Supplemental information

for

Differentiation of chloromethcathinone (CMC) isomers: the new kid on the block after methylmethcathinone (MMC) control in The Netherlands

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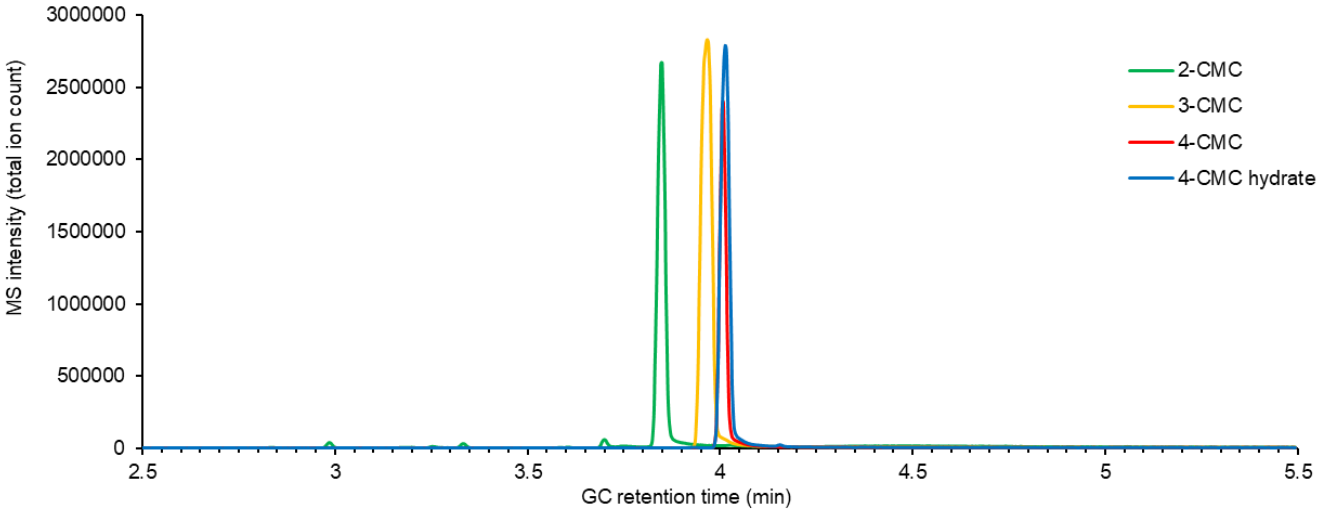

Figure S1. Overlayed total ion GC-MS chromatograms of 2-CMC, 3-CMC, 4-CMC, and 4-CMC hydrate. (1 µL injection of individual 1 mg/mL solutions in acetonitrile)

