Ethnobotanical survey of medicinal plants used by people cured of SARS-CoV-2 in the center of Algeria

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Research

Abstract

Background: The COVID-19 disease has affected more than 760 million people and caused more than 6,780,000 deaths worldwide. These numbers are likely to increase; however, the availability of the SARS-CoV-2 vaccine has slowed its rate of spread. On the other hand, several societies around the world have used many medicinal plants to prevent or treat this disease, particularly in regions with a long history of traditional medicine, like North African countries.

Method: This study was conducted from February to November 2022 in three Algerian provinces (Bejaia, Bouira, and Tizi-Ouzou). The ethnobotanical information was obtained through a direct interview with 459 people cured of COVID-19.

Results: In this investigation, 35 medicinal plants belonging to 21 families were registered, of which 74.29% are local and 25.71% are imported from other countries. The plants mostly used are *Citrus limon* L. (68.49%), *Origanum vulgare* L. (50%), *Syzygium aromaticum* L. (41.66%), *Mentha spicata* L. (35.68%), *Zingiber officinale* Roscoe (26.04%), *Aloysia citrodora* Palau. (21.09%), *Allium sativum* L. (8.59%), *Citrus ×sinensis* L. (8.33%), *Eucalyptus globulus* Labill. (8.07%), and *Allium cepa* L. (7.29%).

Conclusion: This ethnobotanical survey, where information was collected from people cured of COVID-19, is the first in Algeria and probably in the world. Therefore, this study is an interesting contribution to the management of this epidemic, of which at present several cases are recorded throughout the world.

Keywords: SARS-Cov-2, cured people, ethnobotanical survey, Algerian population, medicinal plant

Background

Since its discovery in Wuhan (China) in December 2019, the novel coronavirus, COVID-19 virus or SARS-CoV-2 has affected more than 760 million people and caused more than 6.780.000 deaths worldwide. On January 30, 2020, the World Health Organization (WHO) officially declared the COVID-19 epidemic a public health emergency of international concern (Guo *et al.* 2020).

Coronaviruses are a group of enveloped viruses with a single-strand, positive-sense RNA genome approximately 26–32 kilobases in size (Su *et al.* 2016). They belong to the order Nidovirales, the family Coronaviridae, and the subfamily Orthocoronavirinae (Tang *et al.* 2020). The Orthocoronavirinae comprises four genera, including alpha-CoV, beta-CoV, gamma-CoV, and delta-CoV. SARS-CoV-2 belongs a to beta-coronavirus that is able to infect mammals (Guo *et al.* 2020). SARS-CoV-2 attacks the respiratory system and causes a fatal respiratory disease. Other systems can also be affected by this virus, such as the gastrointestinal system, heart, kidney, liver, and central nervous system (Liu *et al.* 2020).

The images obtained by transmission electron microscopy revealed that SARS-CoV-2 has a spherical form with a diameter varying from about 60 to 140 nm and that its envelope is studded with glycoprotein spikes about 9 to 12 nm, which gave the virus its crown like appearance (Zhu *et al.* 2020). The complete genome sequencing revealed that SARS-CoV-2 RNA has 29.9 kb (Baig *et al.* 2020).

The SARS-CoV-2 virus undergoes mutations over time that give rise to new variants. These mutations can affect the properties of the virus and influence its spread, the severity of the disease it causes, or the effectiveness of vaccines (Grubaugh *et al.* 2021). The WHO reports five variants of concern: alpha, beta, gamma, delta, and omicron (Young *et al.* 2022). Lately, several types of anti-SARS-Cov2 vaccines have been developed, such as mRNA vaccines developed by Pfizer-BioNTech and Moderna; viral vector (adenovirus) vaccines developed by Astra-Zeneca, Johnson & Johnson, Reithera, and Sputnik; inactivated virus vaccines developed by Sinovac, and protein subunit vaccines developed by Novavax (Mascellino *et al.* 2021).

The percentage of deaths and infected cases caused by SARS-CoV-2 differs widely from one country to another. This suggests that environmental factors may be involved, such as diet habits, climate, and the use of traditional treatments (Riggioni *et al.* 2020).

In fact, food types and the attachment of populations to traditional treatments vary considerably from one region to another in the world (Antwi-Baffour *et al.* 2014, Bellik *et al.* 2020). For example, the use of medicinal plants and natural products is more important in poor and developing countries than in developed countries (Mukhtar *et al.* 2008, Mehta *et al.* 2015). In addition, traditional diets, which are usually rich in herbs and spices that contain biologically active components such as antioxidants and immunostimulants, are more commonly followed in less developed societies (Tapsell *et al.* 2006, El Sayed *et al.* 2020).

Although viral infections are treated by synthetic drugs, several virus species remain without an effective remedy to date (Lim *et al.* 2015, Ben-Shabat *et al.* 2020). In such a situation, the bioactive molecules may serve as a proper alternative for treating numerous viral infections with limited side effects (Hussain *et al.* 2017).

Hundreds of bioactive molecules isolated from plants belonging to the alkaloids class, essential oils, phenolic compounds, and vitamins have demonstrated a strong effect against several viral species (Perez 2003, Naithani *et al.* 2010, Khwaza *et al.* 2018, Cui *et al.* 2020), such as influenza virus (Watanabe *et al.* 2014, Dang *et al.* 2015), hepatitis B virus (HBV) (Ortega *et al.* 2019), human immunodeficiency virus (HIV) (Rashed *et al.* 2013), Herpes Simplex Virus (HSV) (Yildirim *et al.* 2016), and severe acute respiratory syndrome coronavirus (SARS-CoV) (Nguyen *et al.* 2012, Chiow *et al.* 2016). Some natural compounds fight especially against the Coronaviridae family, among them oleanane triterpenes from the flowers of *Camellia japonica*, coumarins from *Saposhnikovia divaricata* (Yang *et al.* 2015a, Yang *et al.* 2015b), lectins of several plants (Keyaerts *et al.* 2007), hinokinin (lignin) isolated from some plants such as *Chamecyparis obtusa* (Cui *et al.* 2020), and lycorine of *Lycoris radiata* (Li *et al.* 2005).

Various medicinal plants and foods known for their curative effects have been used in medicine since ancient times (Ben-Shabat *et al.* 2020). The writings indicate that the therapeutic use of natural substances against infectious or non-infectious diseases is as old as 4000–5000 B.C. (Pushpa *et al.* 2013). Today, many populations throughout the world use natural medications as an urgent requirement to treat viral infections and to fill the gap of the unavailability of conventional therapies or vaccines (Ganjhu *et al.* 2015, Mousa 2015, Ben-Shabat *et al.* 2020). Like all diseases that affect humans and pose a threat to their lives, COVID-19 disease prompted scientists to develop treatments and vaccines to eradicate this disease (Mascellino *et al.* 2021, Pascual-Iglesias *et al.* 2021). While ordinary people resorted to their experiences gained in the field of medicinal herbs to prevent or treat this disease (Chaachouay *et al.* 2021, Chebaibi *et al.* 2022).

In Algeria, numerous investigations have reported that people are very attached to folk medicine and use a wide range of medicinal herbs to treat several diseases (Allali *et al.* 2008, Boudjelal *et al.* 2013, Bouasla & Bouasla 2017). Whereas very few ethnobotanical surveys were conducted to enumerate the medicinal herbs used to prevent or treat SARS-CoV-2. In addition, the information reported in these studies was collected from herbalists or healers (Belmouhoub & Aberkane 2021, Brahimi *et al.* 2022, Djouamaa *et al.* 2022). However, to our knowledge, no ethnobotanical survey has been carried out in Algeria, where information is obtained directly from people already infected with COVID-19. For this reason, the purpose of the present investigation is to determine the medicinal plants and natural products mostly used by people recovered from COVID-19 in the center of Algeria.

Materials and Methods

Description of the survey area

This investigation was conducted in three different provinces of Algeria, namely Bejaia, Bouira, and Tizi-Ouzou. These provinces are located in central northern Algeria; they are bordered by the Mediterranean Sea from the North, Jijel province from the East, Sétif, Bordj-Bou-Arreridj, M'sila, and Médéa provinces from the south, and Blida, Boumerdès, and Algiers provinces from the west (Figure 1). The survey area covers 11292 km², with an estimated population of about 3 million inhabitants who speak Arabic and Kabyle. The population density is estimated at 266 inhabitants/km² and the majority occupy urban areas (ONS 2017).

