Supplementary Material

Peptide/β-Peptoid Hybrids with Ultrashort PEG-Like Moieties: Effects on Hydrophobicity, Antibacterial Activity and Hemolytic Properties

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Contents

Estimation of log D values

Table S1. Log D_{max} values and selected ion recording parameters of compounds.

Compound	log D_{max}	m/z		
		z = 6	z = 5	z = 4
1	<−2.662	373.3	466.3	621.4
7	<−3.650	402.3	502.6	669.8
9	<−3.627	352.5	422.7	527.2
10	<−2.994	367.1	440.4	550.2
11	<−2.876	361.8	433.9	542.1
12	<−3.147	383.8	460.4	575.2
13	<−3.911	405.8	486.8	608.3
14	<−2.883	434.9	521.7	651.9
15	<−3.180	345.0	413.7	516.9
16	<−3.922	359.5	431.2	538.8

Calculation of log D values

Table S2. Calculated log D values of compounds.

Subgroup	Cmpd	Sequence [1]	%MeCN [2]	$cLogD_{7.4}$ [3]
I	**1**	H-[X]$_6$-NH$_2$	41.6	−14.22
	2	H-sPEG2-[X]$_6$-NH$_2$	41.4	−16.22
	3	H-sPEG4-[X]$_6$-NH$_2$	41.9	−16.08
II	**4**	H-sPEG2-[X]$_6$-sPEG2-NH$_2$	41.3	−17.42
	5	H-sPEG4-[X]$_6$-sPEG4-NH$_2$	42.2	−17.13
III	**6**	H-[X]$_3$-sPEG1-[X]$_3$-NH$_2$	41.2	−15.37
	7	H-[X]$_3$-sPEG2-[X]$_3$-NH$_2$	41.4	−15.41
	8	H-[X]$_3$-sPEG3-[X]$_3$-NH$_2$	41.7	−15.46
	9	H-[X]$_3$-sPEG4-[X]$_3$-NH$_2$	41.8	−15.27
	10	H-[X]$_3$-sPEG6-[X]$_3$-NH$_2$	42.3	−15.37
IV	**11**	H-sPEG1-[X]$_3$-sPEG1-[X]$_3$-sPEG1-NH$_2$	40.8	−18.20
	12	H-sPEG2-[X]$_3$-sPEG2-[X]$_3$-sPEG2-NH$_2$	41.3	−18.62
	13	H-sPEG3-[X]$_3$-sPEG3-[X]$_3$-sPEG3-NH$_2$	41.9	−18.76
	14	H-sPEG4-[X]$_3$-sPEG4-[X]$_3$-sPEG4-NH$_2$	42.4	−18.19
V	**15**	H-[X]$_2$-sPEG1-[X]$_2$-sPEG1-[X]$_2$-NH$_2$	41.1	−16.52
	16	H-[X]$_2$-sPEG2-[X]$_2$-sPEG2-[X]$_2$-NH$_2$	41.5	−16.61
	17	H-[X]$_2$-sPEG3-[X]$_2$-sPEG3-[X]$_2$-NH$_2$	41.8	−16.71
	18	H-[X]$_2$-sPEG4-[X]$_2$-sPEG4-[X]$_2$-NH$_2$	42.1	−16.33

[1] X = Lys-βNPhe(4-F). [2] Experimental relative hydrophobicity measured as % MeCN at peak elution. RP-HPLC gradient: 0 → 60% B during 15 min. For column specifications, see **Error! Reference source not found.**. [3] $cLogD_{7.4}$ = calculated distribution coefficient at pH 7.4.

Characterization of peptidomimetics

Compound 1

HRMS: calculated for $[M+H]^{1+}$ 1862.05481, found 1862.05565; $\Delta M = 0.5$ ppm.
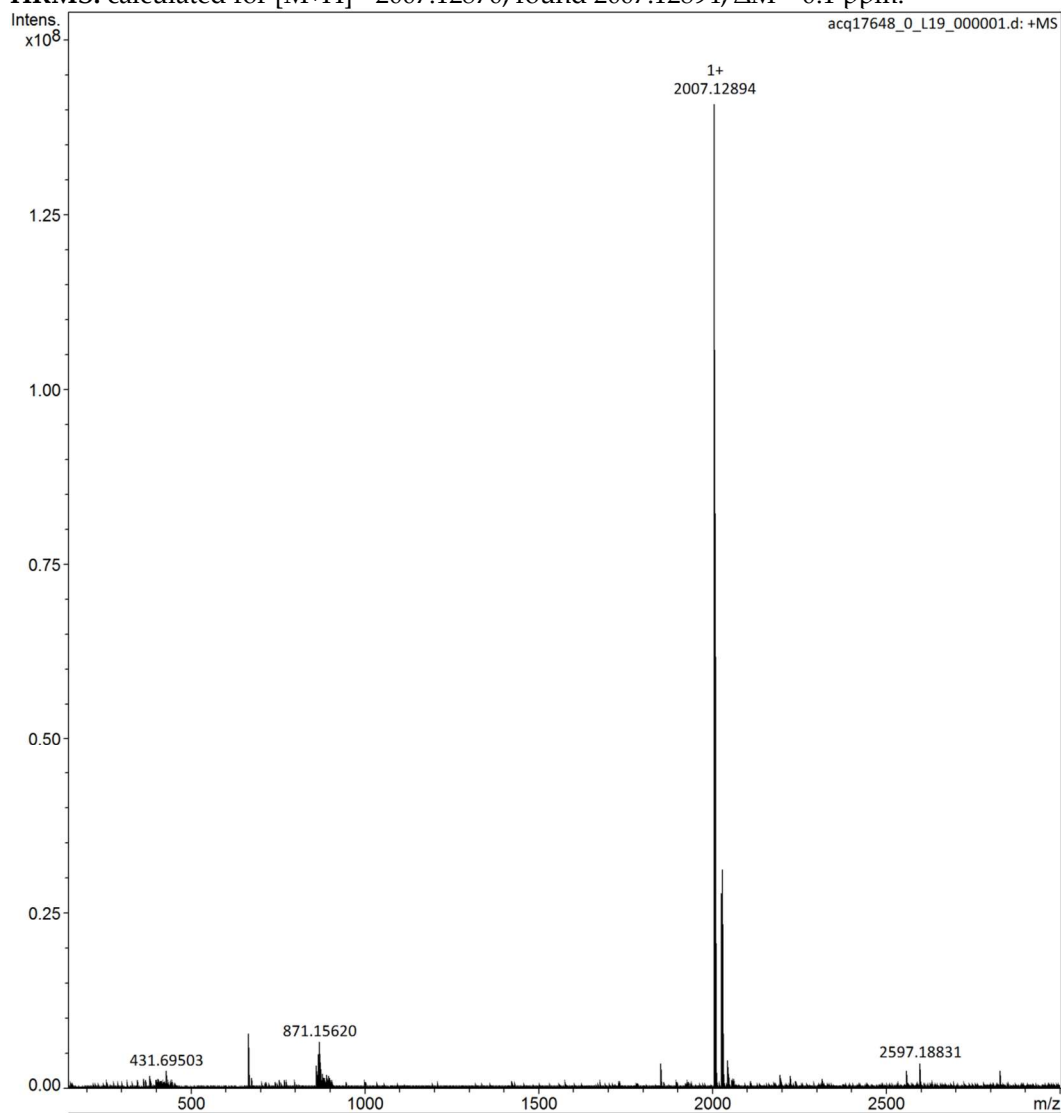