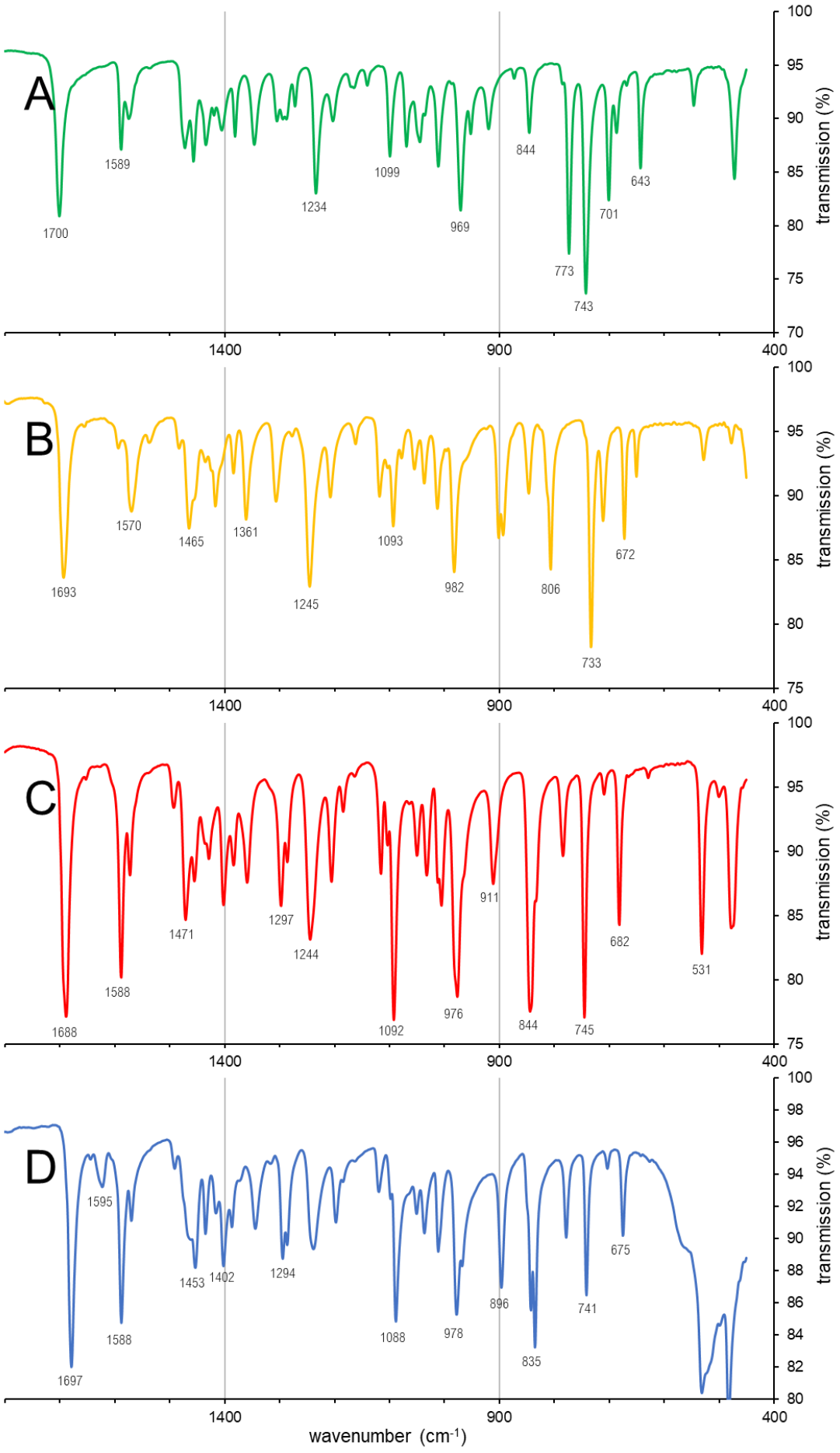

Figure S2. atr-FTIR spectra (450 – 1800 cm^{-1} fingerprint range) of the chloromethcathinone (CMC) isomers. A: 2-CMC HCl, B: 3-CMC HCl, C: 4-CMC HCl, D: 4-CMC HCl hydrate