Figure 1. Location of the study area in Algeria, Bejaia, Bouira, and Tizi-Ouzou provinces

The study area is located in the plain Tellian Atlas; more than half of its total surface is occupied by mountainous terrain. An important vegetation cover characterizes this region, where thousands of plant species are growing. Arboriculture is marked by the predominance of the olive tree, followed by the fig, and citrus trees. The dominant climate is Mediterranean, rainy and mild in winter and dry and hot in summer, but it varies from area to area (ONS 2017).

Ethnobotanical survey and data collection

An ethnobotanical study was conducted from February to November 2022 in several municipalities in the study area. The ethnobotanical information was obtained using a structured questionnaire by a direct interview with 459 people who were already infected by SARS-CoV-2 between 2020 and 2022. The people were chosen randomly, without taking into consideration any parameters about them. The used questionnaire (Appendix 1) was divided into three parts: information concerning people interviewed, information about the disease (COVID-19), and information related to plants used.

Identification of medicinal plants used

The plants used by patients are obtained from local herbalists or from the market, if they are fruits or vegetables. In some regions, plants are picked directly by patients. The vernacular names of plants have been confirmed by respondents if the plant is local and by experienced herbalists if it is imported from other countries or other regions. Then, the binomial nomenclature has been assigned for each plant based on various bibliographical references. The binomial nomenclature, Arabic, Kabyle, and English common names of each plant are listed in Table 3.

Data analysis

The data reported in questionnaires was processed by Microsoft Excel, and several values and parameters were calculated. The results obtained include information related to the patient, the disease, and the plants used.

In addition, ethnobotanical data was analyzed using the relative frequency of citations to determine the well-known and most used species among patients.

Calculations of the different parameters were performed by Microsoft Office Excel 13. The graphs were performed with OriginPro software (Version 10.0.5.157). The comparison between percentages was carried out with Statistica software (Version 7.0.61.0), and the significance level was considered at $p<0.05$.

The ***relative frequency of citations*** shows the local importance of each species and is obtained by dividing the number of informants (patients), who mention the use of the species, by the total number of informants (all patients) participating in the survey. RFC = FC/N. Where RFC is the relative frequency of citation ($0<RFC\leq1$), FC is the number of patients who mention the use of the species, also known as the "Frequency of Citation", and N is the total number of patients using plants (Tardío & Pardo-de-Santayana 2008).

Family importance value (FIV)

The Family Importance Value (FIV) pinpoints the relevance of medicinal plant families. It is assessed by the relative frequency of citations in a given family (RFC family) divided by the total number of species in this family (Ns). Family importance value (FIV) = RFC Family/Ns ($0<FIV\leq1$)

Results

Sociodemographic characteristics

The size of the studied sample is 459 people cured of SARS-CoV-2 infection, including 205 men (44.66%) and 254 women (55.34%), and over 67.10% of them live in urban areas. The age of the respondents varies between 8 and 95 years. More than 74% of them are between 21 and 60 years old. The order of frequency of ABO phenotypes is O > A > B > AB, with respectively 46.84, 32.68, 12.85, 7.62, and 92.38% being Rh+ and 7.62% being Rh-. More than 71% of people interviewed were affected in 2021, and the majority of them (93.6%) were not vaccinated before infection (Table 1).

Table 1. Sociodemographic characteristics

Parameter	Category	Number of patients	Percentage of patients (%)
Gender	Men	205	44.66^{a}
	Women	254	55.34^{b}
Locality	Urban	308	67.10^{a}
	Rural	151	32.90^{b}
Age group (years)	1-20	39	8.50^{c}
	21-40	213	46.40^{a}
	41-60	128	27.89^{b}
	61-80	65	14.16^{c}
	81-100	14	3.05^{c}

Blood group	A	Rh+	150	136	32.68ᵇ	29.63ᵃ
		Rh-		14		3.05ᵇ
	B	Rh+	59	55	12.85ᶜ	11.99ᵃ
		Rh-		4		0.87ᵃ
	O	Rh+	215	200	46.84ᵃ	43.57ᵃ
		Rh-		15		3.27ᵇ
	AB	Rh+	35	33	7.62ᶜ	7.19ᵃ
		Rh-		2		0.43ᵃ
Vaccination before infection	Yes		28		6.1ᵇ	
	No		431		93.9ᵃ	
Year of infection	2020		89		19.39ᵇ	
	2021		327		71.24ᵃ	
	2022		43		9.37ᵇ	

Legend: Percentages in each category with different letters indicate significant differences (p<0.05, a>b>c).

Use of medicinal plants by patients

All the people interviewed (459 respondents) were subjected to pharmacological treatment against SARS-CoV-2. In addition to pharmacological treatment, 384 (83.66%) of patients also used medicinal plants and some natural products. More than half of plant users are women (54.69%).

Moreover, our results show that the use of medicinal herbs differs according to age group. The age groups most attached to medicinal herbs were between 21-40, 41-60, and 61-80 with similar percentages. The age range of 1-20 presented relatively low attachment to plant use but was not statistically different from the latter. However, the oldest people (81-100 years) presented a low attachment to plant uses (Table 2).

Table 2. Distribution of patients using plants by categories

Variable	Category	Number of plant users	Percentage of plant users among all plant users (%)	Percentage of plant users in each category (%)
Gender	Men	174	45.31ᵇ	84.87ᵃ
	Women	210	54.69ᵃ	82.76ᵃ
Age groups (years)	1-20	30	7.81ᵇᶜ	76.92ᵃᵇ
	21-40	181	47.13ᵃ	84.98ᵃ
	41-60	109	28.39ᵇ	85.16ᵃ
	61-80	57	18.84ᵇ	87.69ᵃ
	81-100	7	1.82ᶜ	50ᵇ

Percentages in each category with different letters indicate significant differences (p<0.05, a>b>c).

Combination in the use of plants by patients

Figure 2 represents the combination of medicinal plants used by the patients interviewed. The result shows that only 10.68% of patients used only one species of medicinal plant. However, 16.66% used five different species or more. The majority of patients used two (29.69%), three (24.22%), or four (18.75%) different plant species.

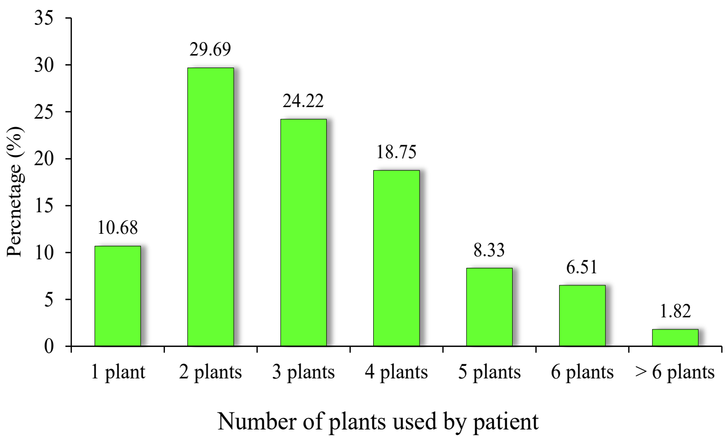


Figure 2. Combination in the use of plants by patients.

Sequelae registered after 2 months of recovery

During this investigation, we noted that some sequelae last longer after healing than others. Most sequelae persist for less than two months. However, some sequelae have persisted for three months. We considered in our study that the longest sequelae were those noticed after 2 months.

The majority of patients did not register sequelae after 2 months of recovery (61.22%), but an important part of 178 patients presented sequelae (38.78%). In this investigation, thirteen different sequelae are noted (Figure 3); the most common is fatigue (37.65%), followed by loss of smell (18.54%), respiratory problems (11.24%), digestive problems (7.3%), a decrease in libido, and memory problems (4.49%). The percentage of other sequelae varies between 1.12 and 3.93%.

Data about plants used by patients

Plant Families

Figure 4A shows that 21 plant families were used by patients. According to the number of species, the most representative families are Lamiaceae with 5 species (14.28% of plants used); Asteraceae and Rutaceae with 3 species (8.57%) for each one; followed by Apiaceae, Lauraceae, Liliaceae, Myrtaceae, Oleaceae, and Zingiberaceae with 2 species (5.71% for each one). The remaining 12 families contributed by one species per family (2.86%).

