DETECTION AND QUANTIFICATION OF PHYTOCHEMICAL MARKERS OF *Ilex paraguariensis* BY LIQUID CHROMATOGRAPHY

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Table 1S. Factors evaluated in the 'Design Space' screening stage

Run	Organic modifier	Gradient time (min)	pH	Column
1	Acetonitrile	12.0	2.4	BEH C_8
2	Acetonitrile	12.0	2.4	CSH PFP
3	Acetonitrile	5.0	2.4	CSH PFP
4	Acetonitrile	12.0	2.4	CSH *phenyl-hexyl*
5	Acetonitrile	5.0	2.4	CSH *phenyl-hexyl*
6	Acetonitrile	8.5	2.4	HSS T_3
7	Acetonitrile	5.0	2.4	CSH PFP
8	Acetonitrile	8.5	5.0	CSH *phenyl-hexyl*
9	Acetonitrile	8.5	5.0	HSS T_3
10	Acetonitrile	8.5	5.0	BEH C_8
11	Acetonitrile	5.0	5.0	BEH C_8
12	Acetonitrile	8.5	5.0	HSS T_3
13	Acetonitrile	8.5	5.0	BEH C_8
14	Acetonitrile	8.5	5.0	CSH PFP
15	Acetonitrile	8.5	5.0	CSH *phenyl-hexyl*
16	Acetonitrile	8.5	5.0	CSH PFP
17	Acetonitrile	8.5	7.0	CSH PFP
18	Acetonitrile	12.0	7.0	CSH PFP
19	Acetonitrile	5.5	7.0	HSS T_3
20	Acetonitrile	12.0	7.0	BEH C_8
21	Acetonitrile	12.0	7.0	CSH *phenyl-hexyl*
22	Acetonitrile	5.0	7.0	CSH *phenyl-hexyl*
23	Methanol	5.0	2.4	BEH C_8
24	Methanol	12.0	2.4	HSS T_3
25	Methanol	8.5	2.4	CSH *phenyl-hexyl*
26	Methanol	5.0	2.4	HSS T_3
27	Methanol	12.0	2.4	HSS T_3
28	Methanol	10.3	2.4	CSH PFP
29	Methanol	8.5	5.0	HSS T_3
30	Methanol	8.5	5.0	HSS T_3
31	Methanol	8.5	5.0	CSH PFP
32	Methanol	8.5	5.0	BEH C_8
33	Methanol	12.0	2.4	BEH C_8
34	Methanol	8.5	5.0	CSH PFP
35	Methanol	8.5	5.0	CSH *phenyl-hexyl*
36	Methanol	8.5	5.0	CSH *phenyl-hexyl*
37	Methanol	12.0	5.0	BEH C_8
38	Methanol	5.0	5.0	CSH *phenyl-hexyl*
39	Methanol	8.5	7.0	BEH C_8
40	Methanol	6.8	7.0	HSS T_3
41	Methanol	12.0	7.0	CSH PFP
42	Methanol	5.0	7.0	CSH PFP
43	Methanol	6.8	7.0	BEH C_8
44	Methanol	10.3	7.0	CSH *phenyl-hexyl*
45	Methanol	12.0	7.0	CSH PFP

[a] Columns: BEH C_8: *Ethylene bridged hybrid*; CSH PFP: *Charged surface hybrid – propyl fluoro phenyl;* HSS T_3: *High strength sílica*; CSH *phenyl-hexyl*: *Charged surface hybrid phenyl-hexyl.*

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Table 2S. Factors evaluated in the 'Design Space' optimization stage

Run	Flow rate (mL. min^{-1})	Final % of organic modifier	Temperature (°C)	pH
1	0.400	70.0	25.0	2.17
2	0.400	62.5	25.0	2.17
3	0.700	70.0	25.0	2.17
4	0.700	55.0	25.0	2.17
5	0.400	55.0	25.0	2.40
6	0.600	62.5	25.0	2.40
7	0.400	70,0	25.0	3.00
8	0.700	70.0	25.0	3.00
9	0.700	55.0	25.0	3.00
10	0.700	62.5	25.0	3.00
11	0.400	70.0	25.0	3.00
12	0.600	66.3	30.0	2.17
13	0.600	58.8	30.0	2.17
14	0.400	55.0	30.0	2.17
15	0.700	62.5	30.0	2.40
16	0.600	62.5	30.0	2.40
17	0.600	62.5	30.0	2.40
18	0.600	55.0	30.0	3.00
19	0.700	70.0	30.0	3.00
20	0.500	66.3	30.0	3.00
21	0.500	58.8	30.0	3.00
22	0.500	66.3	35.0	2.17
23	0.500	58.8	35.0	2.17
24	0.600	66.3	35.0	3.00
25	0.600	58.8	35.0	3.00
26	0.700	62.5	40.0	2.17
27	0.400	55.0	40.0	2.17
28	0.400	62.5	40.0	2.17
29	0.700	70.0	40.0	2.17
30	0.700	70.0	40.0	2.17
31	0.700	55.0	40.0	2.17
32	0.400	70.0	40.0	2.40
33	0.600	55.0	40.0	2.40
34	0.700	55.0	40.0	3.00
35	0.700	62.5	40.0	3.00
36	0.400	55.0	40.0	3.00
37	0.400	62.5	40.0	3.00
38	0.600	70.0	40.0	3.00
39	0.400	55.0	40.0	3.00