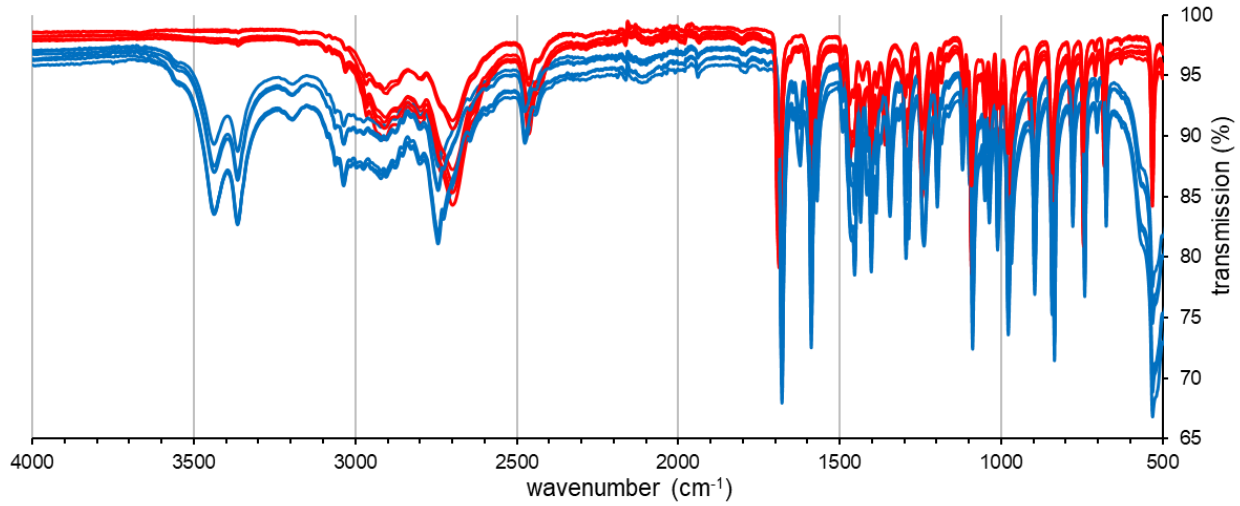

Figure S3. atr-FTIR transmission spectra of six 4-CMC HCl hydrate casework samples (blue) and their spectra obtained after 24 hours heating at 75 ºC (red), that each matched with the reference spectrum of anhydrous 4-CMC HCl.

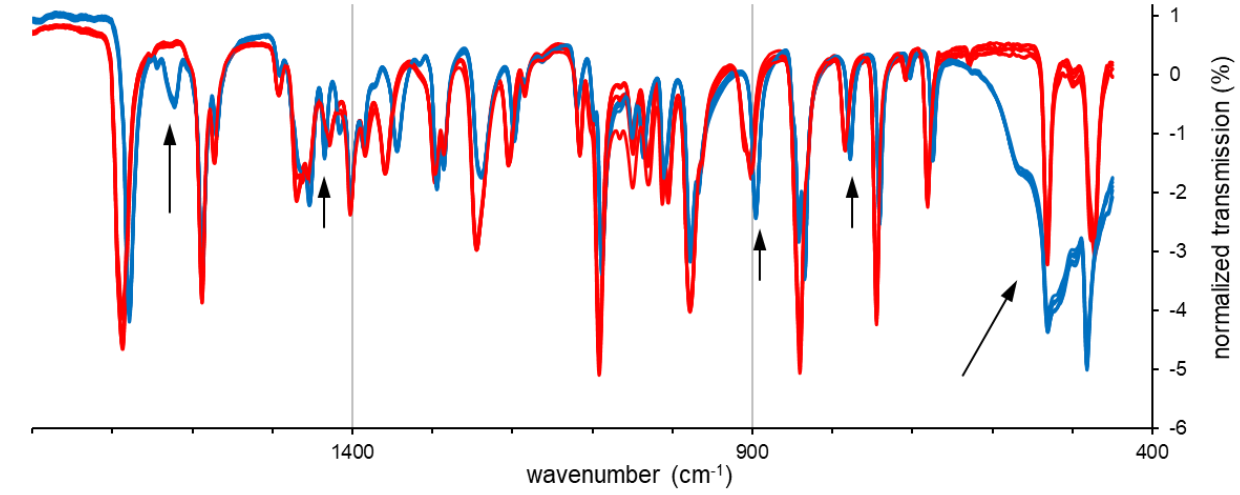

Figure S4. Selection of the 400 – 1800 cm^{-1} fingerprint range of the SNV-normalized atr-FTIR spectra of six 4-CMC HCl hydrate casework samples (blue) and their spectra obtained after 24 hours heating at 75 ºC. Arrows depict the differences.