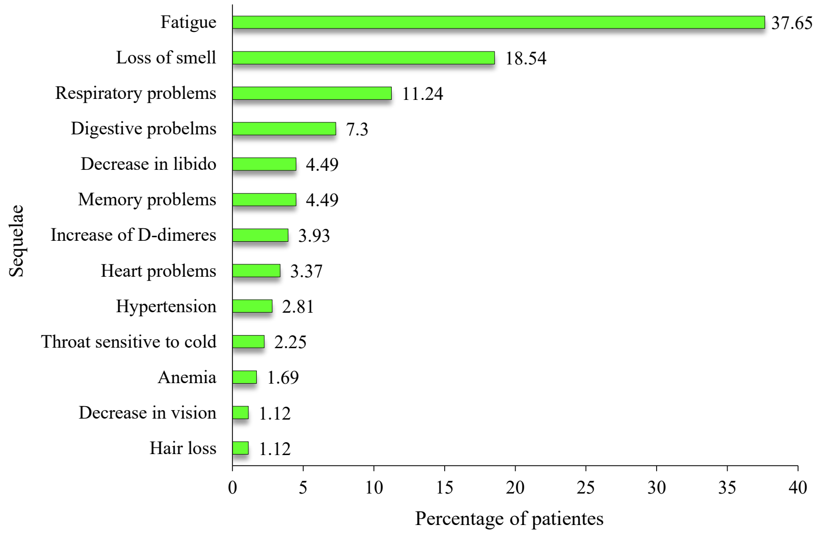


Figure 3. Sequelae registered in patients after 2 months of recovery.

According to the FIV index (Figure 4A), the most cited families are Rutaceae (FIV=0.25), followed by Myrtaceae (FIV=0.24), Verbenaceae (FIV=0.21), Lamiaceae (FIV=0.18), and Zingiberaceae (FIV=0.14), respectively. The FIV index of other plant families varied between 0.003 and 0.07.

Status, origins, and species of plants used

In this investigation, 35 species of medicinal plants belonging to 21 families were registered, of which 74.29% are local and 25.71% are imported from other countries (Figure 4B). Among local plants, 53.85% grow in the wild, and 14.15% are cultivated (Figure 4C). Some species are cited frequently by patients and used by at least 7% of them (RFC>0.06). The use of given species is represented by the percentage of their users compared to all plant users (Figure 5).

The plants mostly used are respectively: *Citrus limon* L. used by 68.49% of plant users, *Origanum vulgare* L. (50%), *Syzygium aromaticum* L. (41.66%), *Mentha spciata* L. (35.68%), *Zingiber officinale* Roscoe (26.04%), *Aloysia citrodora* Parau. (21.09), *Allium sativum* L. (8.59%), *Citrus ×sinensis* L. (8.33%), *Eucalyptus globulus* Labill. (8.07%), and *Allium cepa* L. (7.29%). The plant species recorded in this study, with their names and ethnobotanical use for VOC-19 treatment, are listed in Table 3.

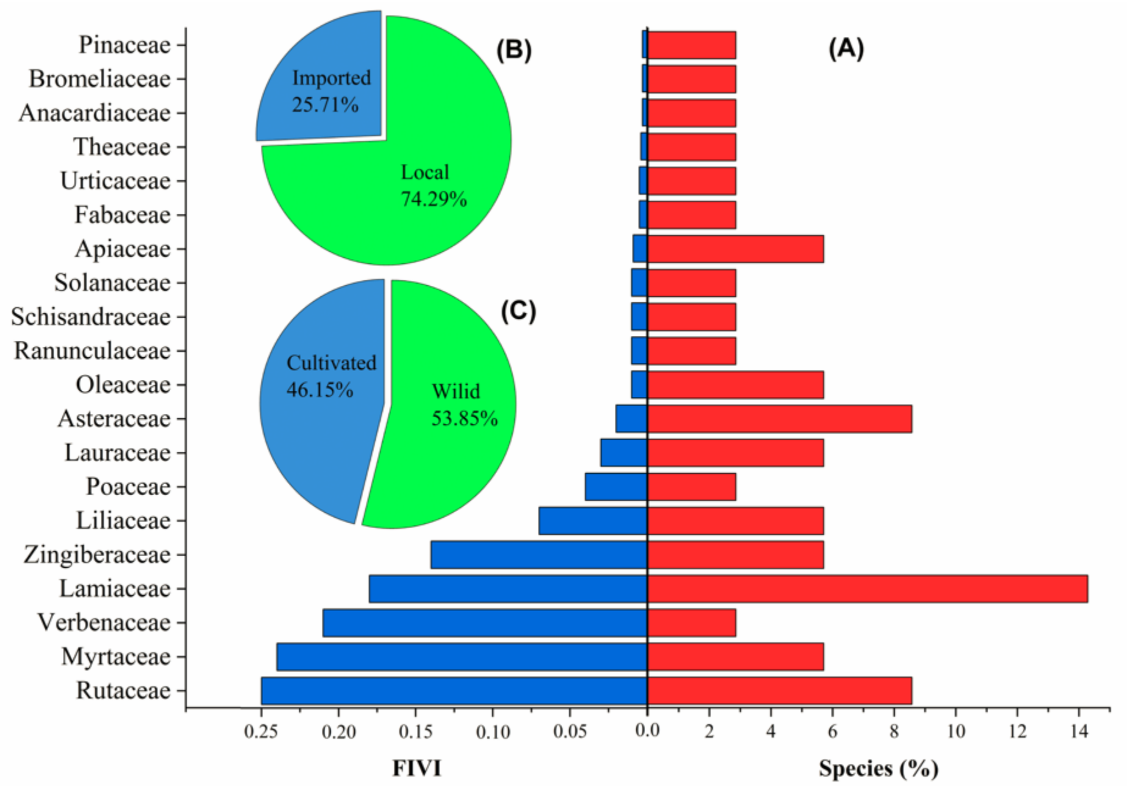


Figure 4. Importance of plant families used by percentage of species and family importance value index (A), status (B), and origins (C) of plants used.

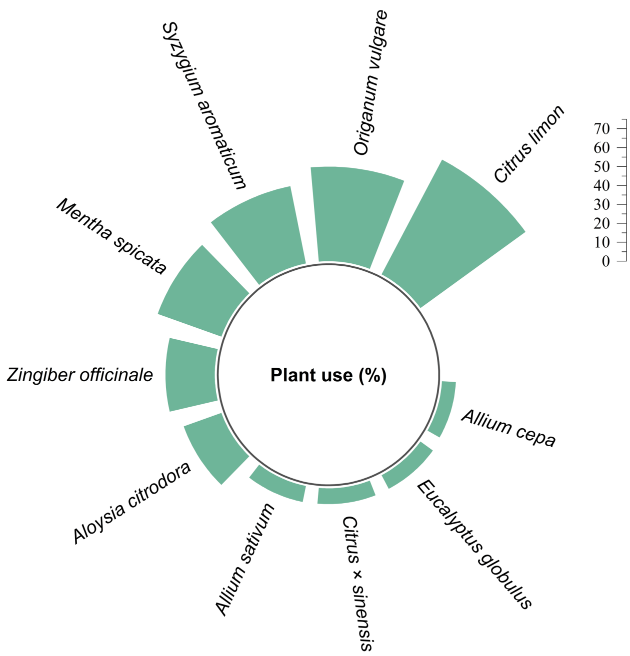


Figure 5. Radial bar plot showing the frequency of popular plants used by the population to treat SARS-CoV-2 infection.

Table 3. List of medicinal plants used to treat SARS-CoV-2 by patients in the study area

