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Original Article

Phytotherapy in response to COVID-19 and risks of intoxication: A field study in the city of Meknes (Morocco)

[Fitoterapia en respuesta al COVID-19 y riesgos de intoxicación: un estudio de campo en la ciudad de Meknes (Marruecos)]

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Abstract

Context: The contagious global pandemic of coronavirus 2019 (COVID-19) has prompted many Moroccans to turn to traditional phytoremedies.

Aims: To highlight the ethnopharmacological information and the risks of intoxication related to the use of herbal medicine to combat COVID-19.

Methods: Through a semi-structured questionnaire and using the "Free listing" technique, an ethnobotanical survey was conducted among 36 herbalists of the Meknes prefecture to collect ethnopharmacological data on species used in the fight against COVID-19. Then, many databases were used to document their pharmacological and toxicological activities.

Results: A total of 36 species in 22 families were reported to be used to prepare traditional recipes against COVID-19. According to the relative frequency index of citation, the species *Artemisia herba-alba* Asso, *Eucalyptus globulus* Labill, *Syzygium aromaticum* (L.) Merr. & L.M. Perry, *Citrus limon* (L.) Osbeck, and *Zingiber officinale* Roscoe. were recommended by all respondents and recorded the highest usage values. Based on the value of the plant parts index, leaves were the most used part (PPV = 0.37). Most of the remedies were prepared as infusions and administered orally. The bibliographic research revealed that the plants used have several biological activities and are frequently used to treat respiratory diseases. However, some of them have been reported to be toxic.

Conclusions: Recommended species are endowed with innumerable biological activities. They can be a promising alternative to combat COVID-19. However, their toxic effects require pharmacotoxicological studies to ensure the safety and efficacy of these natural remedies.

Keywords: COVID-19; ethnobotany; herbalism; Morocco; Meknes; phytotherapy; toxicity.

Resumen

Contexto: La contagiosa pandemia mundial del coronavirus 2019 (COVID-19) ha llevado a muchos marroquíes a recurrir a los fitorremedios tradicionales.

Objetivos: Resaltar la información etnofarmacológica y los riesgos de intoxicación relacionados con el uso de fitoterápicos para combatir el COVID-19.

Métodos: A través de un cuestionario semiestructurado y utilizando la técnica de "Listado Libre", se realizó un relevamiento etnobotánico entre 36 herbolarios de la prefectura de Meknes para recolectar datos etnofarmacológicos sobre especies utilizadas en la lucha contra COVID-19. Luego, se utilizaron muchas bases de datos para documentar sus actividades farmacológicas y toxicológicas.

Resultados: Se informó que un total de 36 especies en 22 familias se utilizaron en la preparación de recetas tradicionales contra COVID-19. Según el índice de frecuencia relativa de citación, las especies Artemisia *herba-alba* Asso, *Eucalyptus globulus* Labill, *Syzygium aromaticum* (L.) Merr. & L.M. Perry, *Citrus limon* (L.) Osbeck y *Zingiber officinale* Roscoe. son recomendados por todos los encuestados y registró los valores de uso más altos. Sobre la base del índice del valor de las partes de la planta, las hojas son la parte más utilizada (VPP = 0,37). La mayoría de los remedios se prepararon como infusiones y se administraron por vía oral. La investigación bibliográfica reveló que las plantas utilizadas tienen varias actividades biológicas y se utilizan con frecuencia en el tratamiento de enfermedades respiratorias. Sin embargo, se ha informado que algunos de ellos son tóxicos.

Conclusiones: Las especies recomendadas están dotadas de innumerables actividades biológicas, pueden ser una alternativa prometedora para combatir el COVID-19. Sin embargo, sus efectos tóxicos requieren estudios farmacotoxicológicos para garantizar la seguridad y eficacia de estos remedios naturales.

Palabras Clave: COVID-19; etnobotánica; fitoterapia; herboristería; Marruecos; Meknes; toxicidad.

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INTRODUCTION

In recent decades, coronaviruses (CoVs) have been the cause of epidemics in East Asia and the Middle East; for example, in 2002 and 2012, severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) appeared, respectively (Dhama et al., 2020). Then, in late December 2019, a new coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), causing Coronavirus 2019 (COVID-19) emerged in Wuhan, China, from where it quickly spread, leading to a nationwide outbreak, followed by an ongoing pandemic around the world (He et al., 2020). In Morocco, the first case of Covid-19 was officially reported on March 2, 2020 (Derraji, 2020).

Coronaviruses belong to one of the major families of viruses, the *Coronaviridae*, and are capable of parasitizing various animal species, including bats, camels and cattle (Zaman et al., 2020). They are enveloped positive-sense RNA viruses, ranging from 60 nm to 140 nm in diameter, and they have spike-like projections on the surface that look like crowns under the electron microscope, hence their name of coronavirus (Bar-On et al., 2020).

From asymptomatic to acute respiratory distress syndrome and multi-organ dysfunction, the clinical signs of COVID-19 vary; in general, they include various respiratory infections, fever, cough, sore throat, headache, fatigue, myalgia, shortness of breath and conjunctivitis (Singhal, 2020). However, in some patients, by the end of the first week, the disease can progress to pneumonia, respiratory failure and death; this progression is related to extreme increases in inflammatory cytokines (Singhal, 2020). In addition to therapeutic protocols for the management of COVID-19, various researchers have proposed the use of medicinal plants as a possible alternative for curing or preventing COVID-19 (Chan et al., 2020). This, like many studies that have used a large number of antiviral compounds produced from plant species (Hussain et al., 2017; Jassim and Naji, 2003). For their part, countries such as China and India combine herbal medicine with modern medicine to boost the immunity of patients with COVID-19 (Ni et al., 2020; Shankar et al., 2020), and the results in symptom management and reduction in deterioration, mortality and recurrence are encouraging (Luo et al., 2020).

In Morocco, the use of phytotherapy is a very common practice (Dossou-Yovo et al., 2017). Indeed, thanks to its privileged geographical situation and its favorable climatic conditions, the country has a very rich and diversified flora (Fennane and Ibn Tattou, 1998). In addition to this wealth of flora, there is medicinal knowledge and traditional therapeutic know-how accumulated over the years and enriched by the mixing of several civilizations (Najem et al., 2020a; 2020b).

Thus, during the COVID-19 pandemic, several citizens resorted to traditional medicinal recipes prepared with plants, both to prevent this disease and to treat its symptoms. For this reason, the present study was undertaken through an ethnobotanical survey in the prefecture of Meknes. The objective was to collect ethnopharmacological information on the therapeutic use of plants against COVID-19 and the possible risks of intoxication associated with this use.

MATERIAL AND METHODS

Presentation of the study area

The city of Meknes is characterized by a semi-continental climate of Mediterranean type, with cool and rainy winters and hot and dry summers (H.C.P., 2013). With a population of about 632,079 inhabitants in 2014 and an area of 370 km², Meknes is placed among the six major cities of the Kingdom (H.C.P., 2018).

Located in the Sais plain, between the Atlantic plains, the pre-Rif hillshills, the Middle Atlas and the high plateaus of the Oriental, its geographical situation is remarkable, especially since it is a crossroads of a multitude of major communication arteries between different cities of the Kingdom (Fig. 1) (H.C.P., 2013). Finally, in terms of health, the public health infrastructure of Meknes consists of two general hospitals and two specialized hospitals and 33 health centers (H.C.P., 2013).

Sample size and inclusion/exclusion criteria

Stratified probability sampling was used; this consisted of subdividing the population into different strata according to certain characteristics and randomly selecting individuals to form a sample containing the same proportion of individuals from each stratum (Kahouadji, 1986). The strata are represented in our case by the following urban districts: Ancienne Medina, El Mechouar Stinia, Marjane, Zitoun, Toulal and Ouislane (Fig. 1). Each stratum was assigned the same number of respondents represented by six herbalists. Thus, our overall sample size was n = 36 respondents.

According to the inclusion criteria adopted, the herbalists surveyed should be natives of the study area, reputedly competent and expert in the practice of herbal medicine or in the trade of aromatic and

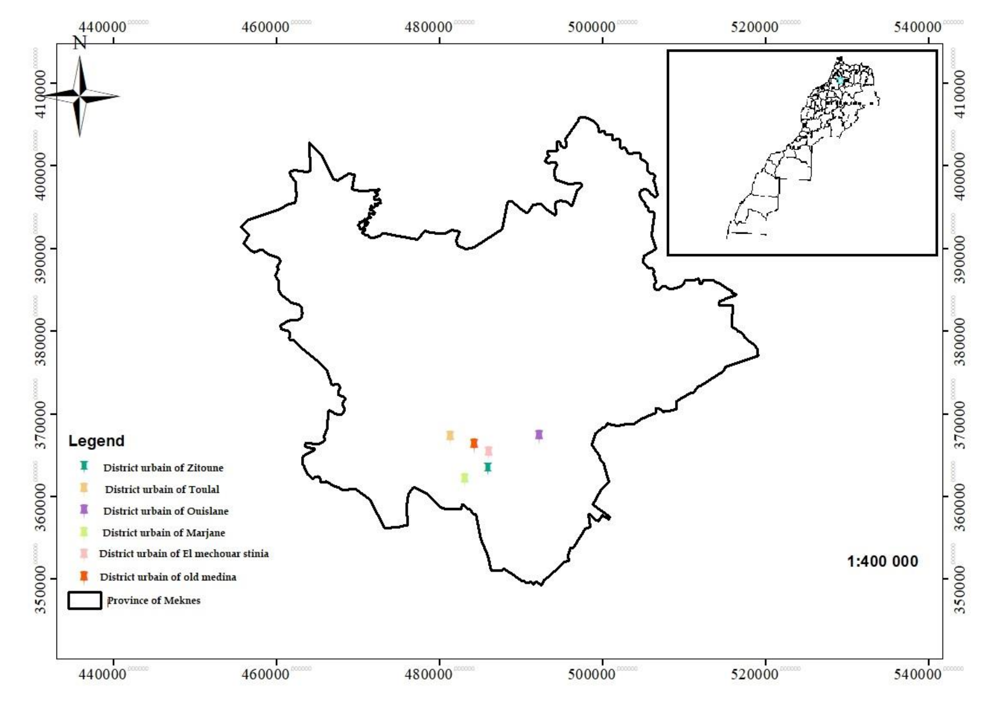

Figure 1. Study area.

medicinal plants; thus, the information provided by them would be correct. As for the exclusion criteria, herbalists who were not from the study area and who were not reputable in the field were not addressed.

