Evaluation the potential of urinary volatilomic patterns of patients infected with SARS-CoV-2 for COVID-19 diagnosis. An exploratory study

Giulia Riccio [1,2], Joana Neto [3], Cristina V. Berenguer [3], Cristina P. Ornelas [4], Viviana Greco [1,2], Jorge A.M. Pereira [3], Rosa Perestrelo [3], José S. Câmara [1,5,*]

SUPPLEMENTARY MATERIAL

Supplementary Table S1.

Identified metabolites in urine samples of COVID patients, patients who recovered from COVID and healthy patients. For each VOM, it is reported the retention time (RT), formula, CAS number and chemical family. For each of the groups that are under analysis it is also registered the frequency of occurrence and mean relative peak areas of each compound.

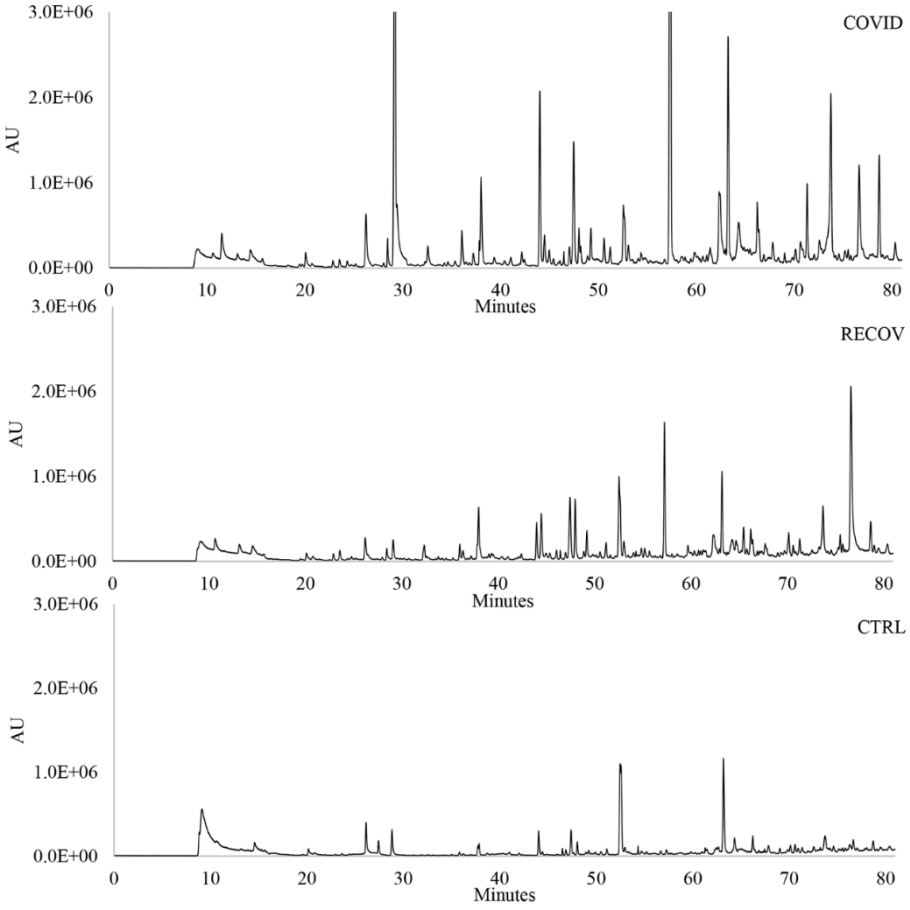
					Frequency of occurrence (%)			Mean Relative Peak Area		
RT (min)	**VOM**	**Formula**	**CAS No.**	**Chemical Family**	**COVID**	**RECOV**	**CTRL**	**COVID**	**RECOV**	**CTRL**
10.58	Methanethiol	CH_4S	74-93-1	SC	27	70	76	13.06	3.61	7.10
13.10	Furan	C_4H_4O	110-00-9	F	34	70	67	13.82	2.71	4.13
15.61	2-Methylfuran	C_5H_6O	534-22-5	F	18	57	43	3.03	1.16	2.30
19.38	2,5-Dimethylfuran	C_6H_8O	625-86-5	F	22	33	0	1.17	0.35	0.00
20.13	6-Methylphenanthridine	$C_{14}H_{11}N$	3955-65-5	HHc	26	90	100	5.85	5.41	14.82
20.66	2-Pentanone	$C_5H_{10}O$	107-87-9	Ket	26	73	48	3.39	2.65	3.10
22.27	(Z)-3,7-Dimethyl-2-octene	$C_{10}H_{20}$	6874-32-4	Ter	12	13	0	1.87	0.17	0.00
22.93	1-Methylcycloheptene	C_8H_{14}	55308-20-8	Hc	7	67	10	0.34	1.96	0.53
23.51	1,3-Dimethyl-1-cyclohexene	C_8H_{14}	2808-76-6	Hc	25	83	33	1.42	2.85	1.76
24.24	Toluene	C_7H_8	108-88-3	BD	26	63	5	1.88	0.85	0.27
24.78	3-Hexanone	$C_6H_{12}O$	589-38-8	Ket	27	53	10	1.57	0.88	0.24
25.11	p-Menth-3-ene	$C_{10}H_{18}$	500-00-5	Ter	18	13	14	0.78	0.27	0.74
26.20	Dimethyl disulfide	$C_2H_6S_2$	624-92-0	SC	37	97	100	25.25	11.96	28.46
26.48	Hexanal	$C_6H_{12}O$	66-25-1	Ald	13	23	19	2.17	1.33	1.19
29.05	4-Heptanone	$C_7H_{14}O$	123-19-3	Ket	34	97	100	80.64	31.95	79.56
30.80	γ-Pyronene	$C_{10}H_{16}$	514-95-4	Ter	11	0	0	0.92	0.00	0.00
32.00	1,4-Cineol	$C_{10}H_{18}O$	470-67-7	Ter	16	53	19	1.41	1.38	1.14
31.96	2-Carene	$C_{10}H_{16}$	554-61-0	Ter	2	20	19	0.08	0.46	2.29
32.06	α-Terpinene	$C_{10}H_{16}$	99-86-5	Ter	5	67	19	0.37	5.58	1.87
32.59	2-Heptanone	$C_7H_{14}O$	110-43-0	Ket	30	70	0	3.43	1.42	0.00
33.50	Limonene	$C_{10}H_{16}$	138-86-3	Ter	10	10	0	0.66	0.36	0.00
33.86	4-Methyl-2-heptanone	$C_8H_{16}O$	6137-06-0	Ket	0	13	0	0.00	0.31	0.00