Family and binomial name of plant used	Arabic name (Local name)	English name	Status	Used parts	Methods of preparation	Daily dose taken (times/day)/ "route of administration"	frequency of citation (FC)	Relative Frequency of Citation (RFC)	Family importance value (FIV)
Anacardiaceae									0.003
Pistacia lentiscus L.	Dharou (Amadagh)	Lentisk	W	Leaf	Dec. or Inf.	2 (Orally)	1	0.003	
Apiaceae									0.009
Cuminum cyminum L.	Kamoune (kamoune)	Cumin	Cu. and Imp	Seed	Inf.	1 to 4 (Orally)	3	0.008	
Foeniculum vulgare var. *azoricum* (Mill.) Thell	Basbasse (Avesvas)	Florence fennel	Cu	Seed	Inf.	1 to 3 (Orally)	5	0.01	
Asteraceae									0.02
Artemisia herba alba Asso.	Chih (Chih)	White wormwood	W	A. part	Dec. or Inf.	2 to 4 (Orally)	11	0.03	
Matricaria recutita L.	Babondje (Wamlal)	wild chamomile	W	A. part	Dec. or Inf.	2 to 4 (Orally)	5	0.01	
Saussurea costus Falc.	Quist hindi (Quist hindi)	Indian costus	Imp	Root	Dec., Inf. Or Vap.	2 to 4 (Orally or by Inhalation)	7	0.02	
Bromeliaceae									0.003
Ananas comosus (L.) Merr.	Ananas (ananas)	Pineapple	Imp	Fruit	Fresh	2 (Orally)	1	0.003	
Fabaceae									0.005
Glycyrrhiza glabra L.	âark essousse (âark essousse)	Licorice	W	Root	Dec. or Inf.	1 to 3 (Orally)	2	0.005	
Lamiaceae									0.18
Marrubium vulgare L.	Elfrassioune (Marnuyeth)	White horehound	W	A. part	Inf.	2 (Orally)	1	0.003	
Mentha spicata L.	Naânaâ (Naânaâ)	Spearmint	Cu	A. part	Dec. or Inf.	1 to 4 (Orally)	137	0.36	
Origanum vulgare L.	Zaâtar (Zaâtar)	Wild thyme	W	A. part	Dec. or Inf.	1 to 4 (Orally)	192	0.50	
Salvia rosmarinus Spenn.	Iklil aldjabal (Amezir,Azzir)	Rosemary	W	Leaf	Dec. or Inf.	1 to 4 (Orally)	5	0.01	
Salvia officinalis L.	Mrimya (Agurim)	Sage	W. and Cu	A. part	Dec. or Inf.	3 (Orally)	3	0.008	
Lauraceae									0.03
Laurus nobilis L.	Rand (Rand)	Laurel	Imp	Leaf	Dec. or Inf.	2 to 3 (Orally)	5	0.01	
Cinnamomum cassia (L.) J. Presl.	Korfa (qurfa)	Chinese cassia	Imp	Bark	Dec. or Inf.	2 to 4 (Orally)	18	0.05	

Liliaceae									0.07
Allium cepa L.	Bassal (lavsal)	Onion	Cu	Bulb	Inf. or Fresh	1 to 4 (Orally or by Inhalation)	28	0.07	
Allium sativum L.	Thoum (Thicherth, thiskerth)	Garlic	Cu	Bulb	Cooked, Dec., Inf. or Fresh	2 to 4 (Orally or by Inhalation)	33	0.08	
Myrtaceae									0.24
Eucalyptus globulus Labill.	kalitous	Eucalyptus	W	Leaf	Inf. or Vap.	1 to 4 (Orally or by Inhalation)	31	0.08	
Syzygium aromaticum (L.) Merr. & L.M. Perry	Coronfel (qranfel)	Clove	Imp.	Flower buds	Dec., Inf. or Vap.	1 to 5 (Orally or by Inhalation)	160	0.41	
Oleacea									0.01
Jasminum polyanthum Franch.	Yasmine (yasmine)	Jasmine	W	Leaf	Inf	2 (Orally)	1	0.003	
Olea europaea L.	Azzitoune (Azmeour)	Olive	Cu, W.	Leaf	Dec. or Inf.	1 to 2 (Orally)	7	0.02	
Pinaceae									0.003
Pinus halepensis Mill.	Sanaoubar (Azimba)	Pine	W	Leaf	Dec. or Inf.	2 (Orally)	1	0.003	
Poaceae									0.04
Hordeum vulgare L.	Chaair (thimzine)	*Barley*	Cu	Seed	Cooked in milk	1 to 3 (Orally)	16	0.04	
Rhamnaceae									0.003
Ziziphus lotus (L.) Lam.	Sidre (hab-ouzeguarre)	*Jujube*	W	Leaf	Inf.	2 (Orally)	1	0.003	
Ranunculaceae									0.01
Nigella sativa L.	Habasaouda (Sinoudj)	Black cumin	W, Imp.	Seed	Dec. or Inf.	3 to 4 (Orally)	4	0.01	
Rutaceae									0.25
Citrus limon (L.) Osbeck	Laymoune (Lqares)	Lemon	Cu	Fruit	Dec. , Fresh or Inf.	1 to 5 (Orally)	263	0.68	
Citrus ×sinensis (L.) Osbeck (pro sp.) [*maxima* × *reticulata*]	Bourtouqualn (tchina)	Orange	Cu	Fruit	Fresh	1 to 4 (Orally)	32	0.08	
Ruta graveolens L.	Sadhab (Awarmi)	Rue	W	A. part	Dec.	2 (Orally)	1	0.003	
Schisandraceae									0.01

Illicium verum Hook.f.	Yanssoun nadjemi (avesass)	Star anise	Imp	Fruit	Dec. or Inf.	1 to 3 (Orally)	4	0.01	
Solanaceae									0.01
Capsicum annuum L.	Folfol (Ifelfel)	Chili pepper	Cu	Fruit	Cooked	1 to 3 (Orally)	5	0.01	
Theaceae									0.004
Camellia sinensis L.	Chay (Tay)	Tea	Imp	Leaf	Inf.	1 (Orally)	1	0.003	
Urticaceae									0.005
Urtica urens L.	Quaras hariq (Azegdhouf)	Burning nettle	W	A. part	Dec.	2 to 3 (Orally)	2	0.005	
Verbenaceae									0.21
Aloysia citrodora Palau.	Louisa (Tizane)	Lemon Verbena	Cu	Leaf	Dec. or Inf.	2 to 4 (Orally)	81	0.21	
Zingiberaceae									0.14
Curcuma longa L.	Korkom (Karkoum)	Turmeric	Imp	Rhizome	Dec. or Inf.	2 to 5 (Orally)	7	0.02	
Zingiber officinale Roscoe	Zindjabil (Zindjabil)	Ginger	Imp	Rhizome	Dec. or inf.	2 to 4 (Orally)	100	0.26	

Used part of the plant

We noticed during this study that plant users exploit the same part of a given plant. Figure 6 shows that the patients used the bulb of *Allium cepa* and *Allium sativum*, the fruit of *Citrus limon* and *Citrus ×sinensis*, the leaf of *Eucalyptus globulus* and *Aloysia citrodora*, the aerial part of *Mentha spicata* and *Origanum vulgare*, the flower bud of *Syzygium aromaticum*, and the rhizome of *Zingiber officinale*. The rest of the plants and their used parts are listed in detail in Table 3.

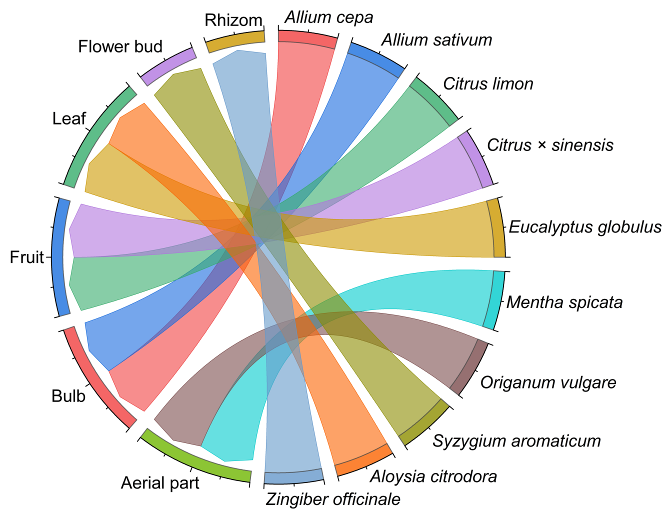


Figure 6. Chord diagram of used plant parts

Methods of preparation and routes of administration

Several methods are followed by patients to use the plants against the SARS-CoV-2 infection. In the majority of cases, the plant or plant extracts were taken orally (Table 3); the solvents mostly used as vehicles are water, milk, tea, olive oil, and honey. The bulb of *Allium cepa* was taken fresh in 96.43% of cases (Figure 7) and by infusion in 3.57% of cases. The bulb of *Allium sativum* was taken orally in all cases, either fresh (84.85%), after decoction (6.06%), cooked (6.06%), or after infusion (3.03%). *Citrus limon* (fruit) was taken orally in all cases, either fresh (48.67%), after infusion (42.58%), or after decoction (8.75%). *Citrus ×sinensis* (fruit) was taken fresh in all cases. The leaves of *Eucalyptus globulus* were taken either by inhalation after evaporation in 61.29% of cases or orally after infusion in water in 38.71% of cases. The flower buds of *Syzygium aromaticum* were either evaporated and taken by inhalation in 1.88% of cases, by infusion (53.12%), or by decoction (45%) in water. *Mentha spicata*, *Origanum vulgare*, *Aloysia citrodora*, and *Zingiber officinale* were taken orally after preparation by two different methods: infusion or decoction in water.