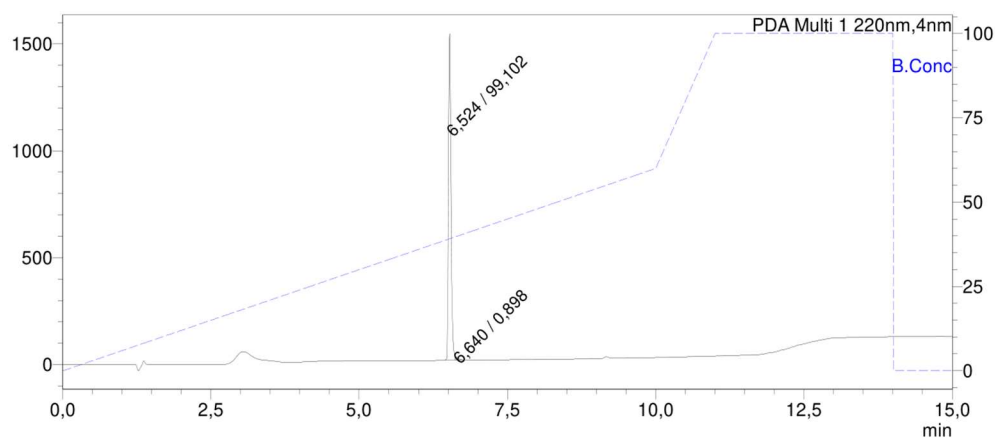**HPLC:** Charge: +7. $t_R = 6.534$ min, purity 98.131%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 2