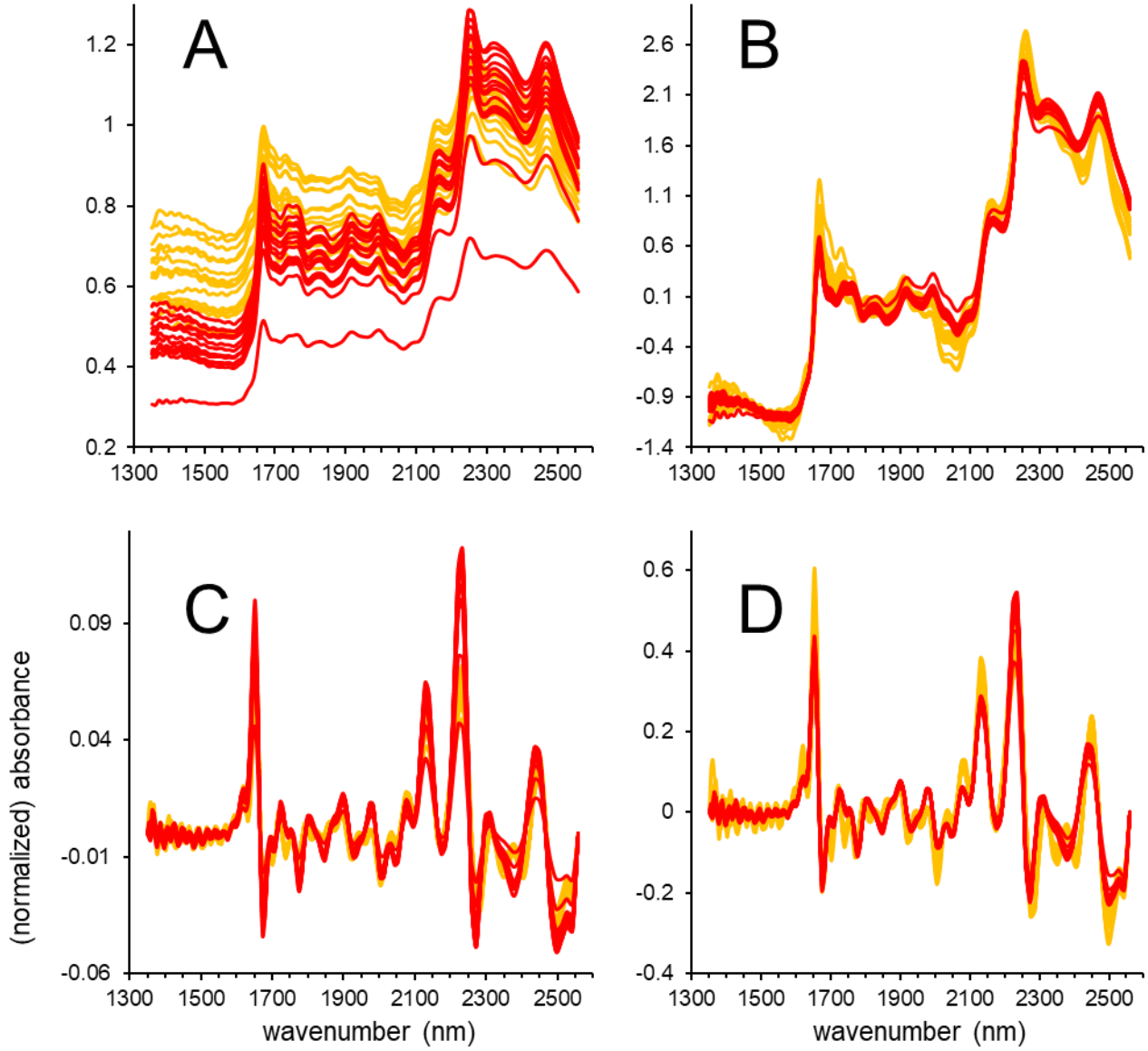

Figure S5. NIR spectra of 15 reference samples of 3-CMC (orange) and 15 reference samples 4-CMC (red) after various pre-processing. Panel A: raw diffuse reflection signal, panel B: SNV normalized data, panel C: first derivative spectrum, panel D: SNV followed by first derivative.