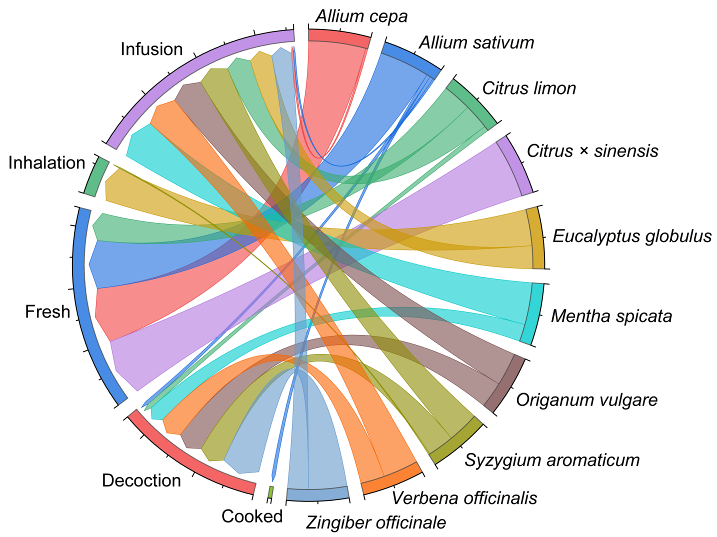


Figure 7. Chord diagram of the preparation method according to the plant

In addition, most patients who used these plants were very satisfied by their anti-SARS-CoV-2 effect (Figure 8).

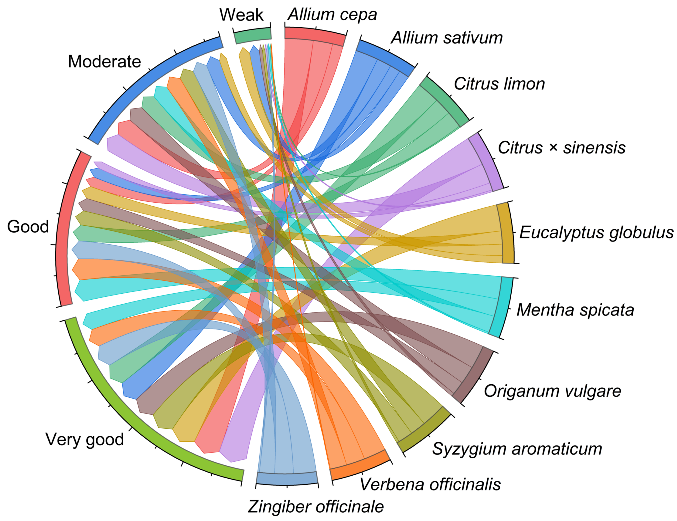


Figure 8. Chord diagram of patients' testimony about the anti-SARS-CoV-2 effect of plants used

Use of natural products and oils with plants

The result obtained shows that over half of plant users (51.4%) also used natural products to treat SARS-CoV-2 infection (Figure 9A). Nearly 43% of them used honey, and 15.88% used olive oil (Figure 9B). Lentisk fixed oil and pine essential oil were used by 1.04% each. Mint essential oil and propolis were used at 0.52 and 0.26%, respectively. The total number of patients can be considered to exceed 51.04% because some patients use two or more products.

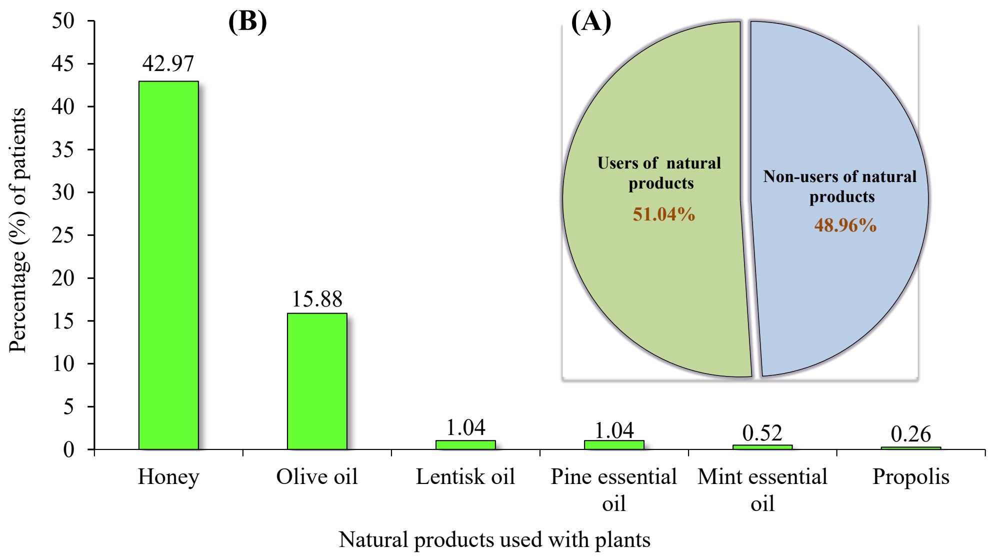


Figure 9. Use of natural products (A) and percentage of natural products used by plant users (B)

Discussion

COVID-19 is a highly transmissible viral infection that kills thousands of people every day across the world. Currently, considerable scientific investigations are focused on the development of vaccines and synthetic drugs, while the solution may be in regular healthy food and natural remedies. Recent studies showed that medicinal plants and natural products may be an important source of antiviral molecules and can serve as a proper alternative for treating numerous viral infections with limited side effects.

In Algeria, for example, since the apparition of COVID-19, people use more medicinal plants and some natural products known for their curative effects against respiratory system infections. In fact, during this investigation, more than 83% of people interviewed used medicinal herbs in addition to pharmacological treatment.

Our sample was chosen randomly, so the data concerning the gender of patients may be different compared to other data found in other parts of Algeria (Bensaber *et al.* 2023). Several epidemiological and clinical studies have revealed that males are more susceptible to SARS-CoV-2 infection than females (Gebhard *et al.* 2020). This difference in the degree of infection can be related to a difference in SARS-CoV-2 receptor expression in tissues, the angiotensin-converting enzyme 2 (ACE2), which is lower in the lung tissues of women compared to men (Tukiainen *et al.* 2017). It has also been suggested that estrogen downregulates the expression of ACE2 (Liu *et al.* 2010).

Concerning age and blood groups, our results agree with other results found in other regions of Algeria (Bouzenda & Ouelaa 2022, Bensaber *et al.* 2023). In this investigation, the age group most infected is between 21 and 40 with 46.40%, followed by those situated between 41 and 60 years with 27.89% (Table 1). The SARS-CoV-2 virus affects significantly more young people, probably because it is the most active category in society and occupies various jobs in the country, such as education, health, trade, and others.

The order of frequency of ABO found in our sample is very close to those found by other investigations carried out in other regions of Algeria (Derouiche *et al.* 2021, Bouzenda & Ouelaa 2022, Bensaber *et al.* 2023). These frequencies do not show a relationship between blood group and SARS-CoV-2 infection, given that the frequencies in the uninfected population are almost the same.

In the present investigation, among the 459 people interviewed, 384 of them (83.66%) used medicinal herbs. The age group most attached to medicinal herbs is situated between 61 and 80 years, representing 87.69% of patients (Table 2). Furthermore, more than 59% of patients used three or more different plants (Figure 2).

In addition, no significant difference was noticed in the use of herbal medicine between men and women (Table 2), unlike the results obtained by other ethnobotanical studies in Algeria, where often women use more medicinal plants than men (Allali *et al.* 2008, Azzi *et al.* 2012, Belmouhoub *et al.* 2022, Djouamaa *et al.* 2022).

These results clearly show the strong attachment of the Algerian population to folk medicine and their vast knowledge in the field of herbal medicine (Allali *et al.* 2008, Boudjelal *et al.* 2013, Telli *et al.* 2016, Belmouhoub *et al.* 2022, Djouamaa *et al.* 2022). Many ethnobotanical studies have reported that North African societies are very attached to medicinal herbs to prevent and treat several diseases (Belayachi *et al.* 2013, Alves-Silva *et al.* 2017, Dehyab *et al.* 2020).

Like all North African countries, in Algeria, since the apparition of this pandemic, people have used more medicinal plants and some natural products known for their curative effect against viral and bacterial infections, especially infections affecting the respiratory system (Belmouhoub & Aberkane 2021, Brahimi *et al.* 2022, Djouamaa *et al.* 2022).