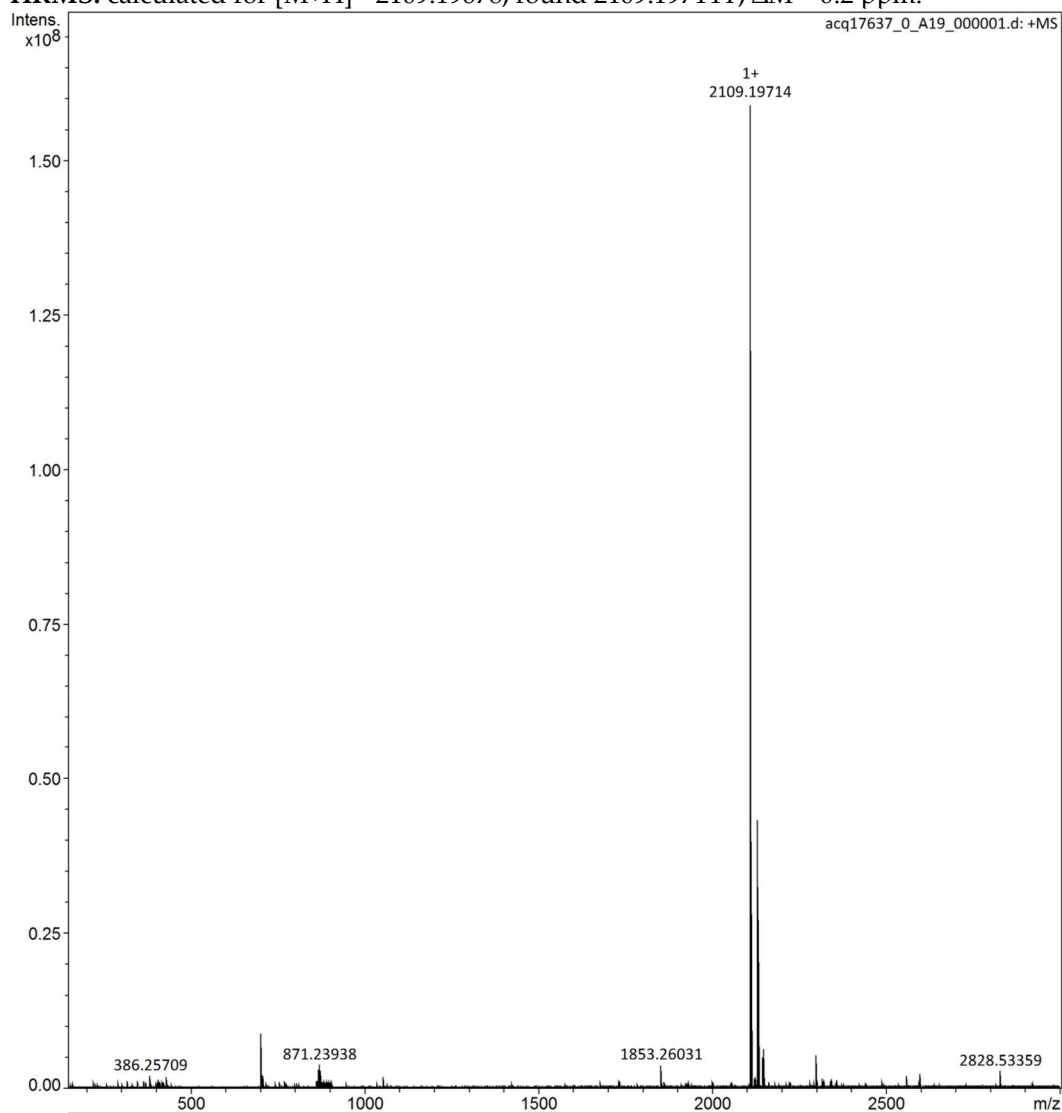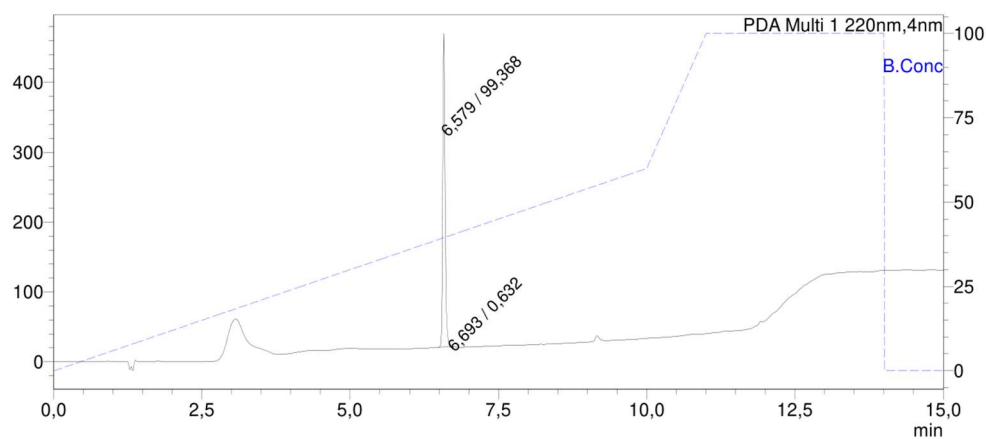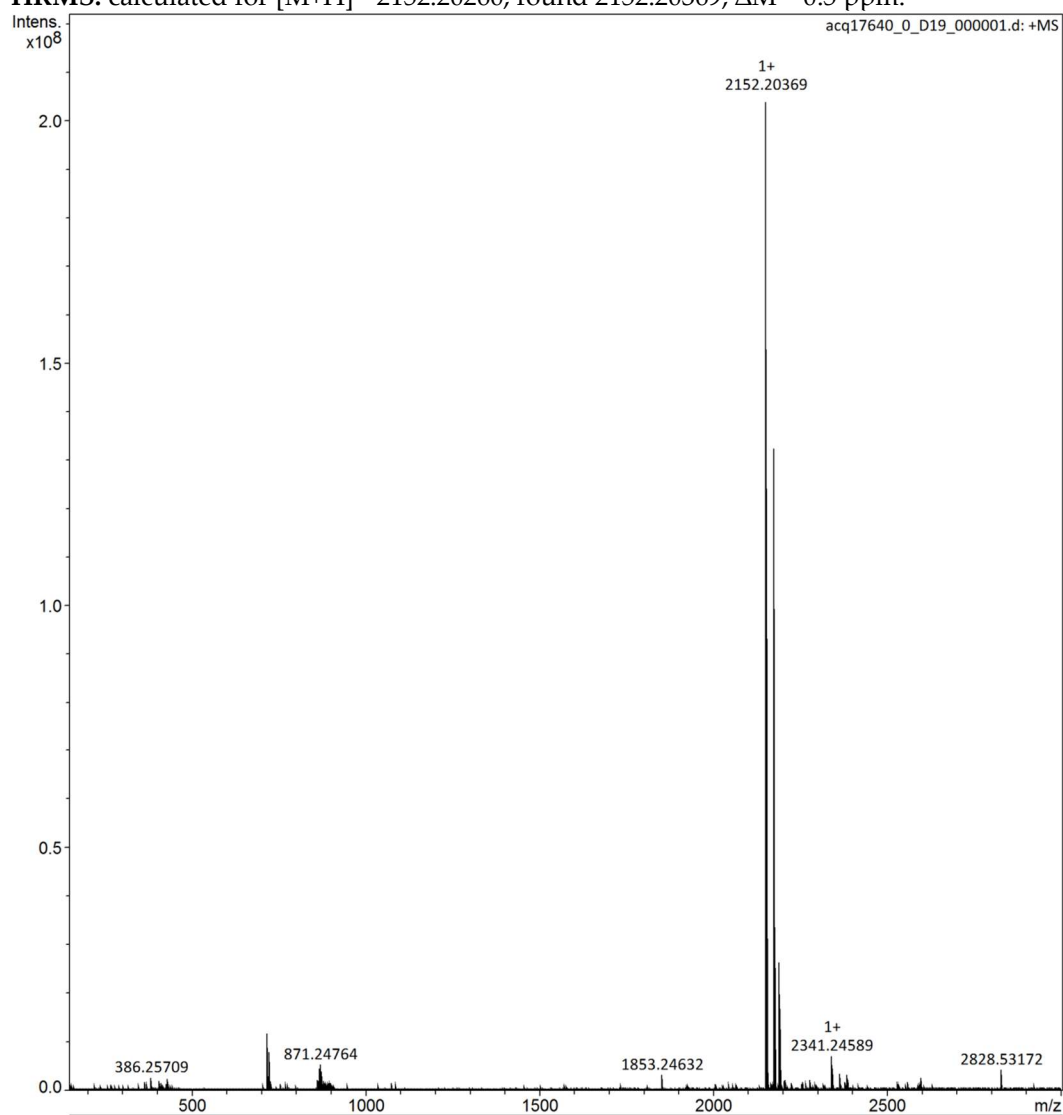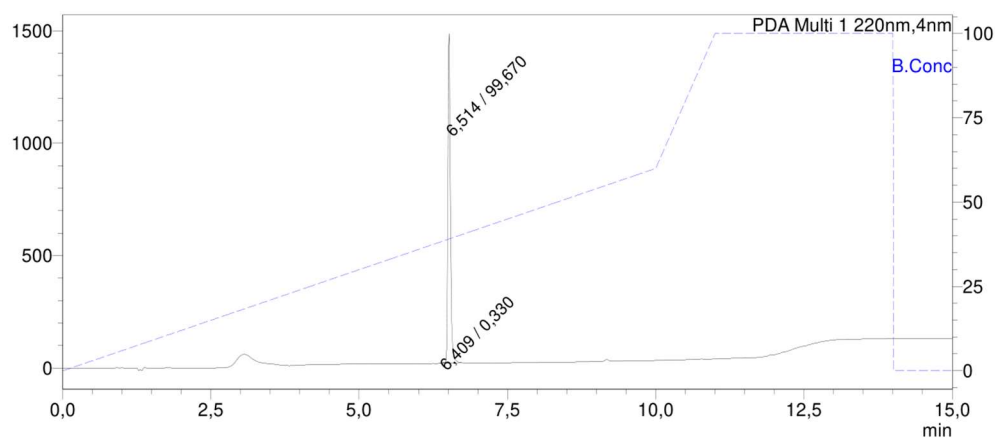