Electronic Supplementary Material (ESI) for Analyst.

Continuous synthesis of $BaFe_2O_4$ and $BaFe_{12}O_{19}$ nanoparticles in droplet microreactor for efficient detection of antihistamine drugs in oral fluid using SALDI-MS

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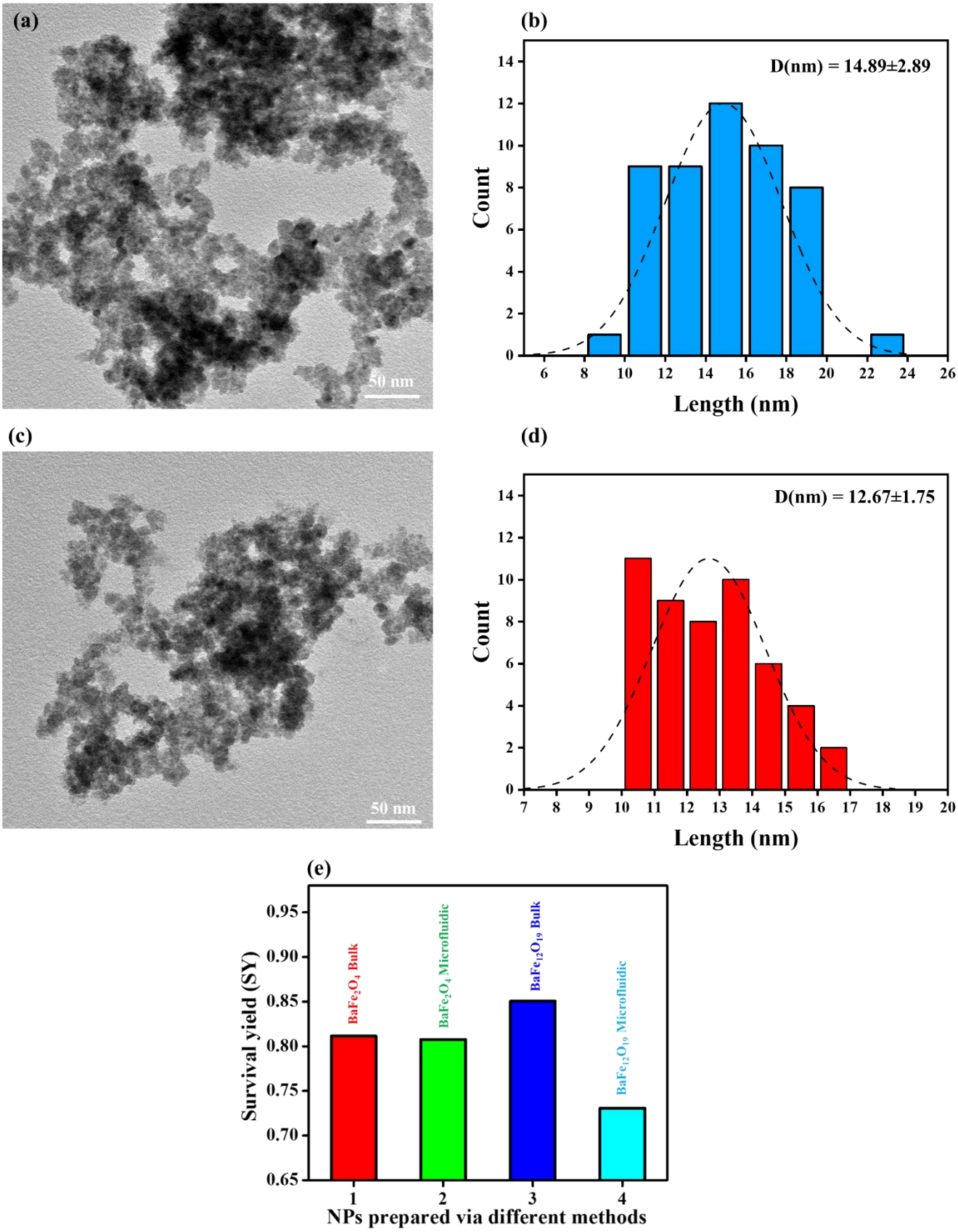
(a)
50 nm
(b)
D(nm) = 14.89±2.89
Count
Length (nm)
(c)
50 nm
(d)
D(nm) = 12.67±1.75
Count
Length (nm)
(e)
Survival yield (SY)
BaFe2O4 Bulk
BaFe2O4 Microfluidic
BaFe12O19 Bulk
BaFe12O19 Microfluidic
NPs prepared via different methods

Figure S1. Transmission electron microscopy (TEM) image of **(a)** $BaFe_2O_4$, **(c)** $BaFe_{12}O_{19}$ NPs, and **(b)** and (**d)** particle size distribution curve for $BaFe_2O_4$ and $BaFe_{12}O_{19}$ NPs synthesized using bulk synthesis. (**e**) Survival yield (SY) measurements as a function of $BaFe_2O_4$ and $BaFe_{12}O_{19}$ NPs prepared *via* different methods.