Ethnopharmacological data collection and interview methods

The present work is based on the results of an ethnobotanical investigation carried out during the period December 2020- March 2021 among herbalists of the prefecture of Meknes via a pre-established semi-structured questionnaire. Using the free listing technique, the respondents were asked to answer closed and semi-closed questions in order to collect information on their knowledge of traditional herbal medicine for the prevention and treatment of COVID-19, adopting the standard methodology proposed by Martin (2014). The interviews were conducted individually; the herbalists were interviewed in the Moroccan Arabic dialect "addarija", each for an average of 30 minutes.

During each interview, all necessary socio-demographic information about the respondents was collected, including education level, age and gender. As for the plants listed, the data collected included the local name of each plant, the part(s) used, the method of preparation, the method of administration, the dose used and the toxicity.

Also, in order to limit bias, we tried to be as neutral as possible to avoid making the respondent feel uncomfortable or influencing his or her opinion. Similarly, value judgments that might influence the respondent's answers or cause bias on their part were avoided.

Ethical declaration and consent to participate

The study was authorized by the scientific research commission of the Faculty of Sciences of Meknes and the research ethics committee of the pole of aromatic and medicinal plants of the Moulay Ismail University of Meknes (EA158/21). Also, before starting each interview, each person concerned gave their agreement and oral consent to participate in the survey. All respondents were informed that the purpose of the study is purely academic with no commercial or profit motive. They were also informed that their responses would be published anonymously and that they had the right to withdraw their information at any time during the survey.

Taxonomic identification of species

The species used by the herbalists surveyed to prevent or cure COVID-19 were sampled, dried, numbered and preserved using the standard method (Jain, 1964). Indeed, each medicinal plant was carefully sampled from the study area or from other regions of Morocco, such as *Lavandula dentata* L. sampled in Marrakech and *Crocus sativus* L. in Taliouine. Samples sold in the herbalists surveyed were used for the species *Cinnamomum verum* J.Presl, *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Nigella sativa* L. and *Zingiber officinale* Roscoe, which do not grow in Morocco. These samples were compared between those sold by the herbalists of the different strata studied for more precision.

The taxonomic identification was carried out in the laboratory of Environment and Valorization of the Microbial and Vegetal Resources by Professor Laila NASSIRI by using the manuals of determination of the vascular plants "Flore pratique du Maroc" (Fennane et al., 1999; 2007; 2014). The denomination of species and families was revised according to the website "Plants of the World online" (http://plantsoftheworldonline.org/). All specimens were deposited for future reference in the herbarium of the research unit "Environnement et Valorisation des Ressources Microbiennes et Végétales", Faculty of Sciences, Moulay Ismail University of Meknes, Morocco.

Statistical analysis

The sociodemographic and ethnopharmacological data collected on the raw questionnaire forms were analyzed by the statistical processing software IBM SPSS Statistics 20 and Excel 2010. Quantitative ethnobotanical indices were also calculated, such as the frequency of citation (FC), the relative frequency of citation (RFC), the use value (UV), the family use value (FUV), the informant agreement ratio (IAR), the fidelity level (FL) and the value of plant parts (PPV).

Frequency of citation and relative frequency of citation

The frequency of citation (FC) corresponds to the number of respondents mentioning a useful species.

The relative frequency of citation (RFC) was calculated according to the formula [1].

$$FRC = \frac{FC}{N} \quad [1]$$

Where: FC: the total number of respondents using a given plant; N: the total number of respondents. The FRC value varies from 0 (when no one mentions a plant as useful), to 1 (when all informants mention it as useful) (Parthiban et al., 2016).

Use value

The use value (UV) is used to demonstrate the relative importance of locally known plants. This index was calculated according to the formula [2].

$$UV = \sum_{i=1}^{i=N} Ui/N \quad [2]$$

Where: Ui= the number of use reports mentioned by each informant i for a given species; N= the total number of informants interviewed (Vitalini et al., 2013).

Family use value

The family use value (FUV) is an index of the cultural importance that can be applied in ethnobotany to identify the significance of plant families. This index was calculated according to the formula [3].

$$FUV = (\sum UVS)/Ns \quad [3]$$

Where: UVs = the use value of species belonging to the same family; Ns = the total number of species present in a given family (Cadena-González et al., 2013).

Fidelity level

The fidelity level (FL) quantified the importance of a species for a given purpose. This index was calculated according to the formula [4].

$$FL\ (\%) = (Ip/Iu) \times 100 \quad [4]$$

Where: Ip = the number of informants who independently suggested the use of a species for the same major purposes; Iu = the number of informants who mentioned the species for any use (Nawash et al., 2013).

Informant agreement ratio

The informant agreement ratio (IAR) is used to determine the agreement between informants about the use of plants for specific use categories. It was calculated using the formula [5].

$$IAR = (Nur - Nt)/(Nur - 1) \quad [5]$$

Where: Nur = the number of mentions in each usage category; Nt = the number of taxa used in each usage category (Collins et al., 2006).

Value of plant parts

The plant part value (PPV) was calculated according to the formula [6].

$$PPV = \frac{RU\ Plant\ part}{RU} \quad [6]$$

Where: RU: the number of reported uses for all parts of the plant; RU Plant part: the sum of reported uses by plant part. The part with the highest PPV was the most used by respondents (Najem et al., 2020a).

RESULTS

Sociodemographic characteristics of informants

A total of 36 herbalists from the study area were selected to participate in the study by means of pre-established questionnaire forms; also, since all the selected participants answered all the questions on the form, 100% of the participants were therefore respondents.

It turns out that in the prefecture of Meknes, herbal medicine was practiced by both men and women, with, however, a male dominance (88.89%) and therefore a sex ratio female/male of 0.12 (Table 1).

Regarding the age of the respondents, the majority were between 50 and 60 years old (33.33%), followed by those between 40 and 50 years old (25%), then the

Table 1. Profile of interviewed informants.

Variable	Category	Percentage (%)
Sex	Female	11.11
	Male	88.89
Age	<30 years	11.11
	30-40 years	13.89
	40-50 years	25.00
	50-60 years	33.33
	> 60 years	16.67
Educational level	Illiterate	16.67
	Primary	27.78
	Secondary	47.22
	University	8.33

age group represented by herbalists older than 60 years old (16.76%), while the age group that was not well represented was that of respondents under 30 years old (11.11%) (Table 1). As for the level of education, most of the participants in the survey (47.22%) had secondary education, 27.78% had primary education, 16.67% were illiterate and only 8.33% had access to higher education (Table 1).

Floristic richness of the plants used

A total of 36 species were recommended by the herbalists interviewed for use against COVID-19. These species are distributed over 33 genera and 22 botanical families (Table 2). With 9 species inventoried, the *Lamiaceae* family was the most presented, followed by the *Apiaceae* (4 species, 11.11%), while the *Amaryllidaceae*, *Asteraceae* and *Myrtaceae* were represented by two species each, compared to only one species for each of the remaining families (Fig. 2).

In Table 2, the inventoried plants were presented in alphabetical order. For each plant, the scientific name, the family, the vernacular name, the part used, the method of preparation and the mode of administration recommended by the actors of traditional medicine, as well as the FC, RFC and UV data were presented. In addition, the biological activities and active compounds of each plant were indicated.

Relative frequency of citation

The relative frequency of citation (RFC) index was calculated to highlight the plants most recommended by herbalists in the study area to prevent or cure COVID-19. The calculations showed that the value of RFC varies from 0.19 to 1. Indeed, 5 species were used by all the respondents to fight against COVID-19 (RFC = 1); they were *Artemisia herba-alba* Asso, *Eucalyptus globulus* Labill., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Citrus limon* (L.) Osbeck and *Zingiber officinale* Roscoe. In contrast, the lowest value (RFC = 0.19) was recorded by *Nerium oleander* L. (Table 2).

Use value of species and families

In order to evaluate the relative importance of medicinal plants recommended by traditional medicine practitioners in the prefecture of Meknes against COVID-19, the use value (UV) was calculated. This value varied from 1.833 to 0.194. The plants with the highest use value were *Citrus limon* (L.) Osbeck (UV = 1.833), *Eucalyptus globulus* Labill. (UV = 1.833), *Zingiber officinale* Roscoe (UV = 1.833), *Syzygium aromaticum* (L.) Merr. & L.M.Perry (UV = 1.556), *Olea europaea* L. (UV = 1.500), *Artemisia herba-alba* Asso (UV = 1.417), *Allium sativum* L. (UV = 1.389), *Cinnamomum verum* J.Presl (UV = 1.333), *Ficus carica* L. (UV = 1.333) and *Lepidium sativum* L. (UV = 1.222). The lowest value was observed in *Nerium oleander* L. (UV = 0.194) (Table 2).

