Supplementary Information

RSM-optimized automated DI-SPME-GC-MS/MS for multi-class trace plasticizers in drinking water

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S1 Chemicals and supplies

HPLC grade ethyl acetate and acetone were purchased from Fisher Scientific (Loughborough, UK). Sodium chloride was purchased from Sinopharm (AR, Shanghai, China). A mixed standard solution of 29 plasticizers in ethyl acetate (1000 μg/mL) was custom-made from TanMo Reference Materials Co., Ltd. (Changzhou, China). The internal standard butyl benzoate (100 mg, purity ≥ 95%) was obtained from Dr. Ehrenstorfer GmbH (Augsburg, Germany) and benzyl benzoate (100 mg, purity ≥ 98%) was obtained from Alta Scientific (Tianjin, China). Butyl benzoate and benzyl benzoate were selected as internal standards due to their similar physicochemical properties to the target analytes, stable responses, absence in the analyzed real samples, low cost, and ready availability. Ultrapure water (18.4 MΩ·cm) was produced in-house using a Milli-Q water purification system acquired from Millipore (Bedford, USA). Drinking water samples were collected locally, stored at 4 °C, and analyzed within 24 h of collection.

The analyte stock solution (100 μg/mL) and the internal standard stock solution (100 μg/mL) were prepared, diluted with ethyl acetate and stored in amber glass bottles at 4 °C. Intermediate solutions were then prepared by diluting the stock solutions with ethyl acetate. Working solutions of all the analytes were prepared by diluting the intermediate solutions with ultrapure water, with the analytes at concentrations ranging from 0.005 to 20 μg/L and both internal standards at 2 μg/L. Additionally, blank solutions spiked with the analytes and internal standards at 2 μg/L each were prepared for experimental condition optimization.

S2 Instrumentation and conditions

The SPME process was performed on an automated sample pretreatment platform based on the PAL (Prep and Load) robotic system (CTC Analytics AG, Zwingen, Switzerland). The platform was constructed on a custom-built RTC850 PAL system (Guangzhou Intelligent Laboratory Technology Co., Ltd., Guangzhou, China), configured with a smart chip identification SPME Arrow replacement module, a SPME Arrow conditioning module, an agitator incubation module, a Heatex stirrer extraction module, a solvent storage module, a temperature-controlled module, and sample tray holders. The debugging and operation of the platform were carried out through the central control panel. The control software written in C++ language was used to set method parameters, establish sequences and trigger the connection with GC-MS/MS via the communication line.

The 1.1 mm outer diameter Smart SPME Arrow kit (Inlab-4AS0-001) and 20 mL sample glass vials

equipped with fitted magnetic screw-on caps with PTFE-faced silicone septa (Inlab-2001) were both provided by the platform supplier as well. The coating types and phase thicknesses of the extraction heads were 100 μm polydimethylsiloxane (PDMS), 100 μm polyacrylate (PA), 120 μm carbon wide range (Carbon WR)/PDMS, 120 μm divinylbenzene (DVB)/PDMS, and 120 μm DVB/Carbon WR/PDMS. The SPME Arrows required a 30-min conditioning before first use and an additional 5-min conditioning after each sample injection, both of which were carried out in the conditioning module. The optimized automated DI-SPME conditions were as follows: stirring rate of 500 rpm, extraction temperature of 66 °C, extraction time of 34 min, desorption time of 336 s, desorption temperature of 270 °C, no addition of NaCl, and immersion depth of the SPME Arrow of 50 mm.

The sample analysis was performed by the 7890B-7000C GC-MS/MS (Agilent Technologies, Santa Clara, CA, USA) equipped with the HP-5MS UI fused-silica capillary column (30 m length × 0.25 mm i.d., 0.25 μm film thickness). The large-volume injection port was adjusted to a temperature of 270 °C in splitless injection mode. High purity helium (99.99%) was employed as the carrier gas at a constant flow rate of 1 mL/min. The oven temperature program was initially held at 80 °C, ramped at 15 °C/min to 180 °C and held for 1 min, then ramped at 5 °C/min to 220 °C and held for 2 min, and finally ramped at 10 °C/min to 260 °C and held for 10 min.

The electron ionization (EI) source was selected with the ion source energy of 70 eV. The ion source temperature was kept at 250 °C, and the transfer line temperature was maintained at 270 °C. High purity nitrogen (99.99%) was employed as the collision gas at a pressure between 1 and 1.2 mTorr.