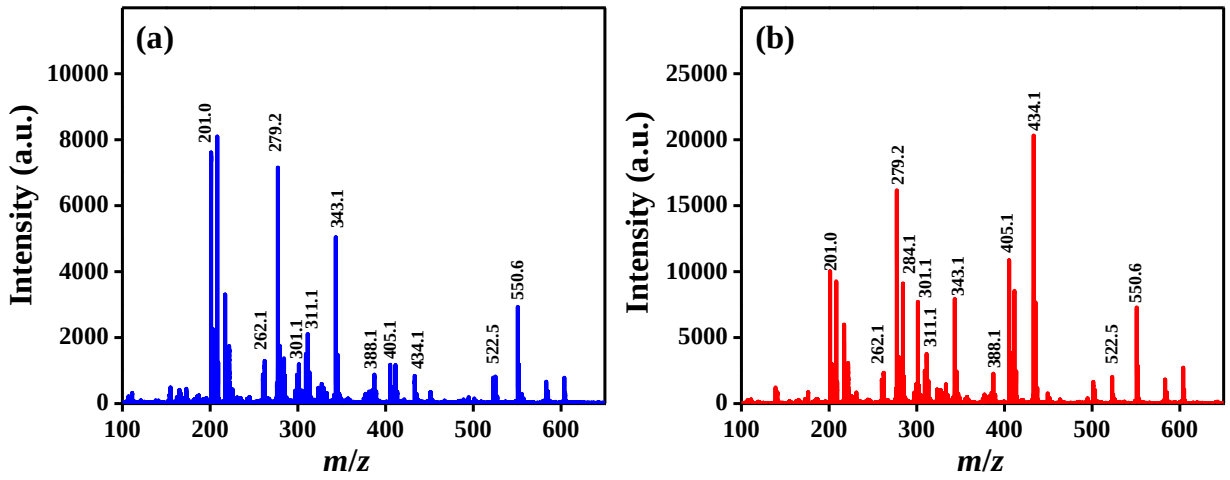

Figure S2. SALDI-MS spectra of methapyrilene, triprolidine, desloratadine, loratadine, and cetirizine mixture in solution using (a) $BaFe_2O_4$ and (b) $BaFe_{12}O_{19}$ NPs.

Table S1: Compounds identification from the standard mixture of antihistamines solution using $BaFe_2O_4$ and $BaFe_{12}O_{19}$ NPs as SALDI-MS substrates. The LODs of the antihistamine drugs were obtained using standard mixture of the five drugs.

$BaFe_2O_4$ NPs							
Compound name	**Possible species**	**Theoretical *m/z***	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**	**LOD**
Methapyrilene	$[Meth + H]^+$	262.137794	262.1386	-3.08	1106.50	11.29	100 ng/mL
	$[Meth + Na]^+$	284.119738	284.1190	2.71	1289.47	13.18	
	$[Meth + 2Na]^+$	307.109507	307.1099	-1.34	305.87	13.16	
Triprolidine	$[Trip + H]^+$	279.186124	279.1875	-4.87	1682.29	7.73	1 pg/mL
	$[Trip + Na]^+$	301.168068	301.1692	-3.86	1248.66	15.75	
Desloratadine	$[Desl + H]^+$	311.131501	311.1324	-2.79	1955.90	13.12	100 pg/mL
	$[Desl + Na]^+$	333.113446	333.1131	1.07	224.75	14.43	
	$[Desl + K]^+$	349.087383	349.0890	-4.64	4367.78	13.60	
Loratadine	$[Lora + H]^+$	383.152631	383.1546	-5.15	319.21	14.70	10 pg/mL
	$[Lora + Na]^+$	405.134575	405.1361	-3.69	1508.32	11.32	
Cetirizine	$[Ceti-C_8H_{15}N_2O_3]^+$	201.04710	201.0482	-5.42	7645.36	12.22	10 ng/mL
	$[Ceti-COOH]^+$	343.15772	343.1562	4.42	4523.24	10.38	
	$[Ceti]^+$	388.155370	388.1545	2.32	836.54	6.90	
	$[Ceti + H]^+$	389.163195	389.1644	-3.07	243.78	15.14	
	$[Ceti+ Na]^+$	411.145140	411.1440	2.88	1292.55	12.35	
	$[Ceti+ 2Na]^+$	434.134909	434.1364	-3.53	712.49	11.14	
$BaFe_{12}O_{19}$ NPs							
Compound name	**Possible species**	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**	**LOD**
Methapyrilene	$[Meth + H]^+$	262.137794	262.1379	-0.27	835.53	12.38	100 ng/mL
	$[Meth + Na]^+$	284.119738	284.1186	4.12	3977.24	13.55	
Triprolidine	$[Trip + H]^+$	279.186124	279.1858	1.06	1392.75	8.59	1 pg/mL
	$[Trip + Na]^+$	301.168068	301.1679823	0.28	3496.41	17.45	
Desloratadine	$[Desl + H]^+$	311.131501	311.1314	0.30	1534.54	5.85	10 pg/mL
	$[Desl + Na]^+$	333.113446	333.1130891	1.07	621.85	17.63	
	$[Desl + K]^+$	349.087383	349.0857	4.88	152.69	8.75	