34.10	Eucalyptol	$C_{10}H_{18}O$	470-82-6	Ter	23	40	10	1.69	0.79	0.29
34.65	2-Pentylfurano	$C_9H_{14}O$	3777-69-3	F	5	57	0	0.47	1.11	0.00
36.06	2,2-dimethyl-5-(1-methyl-1-propenyl)-tetrahydrofuran	$C_{10}H_{18}O$	7416-35-5	F	32	97	100	9.39	5.76	8.03
36.50	γ-Terpinene	$C_{10}H_{16}$	99-85-4	Ter	15	57	10	2.78	2.93	0.48
36.88	3-Octanone	$C_8H_{16}O$	106-68-3	Ket	17	30	0	2.83	0.37	0.00
37.25	3,4-Dimethylthiophene	C_6H_8S	632-15-5	SC	23	43	5	4.23	6.79	0.23
38.03	p-Cymene	$C_{10}H_{14}$	99-87-6	Ter	32	87	90	38.60	28.86	49.85
38.79	Allyl methyl disulfide	$C_4H_8S_2$	2179-58-0	SC	0	3	19	0.00	0.02	0.90
39.07	Isoterpinolene	$C_{10}H_{16}$	586-63-0	Ter	23	50	0	2.97	1.78	0.00
40.41	2-Methoxythiophene	C_5H_6OS	16839-97-7	SC	26	53	0	4.51	1.12	0.00
41.03	2,2,6-Trimethylcyclohexanone	$C_9H_{16}O$	2408-37-9	Ket	25	60	5	2.72	0.99	0.07
42.03	Hemimellitene	C_9H_{12}	526-73-8	BD	34	63	14	5.47	0.89	0.66
43.23	p-Ethyltoluene	C_9H_{12}	622-96-8	BD	24	33	24	0.88	0.40	2.83
44.37	2-Methoxy-5-methylthiophene	C_6H_8OS	31053-55-1	SC	5	13	14	0.25	0.64	0.96
44.49	2-Methyl-5-(methylthio)furan	C_6H_8OS	13678-59-6	F	30	87	71	10.24	7.66	4.10
44.74	Nonanal	$C_9H_{18}O$	124-19-6	Ald	4	33	0	0.09	0.45	0.00
44.98	Dimethyl trisulfide	$C_2H_6S_3$	3658-80-8	SC	23	53	14	5.72	1.99	1.01
45.89	α-Isophorone	C9H14O	78-59-1	Ket	25	17	0	2.05	0.28	0.00
46.10	Tetrahydrideinalool	$C_{10}H_{22}O$	57706-88-4	Ter	20	63	19	4.45	1.60	1.05
46.90	1,1,5,6-tetramethylindane	$C_{13}H_{18}$	942-43-8	Nor	28	87	71	12.06	2.74	5.27
47.49	p-Cymenene	$C_{10}H_{12}$	1195-32-0	Ter	35	97	90	63.09	43.33	53.97
47.64	o-Cymenene	$C_{10}H_{12}$	7399-49-7	Ter	0	10	29	0.00	0.19	3.63
48.03	Dihydromyrcenol	$C_{10}H_{20}O$	18479-58-8	Ter	31	73	86	14.62	12.17	16.15
48.88	t-Furan linalool oxide	$C_{10}H_{18}O_2$	34995-77-2	F	32	47	71	7.87	1.99	3.28
49.25	2-Ethyl-1-hexanol	$C_8H_{18}O$	104-76-7	Alc	37	97	100	12.65	10.61	5.97
50.48	Prehnitene	$C_{10}H_{14}$	488-23-3	Ter	34	70	67	10.99	2.99	4.49
51.22	Theaspirane	$C_{13}H_{22}O$	36431-72-8	Nor	34	90	71	10.15	5.83	5.55
52.25	1,2,5,5,6,7-Hexamethylbicyclo[4.1.0]hept-2-en-4-one	$C_{13}H_{20}O$	100011-05-2	F	2	47	14	10.15	12.88	1.45
52.46	β-Ionone	$C_{13}H_{20}O$	6901-97-9	Nor	9	53	86	4.40	8.79	37.03

