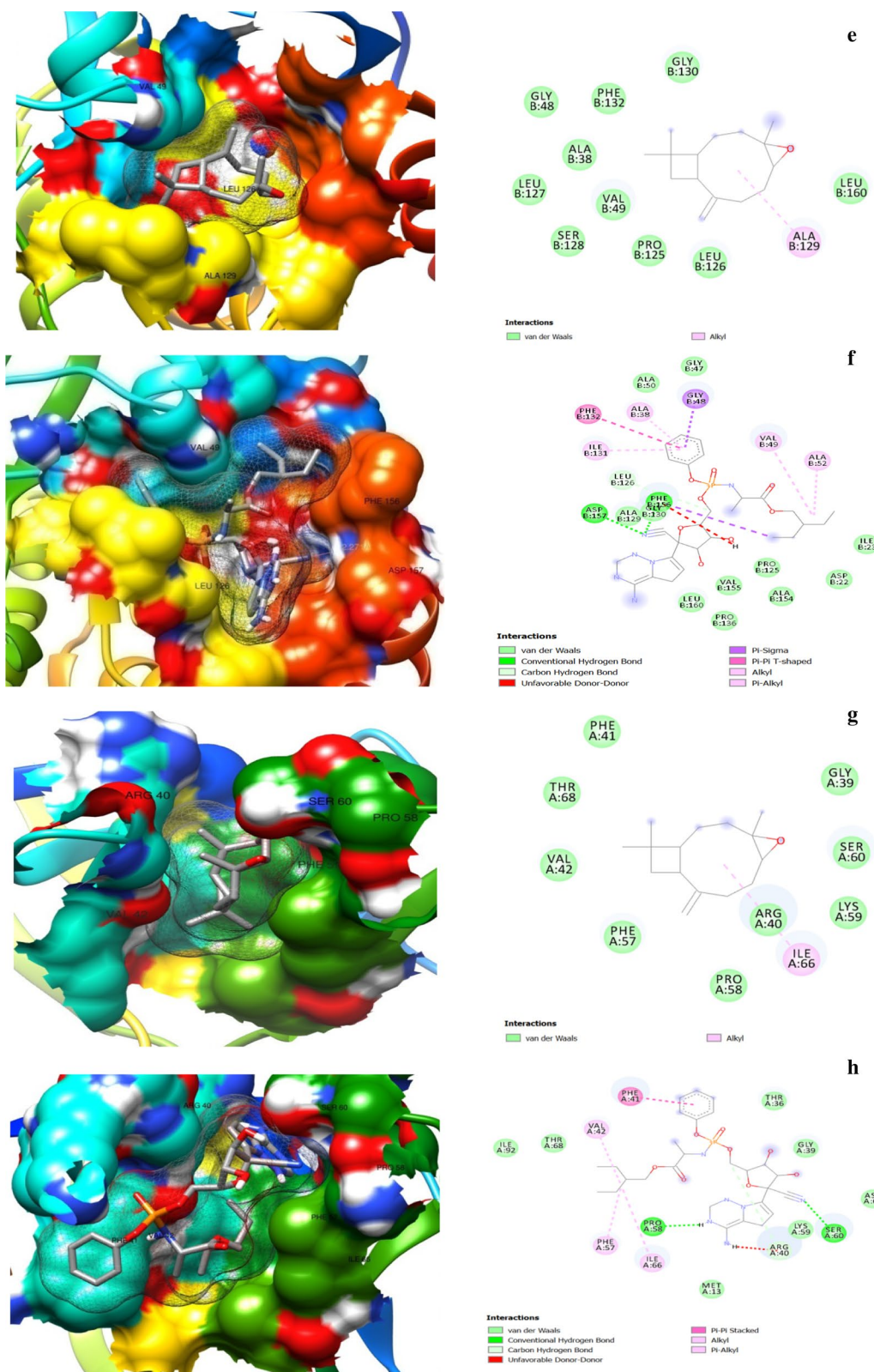


Fig. 5: continued

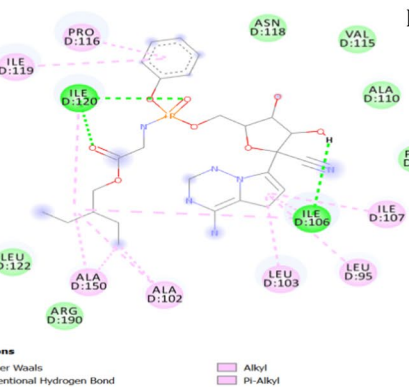
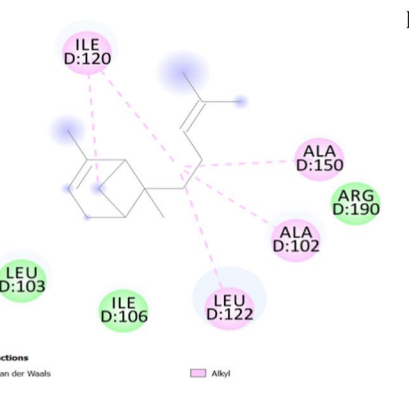
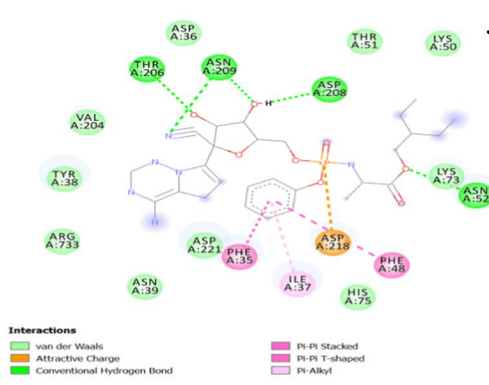