The investigations demonstrated that the practice of traditional medicine varies considerably from one region to another in the world, and this is based on the geography, cultures, and heritage of human societies in medicinal plants and natural treatments (Antwi-Baffour *et al.* 2014, Bellik *et al.* 2020). In addition, the World Health Organization reported that the use of medicinal plants is more important in poor and developing countries than in developed countries (Calixto 2005). These factors can influence the prevalence of diseases and their transmission speed. In fact, the percentages of deaths caused by COVID-19 registered compared to the total population are higher in European Mediterranean countries than in North African Mediterranean countries. According to the WHO, the percentages of deaths in North African countries since the onset of COVID-19 to June 17, 2023, are 0.015% in Algeria, 0.04% in Morocco, 0.22% in Tunisia, 0.09% in Libya, and 0.023% in Egypt, while in European countries they are 0.26% in Spain, 0.31% in Italy, 0.34 in Greece, and 0.24% in France.

Our results concerning plant families used by patients are very close to those recorded by other studies carried out in Algeria (Belmouhoub & Aberkane 2021, Brahimi *et al.* 2022, Djouamaa *et al.* 2022) and Morocco (Benkhaira *et al.* 2021, Chaachouay *et al.* 2021, Chebaibi *et al.* 2022; Flouchi *et al*. 2023). However, there are a few differences in the frequency of plant species used compared to studies performed by other scientists (Brahimi *et al.* 2022, Chebaibi *et al.* 2022, Djouamaa *et al.* 2022; Flouchi *et al*. 2023).

In this investigation, 35 species of medicinal plants belonging to 21 families were registered, 74.29% are local, and 25.71% are imported from other countries (Figure 4B). Among local plants, 53.85% are wild, and 14.15% are cultivated (Figure 4C). Some species are cited frequently by patients and used by at least 7% of them (RFC>0.06).

The choice of the medicinal plants, the part used, the methods of preparation, and the route of administration are not based on scientific knowledge but rather on the traditional medicine heritage and social culture of the population, as has been confirmed by the interviewed people. The plants recorded in this study can be divided into three main groups. The first group is inspired by popular medicine as a remedy for cough and respiratory system diseases, such as *Allium sativum*, *Marrubium vulgare* (Meddour *et al.* 2020), *Allium cepa, Pinus halepensis* (Bendif 2021), *Pistacia lentiscus, Ocimum basilicum* (Chohra & Ferchichi 2019), *Eucalyptus globulus, Syzygium aromaticum* (Souilah *et al.* 2018), *Origanum vulgare*, and *Salvia rosmarinus* (Merouane *et al.* 2022). The second group is inspired by Islamic culture, which is also the case in the majority of Muslim societies (Alqethami *et al.* 2017, Aati *et al.* 2019), such as *Hordeum vulgare* L. (Marwat *et al.* 2012), *Nigella sativa* L. (Maideen 2020), *Saussurea costus* (Abdallah *et al.* 2017), and *Zingiber officinale* (Rene *et al.* 2014). The third group of plants is represented by vegetables, fruits, spices, and condiments, so it is part of the dietary habits of the Algerian population. These plants are consumed even in the absence of diseases, such as *Allium cepa*, *Allium sativum, Capsicum annuum*., *Cinnamomum cassia, Cuminum cyminum, Curcuma longa*, *Laurus nobilis*, *Salvia rosmarinus, Syzygium aromaticum, Zingiber officinale, Citrus limon* and *Citrus ×sinensis.*

In the last decade, many studies have reported the good biological effects of certain plants mentioned in this investigation, namely the antiviral, anti-inflammatory, immunostimulant, and antioxidant effects (San Chang *et al.* 2013, Zhang *et al.* 2014, Lim *et al.* 2015, Li *et al.* 2017, Çifci *et al.* 2018, El-Saber Batiha *et al.* 2020). Recently, other scientific studies have reported that these plants can really exert a potent antiviral effect against SARS-CoV-2 (Brahimi *et al.* 2022, Chebaibi *et al.* 2022, Djouamaa *et al.* 2022; Flouchi *et al*. 2023).

In the present investigation, *Citrus limon* L. was used by 68.49% of plant users (RFC=0.68) (Figure 5, Table 3); in all cases, patients took fruit extract orally (Figure 6), either fresh or infused in water, and in a few cases, by decoction (Figure 7). Recent studies conducted *in vitro* showed that *limonene* and *beta-pinene* found in the essential oil of *C. limon* can block cellular entry of SARS-CoV-2 by inhibiting the ACE2 receptor (Senthil Kumar *et al.* 2020, Torres Neto *et al.* 2022). In addition, hesperidin, a flavanone glycoside extracted from *C. limon,* and its aglycon part, hesperetin, both block the interaction between the spike protein of SARS-CoV-2 and cellular receptor ACE2, and reduce ACE2 and TMPRSS2 expression (Cheng *et al.* 2021). Also, the molecular docking study showed that diosmetin, an O-methylated flavone, can be a potent inhibitor against the SARS-CoV-2 main protease (M^{pro}) (Leal *et al.* 2021).

The second plant most used by patients is *Origanum vulgare* L. This plant is used by 50% of plant users (RFC=0.5). The patients used the extract obtained from the areal part (Figure 6), either by decoction (55.96%) or by infusion (44.04%) (Figure 7). *O. vulgare* is commonly used by the Algerian population to treat colds, flu, coughs, and other respiratory diseases (Meddour *et al.* 2020, Merouane *et al.* 2022, Hassaïne & Benmalek 2023). Besides, other ethnobotanical studies conducted in Algeria showed that this plant was largely used to prevent or treat SARS-CoV-2 infection (Belmouhoub & Aberkane 2021, Brahimi *et al.* 2022, Djouamaa *et al.* 2022). *In vitro* studies showed that flavonoids from *O. vulgare* have a potential effect against SARS-CoV-2 due to their high interaction with the N-terminal and C-terminal RNA binding domains of the SARS-CoV-2 nucleocapsid protein (Husain *et al.* 2022). Another study carried out *in vitro* showed that carvacrol and thymol of *O. vulgare* can block cellular entry of SARS-CoV-2 (Torres Neto *et al.* 2022). On the other hand, the oregano flavonoids can also inhibit SARS-CoV-2 M^{pro} (Guijarro-Real *et al.* 2021).

The third plant most cited is *Syzygium aromaticum* L. (41.66%). This plant is used in many regions of the world to prevent or treat SARS-CoV-2, including Morocco (Benkhaira *et al.* 2021, Chebaibi *et al.* 2022, Flouchi *et al.* 2023), Ethiopia (Tegen *et al.* 2021), Nigeria (Odebunmi *et al.* 2022), Nepal (Chhetri *et al.* 2021), Bangladesh (Islam *et al.* 2021), India (Subitha Shajini *et al.* 2023), and other countries.

Recent experimental studies showed that pectin (Jin *et al.* 2021) crategolic acid (Yunus 2021, Abdelli et al. 2023), campesterol, stigmasterol, oleanolic acid, and bicornin (Abdelli *et al.* 2023) of *S. aromaticum* can block SARS-CoV-2 replication by interaction with the M^{pro}. In addition, the water extract of *S. aromaticum* can also block SARS-CoV-2 replication by suppressing SARS-CoV-2 spike protein–ACE2 binding (Li *et al.* 2022).

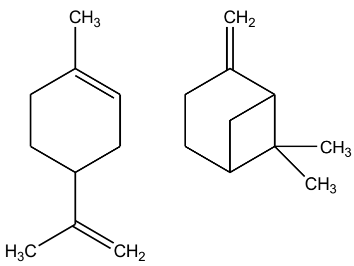
Mentha spicata L. was also widely used by patients (35.68%). In this investigation, the plant users used extract obtained from the infusion or decoction of aerial parts (Figure 6 and Figure 7). In Algeria, this plant is almost daily used by the population as herbal tea. The molecular docking showed that flavonoids and essential oils of *Mentha* species, such as hesperidin, rutin, isorhoifolin, menthol, and pulegone, can inhibit SARS-CoV-2 replication by interaction with its main protease (Wannes & Tounsi 2020, Serlahwaty & Giovani 2021, Ćavar Zeljković *et al.* 2022). On the other hand, the *in vitro* study showed remarkable inhibition of the ACE2 receptor by menthol and other essential oils of *Mentha* species (Demirci *et al.* 2021).