Based on the FUV index, the families that recorded the highest use values were *Lamiaceae* (FUV = 4.949), *Myrtaceae* (FUV = 3.389), *Lauraceae* (FUV = 2.222), *Amaryllidaceae* (FUV = 2.083). The family with the lowest use value was *Apocinaceae* (FUV = 0.194) (Table 3).

Fidelity level

The calculation of "FL" is a very useful way to determine the most effective species for a given use category. The results of this study revealed that the FL values of species used to treat or prevent COVID-19 ranged from 100% to 10%. In addition, the study identified 16 species with a 100% fidelity level used to treat COVID-19 and 4 species with the same fidelity level recommended to prevent COVID-19 (Table 4).

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco.

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Amaranthaceae	*Dysphania ambrosioides* (L.) Mosyakin & Clemants	Mkhinza	MK.Co.12	Fruit, leaves	Decoction, infusion, extract	Oral, brushing	2,5-Dimethyl-3-hexyne-2,5-diol like, carvacrol, 3-isopropyl-4-methyl-1-pentyn-3-ol like, phytol, squalene, vitamin E, sucrose, D-glucose isomer 3, α-linolenic acid, phosphoric acid and glycerol (Reyes-Becerril et al., 2019).	Antifungal, antiaflatoxigenic, antioxidant, intestinal immune and anti-inflammatory (Kumar et al., 2007; Reyes-Becerril et al., 2019).	20	0.56	0.556
Amaryllidaceae	*Allium sativum* L.	Touma	MK.Co.27	Bulb	Cooked	Oral	Ajoenes, allicin, vinyldithiins, diallyl disulfide, diallyl trisulfide, alliin (El-Saber Batiha et al., 2020).	Antibacterial, antifungal, antiprotozoal, antiviral, antioxidant, anti-inflammatory, anticancer, immunomodulatory, anti-obesity, antidiabetic, hypolipidemic, hypocholesterolemic, anti-atherosclerotic, antithrombotic, antihypertensive (El-Saber Batiha et al., 2020).	30	0.83	1.389
Amaryllidaceae	*Allium cepa* L.	Basla	MK.Co.26	Bulb	Cooked	Oral	Alliinase, cysteine, methionine, cysteine sulphoxides, γ-glutamyl peptides, anthocyanins and flavonoids quercetin and kaempferol (Boumediou and Addoun, 2017). Essential oils: Monosulfides (R1-S-R2), disulfides (R1-S-S-R2), trisulfides (R1-S-S-S-R2), tetrasulfides (R1-S-S-S-S-R2) and thiols (RSH) (Boumediou and Addoun, 2017).	antioxidant, antidiabetic, anti-inflammatory, anticancer, antimicrobial, antihyperlipidaemic, anticholesterolaemic, fibrinolytic, antiatherosclerotic, anticataractogenetic, antiplatelet aggregation, immunomodulatory, neuroprotective (Boumediou and Addoun, 2017).	25	0.69	0.694

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Apiaceae	*Visnaga daucoides* Gaertn.	Bachnikha	MK.Co.11	Flowers, fruit	Decoction	Oral	γ-Pyrones, khellin, visnagin, khellinol, ammiol, visammiol, khellol, khellinin, khellinone, visnaginone. Coumarins, visnadin, pyranocoumarins, samidin and dihydrosamidin, furanocomarines, flavonols (quercetin and kaempferol). Essential oils: Amyl isobutyrate, methyl-2-isoamyl butyrate, amyl valerateisoamyl 2-methyl butyrate, isopentyl isovalerate and nonterpene esters (Abdul-Jalil et al., 2010; Amin et al., 2015; Bencheraiet et al., 2011; Talaat et al., 2013).	Antioxidant, cytotoxic, anti-diabetic, antimicrobial, antispasmodic, cardiovascular activity, antimutagenic effect, immunostimulatory, anti-inflammatory and antituberculous activity (Awad et al., 2006; Beltagy and Beltagy, 2015; Bousta et al., 2014; Daoudi et al., 2013; Duarte et al., 2000; Grange and Davey, 1990; Keddad et al., 2016; Semyaril et al., 2011.; Vanachayangkul et al., 2010).	10	0.28	0.278
Apiaceae	*Foeniculum vulgare* Mill.	Besbas	MK.Co.36	Flowers, fruit	Decoction	Oral	3-caffeoylquinic acid, 4-caffeoylquinic acid, 1,5-O-dicaffeoylquinic acid, rosmarinic acid, eriodictyol-7-O-rutinoside, quercetin-3-O-galactoside, kaempferol-3-O-rutinoside, and kaempferol-3-O-glucoside. Essential oils: Trans-anethole and estragole, (*E*)-anethole, fenchone and methyl chavicol (Diao et al., 2014; Mimica-Dukić et al., 2003; Parejo et al., 2004).	Antioxidant, anti-cancer, anti-inflammatory, analgesic, antifungal, hepato-protective, anti-bacterial and estrogenic (Choi and Hwang, 2004; Diao et al., 2014; Esquivel-Ferriño et al., 2012; Kooti et al., 2015; Mimica-Dukić et al., 2003; Mohamad et al., 2011; Wang et al., 2012).	12	0.33	0.417
Apiaceae	*Petroselinum crispum* (Mill.) Fuss	Maadnous	MK.Co.25	Fruit, leaves	Decoction, infusion	Oral	Coumarins and flavonoids, sterols glycosides, saponin, triterpenes and alkaloids. Essential oils: Myristicin, β-phellandrene, 1,3,8-p-menthatriene apiole and β-phellandrene (Craft and Setzer, 2017; Shaza, 2016).	Antimicrobial, antioxidant, immunomodulating, spasmolytic, analgesic, anticancer, antidiabetic, nutraceuticals, cardiovascular activity, neuroprotective and genitourinary activity (Agyare et al., 2017).	14	0.39	0.500

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Apiaceae	*Pimpinella anisum* L.	Habat hlawa	MK.Co.10	Fruit	Decoction, infusion	Oral	Isovitexin, rutin, apigenin 7-glucoside and a luteolin glycoside. Essential oils: Trans-anethole, estragole, γ-himachalen, paraanisaldehyde and methyl cavicol (Kunzemann and Herrmann, 1977; Orav et al., 2008).	Antimicrobial, antifungal, antiviral, anti-inflammatory, muscle relaxant, analgesic, antispasmodic, antiulcer, anti-diabetic, hypolipidemic and anticonvulsant activity (Ahmadipour et al., 2016; Kunzemann and Herrmann, 1977; Orav et al., 2008; Tas et al., 2006; Tirapelli et al., 2007).	15	0.42	0.500
Apocinaceae	*Nerium oleander* L.	Dfla	MK.Co.13	Leaves	Fumigation	Inhalation	Plumericin, alpha-amyrin, beta-sitosterol, kaempferol, odorosides A-H, kaneroside, neriumoside, digitoxigenin, alpha –L-olendroside -5α-adynerin, gentiobiosyl –oleandrin, odoroside A and oleandrin (Kiran and Prasad, 2014).	Antibacterial, antioxidant hepatoprotective, antiproliferative, antidiabetic, anti-inflammatory, antinociceptive, anticancer (Kiran and Prasad, 2014).	7	0.19	0.194
Asteraceae	*Artemisia herba-alba* Asso	Chih	MK.Co.23	Leaves	Decoction	Oral	Sesquiterpene lactones, flavonoids, phenolic compounds and waxes. Essential oils: α-and ß-Thujones, camphor, sabinyl acetate, germacrene D, α-eudesmol, caryophyllene acetate, 1,8-cineole, p-cymene, davanone, camphene, borneol, davana ether and chrysanthenone (Mohamed et al., 2010).	Antibiabetic, cardiovascular action, antimicrobial, antioxidant, antispasmodic, neurological action (Moufid and Eddouks, 2012), anti-venom, nematocidal activity (Mohamed et al., 2010).	36	1.0	1.417

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Asteraceae	*Chamaemelum nobile* (L.) All.	Babounj roumi	MK.Co.8	Leaves, flowers	Infusion	Oral	Angeiic and tiglic acid esters, 1,8 cineole, l-trans-pinocarveol, l-transpinocarvone, chamazulene, farnesol, and nerolidol. Flavonoids: Apigenin, luteolin, quercetin and their glycosides (apiin, luteolin-7-glucoside and rutin); Coumarins: Scopoletin-7-glucoside; germacranolide-type sesquiterpene lactones: nobilin, 3-epinobilin, 1,10-epoxynobilin, and 3-dehydronobilin; Various alcohols: Amyl and isobutyl alcohols (Al-Snafi, 2016).	Antimicrobial, hypotensive, anti-inflammatory, hypoglycemic, nervous effect, antioxidant, cytotoxic and effect in asthma (Al-Snafi, 2016).	9	0.25	0.250
Boraginaceae	*Borago officinalis* L.	Bouchnaf	MK.Co.24	Root, seeds, leaves	Decoction, infusion	Oral	Pyrogallol, salicylic acid, caffeic acid), flavonoids (myricetin, rutin) and isoflavonoid (daidzein), α-linolenic, stearidonic, palmitic, linoleic and γ-linolenic acids, α-linolenic, stearidonic, palmitic, linoleic and γ-linolenic acids. Essential oils: Aldehydes, octanal, nonanal, benzylalcohol, linalool, phenylethyl alcohol, alpha –guaiene (Asadi-Samani et al., 2014; Karimi et al., 2017).	Antioxidant, antibacterial, anti-inflammatory, anticancer, hypoglycemic, antidiabetic, treatment of multiple sclerosis, heart diseases, arthritis and eczema (Asadi-Samani et al., 2014; Karimi et al., 2017).	15	0.42	0.417
Brassicaceae	*Lepidium sativum* L.	Hab erchad	MK.Co.9	Seeds	Infusion	Oral	Glucotropaeolin, 4-methoxyglucobrassicin, esters of caffeic, β-sitosterol, benzylcyanide, calmodulin, sinapoyglucose, p-coumaric, ferulic, quinic acids, protein, mineral, vitamin, 5-4’-dihydroxy 7,8,3,5-tetramethoxyflavone, 5-3’-dihydroxy-7,8,4’ tetramethoxyflavone, and 5-3’-dihydroxy-6,7,4’-tetramethoxyflavone (Baregama and Goyal, 2019).	Antibacterial, antioxidant, antifungal, hemagglutinating activity, management of airways disorders, cytotoxic, diuretic, hepatoprotective, hypoglycemic, antiosteoporotic, antiasthmatic, anti-inflammatory and antiarthritic (Baregama and Goyal, 2019).	34	0.94	1.222