Table S1 Factor levels and coded values of the Plackett-Burman design

Factors	code	levels	
		−1	1
Stirring rate / rpm	A	500	800
Extraction temperature / °C	B	40	70
Extraction time / min	C	30	60
Desorption time / s	D	180	360
Desorption temperature / °C	E	250	280
NaCl addition / g	F	0	2

Table S2 Design and results of the Plackett-Burman experiment

std	run	A	B	C	D	E	F	Y
1	1	1	1	−1	1	1	1	53.3873
2	2	−1	1	1	−1	1	1	48.9983
10	3	−1	1	1	1	−1	−1	51.1698
3	4	1	−1	1	1	−1	1	47.1808
7	5	1	−1	−1	−1	1	−1	43.7729
12	6	−1	−1	−1	−1	−1	−1	44.7631
9	7	1	1	1	−1	−1	−1	48.6454
5	8	−1	−1	1	−1	1	1	43.3525
8	9	1	1	−1	−1	−1	1	48.9940
6	10	−1	−1	−1	1	−1	1	49.0517
4	11	−1	1	−1	1	1	−1	55.3948
11	12	1	−1	1	1	1	−1	46.3191

Table S3 ANOVA results of the Plackett-Burman experiment

Source	Sum of squares	Degree of Freedom	Mean square	*F*-value	*P*-value	significance
Model	143.75	6	23.96	24.73	0.0014	significant
A-Stirring rate	1.64	1	1.64	1.69	0.2505	
B-Extraction temperature	86.13	1	86.13	88.91	0.0002	significant
C-Extraction time	7.84	1	7.84	8.09	0.0361	significant
D-Desorption time	47.91	1	47.91	49.45	0.0009	significant
E-Desorption temperature	0.1681	1	0.1681	0.1735	0.6943	
F-NaCl addition	0.0674	1	0.0674	0.0696	0.8025	
Residual	4.84	5	0.9688			
Cor Total	148.59	11				

Std. Dev. = 0.9843
Mean = 48.42
C.V. % = 2.03

R^2 = 0.9674
Adjusted R^2 = 0.9283
Predicted R^2 = 0.8122
Adeq Precision = 14.3944

Table S4 Design and results of the steepest ascent experiment

Run	length	Extraction temperature / °C	Extraction time / min	Desorption time / s	Y
1	0	55	45	270	43.4282
2	0+1Δ	60	40	300	48.5480
3	0+2Δ	65	35	330	52.5719
4	0+3Δ	70	30	360	46.8864
5	0+4Δ	75	25	390	33.0928

Table S5 Factors and levels of the Box-Behnken design

Factors	code	levels		
		−1	0	1
Extraction temperature / °C	A	60	65	70
Extraction time / min	B	30	35	40
Desorption time / s	C	300	330	360

Table S6 Design and results of the Box-Behnken experiment

std	run	Extraction temperature	Extraction time	Desorption time	Y
4	1	1	1	0	50.2690
5	2	−1	0	−1	45.6884
15	3	0	0	0	53.5200
10	4	0	1	−1	46.0283
17	5	0	0	0	53.7184
16	6	0	0	0	53.9354
13	7	0	0	0	52.6949
8	8	1	0	1	50.6258
11	9	0	−1	1	50.1750
2	10	1	−1	0	48.4206
7	11	−1	0	1	47.0315
1	12	−1	−1	0	48.7287
14	13	0	0	0	54.4678
6	14	1	0	−1	47.1657
9	15	0	−1	−1	47.3768
12	16	0	1	1	46.7480
3	17	−1	1	0	44.8641

Table S7 ANOVA results for the regression model of the Box-Behnken design

Source	Sum of Squares	Degree of Freedom	Mean Square	*F*-value	*P*-value	significance
Model	161.44	9	17.94	44.20	< 0.0001	significant
A-Extraction temperature	12.92	1	12.92	31.85	0.0008	significant
B-Extraction time	5.77	1	5.77	14.21	0.007	significant
C-Desorption time	8.65	1	8.65	21.33	0.0024	significant
AB	8.16	1	8.16	20.11	0.0029	significant
AC	1.12	1	1.12	2.76	0.1406	
BC	1.08	1	1.08	2.66	0.1468	
A^2	32.43	1	32.43	79.92	< 0.0001	significant
B^2	33.51	1	33.51	82.58	< 0.0001	significant
C^2	44.86	1	44.86	110.53	< 0.0001	significant
Residual	2.84	7	0.4058			
Lack of Fit	1.16	3	0.3861	0.9178	0.5084	not significant
Pure Error	1.68	4	0.4207			
Cor Total	164.29	16				