54.08	α-Ionene	$C_{13}H_{18}$	475-03-6	Nor	23	37	38	3.86	1.30	2.29
54.80	5-Methylfurfural	$C_6H_6O_2$	620-02-0	F	9	20	52	1.11	0.63	3.45
55.23	(±)-Neoisomenthol	$C_{10}H_{20}O$	491-02-1	Ter	20	83	62	7.07	4.61	5.29
57.31	Menthol	$C_{10}H_{20}O$	15356-70-4	Ter	35	97	100	42.26	59.48	24.88
58.66	1,1,4,7-Tetramethylindan	$C_{13}H_{18}$	1078-04-2	Hc	4	23	57	0.71	1.29	10.64
59.66	Durene	$C_{10}H_{14}$	95-93-2	Ter	2	17	29	0.19	2.09	1.48
59.86	γ-Vinyl-γ-valerolactone	$C_7H_{10}O_2$	1073-11-6	F	5	47	38	0.86	1.93	2.53
60.18	p-Menth-1(7)-en-2-one	$C_{10}H_{16}O$	15297-07-1	Ter	0	33	29	0.00	31.34	4.62
60.26	1,1,3-Trimethylindane	$C_{12}H_{16}$	2613-76-5	Hc	0	23	33	0.00	1.35	2.78
61.10	1,5,8-Trimethyl-1,2,3,4-tetrahydronaphthalene	$C_{13}H_{18}$	21693-51-6	Nor	21	27	29	4.49	1.06	1.95
61.37	α-Methyl-cinnamaldehyde	$C_{10}H_{10}O$	101-39-3	Ald	2	27	43	0.05	1.82	2.81
61.42	4,7-Dimethylbenzofuran	$C_{10}H_{10}O$	28715-26-6	F	21	47	52	12.70	2.62	6.76
61.89	m-tert-Butylphenol	$C_{10}H_{14}O$	585-34-2	P	13	10	5	9.54	0.57	1.33
62.31	Phellandral	$C_{10}H_{16}O$	21391-98-0	Ter	2	10	19	0.13	0.53	2.53
62.32	3,3,5,7-Tetramethyl-1-indanone	$C_{13}H_{16}O$	54789-23-0	Ket	4	7	24	1.79	0.40	2.26
62.45	6-tert-Butyltetralin	$C_{14}H_{20}$	42044-26-8	ND	15	7	5	12.56	0.93	0.55
62.47	Piperitone	$C_{10}H_{16}O$	89-81-6	Ter	4	40	52	0.92	5.33	11.28
62.68	p-tert-Butylphenol	$C_{10}H_{14}O$	98-54-4	P	4	40	67	1.62	6.21	18.99
63.00	1,2,3,4-tetramethyl-4-(1-methylethenyl)benzene	$C_{13}H_{18}$	61142-76-5	BD	4	23	19	0.63	1.12	0.93
63.23	D-Carvone	$C_{10}H_{14}O$	2244-16-8	Ter	2	50	95	1.76	6.97	60.99
63.27	1,1,6-Trimethyl-1,2-dihydronaphthalene	$C_{13}H_{16}$	30364-38-6	Nor	35	97	19	106.15	34.59	6.27
64.47	3-Methoxy-5-(trifluoromethyl)aniline	$C_8H_8F_3NO$	349-55-3	BD	2	13	90	0.69	2.36	23.30
64.62	p-Acetyltoluene	$C_9H_{10}O$	122-00-9	Ket	0	3	19	0.00	0.06	2.04
64.72	Salicylic acid, methyl ester	$C_8H_8O_3$	119-36-8	Est	24	57	48	14.72	7.11	8.01
64.92	2-Methyl-3-phenylpropanal	$C_{10}H_{12}O$	100013-18-7	Ald	5	37	19	0.76	2.45	2.45
66.25	β-Damascenone	$C_{13}H_{18}O$	23726-93-4	Nor	37	93	69	33.48	10.68	18.02
66.45	2,4-Dimethyl benzaldehyde	$C_9H_{10}O$	15764-16-6	Ald	2	57	21	0.55	5.48	2.95
66.85	1,6,8-trimethyl-1,2,3,4-tetrahydronaphthalene-	$C_{13}H_{18}$	30316-36-0	Nor	7	60	57	1.18	4.34	5.34
67.81	2-methoxyphenol	$C_7H_8O_2$	90-05-1	P	34	93	76	9.31	7.78	9.61

