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Chemotaxonomic Study of the Covid-Organics of Madagascar Based on the Chemical Composition of Their Essential Oils

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Abstract

The aim of this study was to investigate the chemical composition of the essential oils of "Covid-Organics" of Madagascar (62% *Artemisia annua* and two other undisclosed medicinal plants) used as curative and preventive treatments of Covid-19, to identify its constituent species. The essential oils isolated by hydro-distillation from two samples (curative and preventive) were analyzed by GC-FID and GC-MS. These essential oils (curative and preventive) were mainly dominated by camphor (17.9% and 11.9%, respectively), spathulenol (4.8% and 11.8%, respectively), *α*-acorenol (4.3% and 3.7%, respectively), (*E*)-*β*-caryophyllene (3.4% and 4.2%, respectively), 1,8-cineole (3.1% and 3.6%, respectively), hexadecanoïc acid (3.8% and 3.2%, respectively) and caryophyllene oxide (3.4% and 2.4%, respectively). From the chemical composition, two species were identified, *A. annua* characterised by camphor and *Cinnamomumcamphora* (Ravintsara) characterised by 1,8-cineole and sabinene. However, we were unable to identify the third species.

Keywords

Covid-19, Covid-Organics, *Artemisia annua*, Essential Oils, Chemotaxonomic

1. Introduction

Since the end of December 2019, a new coronavirus (Covid-19) with human-to-human transmission and serious human infection was identified. This virus affected many people in a very short time [1] [2]. On January 30, 2020, the Director-General of the World Health Organization declared the Covid pandemic a public health emergency of international concern and issued temporary recommendations under the International Health Regulations [3].

This pandemic was still ongoing, so there was an urgent need to find new preventive and therapeutic agents as soon as possible. Although specific vaccines and antiviral agents are the most effective methods to prevent and treat viral infection, there are not yet effective treatments that target Covid-19. The development of these treatments could take months or years, which means that a more immediate treatment or control mechanism should be found if possible [4]. Medicinal plants present a potentially valuable resource for this purpose [5].

Thus, in April 2020, the Malagasy Institute for Applied Research developed an herbal tea composed of 62% Artemisia annua and two other medicinal plants whose names were not revealed that grow in Madagascar (Covid-Organics), claiming preventive and curative properties against Covid-19 [6]. *Artemisia annua* L. (Asteraceae) is native to China, well known as the source of artemisinin and used in the treatment of the malaria. In addition, its essential oils have several therapeutic properties [7] [8] [9] [10] [11].

In May, Senegal placed its order for "Covid-Organics", but the National Scientific Committee demanded that we first carry out in-depth scientific examinations on this product made in Madagascar before possibly using it on patients with coronavirus because reliable botanical, chemical, toxicological and pharmacological data were lacking.

Therefore, the aim of this study was to investigate the chemical composition of the essential oils of "Covid-Organics" to identify its constituent species.

2. Experimental

2.1. Plant Material

Samples (two remedies in the form of herbal teas: curative and preventive) were provided by the Pharmacy and Drug Directorate. The two remedies were composed of 62% *Artemisia annua* and two other medicinal plants whose names were not revealed. The only difference was the dosage: the curative remedy was administered 3 times/day, while the preventive was administered 2 times/day.

2.2. Extraction of Essential Oils

Samples were hydrodistilled (6 h) using a Clevenger-type apparatus according to the method recommended in the European Pharmacopoeia [12]. The yields of essential oils (w/w, calculated on dry weight basis) were given in **Table 1**.

2.3. Chemical Compositions

The chromatographic analyses were carried out using a Perkin-Elmer Autosystem XL GC apparatus (Walthon, MA, USA) equipped with dual flame ionization detection (FID) system and fused-silica capillary columns, namely, Rtx-1 (polydimethylsiloxane) and Rtx-wax (poly-ethyleneglycol) (60 m × 0.22 mm i.d;

Table 1. Chemical composition of the essential oils of the two remedies.

N[a]	Compounds	lRI*a*[b]	RI*a*[c]	RI*p*[d]	Remedies	
					Curative	**Preventive**
1	*α*-thujene	766	922	1023	0.1	0.1
2	*α*-pinene	936	931	1015	0.4	0.7
3	Camphene	950	943	1066	0.4	0.6
4	Sabinene	973	964	1120	0.6	1.4
5	*β*-pinene	978	970	1110	0.3	0.5
6	Myrcene	987	980	1159	0.1	0.2
7	*p*-cymene	1015	1011	1268	0.3	0.8
8	1,8-cineole	1024	1020	1209	3.1	3.6
9	*γ*-terpinene	1051	1047	1243	0.1	0.2
10	Camphor	1123	1123	1517	17.9	11.9
11	Borneol	1150	1148	1698	0.2	0.8
12	Terpinen-4-ol	1164	1161	1600	2.6	0.1
13	*α*-terpineol	1176	1179	1700	2.6	2.7
14	*Trans*-carvyl acetate		1316	1731	0.4	0.6
15	*Cis*-carvyl acetate		1343	1767	0.2	0.4
16	*α*-copaene	1379	1379	1488	0.8	0.9
17	(*E*)-*β*-caryophyllene	1421	1420	1591	3.4	4.2
19	(E)-*β*-farnesene	1446	1448	1661	0.2	2.1
18	*α*-humulene	1455	1456	1665	2.1	5.3
20	*α*-himachalene	1449	1450	1639	0.9	0.4
21	*g*-gurjunene	1413	1470	1654	2.1	2.2
22	Germacrene-D	1479	1480	1704	0.9	2.8
23	*β*-selinene	1486	1483	1712	1.8	2.0
24	Ledene	1491	1494	1695	0.9	1.1
25	Spathulenol	1572	1557	2119	4.8	11.8
26	Caryophyllene oxyde	1570	1569	1980	3.4	2.4
27	Humulene epoxyde II	1602	1601	2044	2.9	3.1
28	1,10-di-epi-cubenol	1615	1608	2031	2.9	5.3
29	*α*-acorenol	1623	1616	2123	4.3	3.7
30	Cadina-4-en-7-ol	1627	1627	2096	0.4	1.0
31	Hexadecanoïc acid	1962	1947	2886	3.8	3.2
32	Linoleic acid	2123	2123	3176	-	0.6
		Hydrocarbon monoterpenes			2.3	4.5
		Oxygenated monoterpenes			27.0	20.1
		Hydrocarbon sesquiterpenes			13.1	21
		Oxygenated sesquiterpenes			22.5	30.5
		Other compounds			-	0.6
		Total identified (%)			64.9	76.7
		Yields (w/w vs dry material)			0.16	0.2