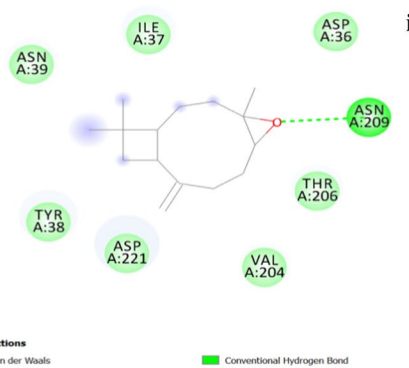
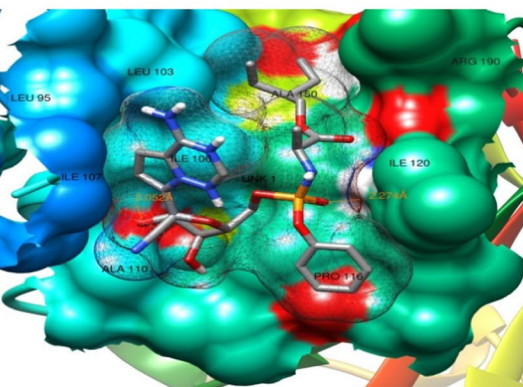
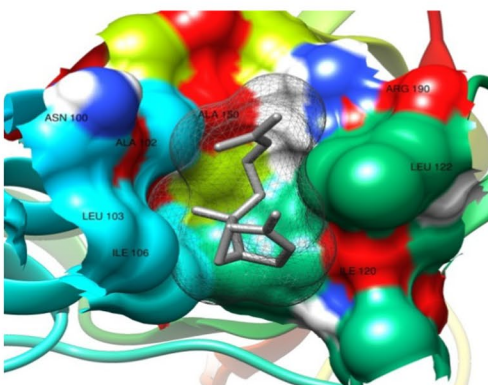
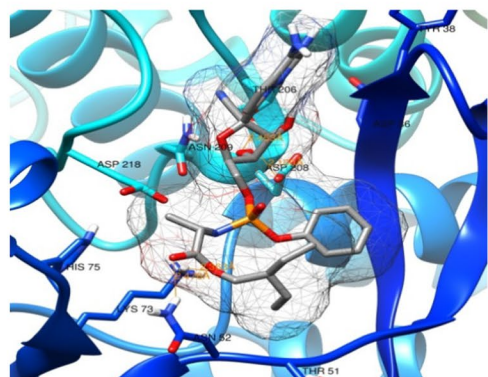
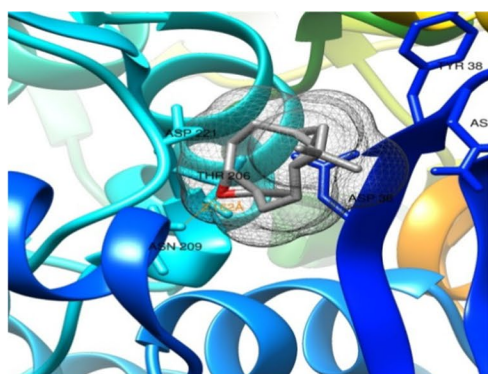