Std. Dev. = 0.6371	R^2 = 0.9827
Mean = 49.5	Adjusted R^2 = 0.9605
C.V. % = 1.29	Predicted R^2 = 0.8712
	Adeq Precision = 18.7167

Table S8 Concentrations of plasticizer residues in end-use water samples after microextraction by DI-SPME and determination by GC-MS/MS

Components	Concentration of plasticizers in samples (μg/L)																	
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	Sample 8	Sample 9	Sample 10	Sample 11	Sample 12	Sample 13	Sample 14	Sample 15	Sample 16	Sample 17	Sample 18
DMA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.324±0.024	ND	ND	ND	ND	ND	1.34±0.031	0.158±0.0096
DEA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DMP	3.06±0.062	2.62±0.22	0.546±0.035	0.491±0.034	0.900±0.014	0.709±0.025	0.714±0.023	0.419±0.044	0.293±0.029	2.68±0.15	0.628±0.045	0.458±0.016	0.0940±0.0016	0.185±0.0055	0.360±0.012	0.201±0.0079	0.148±0.0068	1.04±0.014
DEP	5.68±0.055	1.19±0.052	0.373±0.020	0.276±0.0014	0.600±0.034	0.527±0.016	0.237±0.031	0.351±0.028	0.368±0.0095	0.584±0.057	0.137±0.0069	0.124±0.0044	0.0504±0.0054	0.298±0.0088	0.419±0.017	0.0818±0.0046	0.0480±0.0039	0.119±0.0066
TBP	0.0730±0.0025	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.0377±0.0025	ND	ND	ND	ND	ND	ND	ND
DIPrP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DIBA	0.0326±0.0027	ND	0.111±0.0071	0.0532±0.0022	0.0780±0.00054	0.106±0.0078	ND	ND	ND	ND	0.238±0.0064	0.159±0.011	0.0791±0.0031	0.150±0.0075	0.173±0.0054	0.117±0.0032	0.0644±0.0032	0.0567±0.0025
DALP	ND	ND	D	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DBA	0.237±0.0045	ND	0.0936±0.0054	0.183±0.0031	0.179±0.0053	ND	0.0655±0.0027	0.0417±0.0010	ND	ND	0.495±0.024	0.249±0.017	0.130±0.013	0.597±0.032	0.746±0.031	0.0883±0.0087	0.0549±0.0051	0.0361±0.0030
DPrP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DIBP	5.02±0.21	0.456±0.015	0.0531±0.0025	0.230±0.0093	0.0904±0.0030	0.0645±0.0039	0.0326±0.00028	0.0863±0.00074	0.0566±0.0020	0.0845±0.0021	0.00933±0.00033	0.0340±0.0029	0.0803±0.0056	0.0523±0.0042	0.00683±0.00025	0.0152±0.00085	0.0171±0.0013	0.0222±0.00083
DBP	4.48±0.16	6.36±0.40	ND	2.38±0.019	2.03±0.023	ND	1.36±0.099	ND	2.43±0.11	ND	2.16±0.049	0.566±0.050	ND	1.74±0.16	3.17±0.12	0.345±0.012	ND	0.0882±0.0052
DIPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DMPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.0279±0.0017	D	ND	ND	D	ND	ND	ND