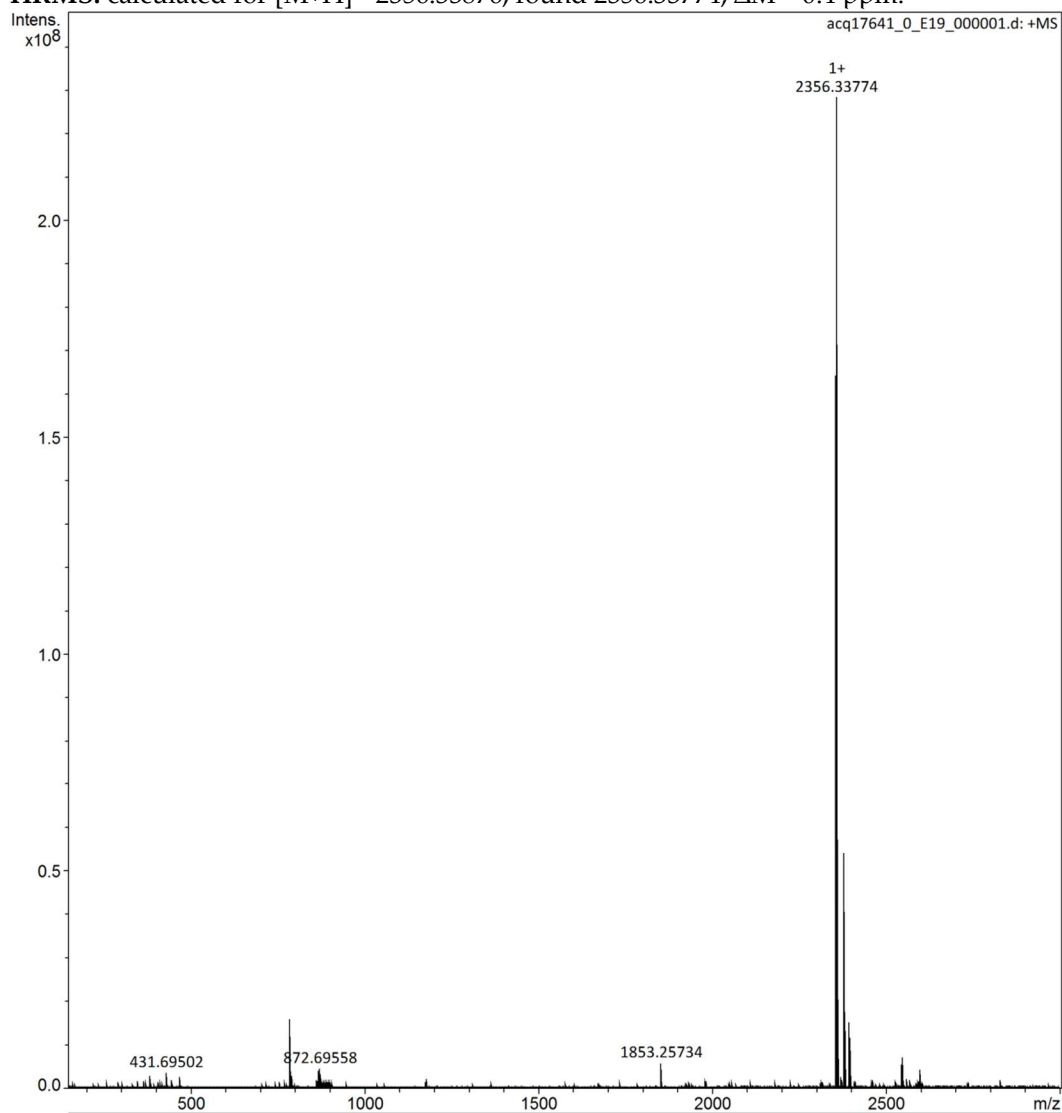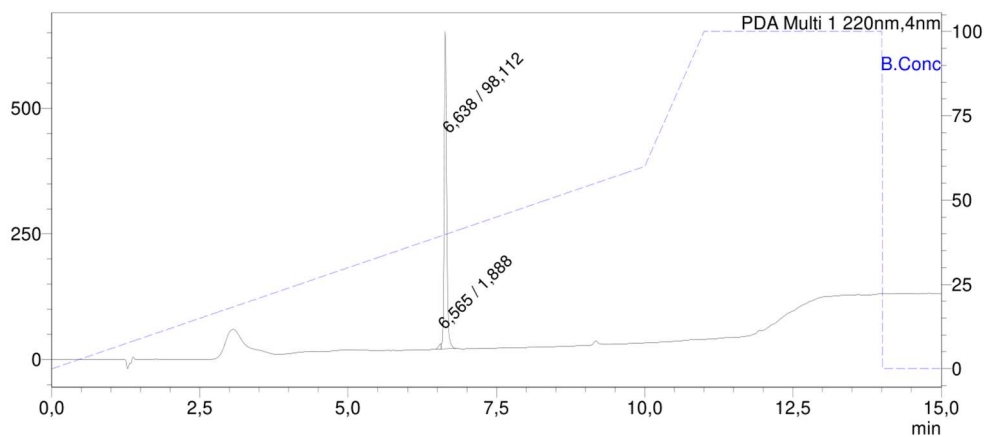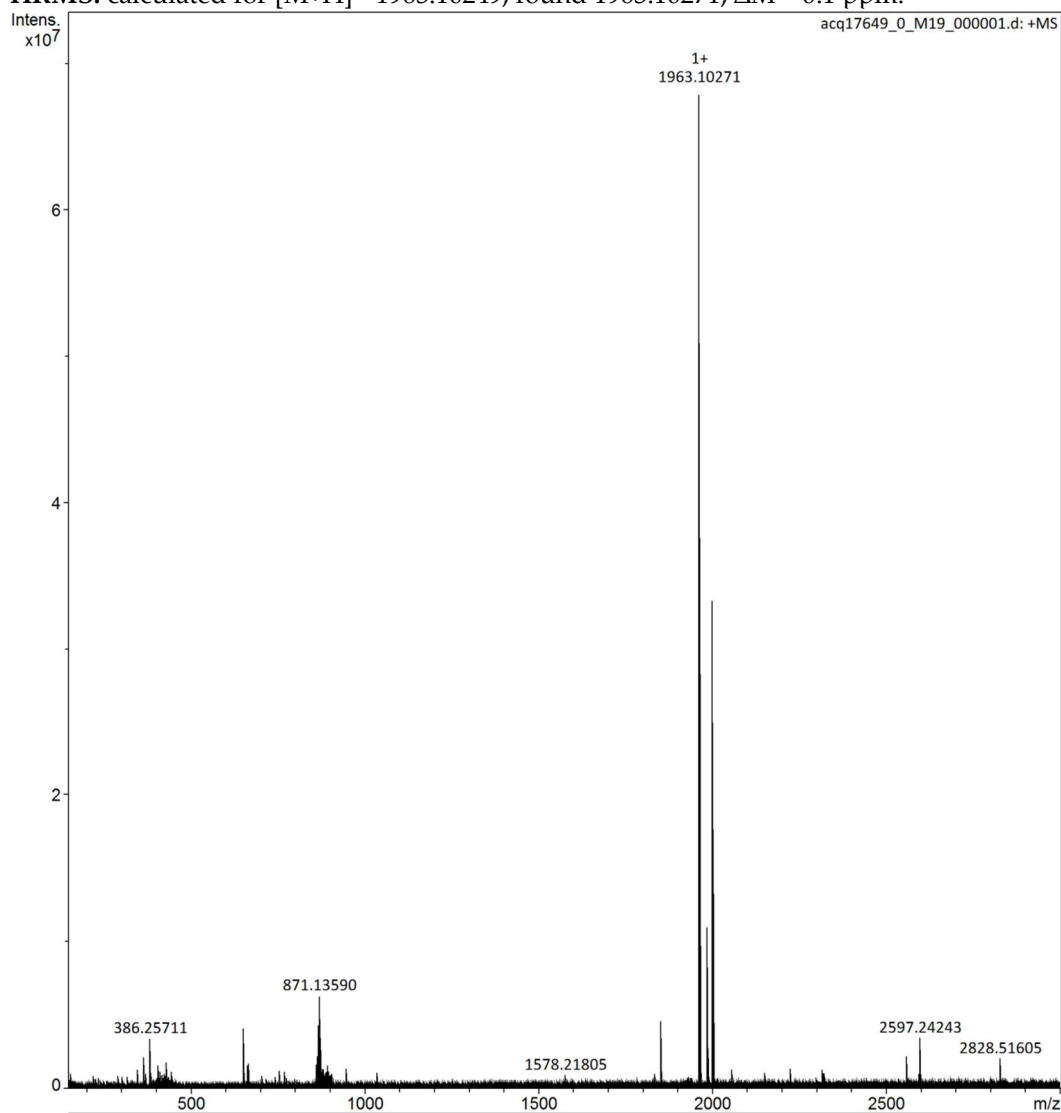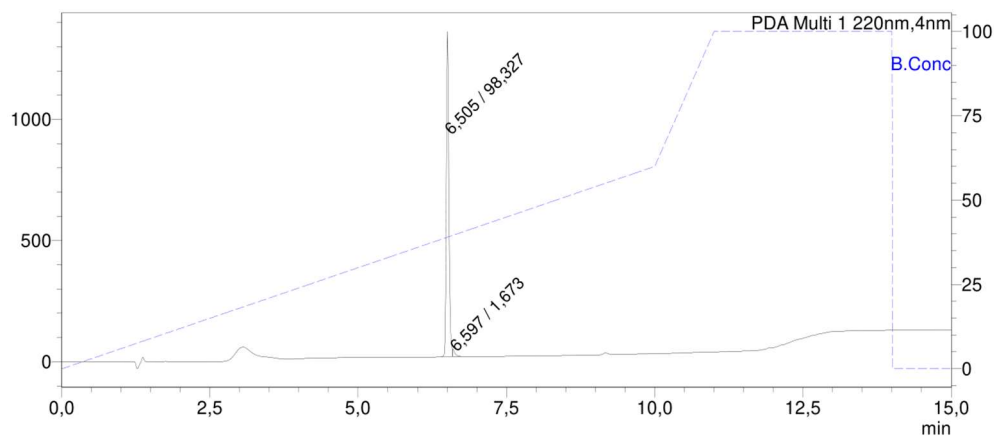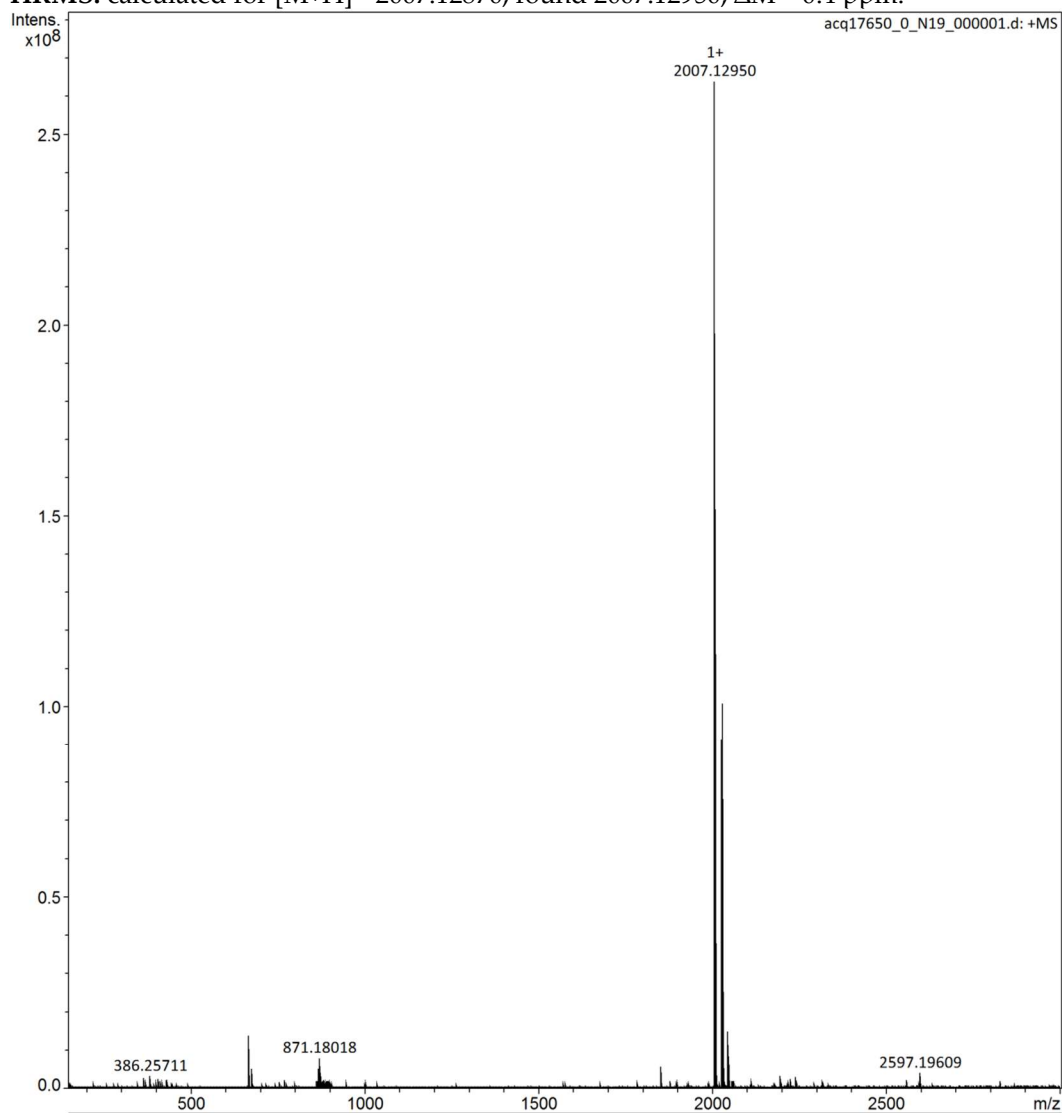