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Caryophyllaceae	*Corrigiola telephiifolia* Pourr.	Serguina	MK.Co.5	Root	Decoction, infusion, fumigation	Oral, inhalation	Saponins and terpenes (Lakmichi et al., 2011).	Antidiabetic, antibacterial, diuretic, hypolipidemic and antioxidant activities (Daoudi et al., 2017; Hebi and Eddouks, 2019; 2020; Zakariya et al., 2020).	28	0.78	0.778
Iridaceae	*Crocus sativus* L.	Zaefran hor	MK.Co.28	Flowers	Infusion, decoction	Oral	Apocarotenoids such as crocetin, crocin, safranal (the bio-oxidative cleavage products of zeaxanthin) and picrocrocin (Bukhari et al., 2018).	Antioxidant, cardiovascular effects, respiratory effects, anticancer, anti-inflammatory and analgesic effects, protective effects, antidiabetic effects, dermatological effects (Al-Snafi, 2016).	20	0.56	0.611
Lamiaceae	*Lavandula dentata* L.	Lhlhal lmrrakchi	MK.Co.22	Leaves, flowers	Infusion, decoction, fumigation	Oral, inhalation	Polyphenols and flavonoid (Pereira et al., 2019). Essential oils: Eucalyptol, fenchone, linalool, myrtenol, citronellol, camphor, sabinene, ß-caryophyllene, α-bisabolene, α -selinene, ß- caryophyllene oxide and p-cymene (Martins et al., 2019).	Antioxidant, antibacterial, antifungal antispasmodic, anti-Inflammatory, hepatoprotective (Pereira et al., 2019).	21	0.58	0.583
Lamiaceae	*Lavandula stoechas* L.	Lhalhal	MK.Co.35	Leaves, flowers	Infusion, decoction, fumigation	Oral, inhalation	Protocatechuic, caffeic, ferulic, chlorogenic and rosmarinic acids, pinobanksin, pinocembrin, quercetin and luteolin (Ez Zoubi et al., 2020). Essential oils: Camphor, cineole, camphene, linalyl acetate, γ-terpinene, linalool, lavandulyl acetate, myrtenyl acetate, bornyl acetate, borneol and caryophyllene (Ez Zoubi et al., 2020).	Antifungal, antioxidant, cytotoxic, antibacterial, antispasmodic, sedative, anti-inflammatory (Ez Zoubi et al., 2020).	21	0.58	0.806

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Lamiaceae	*Marrubium vulgare* L.	Mariouta	MK.Co.14	Flowers, leaves	Infusion, extract	Oral, inhalation	β-sitosterol, lupeol, and β-amyrin types of triterpenoids such as oleanolic acid, peregrinol, peregrinin, dihydroperegrinin, vulgarol, vulgarcoside A, deacetylvitexilactone, carnosol, deacetylforskolin, marrubiin, marrubic acid. Essential oils: camphene, p-cymol, fenchene, limonene, α-pinene, sabinene, and α-terpinolene (Lodhi et al., 2017).	Antimicrobial, antioxidant, immunomodulatory, anti-inflammatory, anticancer, antiedematogenic, antispasmodic, gastroprotective, antihypertensive, antidiabetic, analgesic, antihepatotoxic, antihyperlipidemic, antinociceptive (Lodhi et al., 2017).	25	0.69	0.694
Lamiaceae	*Mentha pulegium* L.	Fliyou	MK.Co.29	Leaves, flowers	Decoction, infusion	Oral	Luteolin-7-rutinoside, diosmin, and apigenin and respective derivatives. Essential oils: Menthone, pulegone, neo-menthol and 8-hydroxy--4(5)-p-menthen-3-one (Miraj and Kiani, 2016b; Teixeira et al., 2012).	Antimicrobial, antioxidant, antidiabetic, anti-genotoxic, spasmolytic, relaxant, hepatoprotective, anti-myometrium, metabolic effect (Miraj and Kiani, 2016b).	12	0.33	0.500
Lamiaceae	*Salvia rosmarinus* Spenn.	Azir	MK.Co.34	Leaves	Infusion, decoction, fumigation	Oral, inhalation	Rosmarinic acid, camphor, caffeic acid, ursolic acid, betulinic acid, carnosic acid and carnosol. Essential oils: camphor, 1,8-cineole, α-pinene, borneol, camphene, β-pinene and limonene (Andrade et al., 2018; Kompelly et al., 2019).	Antibacterial, antidiabetic, anti-inflammatory, antitumor antioxidant, analgesic, anti-infectious, antidepressant, neuroprotective, cholinergic, antiproliferative, hepatoprotectivity (Andrade et al., 2018; Kompelly et al., 2019).	25	0.69	0.694
Lamiaceae	*Salvia officinalis* L.	Salmiya	MK.Co.30	Leaves	Decoction, infusion	Oral	1,8-Cineole, camphor, α-thujone, β-thujone, borneol, and viridiflorol (Miraj and Kiani, 2016a).	Anticancer, antimutagenic, antioxidant, anti-inflammatory, antinociceptive, antimicrobial, antifungal, antiviral, anti-malarial antimutagenic, antidementia, hypoglycemic, hypolipidemic (Ghorbani and Esmaeilizadeh, 2017).	14	0.39	0.389

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Lamiaceae	*Teucrium polium* L.	Jaâda	MK.Co.7	Leaves, fowers	Decoction, infusion	Oral	Tannin, terpenoid, saponin, flavonoid, sterol, β-caryophyllene, diterpenoids, caryophyllene oxide, asparagine, ditryne and resinous substances (El Atki et al., 2019a; 2019b; 2020; Khazaei et al., 2018).	Antidiabetic, antioxidant, antimicrobial, anticancer and hypoglycemic effect (El Atki et al., 2019a; 2019b; 2020; Khazaei et al., 2018).	14	0.39	0.444
Lamiaceae	*Thymus vulgaris* L.	Zaatar	MK.Co.21	Leaves, flowers	Decoction, infusion	Oral	Thymol, p-cymene, caryophyllene, α-pinene, β-myrcene, thymyl methyl ether, carvacrol, β-pinene, α-cadinol and 3-carene (Al-Maqtari et al., 2011).	Anti-inflammatory, antibacterial, antiviral, antioxidant (Prasanth Reddy et al., 2014).	20	0.56	0.889
Lauraceae	*Cinnamomum verum* J.Presl	Lqarfa	MK.Co.31	Bark	Infusion	Oral	Hydrocinnamaldehyde, benzaldehyde, 3-phenylpropyl Acetate, N-heptadecane, 2-hexadecanone (Ranasinghe et al., 2013).	Antimicrobial, antiparasitic, antioxidant, effects on blood pressure, glycemic control and lipids (Ranasinghe et al., 2013).	28	0.78	1.333
Lauraceae	*Laurus nobilis* L.	Assa moussa	MK.Co.6	Leaves	Fumigation	Inhalation	1, 8-Cineole, α-pinene, β-pinene, sabinene, limonene and linalool (Chahal et al., 2017).	Antiviral, antibacterial, antifungal, wound healing, neuroprotective, antioxidant, antiulcerogenic, anticonvulsant, antimutagenic, anticholinergic (Patrakar et al., 2012).	18	0.50	0.889
Fabaceae	*Trigonella foenum-graecum* L.	Lhalba	MK.Co.15	Seeds	Infusion, cooked	Oral	Galactomannan, diosgenin isoleucine, lecithin and choline, mineral, B-complex, iron, phosphate, para-benzoic acid, vitamins A and D (Olaiya and Soetan, 2014).	Antibacterial, antifungal, antiviral, antidiabetic, antiplasmodic, hepatoprotective, hypolipidemic, analgesic activity, anthelmintic, anti-inflammatory, antioxidant, antiulcer, anticarcinogenic, antifertility, immunomodulatory effect (Haque et al., 2015; Olaiya and Soetan, 2014).	18	0.50	0.500