[a]Order of elution is given on apolar column (Rtx-1); [b]Retention indices of literature on the apolar column (lRIa); [c]Retention indices on the apolarRtx-1 column (RIa); [d]Retention indices on the polar Rtx-Wax column (RIp).

film thickness 0.25 µm). The oven temperature was programmed from 60 to 230˚C at 2˚C/min and then held isothermally at 230˚C for 35 min: hydrogen was employed as carrier gas (1 mL/min). The injector and detector temperatures were maintained at 280˚C, and samples were injected (0.2 µL of pure oil) in the split mode (1:50). Retention indices (RI) of compounds were determined relative to the retention times of a series of n-alkanes (C5-C30) by linear interpolation using the Van den Dool and Kratz (1963) equation with the aid of software from Perkin-Elmer (Total Chrom navigator). The relative percentages of the oil constituents were calculated from the GC peak areas, without application of correction factors.

Samples were also analysed with a Perkin-Elmer Turbo mass detector (quadrupole) coupled to a Perkin-ElmerAutosystem XL, equipped with fused-silica capillary columns Rtx-1 and Rtx-Wax. The oven temperature was programmed from 60 to 230˚C at 2˚C /min and then held isothermally at 230˚C (35 min): hydrogen was employed as carrier gas (1 mL/min). The following chromatographic conditions were employed: injection volume, 0.2 µL of pure oil; injector temperature, 280˚C; split, 1:80; ion source temperature, 150˚C; ionization energy, 70 eV; MS (EI) acquired over the mass range, 35 - 350 Da; scan rate, 1 s. Identification of the components was based on: (a) comparison of their GC retention indices (RI) on non-polar and polar columns, determined from the retention times of a series of n-alkanes with linear interpolation, with those of authentic compounds or literature data; (b) on computer matching with commercial mass spectral libraries [13] [14] [15] and comparison of spectra with those of our personal library; and (c) comparison of RI and MS spectral data of authentic compounds or literature data.

3. Results and Discussion

The essential oil yields of the two remedies (curative and preventive) were 0.16% and 0.2%, respectively.

Chemical analysis by Gas Chromatography (GC) showed that the two essential oils of the two remedies (curative and preventive) have identical chromatographic profiles. This analysis allowed the identification of 32 compounds representing 64.9 and 76.7%, respectively, of the total chemical compositions. This confirms that the two remedies are made from the same plants. These essential oils (curative and preventive) were mainly dominated by camphor (17.9% and 11.9%, respectively), spathulenol (4.8% and 11.8%, respectively), *α*-acorenol (4.3% and 3.7%, respectively), (*E*)-*β*-caryophyllene (3.4% and 4.2%, respectively), 1,8-cineole (3.1% and 3.6%, respectively), Hexadecanoïc acid (3.8% and 3.2%, respectively) and caryophyllene oxide (3.4% and 2.4%, respectively). Camphor is a characteristic compound of the essential oil of *A. annua* and its content can be up to 50% in *A. annua* [7] [8] [16] [17]. It was the main compound of the essential oil of *A. annua* grown in Senegal [17]. 1,8-cineole was found at significant levels in both essential oils (3.1% and 3.6%, respectively) along with sabinene. These two compounds constitute the chemotype of Ravintsara (*Cinnamomum camphora*, ct 1,8-cineole and sabinene) from Madagascar [18] [19] [20] [21] [22]. These results show that both remedies contain *A. annua* and *C. camphora*. However, we were unable to identify the third species. This hypothesis was confirmed by the capsule form (Artemisinin and essential oil of *C. camphora*) [23].

Ravintsara oil is distilled from the leaves of *C. camphora* belongs to the family Lauraceae in Madagascar. True Ravintsara essential oils contain at least 45% of 1,8-cineole [19] [20] [21] [22]. During the recent outbreak of coronavirus (SARS-CoV-2), Ravintsara oil is found to inhibit the coronavirus *in vitro* and *in vivo* due to its antiviral properties [24] [25]. Ravintsara oil is an excellent germ fighter and has antiviral, anti-inflammatory, and anti-spasmodic properties which can calm muscles and soothe coughs [19] [20] [21] [25].

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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