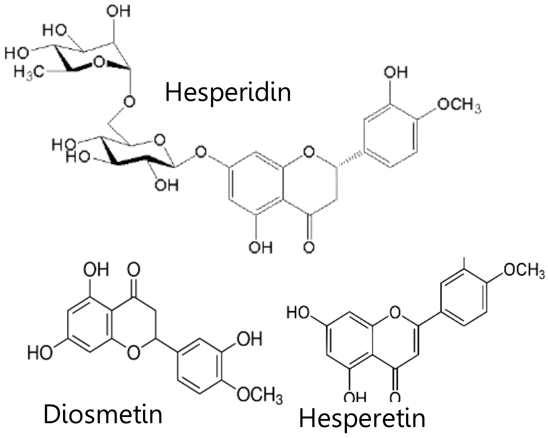
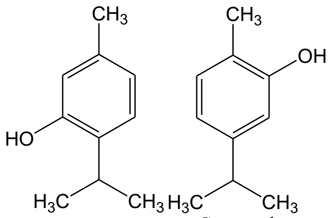
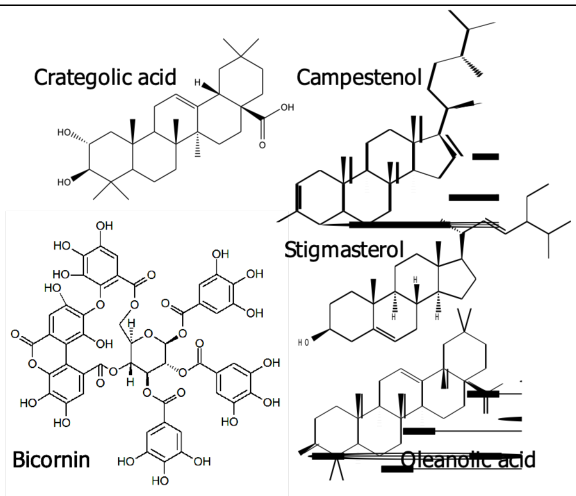
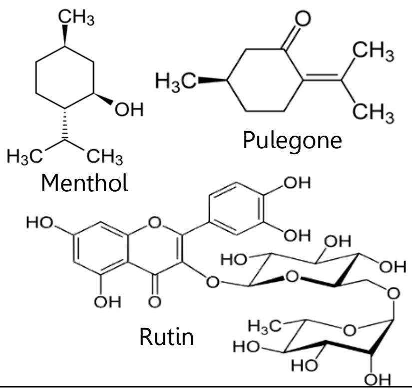
Concerning other plants, several molecular docking and *in vitro* studies showed the probable anti-SARS-CoV-2 effect of their compounds. Some compounds can act by inhibition of SARS-CoV-2 M^{pro}, such as S-Allylcysteine sulfoxide (Alliin), diallyl trisulfide, diallyl disulfide, and diallyl sulfide of *Allium sativum* (Pandey *et al.* 2021), quercetin, oleanolic acid, and cyanidin of *Allium cepa* (Fitriani *et al.* 2020, Bondhon *et al.* 2021), zingiberenol, zingiberol, and 6-gingerol of *Zingiber officinale* (Rathinavel *et al.* 2020, Rabie 2022), eucalyptol (1,8 cineole) of *Eucalyptus globulus* (Sharma 2020, Torres Neto *et al.* 2022), Apigenine-7-glucoside and oleuropein of *Olea europaea* (Khaerunnisa *et al.* 2020), nigellidine and α-hederin of *Nigella sativa* (Bouchentouf & Missoum 2020), tangshenoside III, rutin, and hesperidin of *Saussurea costus* (Houchi & Messasma 2022), and curcumin of *Curcuma longa* (Nidom *et al.* 2023).

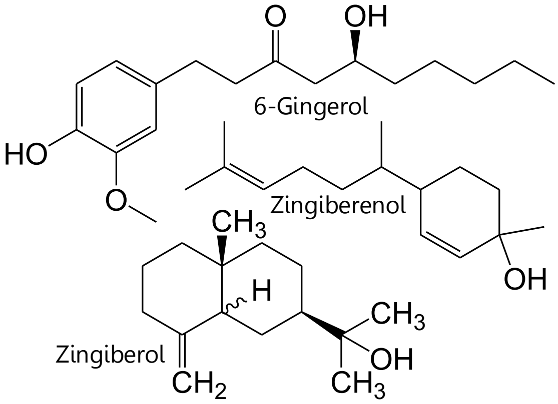
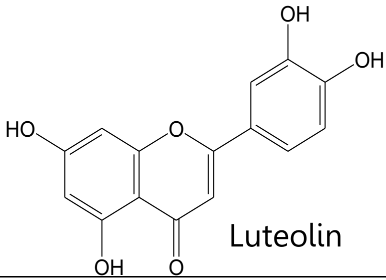
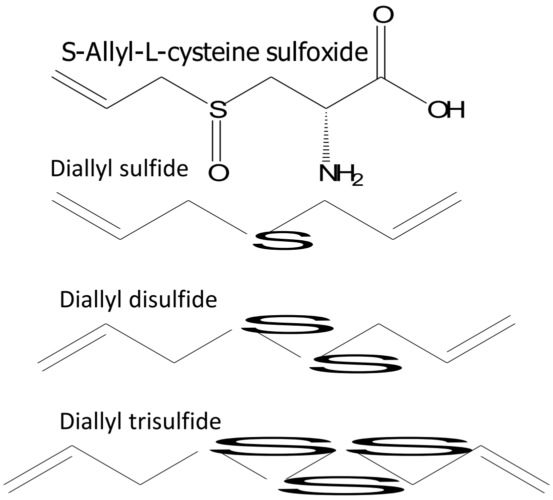
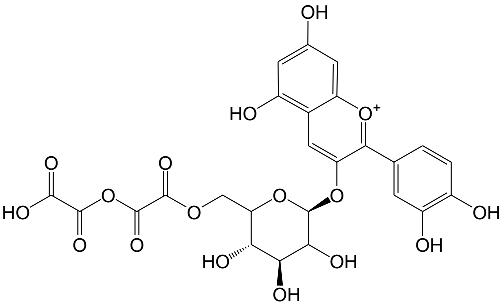
Other compounds can prevent the entry of SARS-CoV-2 to host cells either by binding on the ACE2 receptor, such as luteolin 7-galactoside of *verbenacea* (Iheagwam & Rotimi 2020), and luteolin and quercetin of *Aloysia citrodora* (Hamdani and Houari 2020), or by binding on viral spike protein, such as 1,6-dimethylhepta-1,3,5-triene, chrysanthone, eucalyptol, and α-pinene of *Artemisia herba alba* (Diass *et al.* 2023), or by binding on both molecules, such as curcumin of *Curcuma longa* (Maurya *et al.* 2020, Patel *et al.* 2022), cyanidin3-O-(6''-dioxalylglucoside) and Peonidin3-(6''-malonylglucoside) of *Citrus sinensis* (Fouedjou *et al*. 2022), and bromelain of *Ananas comosus* (Sagar *et al.* 2021). Some foods consumed by patients, such as *Chili pepper*, *Allium cepa,* and *Camellia sinensis*, are very rich in quercetin, a flavonol with a potent inhibition action on transmembrane serine protease 2 (TMPRSS2), a membrane enzyme involved in the entry of SARS-CoV-2 into the host cells (Manjunathan *et al.* 2022).

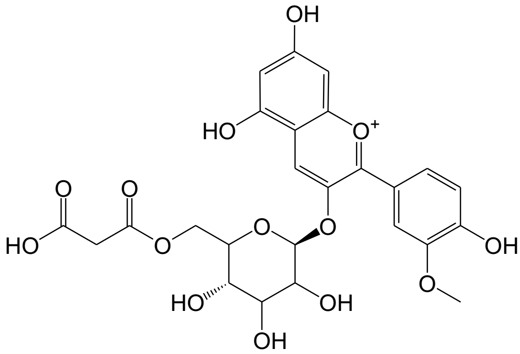
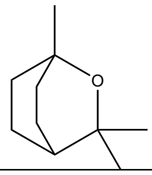
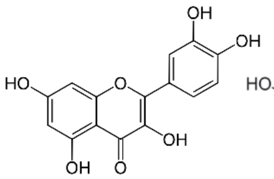
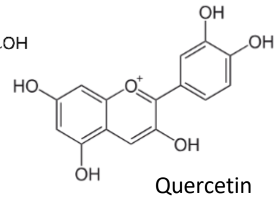
The compounds of some plants can also fight indirectly against SARS-CoV-2 due to their anti-inflammatory and immunomodulatory effects, such as ascorbic acid (vitamin C) (Colunga Biancatelli *et al.* 2020), found in *Citrus limon*, *Citrus sinensis, and Capsicum annuum*, curcumin of *Curcuma longa* (Liu *et al.* 2020), bromelain of *Ananas comosus* (Kritis *et al.* 2020), nigellidin and thymoquinone *of Nigealla sativa* (El Sayed *et al.* 2020), diallyl trisulfide of *Allium sativum* (Moutia *et al.* 2018), ursolic acid and verbascosid of *Salvia officianlis* (Salomón *et al.* 2020), various flavonoids and essential oils of *Ocimum basilicum* (Eftekhar *et al.* 2019), and other compounds. The bioactive components of most plant species used by patients with the proposed mechanism of action are summarized in Table 4.