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Meliaceae	*Azadirachta indica* A.Juss.	Neem	MK.Co.32	Leaves	Infusion	Oral	Myricetin, linalool, urosolic acid, apigenin, quercetin, narasin (Pankaj et al., 2011).	Anti-inflammatory, antiarthritic, antipyretic, hypoglycemic, antigastric ulcer, spermicidal, antifungal, antibacterial, diuretic, immunomodulatory, antimalarial (Pankaj et al., 2011).	10	0.28	0.556
Moraceae	*Ficus carica* L.	Karmous	MK.Co.33	Fruit	Cooked, raw, maceration	Oral	3-*O*- and 5-*O*-Caffeoylquinic acids, ferulic acid, quercetin-3-*O*-glucoside, quercetin-3-*O*-rutinoside, psoralen, bergapten, oxalic, citric, malic, quinic, shikimic and fumaric acids (Oliveira et al., 2009).	Antiviral, antimicrobial, antipyretic, anti-inflammatory, antispasmodic and antiplatelet, anthelmintic, hepatoprotective, anticonstipation, hypoglycemic, hypocholesterolemic, hypolipidemic, anticancer, antimutagenic, anti-angiogenic, erythropoietic, hemostatic, antioxidant, immunostimulant (Badgujar et al., 2014).	28	0.78	1.333
Myrtaceae	*Eucalyptus globulus* Labill.	kalitous	MK.Co.4	Leaves	Fumigation	Inhalation	Eucalyptol, α-pinene, α-terpineol acetate, alloaromadendrene, β-pinene, sabinene, limonene, isoledene, α-gurjunene, aromadendrene (Abdossi et al., 2015).	Anti-inflammatory, antimicrobial, antiviral, antiseptic, antioxidant, antimalarial, respiratory and gastrointestinal disorder treatment, antitumor, antihistaminic, antidiabetic (Hardel and Laxmidhar, 2011).	36	1.0	1.833
Myrtaceae	*Syzygium aromaticum* (L.) Merr. & L.M.Perry	Lqronfil	MK.Co.16	Flower bud	Maceration	Oral	Eugenol, eugenyl acetate, β-caryophyllene (Mittal et al., 2014).	Antibacterial, antifungal, antioxidant, anticarcinogenic, analgesic, anti-inflammatory, antithrombotic, anesthetic (Mittal et al., 2014).	36	1.0	1.556
Oleaceae	*Olea europaea* L.	Zitoun	MK.Co.20	Leaves	Decoction, vegetable oil	Oral	Flavonoids, flavone glycosides, flavanones, iridoids, triterpenes, biophenols (Hashmi et al., 2015).	antioxidant, antiviral, antimicrobial, cardioprotective, antidiabetic, against respiratory diseases (Hashmi et al., 2015).	34	0.94	1.500

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Ranunculaceae	*Nigella sativa* L.	Habit El baraka	MK.Co.3	Seeds	Powder	Oral	Thymoquinone, thymohydroquinone, dithymoquinone, p-cymene, carvacrol, 4-terpineol, t-anethol, sesquiterpene longifolene, α-pinene and thymol (Ahmad et al., 2013).	Antimicrobial, antioxidant, immunomodulator, pulmonary-protective activity and anti-asthmatic effects, antidiabetic, anticancer, analgesic, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, renal protective, gastro-protective, cardiovascular activity, anti-schistosomiasis (Ahmad et al., 2013).	30	0.83	0.833
Rhamnaceae	*Ziziphus lotus* (L.) Lam.	Nbag	MK.Co.19	Fruit, root, leaves	Decoction	Oral	Polyphenols, cyclopeptide alkaloids, dammarane saponins, vitamins, minerals, amino acids, and polyunsaturated fatty acids (Abdoul-Azize, 2016).	Antimicrobial, antifungal, anti-inflammatory, antioxidant, immunomodulatory, antidiabetic, hypoglycemic, antiulcerogenic, gastroprotective, analgesic and antispasmodic (Abdoul-Azize, 2016).	15	0.42	0.417
Rutaceae	*Citrus limon* (L.) Osbeck	lhamed	MK.Co.2	Fruit	Extract	Oral	Diosmin, hesperidin, limocitrin, ferulic, synapic, p-hydroxybenzoic acids. Essential oils: D-limonene, β-pinene, γ-terpinene (Klimek-Szczykutowicz et al., 2020).	Antimicrobial, antioxidant, antiparasitic, anticancer, anti-inflammatory, gastroprotective, hepatoregenerating, antidiabetic, anti-allergic, effects on the cardiovascular system (Klimek-Szczykutowicz et al., 2020).	36	1.0	1.833
Scrophulariaceae	*Verbascum sinuatum* L.	Maslah ndar	MK.Co.17	Root. leaves, flowers	Decoction, infusion	Oral	Mulleinsaponin II, mulleinsaponin III, catalpol, 2'-O-acetylacteoside, martynoside, cistanoside (Tatli and Akdemir, 2004).	Antimicrobial, anti-inflammatory, antioxidant (Jamshidi-Kia et al., 2018).	10	0.28	0.278

Table 2. Plants used to prevent or cure COVID-19 in the prefecture of Meknes, Morocco (continued…)

Family	Scientific name	Vernacular name	Specimen number	Parts used	Preparation methods	Routes of administration	Bioactive compounds	Biological activities	Fc	RFC	UV
Verbenaceae	*Verbena officinalis* L.	Lwîsa	MK.Co.1	Leaves, fruit	Decoction, infusion	Oral	Verbascoside, isoverbascoside, campneoside II, isocampneoside II, verbenalin, hastatoside, luteolin 7-O diglucuronide, apigenin 7-O diglucuronide. Essential oils: β-citral, isobornyl formate, carvone, geranial, caryophyllene oxide, α-curcumene (Kubica et al., 2020).	Antioxidant, antibacterial, antifungal, anti-inflammatory, analgesic, anticonvulsant, anxiolytic, sedative, anticancer, wound healing, gastroprotective (Kubica et al., 2020).	8	0.22	0.222
Zingiberaceae	*Zingiber officinale* Roscoe	Skinjbir	MK.Co.18	Rhizome	Powder, infusion	Oral	Gingerols, zingibain, shogaols, paradols and zingerone (Kumar Gupta and Sharma, 2014). Essential oils: Zingeberene, curcumene and farnesene (Kumar Gupta and Sharma, 2014).	Anti-inflammatory, antimicrobial, antidiabetic, antioxidant, hepatoprotective, hypocholesterolemic, hypolipidemic, anticancer (Kumar Gupta and Sharma, 2014).	36	1.0	1.833

FC: Frequency of citation of species; RFC: Relative frequency of citation of species; UV: Use value of species. The scientific names were proposed according to The Plant List (2020) (http://www.theplantlist.org)

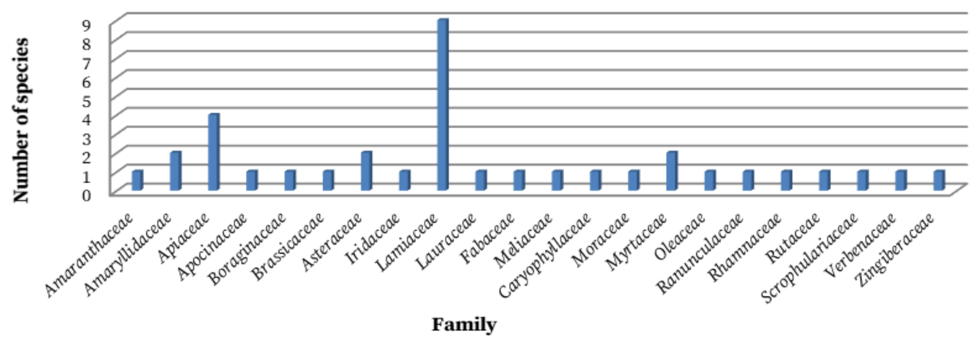

Figure 2. Richness of plant families used against COVID-19.

Table 3. Use value of families of medicinal plants used against COVID-19 in the prefecture of Meknes, Morocco.

Families	FUV	Families	FUV
Amaranthaceae	0.556	*Lamiaceae*	4.949
Amaryllidaceae	2.083	*Lauraceae*	2.222
Apiaceae	1.695	*Meliaceae*	0.556
Apocinaceae	0.194	*Moraceae*	1.333
Asteraceae	1.667	*Myrtaceae*	3.389
Boraginaceae	0.417	*Rhamnaceae*	0.417
Brassicaceae	1.222	*Rutaceae*	1.833
Caryophyllaceae	0.778	*Scrophulariaceae*	0.278
Fabaceae	0.500	*Verbenaceae*	0.222
Iridaceae	0.611	*Zingiberaceae*	1.833

Table 4. Degree of fidelity of medicinal plants used against COVID-19 in the prefecture of Meknes, Morocco.