Loratadine	[Lora + H]$^+$	383.152631	383.1546	-5.23	220.60	14.80	1 pg/mL
	[Lora + Na]$^+$	405.134575	405.1361071	-3.78	5253.53	16.72	
Cetirizine	[Ceti-$C_8H_{15}N_2O_3$]$^+$	201.04710	201.047	0.62	5583.23	12.62	10 ng/mL
	[Ceti-COOH]$^+$	343.15772	343.1585	-2.16	3721.82	13.73	
	[Ceti]$^+$	388.155370	388.1561	-1.93	340.94	6.46	
	[Ceti + H]$^+$	389.163195	389.1619	3.33	249.30	12.02	
	[Ceti+ Na]$^+$	411.145140	411.1460956	-2.32	3267.7	18.31	

Table S2: Compounds identification of oral fluid obtained from healthy donor using $BaFe_2O_4$ and $BaFe_{12}O_{19}$ NPs as SALDI-MS substrates.

$BaFe_2O_4$ NPs					
Possible species	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**
[Lactic acid +Na]$^+$	113.021463	113.0220	-4.99	8999.83	14.66
[Glycine+Ca]$^+$	114.994619	114.9949	-2.35	4452.72	12.01
[Threonine+H]$^+$	120.066068	120.0660	0.95	3840.04	18.67
[Lactic acid +2Na]$^+$	136.011233	136.0104	6.42	399.87	11.86
[Phenol+Na+Mg]$^+$	141.016676	141.0160	4.83	318.13	13.60
[Phenol+K+Mg]$^+$	156.990613	156.9911	-3.37	768.06	16.77
[Taurine +2Na]$^+$	170.994203	170.9934	4.41	438.48	14.49
[Phenol +K +Ca]$^+$	172.968162	172.9686	-2.27	341.74	11.14
[Taurine +Na +K]$^+$	186.968140	186.9683	-1.04	705.69	11.06
[Taurine + Ca+ Mg]$^+$	188.962297	188.9635	-6.21	588.13	8.54
[Aspartic acid Ca + Mg]$^+$	196.985140	196.9849	1.23	531.70	13.23
$BaFe_{12}O_{19}$ NPs					
Possible species	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**
[Lactic acid +Na]$^+$	113.021463	113.0222	-6.17	65353.44	12.33
[Glycine+Ca]$^+$	114.994619	114.9951	-4.56	38007.84	14.15
[Phenol+Na]$^+$	117.031634	117.0320	-3.42	3259.16	12.69
[Threonine+H]$^+$	120.066068	120.0657	2.77	18040.33	13.88
[Lactic acid +2Na]$^+$	136.011233	136.0122	-7.04	972.65	14.53
[Phenol+Na+Mg]$^+$	141.016676	141.0173	-4.09	1637.94	15.66
[Phenol+K+Mg]$^+$	156.990613	156.9915	-5.53	11670.18	14.71
[Threonine + Ca]$^+$	159.020834	159.0200	5.23	1335.53	15.53
[Taurine +2Na]$^+$	170.994203	170.9939	1.78	3409.37	15.85

[Phenol +K +Ca]$^+$	172.968162	172.9688	-3.46	2298.37	14.29
[Taurine +Na +K]$^+$	186.968140	186.9686	-3.155	7930.33	15.97
[Taurine + Ca+ Mg]$^+$	188.962297	188.9616	3.79	6576.17	15.86
[Creatinine + 2K]$^+$	190.986325	190.9866	-1.32	1469.63	14.58
[Asparagine + Na+ K]$^+$	194.006968	194.0074	-2.23	1274.55	15.59
[Aspartic acid Ca + Mg]	196.985140	196.9840	5.91	2537.35	14.30