69.04	1,2,3-Trimethylindene	$C_{12}H_{14}$	4773-83-5	Hc	9	50	38	1.38	3.60	2.28
69.84	1,1,6,8-Tetramethyl-1,2-dihydronaphthalene	$C_{14}H_{18}$	100018-66-3	ND	4	33	29	0.63	2.00	3.26
69.99	2,3-Dihydro-1,1,5,6-tetramethyl-1H-indene	$C_{13}H_{18}$	942-43-8	Nor	5	57	29	2.52	7.42	6.56
70.67	Acetate, (2,5,5,8a-tetramethyl-1,2,3,5,6,7,8,8a-octahydro-1-naphthalenyl) ester	$C_{16}H_{26}O_2$	101447-86-3	Est	0	10	57	0.00	3.15	7.78
70.95	Heptanoic acid	$C_7H_{14}O_2$	3665-80-3	CA	2	23	43	0.59	1.46	2.79
71.27	5,6-Dimethyltetralin	$C_{12}H_{16}$	20027-77-4	ND	4	57	19	0.93	5.42	3.21
71.38	N-Ethyl-4-nitroaniline	$C_8H_{10}N_2O_2$	3665-80-3	BD	0	0	52	0.00	0.00	4.86
72.59	2-Bromophenol	C_6H_5BrO	95-56-7	P	35	80	100	11.91	4.75	15.37
73.73	Phenol	C_6H_6O	108-95-2	P	31	80	100	23.77	18.62	32.40
74.11	3,5,8-trimethyl-1,2-dihydronaphthalene	$C_{13}H_{16}$	30316-18-8	Nor	0	20	14	0.00	2.22	0.50
74.57	1,7-Dimethylnaphthalene	$C_{12}H_{12}$	575-37-1	ND	30	57	57	9.65	3.76	4.83
75.18	Octanoic Acid	$C_8H_{16}O_2$	124-07-2	CA	21	87	57	11.85	8.39	4.14
75.47	1-Methyl-2-phenylpiperidin-4-one	$C_{12}H_{15}NO$	91640-05-0	Ket	0	27	10	0.00	3.92	0.71
76.27	2,5,8-Trimethyl-1,4-dihydronaphthalene	$C_{13}H_{16}$	30316-19-9	Nor	25	17	52	9.56	1.88	6.14
76.65	p-Cresol	C_7H_8O	106-44-5	P	37	97	100	64.50	76.39	76.37
78.06	Eudalene	$C_{14}H_{16}$	490-65-3	ND	2	13	62	0.80	1.01	4.25
78.69	3,3,5,6-Tetramethyl-1-indanone	$C_{13}H_{16}O$	54789-22-9	Ket	35	87	81	52.65	12.66	11.55
79.48	Nonanoic acid	$C_9H_{18}O_2$	112-05-0	CA	4	77	43	0.13	6.45	2.97
80.35	2,3,3-Trimethylindanone	$C_{12}H_{14}O$	54484-71-8	Ket	12	70	14	4.60	5.24	1.02
80.45	Eugenol	$C_{10}H_{12}O_2$	97-53-0	P	0	7	19	0.00	0.99	2.90

Abbreviations: Alc, Alcohols; Ald, Aldehydes; BD, Benzene Derivatives; CA, Carboxylic Acid; Est, Esters; F, Furans; Hc, Hydrocarbons; HHc, Heterocyclic Hydrocarbons; Ket, Ketones; ND, Naphthalene Derivatives; Nor, Norisoprenoids; P, Phenols; SC, Sulfur Compounds; Ter, Terpenes; COVID, COVID group; RECOV, recovered group; CTRL, control group.



Supplementary Figure S1. Typical chromatograms of the analysed groups. COVID, patients infected with SARS-CoV-2; RECOV, recovered COVID-19 patients; CTRL, healthy subjects.