Category of use	Species fidelity level
Treatment	*Allium sativum* L. (100%), *Lepidium sativum* L. (100%), *Artemisia herba-alba* Asso (100%), *Dysphania ambrosioides* (L.) Mosyakin & Clemants (100%), *Nerium oleander* L. (100%), *Crocus sativus* L. (100%), *Thymus vulgaris* L. (100%), *Cinnamomum verum* J.Presl (100%), *Laurus nobilis* L. (100%), *Lavandula stoechas* L. (100%), *Azadirachta indica* A.Juss. (100%), *Eucalyptus globulus* Labill. (100%), *Syzygium aromaticum* (L.) Merr. & L.M.Perry (100%), *Citrus limon* (L.) Osbeck (100%), *Nigella sativa* L. (100%), *Zingiber officinale* Roscoe (100%), *Teucrium polium* L. (92.86%), *Olea europaea* L. (82.35%), *Marrubium vulgare* L. (80%), *Salvia rosmarinus* Spenn. (72%), *Ficus carica* L. (71.43%), *Petroselinum crispum* (Mill.) Fuss (71.43%), *Allium cepa* L. (60%), *Pimpinella anisum* L. (53.33%), *Mentha pulegium* L. (50%), *Verbascum sinuatum* L. (50%), *Verbena officinalis* L. (50%), *Trigonella foenum-graecum* L. (50%), *Lavandula dentata* L. (42.86%), *Corrigiola telephiifolia* Pourr. (42.86%), *Foeniculum vulgare* Mill. (41.67%), *Borago officinalis* L. (40%), *Ziziphus lotus* (L.) Lam. (33.33%), *Salvia officinalis* L. (28,57%), *Visnaga daucoides* Gaertn. (20%), *Chamaemelum nobile* (L.) All. (11.11%)
Prevention	*Azadirachta indica* A.Juss. (100%), *Ficus carica* L. (100%), *Mentha pulegium* L. (100%), *Chamaemelum nobile* (L.) All. (88.89%), *Allium sativum* L. (83.33%), *Citrus limon* (L.) Osbeck (83.33%), *Foeniculum vulgare* Mill. (83.33%), *Eucalyptus globulus* Labill. (83.33%), *Zingiber officinale* Roscoe (83.33%), *Visnaga daucoides* Gaertn. (80%), *Laurus nobilis* L. (77.78%), *Olea europaea* L. (76.47%), *Cinnamomum verum* J.Presl (71.43%), *Salvia officinalis* L. (71.43%), *Ziziphus lotus* (L.) Lam. (66.67%), *Pimpinella anisum* L. (66.67%), *Borago officinalis* L. (60%), *Thymus vulgaris* L. (60%), *Petroselinum crispum* (Mill.) Fuss (57.14%), *Lavandula dentata* L. (57.14%), *Corrigiola telephiifolia* Pourr. (57.14%), *Syzygium aromaticum* (L.) Merr. & L.M.Perry (55.56%), *Trigonella foenum-graecum* L. (50%), *Verbascum sinuatum* L. (50%), *Verbena officinalis* L. (50%), *Artemisia herba-alba* Asso (41.67%), *Allium cepa* L. (40%), *Lavandula stoechas* L. (38.10%), *Lepidium sativum* L. (29.41%), *Salvia rosmarinus* Spenn. (28%), *Teucrium polium* L. (21.43%), *Marrubium vulgare* L. (20%), *Crocus sativus* L. (10%)

Table 5. The informant agreement ratio values by categories of use against COVID-19 in the prefecture of Meknes, Morocco.

Category of use	Nt	Nur	IAR
Treatment	36	618	0.943
Prevention	33	423	0.924

IAR = informant agreement ratio; Nur = number of mentions in each usage category; Nt = number of taxa used in each usage category.

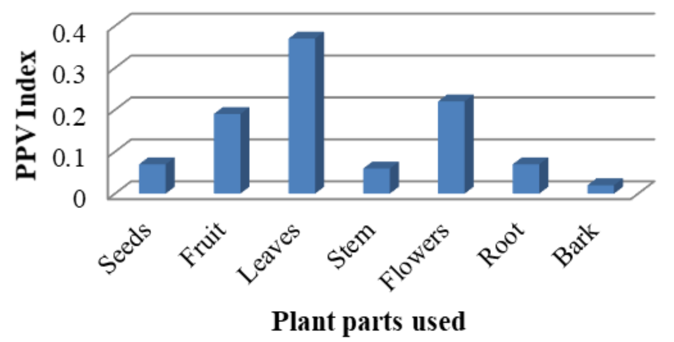

Figure 3. Plant parts used against COVID-19.

Furthermore, some species were only used by the traditional medicine actors interviewed for the treatment of COVID-19, such as *Dysphania ambrosioides* (L.) Mosyakin & Clemants, *Nerium oleander* L. and *Nigella sativa* L. (Table 4).

Informant agreement ratio

To assess the consistency of information provided by different informants on the species used against COVID-19 the informant agreement ratio was calculated. An IAR value close to 1 indicates agreement on the selection of taxa among informants. The results showed a consensus between the traditional medicine actors of the Meknes prefecture on both the plants used for treatment (IAR = 0.943) and those used for prevention (IAR = 0.924) (Table 5).

Parts of plants used

In the prefecture of Meknes, herbalists used different plant parts (leaves, flowers, fruits, roots, seeds, stems and barks) to prepare traditional remedies against COVID-19. Thus, based on the value of plant parts (PPV Index), leaves were reported as the most recommended plant part (PPV = 0.37), followed by flowers (PPV = 0.22), fruit (PPV = 0.19); roots and seeds both came fourth (PPV = 0.07) and bark came last (PPV = 0.02) (Fig. 3).

Methods of preparation of remedies

Remedies against COVID-19 were prepared in different ways. Infusion and decoction were the two most common methods of preparation reported by the respondents with a rate of 35.94% and 29.69%, respectively; fumigation came in third place with a percentage of 14.06%. Also, the recommended plants can be cooked (6.25%), or their juices were extracted by chewing them or grinding them with a mortar (4.69%). Some of them were powdered (3.13%) or used after maceration (3.13%). On the other hand, vegetable oils and the use of the raw plant represented only 1.56% for each (Fig. 4).

In general, the ethnomedicinal preparations used by the herbalists surveyed were based on the separate use of plants, but mixtures were also used. These preparations may be accompanied by milk or honey.

Methods of administration of remedies

The mode of administration varied according to the active ingredient of the plant and the symptom treated. Thus, in the study area, herbalists recommended mainly the oral route to treat COVID-19 (76.74%), but they also resorted to inhalation (20.93%) and brushing (2.33%) (Fig. 5).

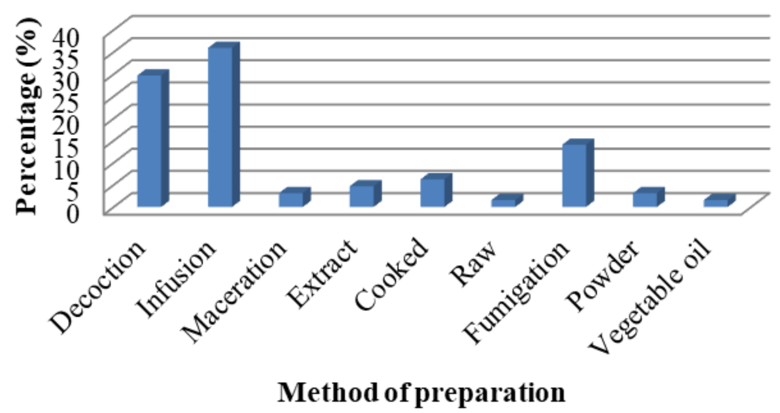

Figure 4. Frequency of different preparation methods.

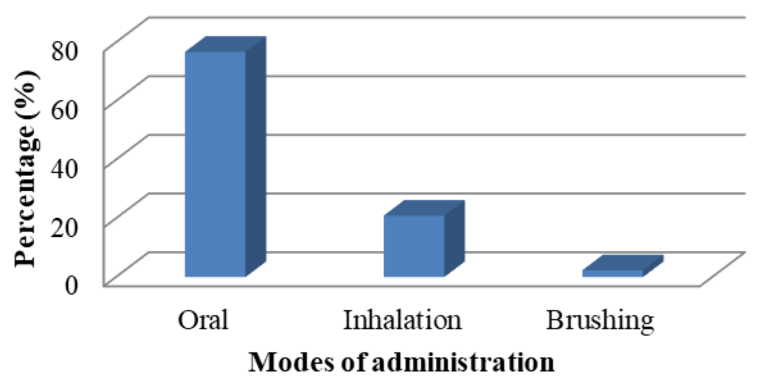

Figure 5. Frequency of different modes of administration.

DISCUSSION

Since antiquity and through many civilizations, man has always sought to use plants to survive and develop remedies to treat various diseases (Bouyahya et al., 2017). Indeed, plants have always attracted the attention of researchers for the discovery of bioactive molecules. In addition, in North Africa, phytotherapy is very anchored in the culture of the populations and holds a very important place in traditional medicine (Najem et al., 2018a). Currently, and during the pandemic of COVID-19, the Moroccan population has resorted to traditional herbal medication to prevent this disease or cure its symptoms; this is also the case in Meknes city.

Thus, ethnobotanical investigations conducted among herbalists in this region have shown that the herbal medicine and phytotherapy sectors are dominated by the male sex, the same as other works carried out in other regions of Morocco (Bachiri et al., 2015; Daoudi et al., 2015).

Moreover, the ethnomedicinal know-how is found in different age groups; also, the presence of young people in the field of herbal medicine is quite visible, demonstrating the persistence of natural and traditional treatments and the durability of the transmission of knowledge from one generation to another (Najem et al., 2019a). Nevertheless, the knowledge of the uses of the medicinal plants and their properties, particularly their toxicity, is generally acquired after a long accumulated experience (Anyinam. 1995). In addition, the survey revealed that information on the plants used against COVID-19 varies from one respondent to another; in fact, each individual holds a secret that has been transmitted either by his ancestors, or during training with the holders of traditional know-how, or through the accumulation of knowledge after several years of experience. Finally, concerning the level of education, most of the respondents have secondary school education. Also, the herbalists who have a university academic level, although they represent only 8.33%, can positively influence the practice of herbal medicine because they are able to document themselves on each plant and to become aware of the degree of seriousness of each reported toxic principle and also can ensure the written transcription of their knowledge and thus avoid its erosion or its bad transmission, when only orality is adopted (Najem et al., 2021a).

On the one hand, during this study, the interviews undertaken with herbalists in the city of Meknes allowed listing 36 species used against COVID-19. These species are distributed over 33 genera and 22 botanical families. The most presented family is *Lamiaceae,* followed by *Apiaceae* and *Asteraceae.* These families are the most represented in the Mediterranean countries (Benítez et al., 2010; Savo et al., 2011) and include many spontaneous species (Nassiri et al., 2016) beneficial but also toxic (Najem et al., 2018b; Najem et al., 2019b). Taking into account the use value of the families, the most represented families are *Lamiaceae*, *Myrtaceae* and *Lauraceae*. This predominance is due to the possession of species of these families of many secondary metabolites, in particular, sesquiterpene lactones, volatile oils and terpenoids, all effective against respiratory diseases (Adekenov, 1995; Cronquist, 1982) and with antiviral activity (GabAllah et al., 2020; Nolkemper et al., 2006).