Table S3: Compounds identification obtained from antihistamine drugs standards spiked in oral fluid samples using $BaFe_2O_4$ and $BaFe_{12}O_{19}$ NPs as SALDI-MS substrates

$BaFe_2O_4$ NPs							
Compound name	**Possible species**	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**	**LOD**
Methapyrilene	[Meth + Na]$^+$	284.119738	284.1202	-1.63	5569.97	8.73	900 ng/mL
	[Meth + K]$^+$	300.093675	300.0948	-3.64	1231.05	10.39	
Triprolidine	[Trip + Na]$^+$	301.168068	301.1691	-3.49	15591.67	10.07	100 pg/mL
	[Trip + K]$^+$	317.142005	317.1404	5.19	4618.31	13.66	
Desloratadine	[Desl + Na]$^+$	333.113446	333.1130	1.45	9487.55	7.83	1 ng/mL
	[Desl + K]$^+$	349.087383	349.0891	-5.01	1352.97	9.19	
Loratadine	[Lora + Na]$^+$	405.134575	405.1343	0.68	5144.80	11.35	100 ng/mL
	[Lora + K]$^+$	421.108512	421.1094	-2.10	466.11	11.18	
Cetirizine	[Ceti-$C_8H_{15}N_2O_3$]$^+$	201.047100	201.0509	-4.55	4291.05	16.48	100 ng/mL
	[Ceti + Na]$^+$	411.145140	411.1436	3.72	4297.91	17.69	
	[Ceti + K]$^+$	427.119077	427.1181	2.17	354.29	12.67	
	[Ceti + 2Na]$^+$	434.134909	434.1362	-2.98	8510.79	13.59	
	[Ceti +Na+ K]$^+$	450.108846	450.1080	1.95	12012.37	10.34	
	[Ceti + 2K]$^+$	466.082780	466.0823	1.10	3481.31	15.27	
$BaFe_{12}O_{19}$ NPs							
Compound name	**Possible species**	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**	**LOD**
Methapyrilene	[Meth + Na]$^+$	284.119738	284.1185	4.29	10940.82	10.72	900 ng/mL
	[Meth + K]$^+$	300.093675	300.0928	2.88	978.33	12.48	
Triprolidine	[Trip + Na]$^+$	301.168068	317.1415	1.75	27598.42	13.72	100 pg/mL
	[Trip + K]$^+$	317.142005	317.1415	-4.57	9019.15	8.65	
Desloratadine	[Desl + Na]$^+$	333.113446	333.1125	2.87	10518.29	15.89	100 ng/mL

	[Desl + K]$^+$	349.087383	349.0878	-1.22	1347.57	11.65	
Loratadine	[Lora + Na]$^+$	405.134575	405.1327	4.70	4022.83	15.21	100 ng/mL
	[Lora + K]$^+$	421.108512	421.1090	-1.23	385.66	13.64	
Cetirizine	[Ceti-$C_8H_{15}N_2O_3$]$^+$	201.047100	201.0473	-1.16	1626.76	13.30	100 ng/mL
	[Ceti + Na]$^+$	411.145140	411.1466	-3.58	2998.24	13.70	
	[Ceti + K]$^+$	427.119077	427.1215	-5.63	585.86	8.85	
	[Ceti + 2Na]$^+$	434.134909	434.1348	0.20	6526.57	15.04	
	[Ceti +Na+ K]$^+$	450.108846	450.1074	3.20	8742.96	10.98	
	[Ceti + 2K]$^+$	466.082780	466.0831	-0.75	3511.83	14.92	

Table S4: Compounds identification from the levocetirizine tablet (1mg mL^{-1}) in solution using $BaFe_2O_4$ and $BaFe_{12}O_{19}$ NPs as SALDI-MS substrates.