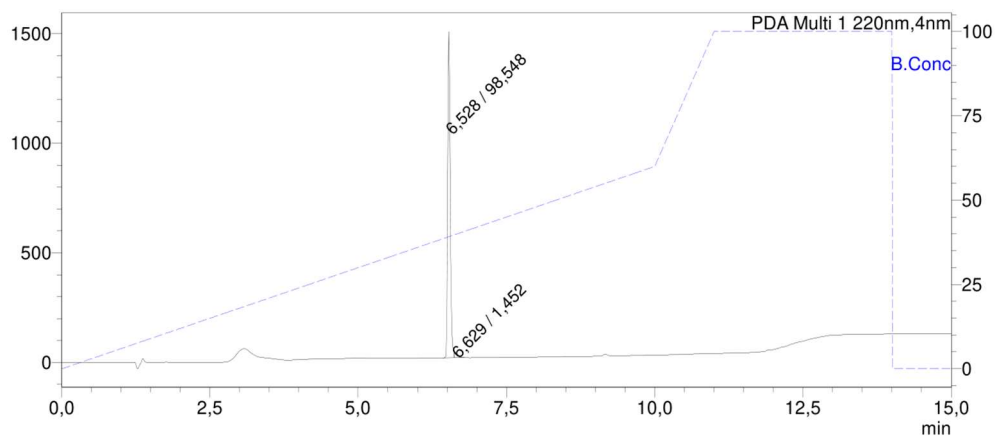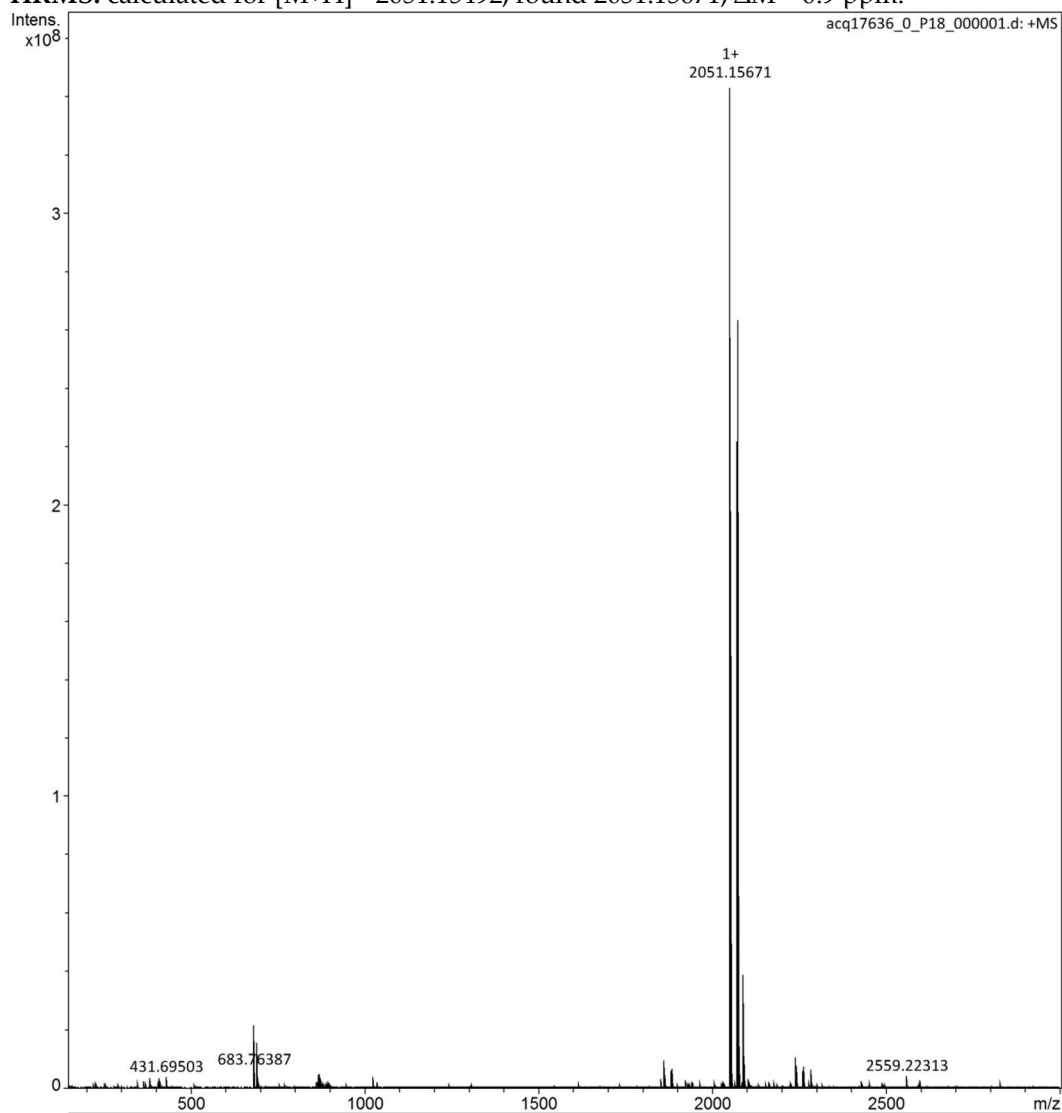**HRMS:** calculated for $[M+H]^{1+}$ 2007.12870, found 2007.12894; $\Delta M = 0.1$ ppm.