Table 4. Bioactive components of most plant species used and their mechanisms of action

Plant species	**Bioactive components and their structure**	**Mechanism of action**	**Reference**
Citrus limon L.	 Limonene β-pinene	Prevent the interaction between the Spike protein of Sars-CoV-2 and cellular receptor ACE2 Prevent the interaction between the spike protein of SARS-CoV-2 and cellular receptor ACE2, and reduce ACE2 and TMPRSS2 expression	(Senthil Kumar *et al.* 2020, Torres Neto *et al.* 2022) (Cheng *et al.* 2021)

	 Hesperidin, Diosmetin, Hesperetin	Inhibition of SARS-CoV-2 main protease (M^pro^)	(Leal *et al.* 2021)
Origanum vulgare L.	 Thymol, Carvacrol	Block cellular entry of SARS-CoV-2	(Torres Neto *et al.* 2022)
Syzygium aromaticum L.	 Crategolic acid, Campestenol, Stigmasterol, Bicornin, Oleanolic acid	Inhibition of SARS-CoV-2 main protease	(Jin *et al.* 2021, Yunus 2021, Abdelli *et al*. 2023)
Mentha spicata L.	 Menthol, Pulegone, Rutin	Inhibition of SARS-CoV-2 main protease and prevent cellular entry of SARS-CoV-2	(Wannes & Tounsi 2020, Demirci *et al*. 2021, Serlahwaty & Giovani 2021, Ćavar Zeljković *et al.* 2022)

Zingiber officinale Roscoe.	 6-Gingerol Zingiberenol Zingiberol	Inhibition of SARS-CoV-2 main protease	(Rathinavel *et al.* 2020, Rabie 2022)
Aloysia citrodora Palau.	 Luteolin	Prevent the entry of SARS-CoV-2 into host cells	(Hamdani & Houari 2020)
Allium sativum L.	 S-Allyl-L-cysteine sulfoxide Diallyl sulfide Diallyl disulfide Diallyl trisulfide	Inhibition of SARS-CoV-2 main protease	(Pandey *et al.* 2021)
Citrus ×sinensis L.	 Cyanidin3-O-(6''-dioxalylglucoside)	Prevent the entry of SARS-CoV-2 intof host cells and inhibit its main protease	(Fouedjou *et al*. 2022)

		 Peonidin 3-(6''-malonylglucoside)		
Eucalyptus globulus Labill.	Eucalyptol (1,8 cineole)		Inhibition of SARS-CoV-2 main protease	(Sharma 2020, Torres Neto *et al.* 2022)
Allium cepa L.		  Quercetin Cyanidin	Inhibition of SARS-CoV-2 main protease	(Fitriani *et al.* 2020, Bondhon *et al.* 2021)

Moreover, half of plant users (51.04%) use natural products and plant-prepared oils with plant extracts (Figure 9A). Nearly 43% of them used honey, and 15.88% used olive oil (Figure 9B). In the majority of cases, honey is added not only to sweeten herbal teas but also for its therapeutic virtues. In Algeria and other Muslim societies, honey is known much more as a natural remedy than food because it was recommended in the Quran (chapter 16 -bees, verses 68-69) and in the hadith of the Prophet Muhammad, peace be upon him (El Sayed *et al.* 2020). In Algeria, honey is used to treat several diseases related to infections caused by microorganisms, especially respiratory system infections.

Molecular docking studies suggest that some phenolic compounds contained in honey, such as caffeic acid phenylethyl ester (CAPE), galangin, and chrysin, can protect and treat SARS-CoV-2 infection by inhibiting its M^{pro} activity (Hashem 2020). Other phenolic compounds such as rutin, luteolin, and quercetin can prevent the attachment of SARS-CoV-2 to cell hosts by blocking TMPRSS2, ACE2, and Protein S (Ali & Kunugi 2021). On the other hand, natural compounds contained in honey can also fight against SARS-CoV-2 infection through their anti-inflammatory and antioxidant activities (Vallianou *et al.* 2014).

In addition, 15.88% of plant users used olive oil as a natural remedy. In all cases, the olive oil was taken alone or added to food, but not to herbal extracts. In fact, in the study area, like in all Mediterranean countries, olive oil is part of the daily diet of the inhabitants and represents the traditional symbol of the Mediterranean diet (Colomer & Menéndez 2006, Mazzocchi *et al.* 2019, Djelloul *et al.* 2020). In Algerian traditional medicine, old olive oil was widely used to treat respiratory diseases (Boukhebti *et al.* 2016).

Furthermore, the benefits of olive oil are also recommended in Islamic medicine. The olive tree and its oil are blessed in the Quran (Chapter 24: verse 35), and their health benefits have been mentioned in Prophetic medicine. For example, the Prophet Muhammad (PBUH) said: "Use olive oil as a food and ointment for it comes from a blessed tree (At-Tirmdhi)" (Iqbal *et al.* 2021).

Recently, in silico molecular docking studies have indicated that phytochemicals present in olive oil are a potential candidate to act against SARS-CoV-2. The study carried out by Geromichalou *et al.* (2022) reported that oleuropein and oleocanthal of extra virgin olive oil exhibited high binding affinity to the SARS-CoV-2 Spike protein and prevented its initial interaction with the ACE2 host cell receptor. In another molecular study, it was reported that Demethyloleuropein aglycone extracted from olive fruit can limit SARS-CoV-2 infection by inhibiting papain-like protease activity (Thangavel & Albratty 2023).

On the other hand, bioactive compounds of olive oil, like phenolic compounds, can also fight against SARS-CoV-2 infection through their potent anti-inflammatory (Wongwarawipat *et al.* 2018), immunomodulatory (Alvarez-Laderas *et al.* 2020), and antioxidant effects (Papadopoulos & Boskou 1991).

Conclusion

The present investigation shows that the Algerian population is closely attached to medicinal plants and folk medicine. The majority of people use medicinal herbs not because of a lack of treatment or access to modern medicine but because they believe in their healing effects. In addition, the studied population showed significant knowledge of the traditional treatment. As proof, the possible anti-SARS-CoV-2 effect of many plants used has been demonstrated either *in vitro* or *in silico* studies; however, their effects *in vivo* and in clinical trials have not yet been confirmed, so these tests are very necessary. Finally, this investigation constitutes a good contribution to the Algerian heritage in medicinal herbs and natural products to fight against the SARS-CoV-2 infection. Moreover, thorough pharmacological and phytochemical investigations are needed to reveal the real effects of these plants as well as their active components involved in anti-SARS-CoV-2 action.

Declarations

List of abbreviations: A. part - Aerial part; Cu - Cultivated; Dec. - Decoction; FC - Frequency of Citation; FIV - Family importance value; HIV - human immunodeficiency virus; HSV - Herpes Simplex Virus; Imp. - Imported; Inf. - Infusion; Inh. - Inhalation; Mac. - Maceration; RFC - relative frequency of citation; Vap. - Vaporization; W. - Wild; WHO - World Health Organization

Ethics approval and consent to participate: The author discussed with individual people before the interviews, and permission was obtained from all participants prior to each interview, discussion, or filling out the questionnaire.

Consent for publication: Not applicable

Ethical statements: This article contains questionnaire-based survey research conducted through verbal communication between the authors and people cured of COVID-19. This article does not contain any studies involving animals performed by any of the authors. This article does not contain any studies involving animals performed by any of the authors.

Conflict of interest: All authors of this work declare that there is no conflict of interest.

Availability of data and materials: The data collected in this research is available upon reasonable request to the corresponding author.

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Appendix 1. Questionnaire used during the investigation.

Information about patients	**Information about disease**	**Information about plants used**
1. Gender 2. Age 3. Place of residence (city or companion) 4. Blood group 5. Vaccination before infection	1. Year and month of infection 2. Infection confirmed or not? 3. Taking pharmacological treatment, or no? 4. Hospitalized or not? 5. Sequelae after recovery	1. Common name of plants used 2. Mode of preparation 3. Plant parts used 4. Daily dose taken 5. Plant effect 6. Cultivated, wild or imported 7. Other natural product taken with plants