Table S1. Results of the LDA- and SVM-models applied on NIR-spectra of 27 casework samples.

sample	identity	LDA					SVM
		LDA scores (on 4 PCs)					nu-SVC
	(FTIR & GC-MS)	2-CMC	3-CMC	4-CMC	4-CMC hydr	prediction	prediction
Sample N1	4-CMC	-392.4	-362.9	**-3.9**	-1084.7	4-CMC	4-CMC
Sample N2	4-CMC hydr	-718.1	-792.9	-554.8	**-139.3**	4-CMC hydr	4-CMC hydr
Sample N3	3-CMC	-200.5	**-6.6**	-394.6	-1301.8	3-CMC	3-CMC
Sample N4	4-CMC	-488.2	-477.0	**-6.3**	-1193.7	4-CMC	4-CMC
Sample N5	3-CMC	-224.2	**-5.1**	-383.3	-1245.8	3-CMC	3-CMC
Sample N6	3-CMC	-234.8	**-3.1**	-443.2	-1354.1	3-CMC	3-CMC
Sample N7	3-CMC	-179.7	**-4.5**	-358.1	-1241.5	3-CMC	3-CMC
Sample N8	3-CMC	-204.2	**-2.3**	-388.9	-1284.4	3-CMC	3-CMC
Sample N9	3-CMC	-204.7	**-2.6**	-405.9	-1344.6	3-CMC	3-CMC
Sample N10	3-CMC	-209.0	**-2.8**	-411.6	-1309.1	3-CMC	3-CMC
Sample N11	3-CMC	-180.7	**-6.9**	-341.4	-1205.4	3-CMC	3-CMC
Sample N12	3-CMC	-228.0	**-2.5**	-429.1	-1309.2	3-CMC	3-CMC
Sample N13	3-CMC	-199.0	**-2.5**	-391.5	-1309.9	3-CMC	3-CMC
Sample N14	3-CMC	-168.5	**-6.9**	-352.4	-1193.2	3-CMC	3-CMC
Sample N15	3-CMC	-137.0	**-12.3**	-331.5	-1210.8	3-CMC	3-CMC
Sample N16	MDMA + 3-CMC	-69.6	**-68.0**	-408.7	-1124.6	3-CMC*	2-CMC
Sample N17	3-CMC	-197.0	**-3.7**	-389.9	-1302.9	3-CMC	3-CMC
Sample N18	4-CMC hydr	-995.3	-1089.8	-1061.6	**-16.8**	4-CMC hydr	4-CMC hydr
Sample N19	4-CMC hydr	-877.2	-983.3	-778.0	**-40.6**	4-CMC hydr	4-CMC hydr
Sample N20	4-CMC hydr	-701.3	-778.8	-534.4	**-126.6**	4-CMC hydr	4-CMC hydr
Sample N21	3-CMC	-276.8	-104.5	-620.0	-868.4	3-CMC	3-CMC
Sample N22	4-CMC hydr	-1165.9	-1298.0	-1148.7	**-2.8**	4-CMC hydr	4-CMC hydr
Sample N23	4-CMC hydr	-1015.9	-1127.1	-1041.5	**-10.0**	4-CMC hydr	4-CMC hydr
Sample N24	4-CMC hydr	-978.2	-1081.4	-1012.3	**-14.6**	4-CMC hydr	4-CMC hydr
Sample N25	4-CMC hydr	-1063.5	-1162.6	-1094.4	**-13.1**	4-CMC hydr	4-CMC hydr
Sample N26	4-CMC	-380.0	-357.4	**-5.2**	-1073.5	4-CMC	4-CMC
Sample N27	4-CMC hydr	-963.4	-1076.8	-989.2	**-14.6**	4-CMC hydr	4-CMC hydr

Average scores of 3 replicate analyses. * for sample N16, 3-CMC was correctly predicted in 2 out of 3 of the LDA results. In one measurement, 2-CMC was predicted.