HPLC: Charge: +7. t_R = 6.524 min, purity 99.102%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 3

HRMS: calculated for $[M+H]^{1+}$ 2109.19678, found 2109.19714Y; ΔM = 0.2 ppm.

HPLC: Charge: +7. t_R = 6.579 min, purity 99.368%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
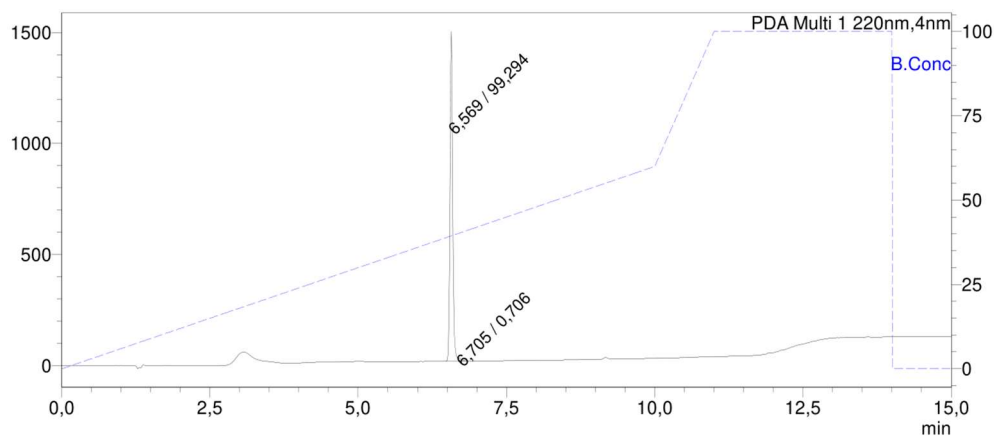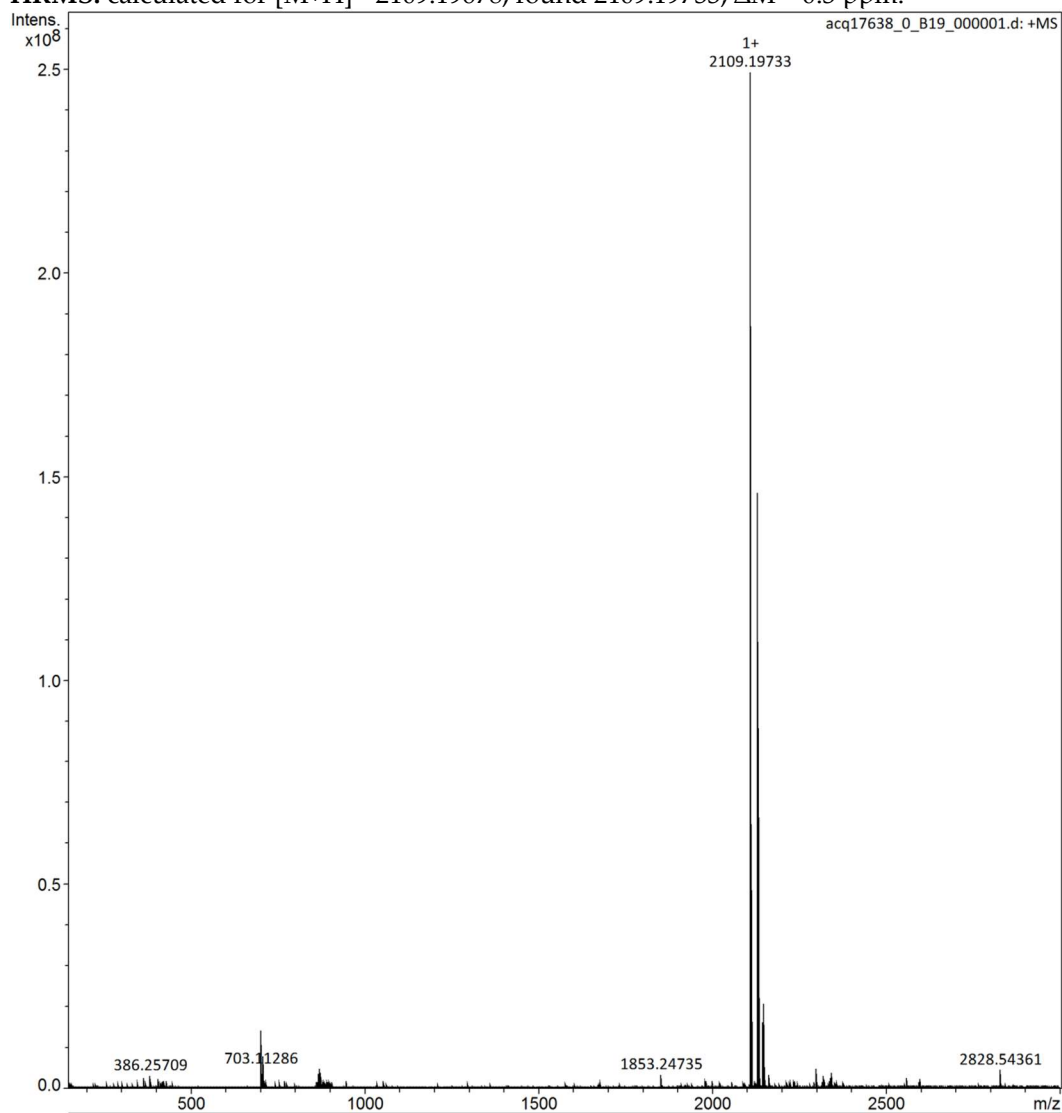
Compound 4