DAP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ATBC	ND	ND	ND	0.216±0.0068	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TDCPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DHxP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.116±0.0054	0.0497±0.0049	0.0240±0.00070	ND	0.0330±0.0017	ND	ND	ND
BBP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.0790±0.0029	0.187±0.0066	0.123±0.0072	0.0860±0.0026	ND	0.0360±0.0018	0.0470±0.0032	0.193±0.018
DEHA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.0332±0.00090	D	ND	ND	ND	ND	ND	0.0462±0.0042
TPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
BBPA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TEHP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DCHP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DHP	ND	1.49±0.037	ND	ND	ND	0.229±0.025	ND	D	ND	ND	D	ND	0.0205±0.0015	ND	ND	D	0.0216±0.0016	ND
DEHP	0.807±0.059	0.663±0.064	2.26±0.13	3.60±0.15	3.25±0.099	1.23±0.027	2.15±0.041	2.30±0.21	2.09±0.016	1.83±0.040	2.12±0.047	1.29±0.085	0.728±0.054	2.29±0.20	3.33±0.11	1.13±0.056	0.959±0.085	2.57±0.14
DPhP	0.125±0.0045	ND	ND	ND	0.128±0.011	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TOCP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DNOP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TOTAL	19.5±0.30	12.8±0.70	3.44±0.12	7.43±0.15	7.25±0.12	2.87±0.031	4.56±0.18	3.21±0.28	5.23±0.13	5.18±0.24	6.42±0.011	3.15±0.087	1.33±0.055	5.40±0.17	8.25±0.080	2.03±0.084	2.70±0.080	4.34±0.14

ND: not detected (concentration < LOD); D: detected (LOD < concentration < LOQ), values are included in total concentration calculations.

Table S9 Concentrations of plasticizer residues in bottled water samples after microextraction by DI-SPME and determination by GC-MS/MS

Components	Concentration of plasticizers in samples (μg/L)											
	Sample 19	Sample 20	Sample 21	Sample 22	Sample 23	Sample 24	Sample 25	Sample 26	Sample 27	Sample 28	Sample 29	Sample 30
DMA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DEA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DMP	0.107±0.0089	0.194±0.0044	0.509±0.025	0.0609±0.0028	0.246±0.0064	0.145±0.0093	ND	0.255±0.016	0.0896±0.0051	ND	0.219±0.015	0.117±0.0038
DEP	ND	ND	ND	ND	0.105±0.0048	0.272±0.014	0.434±0.022	0.125±0.012	0.268±0.011	ND	0.329±0.013	0.170±0.0031
TBP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DIPrP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DIBA	ND	ND	0.0211±0.0012	ND	ND	ND	ND	ND	ND	ND	ND	ND
DALP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DBA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DPrP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.0547±0.0057	ND
DIBP	2.56±0.22	3.43±0.16	0.636±0.015	3.78±0.37	0.269±0.019	0.0768±0.0012	0.848±0.017	0.217±0.020	1.51±0.052	0.447±0.028	0.103±0.0098	1.12±0.093
DBP	3.31±0.13	3.78±0.37	1.47±0.10	4.85±0.14	0.876±0.0065	0.633±0.014	1.32±0.024	1.64±0.024	2.03±0.014	3.54±0.15	1.82±0.11	2.24±0.011
DIPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DMPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DAP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ATBC	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TDCPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DHxP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
BBP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DEHA	ND	D	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TPP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
BBPA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TEHP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DCHP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DHP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DEHP	2.42±0.11	1.31±0.27	2.78±0.15	2.51±0.25	2.99±0.10	0.334±0.023	1.76±0.067	3.27±0.058	0.745±0.0085	4.15±0.062	3.39±0.26	1.51±0.14

DPhP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.0225±0.0022
TOCP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
DNOP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TOTAL	8.39±0.32	8.73±0.48	5.42±0.21	11.2±0.66	4.49±0.10	1.46±0.046	4.36±0.064	5.51±0.094	4.65±0.050	8.14±0.21	5.92±0.31	5.18±0.034

ND: not detected (concentration < LOD); D: detected (LOD < concentration < LOQ), values are included in total concentration calculations.