$BaFe_2O_4$ NPs					
Possible species	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**
[Ceti-$C_8H_{15}N_2O_3$]$^+$	201.047100	201.0479	-4.03	24645.89	16.35
[Ceti-COOH]$^+$	343.157720	343.1563	4.23	3402.41	10.99
[Ceti]$^+$	388.155370	388.1555	-0.31	1166.50	15.77
[Ceti + Na]$^+$	411.145140	411.1423	6.95	6405.80	10.37
[Ceti - H + 2Na]$^+$	433.127084	433.1279	-1.89	6081.44	11.37
$BaFe_{12}O_{19}$ NPs					
Possible species	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**
[Ceti-$C_8H_{15}N_2O_3$]$^+$	201.047100	201.0461	4.83	14132.25	17.40
[Ceti-COOH]$^+$	343.157720	343.1561	4.64	3259.07	15.53
[Ceti]$^+$	388.155370	388.1548	1.46	1524.12	9.86
[Ceti + Na]$^+$	411.145140	411.1436	3.79	8776.81	16.01
[Ceti - H + 2Na]$^+$	433.127084	433.1279	-1.88	9086.02	10.90

Table S5: Compounds identification from 500 µg mL^{-1} levocetirizine tablet spiked oral fluid using $BaFe_2O_4$ and $BaFe_{12}O_{19}$ NPs as SALDI-MS substrates.

$BaFe_2O_4$ NPs						
Possible species	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**	**LOD**
[Lactic acid +Na] $^+$	113.021463	113.0220	-4.62	24212.07	16.40	250 ng/mL
[Glycine+Ca] $^+$	114.994619	114.9951	-4.56	15239.87	17.22	
[Threonine+H] $^+$	120.066068	120.0657	3.01	7212.82	13.85	
[Lactic acid +2Na] $^+$	136.011233	136.0118	-4.33	497.50	15.58	
[Phenol+Na+Mg] $^+$	141.016676	141.0173	-4.09	3543.80	9.96	
[Phenol+K+Mg] $^+$	156.990613	156.9913	-4.38	7274.75	11.73	
[taurine +2Na] $^+$	170.994203	170.9938	2.36	2143.41	12.89	
[Phenol +K +Ca] $^+$	172.968162	172.9692	-5.61	1659.94	11.96	
[taurine +Na +K] $^+$	186.968140	186.9683	-1.04	4169.31	15.62	
[taurine + Ca+ Mg] $^+$	188.962297	188.9633	-5.56	3440.21	12.46	
[Aspartic acid Ca + Mg] $^+$	196.985140	196.9843	4.21	1623.48	15.51	
[Ceti-$C_8H_{15}N_2O_3$]$^+$	201.04710	201.0485	-7.15	2522.04	5.89	
[Ceti + Na]$^+$	411.145140	411.1436	3.85	1565.26	9.04	
[Ceti - H + 2Na]$^+$	433.127084	433.1280	-2.19	3237.75	4.73	
$BaFe_{12}O_{19}$ NPs						
Possible species	**Theoretical m/z**	**Detected *m/z***	**m/z error (ppm)**	**Average intensity**	**%RSD**	**LOD**
[Lactic acid +Na] $^+$	113.021463	113.0221	-5.51	85587.91	15.35	250 ng/mL
[Glycine+Ca] $^+$	114.994619	114.9951	-4.56	66040.51	11.42	
[Phenol+Na] $^+$	117.031634	117.0322	-5.22	1176.74	18.26	
[Threonine+H] $^+$	120.066068	120.0669	-6.89	13835.88	18.26	
[Lactic acid +2Na] $^+$	136.011233	136.0107	3.95	401.52	13.27	
[Phenol+Na+Mg] $^+$	141.016676	141.0174	-5.09	5215.67	14.73	
[Phenol+K+Mg] $^+$	156.990613	156.9914	-4.90	24416.89	13.07	
[Threonine + Ca] $^+$	159.020834	159.0218	-6.27	2738.86	15.86	
[Taurine +2Na] $^+$	170.994203	170.9938	2.55	10179.73	19.42	
[Phenol +K +Ca] $^+$	172.968162	172.9688	-3.46	7815.15	17.10	

[Taurine +Na +K] $^{+}$	186.968140	186.9669	6.64	21297.47	16.71	
[Taurine + Ca+ Mg] $^{+}$	188.962297	188.9634	-5.90	17544.38	18.12	
[Creatinine + 2K] $^{+}$	190.986325	190.9876	-6.56	4295.26	12.70	
[Asparagine + Na+ K] $^{+}$	194.006968	194.0074	-2.26	1343.47	13.83	
[Aspartic acid Ca + Mg] $^{+}$	196.985140	196.9860	-4.50	4240.59	16.57	
[Ceti-$C_8H_{15}N_2O_3$]$^{+}$	201.047100	201.0462	4.44	3030.85	4.97	
[Ceti + Na]$^{+}$	411.145140	411.1442	2.34	3576.36	12.63	
[Ceti - H + 2Na]$^{+}$	433.127084	433.1273	-0.55	3735.06	11.31	
[Ceti-H+Na]$^{+}$	449.101021	449.1039	-6.51	6884.07	16.05	