HRMS: calculated for $[M+H]^{1+}$ 2152.20260, found 2152.20369; $\Delta M = 0.5$ ppm.

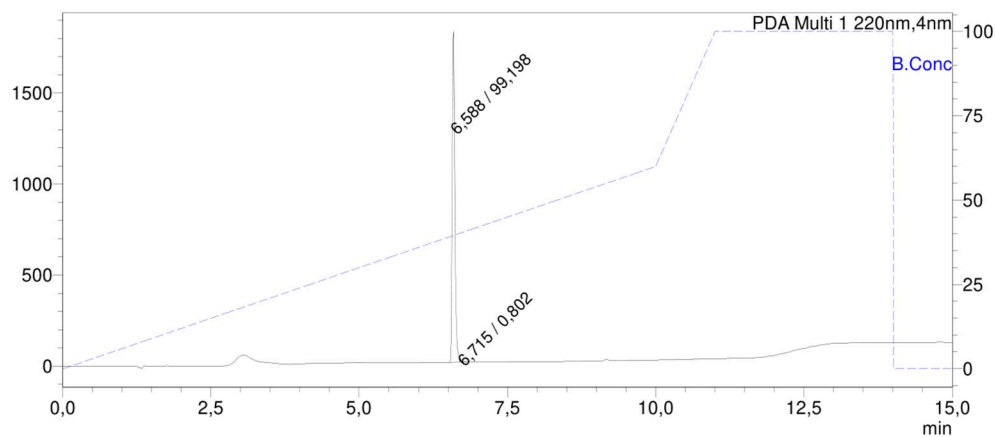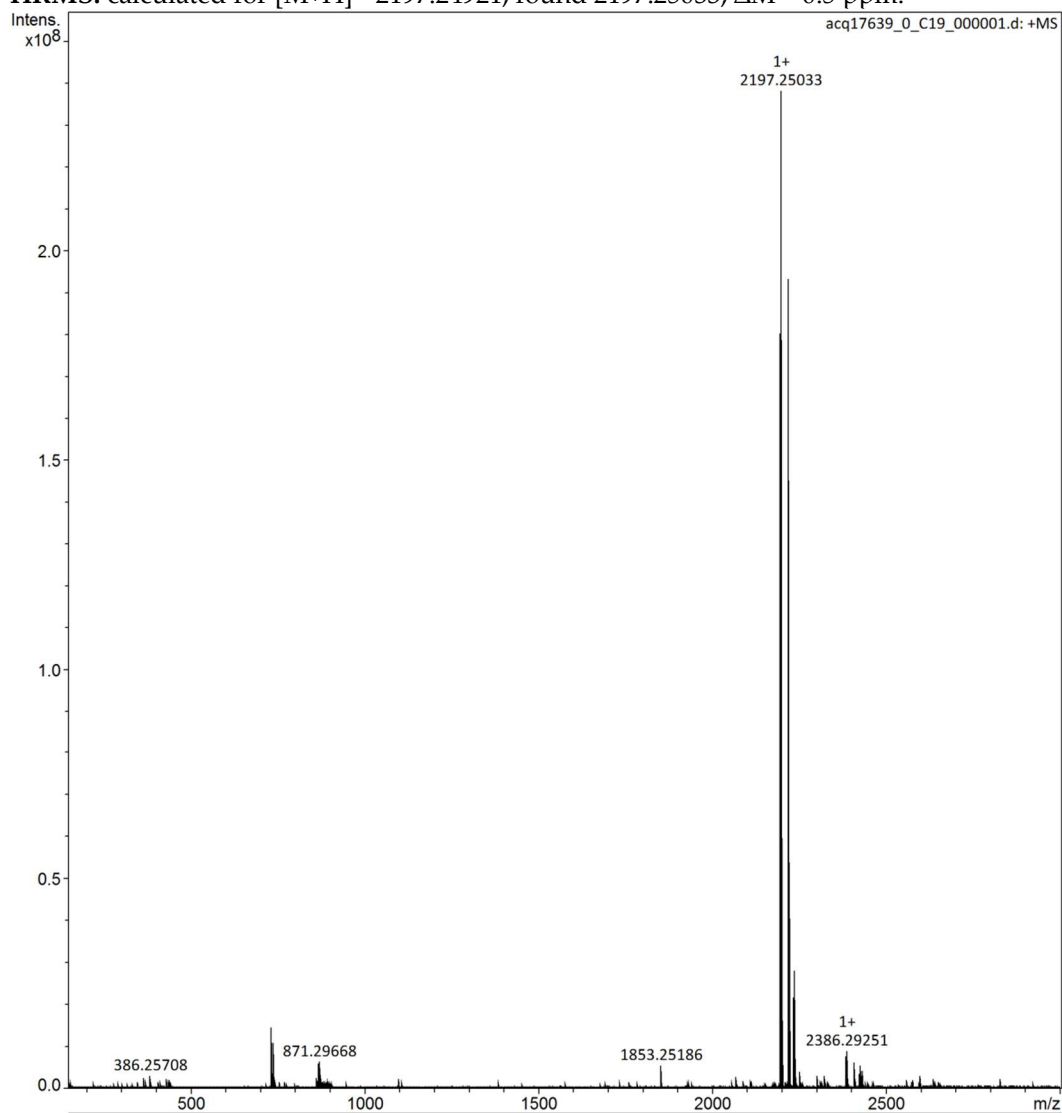**HPLC:** Charge: +7. t_R = 6.514 min, purity 99.670%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 5

HRMS: calculated for $[M+H]^{1+}$ 2356.33876, found 2356.33774; $\Delta M = 0.4$ ppm.