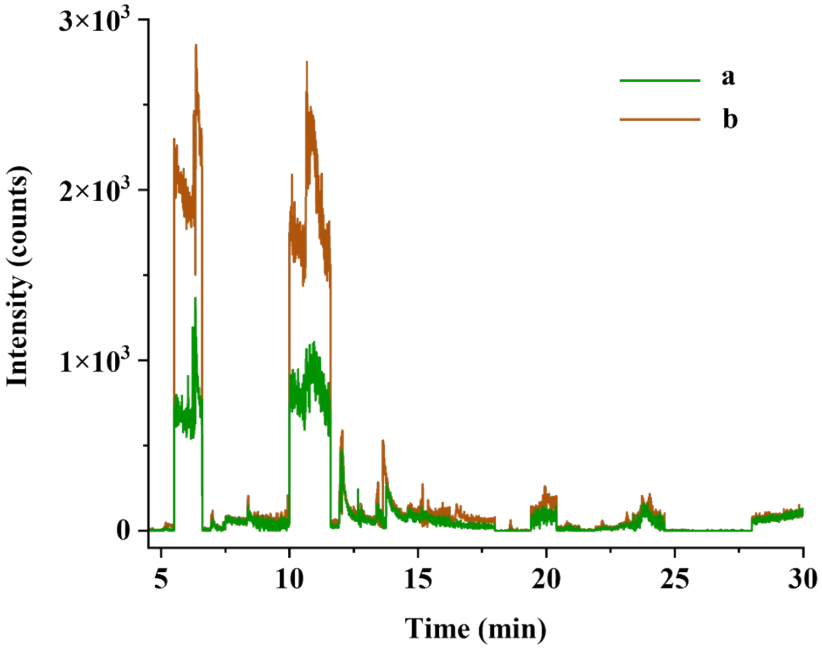

Fig. S1. Comparison of procedural blank chromatograms obtained (a) under routine conditions before the sample sequence and (b) after analysis of a 5 µg/L spiked sample. No internal standards were added to the procedural blanks.

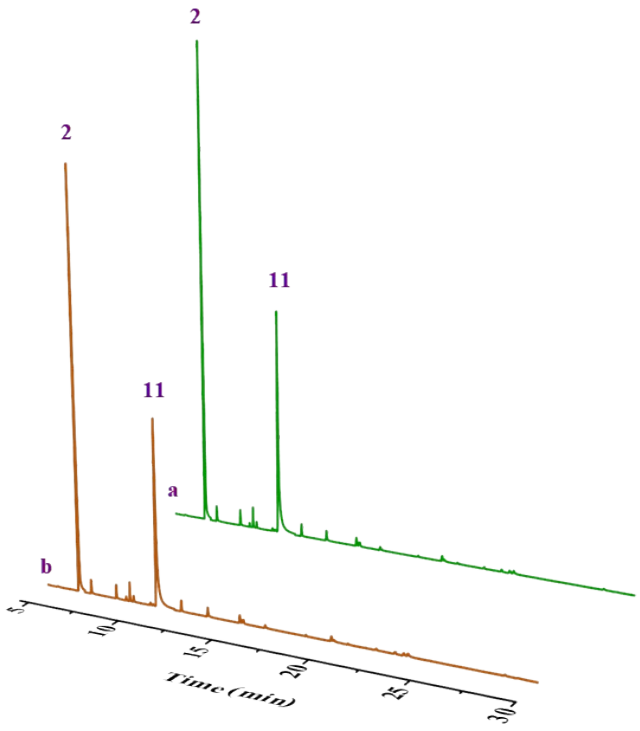

Fig. S2. Comparison of TICs obtained using the same SPME Arrow for a spiked water sample (a) before and (b) after 100 extraction cycles. The 29 analytes were spiked at 0.5 µg/L, and the two internal standards were added at 2 µg/L.

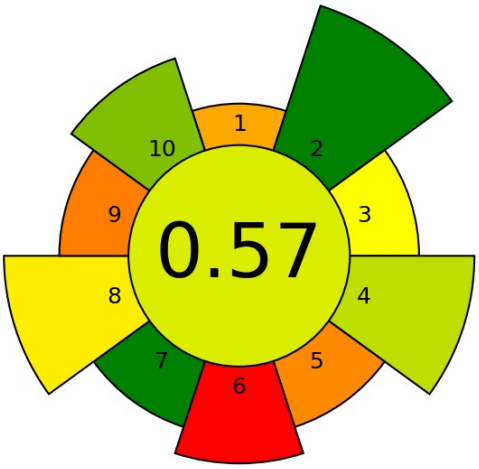

Fig. S3. AGREEprep assessment of the developed DI-SPME-GC-MS/MS method.

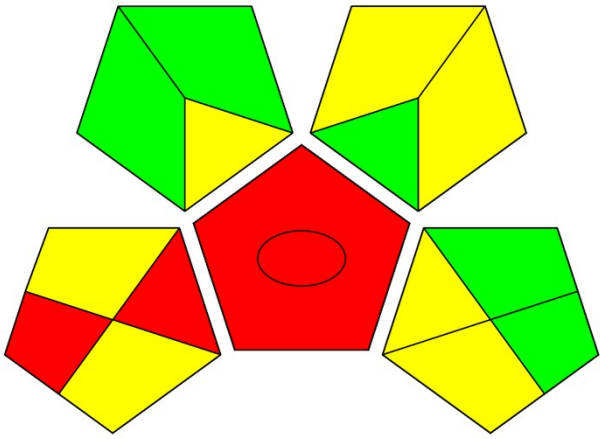

Fig. S4. GAPI assessment of the developed DI-SPME-GC-MS/MS method.