Fig. 5: continued

Table 4 Protein residue interactions with the compounds and Remdesivir

Protein–ligand complex	Interacting residues						
	Hydrogen bond	Unfavorable donor–donor	Pi-sigma	Pi-alkyl	Alkyl	Carbon–hydrogen	Attractive charge
3CLpro-Caryophyllene oxide	–	–	PHE294	–	–	–	–
3CLpro-Remdesivir	SER158; THR111	SER158; THR292	–	–	1LE249; PRO293	–	–
ACE2- β -bisabolene	–	–	–	HIS450; LYS541; LYS441	HIS540; PRO415; PHE438; ILE291	–	–
ACE2-Remdesivir	GLU398; ALA348; ASP350	–	TRP349	TRP349; ARG393	–	GLU402; ALA348; ASP382	ASP382; ASP350
NSP3-Cryophyllene oxide	–	–	–	–	ALA129	–	–
NSP3-Remdesivir	ASP157; PHE156	PHE156	GLY48; PHE156	ALA38; ILE131	VAL49; ALA52	LEU126	–
NSP9-Cryophyllene oxide	–	–	–	–	ILE68	–	–
NSP9-Remdesivir	PRO58; SER60	ARG40	–	VAL42; PHE56	ILE66	ARG40	–
RDRP-Cryophyllene oxide	ASN209	–	–	–	–	–	–
RDRP-Remdesivir	ASN52; THR206; ASN209; ASP208	–	–	ILE37	–	–	ASP218
RP1A- α -bergamotene	–	–	–	–	ILE120; ALA150; ALA102; LEU122	–	–
RP1A-Remdesivir	ILE120; ILE106	–	–	PRO116; ILE119; ILE107; LEU95; LEU103	ILE120; ILE106; ALA150; ALA102	–	–

GC–MS analysis of the oil showed that it contained many compounds with known biological and therapeutic activities. The docking studies of these compounds against some major targets on the SARS-CoV-2 revealed that caryophyllene oxide, α -bergamotene, and β -bisabolene were promising candidates in the inhibition of the activity of these proteins. Their ADMET results further indicated that they would have good pharmacological and pharmacodynamic properties in the human system. There is therefore need for further in vitro, in vivo, and clinical trials to validate the potentials of these compounds in the eradication of the coronavirus pandemic.

Abbreviations

COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; GC–MS: Gas chromatography–mass spectrometer; MSD: Mass selective detector; NIST: National Institute of Standards and Technology; RP1A: Replicase polyprotein; NSP9: Nonstructural protein 9; NSP3: Nonstructural protein 3; 3CLpro: 3-Chymotrypsin-like protease; RDRP: RNA-dependent RNA polymerase; ACE2: Angiotensin-converting enzyme; CASTp: Computed atlas for surface topography of proteins; ADMET: Absorption, distribution, metabolism and elimination and toxicity; FDA: Food and drug administration; TYR: Tyrosine; MET: Methionine; TRP: Tryptophan; ILE: Isoleucine; SER: Serine; ALA: Alanine; PHE: Phenylalanine; THR: Threonine; VAL: Valine; ARG: Arginine; PRO: Proline; LEU: Leucine; HIS: Histidine; ASN: Asparagine; GLY: Glycine; LYS: Lysine; GLU: Glutathione.

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Authors' contributions

CED conceived, designed, and wrote the research, and performed the DFT studies. IAD extracted and characterized the oil sample, and proof-read the manuscript. AEA performed the docking studies and post docking analysis. All authors have approved the manuscript in the present form and gave the permission to submit the manuscript for publication. All authors read and approved the final manuscript.

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Declarations

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Not applicable.

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Competing interests

The authors declare that they have no competing interests.

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