On the other hand, the calculation of the relative frequency of citation (RFC) revealed that some species are more recommended than others, probably because they are well known among the traditional medicine practitioners surveyed for their frequent use in the treatment of various respiratory diseases and the cure of symptoms similar to those accompanying COVID-19 (Kayani et al., 2014). Thus, the species *Artemisia herba-alba* Asso. *Eucalyptus globulus* Labill. *Syzygium aromaticum* (L.) Merr. & L.M.Perry. *Citrus limon* (L.) Osbeck and *Zingiber officinale* Roscoe are used by all respondents to prepare remedies against COVID-19. Similarly, these species have the highest recorded use values (Table 2). Therefore, they should be subject to biochemical, pharmacological and toxicological analyses that would allow the identification of the active principles that will be useful in treating or preventing the said disease. Plants with low UV should not be ignored to ensure better the transmission of ancestral knowledge to future generations (Najem et al., 2020a).

The high IAR values found in the study indicate reasonable reliability of informants on the use of medicinal plants to prevent or cure COVID-19. Similarly, these values highlighted the sharing of medicinal knowledge among traditional medicine actors in the study area (Lin et al., 2002).

Also, various parts of plants are used in the preparation of ethnomedical remedies in the city of Meknes, and the choice of one part or the other is based on the utility sought, the method of preparation, the content of active principles, the know-how of each herbalist and the endogenous knowledge related to the use of this part. In this framework, the calculation of the index of the value of the parts of the plant "PPV" showed that the leaves are the most recommended part, and this is probably due to the ease of their collection without the cycle of life of the plant being affected (Bhat et al., 2013). Moreover, the leaves are the photosynthetic seat from their richness in secondary bioactive metabolites (Ould El Hadj et al., 2003). Also, previous studies have shown that the leaves are the most used part in the treatment of respiratory diseases (Alamgeer et al., 2018; Najem et al., 2021b).

Moreover, the modes of preparation and administration of the medicinal recipes are among the key parameters which condition the effectiveness, safety or toxicity of a plant (Najem et al., 2020c). Some preparation methods allow to extract higher concentrations of active principles than others, and the best use of a plant would be the one that would preserve all its properties while allowing the extraction and assimilation of these active principles (Dextreit, 1984). Indeed, the preparation mode is related to the nature of the chemical compounds and the mode of use, and generally, decoction, infusion, maceration are recommended for internal use, while fumigation is used by nasal route (inhalation) (Najem et al., 2021b). Also, in the study area, the three most commonly used modes of use against COVID-19 are infusion, decoction and fumigation. Finally, the preference for a method of administration or preparation is also related to the symptoms treated; thus, inhalation allows direct contact of the curative active ingredients with the respiratory tract (Najem et al., 2021b); as for the predominance of oral administration, it is due to both its ease and its acceptability by the patient. In addition, the results of the investigations carried out showed that the majority of the recipes prepared by the herbalists interviewed against COVID-19 use water as a diluent; this is in agreement with the results found by other researchers (Bouyahya et al., 2017). Milk, olive oil, and honey are also used as a diluent or accompaniment because these products are part of the culture of the local population and are considered essential food, even a remedy for many diseases.

On the other hand, the present study showed that most of the species had a fidelity level equal to 100%, reflecting their efficacy against COVID-19; only 4 species used for treatment and 6 species used for prevention recorded a level of fidelity below 40% (Table 4). Thus, the medicinal plants used by the herbalists in the preparation of curative and preventive recipes against COVID-19 contain an important number of active principles such as flavonoids, terpenes, saponins, tannins, lignans, coumarins, alkaloids, anthraquinones, organosulfur compounds, secoiridoids, phenolic lipids, glycosides, carotenoids, steroids, essential oils, and many other active molecules (Table 2). These compounds have several biological and pharmacological activities, including antimicrobial, antioxidant, anti-inflammatory, antiviral, antiasthmatic, bronchodilator, immunomodulator, antidiabetic, anticancer, analgesic, antifungal, lung-protective, hepato-protective, kidney-protective, gastro-protective, cardiovascular, antitumor, anticancer, antiallergic, antiatherogenic, antimutagenic and many others (Table 2).

Thus, polyphenols, flavonoids, proanthocyanidins, saponins, monoterpenoids, triterpenoids, glycosides, sesquiterpenes and alkaloids isolated from various medicinal plants have diverse antiviral activities and may act through different mechanisms towards SARS-CoV-2 (Adhikari et al., 2020). These mechanisms include viral protease inhibition, where inhibitors modify or deactivate the configuration of proteases involved in the proteolytic activity associated with the disease (Adhikari et al., 2020). Also, secondary plant metabolites may act by inhibiting viral replication steps; the coronavirus genome encodes a protein called RNA-dependent RNA polymerase (RdRP), which allows the viral genome to be transcribed into new RNA copies using the host cell machinery, and inhibition of this RdRP may be a potential target for controlling viral infection (Adhikari et al., 2020). Similarly, inhibition of the spike protein and viral receptor can be used as a means of control; in fact, the SARS-CoV-2 spike glycoprotein contains a receptor-binding domain (RBD) that recognizes the target receptor, and the angiotensin-converting enzyme-2 (ACE-2) receptor is a preferred receptor for SARS-CoV-2 (Peng et al., 2020). Secondary metabolites such as hesperidin, pectolinarin, cannabinoids, rhoifolin, diosmin, apiin, diacetylcurcumin from medicinal plants are bioactive against the major SAR protease S-CoV-2 and the spike glycoprotein (Adhikari et al., 2020).

In the present study, medicinal plants recommended by the surveyed herbalists such as *Crocus sativus* L., *Nerium oleander* L. and *Lauris nobilis* L., containing crocin, digitoxigenin and β-eudesmol, respectively were shown to be able to inhibit SARS CoV-2 by the molecular docking method based on the types of interaction energies between these molecules and the main protease inhibitor of coronavirus (nCoV-2019) (Aanouz et al., 2020). For its part, *Nigella sativa* L., which has always been considered as a panacea by many Muslim and Christian populations of North Africa, has been shown to inhibit COVID-19 ; its active components, nigellidine and α hederine act on the main protease (Mpro), giving the same or higher energy score than drugs submitted to clinical tests such as chloroquine, hydroxychloroquine, azithromycin, arbidol, remdesivir, lopinavir/ritonavir, ribavirin, chloroquine phosphate and favipiravi (Bouchentouf and Missoum, 2020).

Moreover, essential oils can be potential antiviral agents against SARS-COV-2. In this sense, the essential oil of *Eucalyptus globulus* Labill. has demonstrated its antiviral action against coronaviruses, in particular COVID-19, thanks to its major compound eucalyptol made up of ether, ketone and hydroxyl groups, which play the main inhibitory role against SARS-CoV-2 (Sharma and Kaur, 2020). Also, essential oils can be used as an antiviral drug alone or in synergy with synthetic antiviral agents (Bary and El Amraoui, 2020). In addition, they are used as dietary supplements to relieve symptoms or strengthen the immune system of affected patients; in fact, linalool, β-caryophyllene and 1,8-cineole have anti-inflammatory and anti-nociceptive activity (Klauke et al., 2014; Li et al., 2016; Peana et al., 2003; Santos and Rao, 2000). Thymol and camphor have antitussive activity (Gavliakova et al., 2013a; 2013b). Similarly, essential oils can be used as an adjuvant in hydro-alcoholic solutions or gels to increase their effectiveness in the external control of COVID 19 (Bary and El Amraoui, 2020).

Nevertheless, to date, there is no absolute therapy against COVID-19 (Rodríguez-Morales et al., 2020); the exploration of different remedies is a priority for the scientific community, and experts in herbal medicine focus on medicinal plants that can be effective in treating COVID-19 and strengthening the immune system to inhibit the spread of this disease. However, despite the therapeutic properties of medicinal plants, they may contain toxic substances that can cause various disorders and intoxications. Indeed, in the framework of ethnobotanical investigations carried out by our research team, in particular, on toxic medicinal plants, it turned out that 52.78% of the plants recommended by herbalists against COVID-19 in the city of Meknes have already been declared toxic by the practitioners of traditional medicine in the Moroccan central Middle Atlas. These plants are: *Dysphania ambrosioides* (L.) Mosyakin & Clemants, *Visnaga daucoides* Gaertn., *Foeniculum vulgare* Mill., *Pimpinella anisum* L., *Nerium oleander* L., *Borago officinalis* L. *Lepidium sativum* L., *Artemisia herba-alba* Asso, *Chamaemelum nobile* (L.) All., *Marrubium vulgare* L., *Mentha pulegium* L., *Salvia rosmarinus* Spenn., *Salvia officinalis* L., *Teucrium polium* L., *Laurus nobilis* L., *Trigonella foenum-graecum* L., *Corrigiola telephiifolia* Pourr., *Ziziphus*

Table 6. Summary of toxic principles and symptoms of intoxication by some plants used to treat COVID-19.