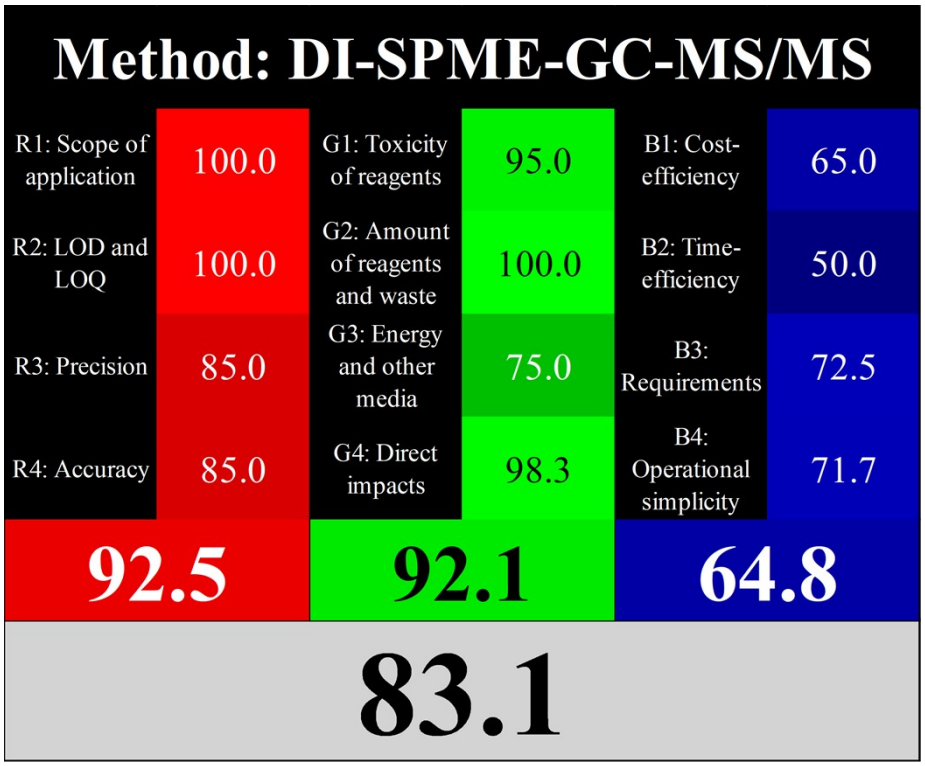

Fig. S5. RGB12 Whiteness assessment of the developed DI-SPME-GC-MS/MS method.

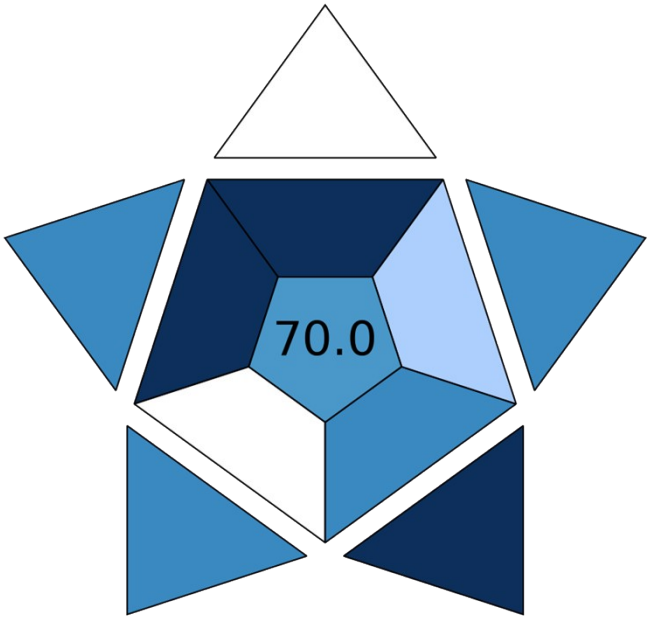

Fig. S6. BAGI assessment of the developed DI-SPME-GC-MS/MS method.