Table S2. (part 1 of 3) Results of the LDA-model applied to 70 eV ei mass spectra for 50 casework samples analyzed over a 6-month timespan. Samples were afterwards divided in groups based on their identify determined by FTIR and/or Raman spectroscopy (ground truth).

sample	identity	LDA LDA scores (on 3 PCs)			
	(FTIR & Raman)	2-CMC	3-CMC	4-CMC	prediction
Sample 1#01	4-CMC hydr	-1570.4	-382.2	-2.5	4-CMC
Sample 1#02	4-CMC hydr	-1556.1	-380.7	-2.3	4-CMC
Sample 1#03	4-CMC hydr	-1536.2	-382.1	-1.8	4-CMC
Sample 1#04	4-CMC hydr	-1477.8	-352.8	-3.5	4-CMC
Sample 1#05	4-CMC hydr	-1486.9	-413.9	-2.4	4-CMC
Sample 1#06	4-CMC hydr	-1514.5	-407.2	-1.5	4-CMC
Sample 1#07	4-CMC hydr	-1490.7	-383.9	-2.1	4-CMC
Sample 1#08	4-CMC hydr	-1502.0	-425.1	-2.3	4-CMC
Sample 1#09	4-CMC hydr	-1586.1	-421.6	-1.3	4-CMC
Sample 1#10	4-CMC hydr	-1531.7	-399.1	-1.2	4-CMC
Sample 1#11	4-CMC hydr	-1524.1	-394.3	-1.3	4-CMC
Sample 1#12	4-CMC hydr	-1515.2	-386.3	-1.5	4-CMC
Sample 1#13	4-CMC hydr	-1571.6	-391.1	-1.7	4-CMC
Sample 1#14	4-CMC hydr	-1480.8	-353.3	-3.3	4-CMC
Sample 1#15	4-CMC hydr	-1569.1	-431.2	-1.4	4-CMC
Group 2 Sample 1	3-CMC	-1002.1	-32.1	-591.5	3-CMC
Group 2 Sample 2	3-CMC	-1122.6	-8.8	-315.0	3-CMC
Group 2 Sample 3	3-CMC	-1211.2	-7.3	-323.8	3-CMC
Group 2 Sample 4	3-CMC	-1221.3	-3.9	-358.7	3-CMC
Group 2 Sample 5	3-CMC	-1251.5	-4.3	-370.8	3-CMC
Group 2 Sample 6	3-CMC	-1129.0	-19.9	-590.8	3-CMC
Group 2 Sample 7	3-CMC	-1321.2	-19.8	-290.6	3-CMC
Group 2 Sample 8	3-CMC	-1211.2	-7.3	-323.8	3-CMC
Group 2 Sample 9	3-CMC	-1221.3	-3.9	-358.7	3-CMC
Group 2 Sample 10	3-CMC	-1251.5	-4.3	-370.8	3-CMC
Group 2 Sample 11	3-CMC	-1129.0	-19.9	-590.8	3-CMC
Group 2 Sample 12	3-CMC	-1321.2	-19.8	-290.6	3-CMC

Table S2. (part 2 of 3)