Scientific name	**Vernacular name**	**Toxic principles**	**Symptoms of intoxication**
Artemisia herba-alba Asso	Chih	β-thujone (Bellakhdar, 1997)	- Neurological disorders: Thujone inhibits the gamma-aminobutyric acid A (GABA(A)) receptor, causing excitation and convulsions in a dose-dependent manner (Pelkonen et al., 2013); - Visual disorders, gastrointestinal disorders (Sijelmassi, 1993); - Abortive, hemorrhagic (Pierre and Lis, 1992).
Azadirachta indica A.Juss.	Neem	Azadirachtin (Durasnel et al., 2014)	- Hypoglycemia, coma, tachycardia, mydriasis, hypothermia, renal failure, hepatic cytolysis, diarrhea, vomiting (Durasnel et al., 2014).
Borago officinalis L.	Bouchanaf	Pyrrolizidine alkaloids (Bellakhdar, 1997)	- Genotoxic, carcinogenic, teratogenic, and hepatotoxic effects (Durnev and Lapitskaya, 2013); - Veno-occlusive (Aouadhi, 2010).
Chamaemelum nobile (L.) All.	Babounj roumi	Anthecotulid and matricarin (Gardiner, 1999)	- Allergic contact dermatitis (Cabanillas et al., 2006).
Cinnamomum verum J.Presl	Lqarfa	Cinnamic acid, coumarin compound (Singh et al., 2021)	- Intraoral allergic contact dermatitis; - Hepatotoxic effects (Singh et al., 2021).
Corrigiola telephiifolia Pourr.	Serguina	Saponins (Lakmichi et al., 2011)	- Nephrotoxicity, hepatic injury, nutrient deficiency, abdominal contractions, inactivity, prostration, intense diarrhea, and respiratory complications (Lakmichi et al., 2011).
Dysphania ambrosioides (L.) Mosyakin & Clemants	Mkhenza	Carvacrol, ascaridole and caryophyllene oxide (Gille et al., 2010)	- Headache and unconsciousness (Bellakhdar, 1997); - Congestion of the lungs, metaplastic changes in the mucosal surface of the stomach, and necrosis of the kidney tubules (Amole and Izegbu, 2005); - Liver toxicity (Derraji et al., 2014); - Inhibition of the respiratory chain (Gille et al., 2010).
Eucalyptus globulus Labill.	Kalitous	Monoterpenes, α and β-pinene, limonene, 1,8-cineole (Lobstein et al., 2018)	- Kidney irritation, heartburn, nausea, vomiting, coma (Lobstein et al., 2018).
Foeniculum vulgare Mill.	Besbas	Estragole or methyl chavicol (Levorato et al., 2018) and anethole or trans-anethole (Lamarti et al., 1993)	- Neurological disorders: daze, hallucinations and convulsions (Bellakhdar, 1997); - Hepatotoxicity and nephrotoxicity (Al-Hizab et al., 2018); - Respiratory distress, movement disorder and unresponsiveness to external stimulation (Ostad et al., 2001).
Laurus nobilis L.	Assa moussa	Sesquiterpene lactones (Cheminat et al., 1984)	- Allergic contact dermatitis (Cheminat et al., 1984).
Lepidium sativum L.	Hab erchad	Not identified	- Enterohepato-nephrotoxicity; - Organ damage with anemia and leukopenia correlated with alterations in serum AST, ALT, total protein, cholesterol, urea, and other serum constituents (Adam, 1999).
Marrubium vulgare L.	Mariouta	Psoralen (Tahri et al., 2012; Zenjari et al., 2019)	- Irritation of the skin and mucous membranes (Tahri et al., 2012; Zenjari et al., 2019).
Mentha pulegium L.	Fliyou	Pulegone (Hadi et al., 2017)	- Reproductive performance of female rats and induces fetotoxicity (Gerenutti et al., 2014).

Table 6. Summary of toxic principles and symptoms of intoxication by some plants used to treat COVID-19 (continued...)

Scientific name	Vernacular name	Toxic principles	Symptoms of intoxication
Nerium oleander L.	Dfla	Cardiotonic glycosides, the main one being oleandrin (Al-Farwachi et al., 2008)	- Digestive disorders: nausea, vomiting, abdominal pain, gastroenteritis; - Neurosensory disorders: agitation, obnubilation, headache; - Color vision disorders and mydriasis; - Cardiac disorders: conduction and/or automatism disorders and arrhythmia; - Skin disorders: skin burning dermatitis (Bakkali et al., 2010; Flesch, 2005).
Nigella sativa L.	Habit El baraka	Thymoquinone (Anlar and Bacanli, 2020)	-Toxic effects on the histological structure of the kidney, hepatic toxicity (Zaghlol et al., 2012); -Changes in hemoglobin metabolism and the fall in leukocyte and platelet (Zaoui et al., 2002).
Pimpinella anisum L.	Habat hlawa	Anethol (Bellakhdar, 1997)	- Neurological disorders: general excitement, hallucinations and epileptiform seizures (Bellakhdar, 1997)
Salvia officinalis L.	Salmiya	Ketones (alpha, beta-thujone and camphor) (Milpied-Homsi, 2009)	- Epileptiform convulsion (Brneuton, 1996); -Hepatotoxicity (Lima et al., 2003)
Salvia rosmarinus Spenn.	Azir	Verbenone and camphor (Hedayat et al., 2020)	- Irritations and gastrointestinal bleeding; - Epilepsy; - Hepatotoxicity; - Nephritis; - Neurotoxicity (Aouadhi, 2010)
Syzygium aromaticum (L.) Merr. & L.M.Perry	Lqronfil	Eugenol (Mohammadi Nejad et al., 2017)	- Significant decrease in sperm count, motility and testosterone (Dehghani et al., 2012); - Hepatotoxic effects, acute respiratory distress with hemorrhagic pulmonary edema, toxic effects on mitochondrial function, damage in kidney and some morphological alteration and cell apoptosis in renal cells and changes in blood chemistry (Mohammadi Nejad et al., 2017).
Teucrium polium L.	Jaada	Furancontaining diterpenoids (Bunchorntavakul and Reddy, 2013)	- Hepatic necrosis (Mazokopakis et al., 2004) - Renal tubular damage (Rafieian-Kopaei et al., 2014)
Trigonella foenum-graecum L.	Lhalba	Trigonelline (Kharchoufa et al., 2018)	- Fore-limb inflammation and alopecia, spermatotoxic effects (Al-Ashban et al., 2010). - Fenugreek in teratogenic dosages can decrease the severity of bone marrow cell proliferation and increase fetal mortality rate (Araee et al., 2009).
Visnaga daucoides Gaertn.	Bachnikha	Khellin (Al-Shoubaki et al., 2020)	- Photosensitization, hepatotoxicity, allergy (Boudghene Stambouli, 2017). - Nausea, dizziness and collapse (Gattefossé, 1952).

lotus (L.) Lam. and *Verbascum sinuatum* L. (Najem et al., 2020c; 2021c).

In addition, the consultation of some review works, and the analysis of several articles related to clinical tests and research conducted in laboratories confirmed the toxicity of several plants recommended by herbalists of the prefecture of Meknes in the treatment of COVID-19 (Table 6). The degree of severity of intoxications by these plants and their impact on the organism are variable. They are responsible for the alteration of several systems and organs, notably the nervous system, the gastrointestinal tract, the liver, the kidneys, the heart, and are also involved in allergic reactions and dermatoses (Table 6).

The toxicity of these plants is mainly due to the toxicity of their active ingredients, whose nature is extremely diverse both from the point of view of molecular structure and biological impacts (Najem et al., 2021c). The most dangerous are alkaloids, cardiotonic heterosides, terpenoids of essential oils; then, in second place, there are quinones, saponosides, furanocoumarins, glucosinolates, polyenes and calcium oxalates (Alison and Paul, 2008).

In addition, the safety or toxicity, the effectiveness or ineffectiveness of a remedy depends strongly on other parameters such as the dosage and the method of preparation or administration (Najem et al., 2020c). Indeed, a plant that is medicinal at a low dose and in rigorous conditions of use can become a danger for the health if it is not used correctly (Hammiche et al., 2013). Overdosing is dangerous even for non-toxic plants and synthetic drugs, so it is essential to know the useful dose that acts without causing metabolic disorders, even if this is sometimes difficult with natural substances, especially when it is the totality of the active ingredients that gives a plant its activity and clinical efficacy "*Notion of totum*" and not an isolated compound (Bone and Mills, 2013). In addition, the risk of medicinal plants also depends on factors related to the consumers, such as age, physiological state and concomitant diseases, the elderly, people with altered health conditions being the most sensitive (Zeggwagh et al., 2013).

CONCLUSION

The present study conducted among herbalists in the city of Meknes, listed 36 species belonging to 22 different families used to prevent coronavirus disease 2019 or treat any of its symptoms. The species most recommended by the herbalists interviewed are *Artemisia herba-alba* Asso, *Eucalyptus globulus* Labill., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Citrus limon* (L.) Osbeck and *Zingiber officinale* Roscoe. The leaves are the most commonly used part of the plants, most often orally and as an infusion. Thus, ethnobotanical and ethnopharmacological data collected during this critical period of the COVID-19 pandemic reveal that traditional medicine, especially herbal medicine, is still embedded in the primary health care system of Moroccans.

Although ethnobotanical and ethnopharmacological studies have often been the basis for the discovery of new natural molecules with important biological activities, seemingly innocuous herbal remedies can present a major risk of intoxication if misused. Therefore, it is imperative to investigate the means of circumventing the risks of intoxication since the prohibition of the use of these plants is difficult, even impossible. In this context, phytochemical, pharmacological and toxicological research, and clinical tests are necessary in order to integrate traditional medicine into conventional treatment, particularly that of COVID-19.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTION:

Contribution	Najem M	Ibijbijen J	Nassiri L
Concepts or ideas	x		x
Design	x		x
Definition of intellectual content	x		x
Literature search	x		x
Experimental studies	x		x
Data acquisition	x		x
Data analysis	x	x	x
Statistical analysis	x		x
Manuscript preparation	x	x	x
Manuscript editing	x	x	x
Manuscript review	x	x	x

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