sample	identity	LDA			
		LDA scores (on 3 PCs)			
	(FTIR & Raman)	2-CMC	3-CMC	4-CMC	prediction
Group 3 Sample 1	3-CMC	-1387.0	-84.5	-155.1	3-CMC
Group 3 Sample 2	3-CMC	-1292.6	-34.2	-236.5	3-CMC
Group 3 Sample 3	3-CMC	-1142.3	-7.0	-325.9	3-CMC
Group 3 Sample 4*	3-CMC	-1745.1	-127.5	-253.4	3-CMC
Group 3 Sample 5*	3-CMC	-1738.2	-120.7	-257.4	3-CMC
Group 3 Sample 6*	3-CMC	-1713.5	-117.1	-249.2	3-CMC
Group 3 Sample 7*	3-CMC	-1705.8	-113.4	-251.8	3-CMC
Group 3 Sample 8*	3-CMC	-1712.3	-121.3	-238.0	3-CMC
Group 3 Sample 9	3-CMC	-1095.8	-28.4	-622.7	3-CMC
Group 3 Sample 10	3-CMC	-1087.6	-20.6	-577.2	3-CMC
Group 3 Sample 11	3-CMC	-1247.5	-2.9	-393.7	3-CMC
Group 3 Sample 12	3-CMC	-1248.7	-2.8	-399.7	3-CMC
Group 3 Sample 13	3-CMC	-1174.2	-2.9	-359.0	3-CMC
Group 3 Sample 14	3-CMC	-1212.7	-6.0	-328.7	3-CMC
Group 4 Sample 1	4-CMC hydrate	-1545.8	-559.5	-16.4	4-CMC
Group 4 Sample 2*	4-CMC hydrate	-3109.0	-1104.0	-345.4	4-CMC
Group 4 Sample 3*	4-CMC hydrate	-2358.1	-879.5	-126.1	4-CMC
Group 4 Sample 4*	4-CMC hydrate	-2185.2	-829.0	-91.8	4-CMC
Group 4 Sample 5	4-CMC hydrate	-1144.1	-282.5	-40.6	4-CMC
Group 4 Sample 6	4-CMC hydrate	-1211.5	-328.1	-27.2	4-CMC
Group 4 Sample 7	4-CMC hydrate	-1211.3	-398.6	-32.0	4-CMC
Group 4 Sample 8	4-CMC hydrate	-1188.1	-317.5	-31.9	4-CMC
Group 4 Sample 9	4-CMC hydrate	-1645.1	-506.9	-7.0	4-CMC
Group 4 Sample 10	4-CMC hydrate	-1630.5	-487.6	-4.9	4-CMC
Group 4 Sample 11	4-CMC hydrate	-1405.2	-357.2	-5.5	4-CMC
Group 4 Sample 12	4-CMC hydrate	-1409.6	-383.0	-5.8	4-CMC
Group 4 Sample 13	4-CMC hydrate	-1339.7	-349.2	-10.2	4-CMC
Group 4 Sample 14	4-CMC hydrate	-1802.1	-599.1	-22.9	4-CMC
Group 4 Sample 15	4-CMC hydrate	-1806.8	-590.7	-21.1	4-CMC
Group 4 Sample 16	4-CMC hydrate	-1550.0	-464.1	-3.4	4-CMC

after retrospective investigation, samples marked with an asterisk (*) were found to be acquired in GC-MS sequences ran shortly after instrument maintenance and the installation of a new column in August 2023. Laboratory staff reported an increased baseline for these sequences (although data was suitable for analysis according to the criteria in their routine analysis procedures)

Table S2. (part 3 of 3)

sample	identity	LDA			
		LDA scores (on 3 PCs)			
	(FTIR & Raman)	2-CMC	3-CMC	4-CMC	prediction
Group 5 Sample 1	4-CMC	-1368.0	-438.9	-11.6	4-CMC
Group 5 Sample 2	4-CMC	-1416.7	-437.4	-7.2	4-CMC
Group 5 Sample 3	4-CMC	-1828.8	-635.3	-28.4	4-CMC
Group 5 Sample 4	4-CMC	-1658.0	-507.0	-6.8	4-CMC
Group 5 Sample 5	4-CMC	-1623.4	-503.2	-6.1	4-CMC
Group 5 Sample 6	4-CMC	-1288.6	-393.5	-17.6	4-CMC
Group 5 Sample 7	4-CMC	-1446.8	-391.1	-2.9	4-CMC
Group 5 Sample 8	4-CMC	-1438.0	-360.3	-3.7	4-CMC