HPLC: Charge: +7. t_R = 6.638 min, purity 98.112%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
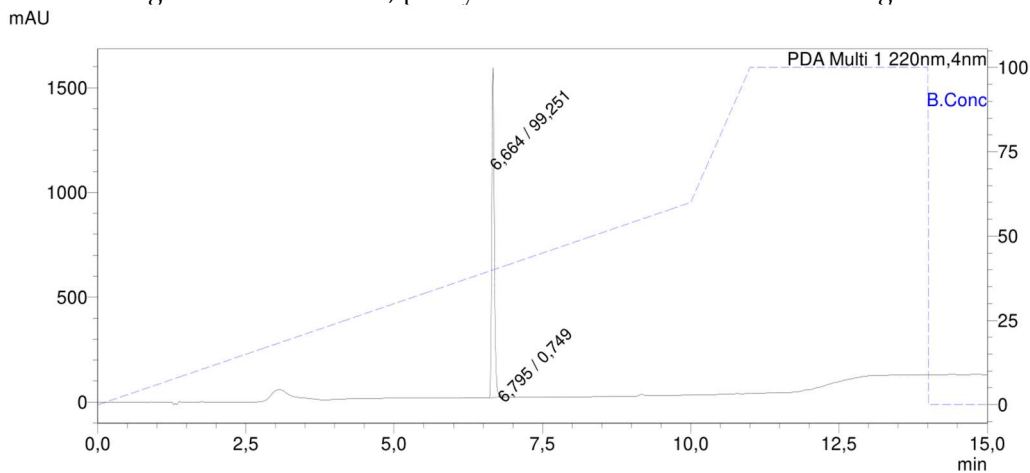
Compound 6

HRMS: calculated for [M+H]$^{1+}$ 1963.10249, found 1963.10271; ΔM = 0.1 ppm.
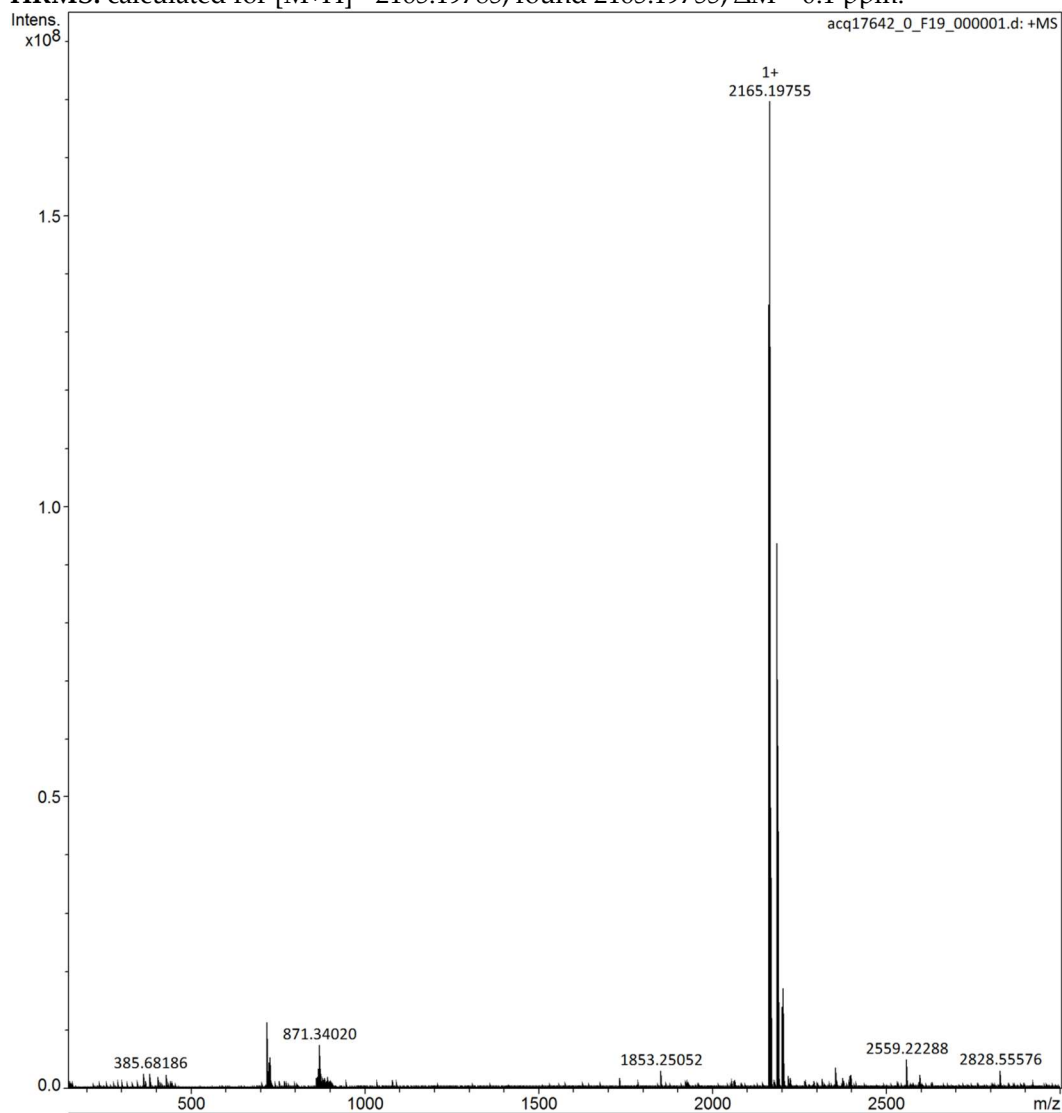

HPLC: Charge: +7. t_R = 6.505 min, purity 98.327%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 7

HRMS: calculated for $[M+H]^{1+}$ 2007.12870, found 2007.12950; $\Delta M = 0.4$ ppm.

HPLC: Charge: +7. t_R = 6.528 min, purity 98.548%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
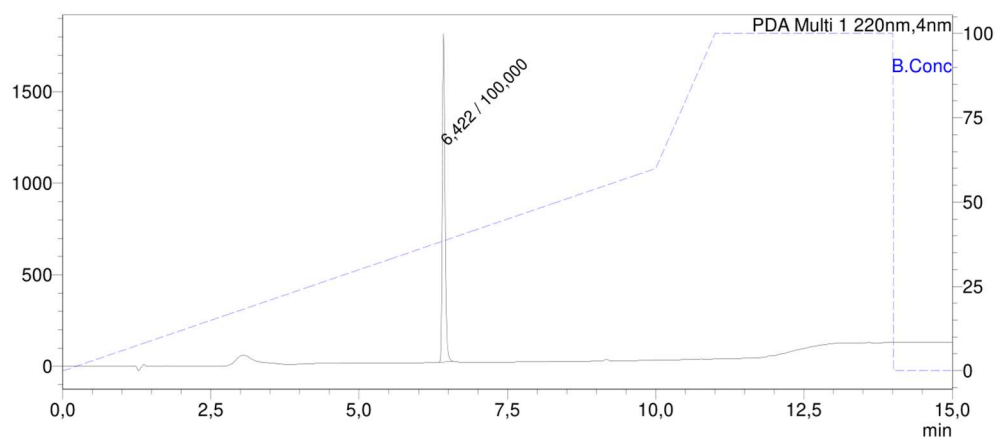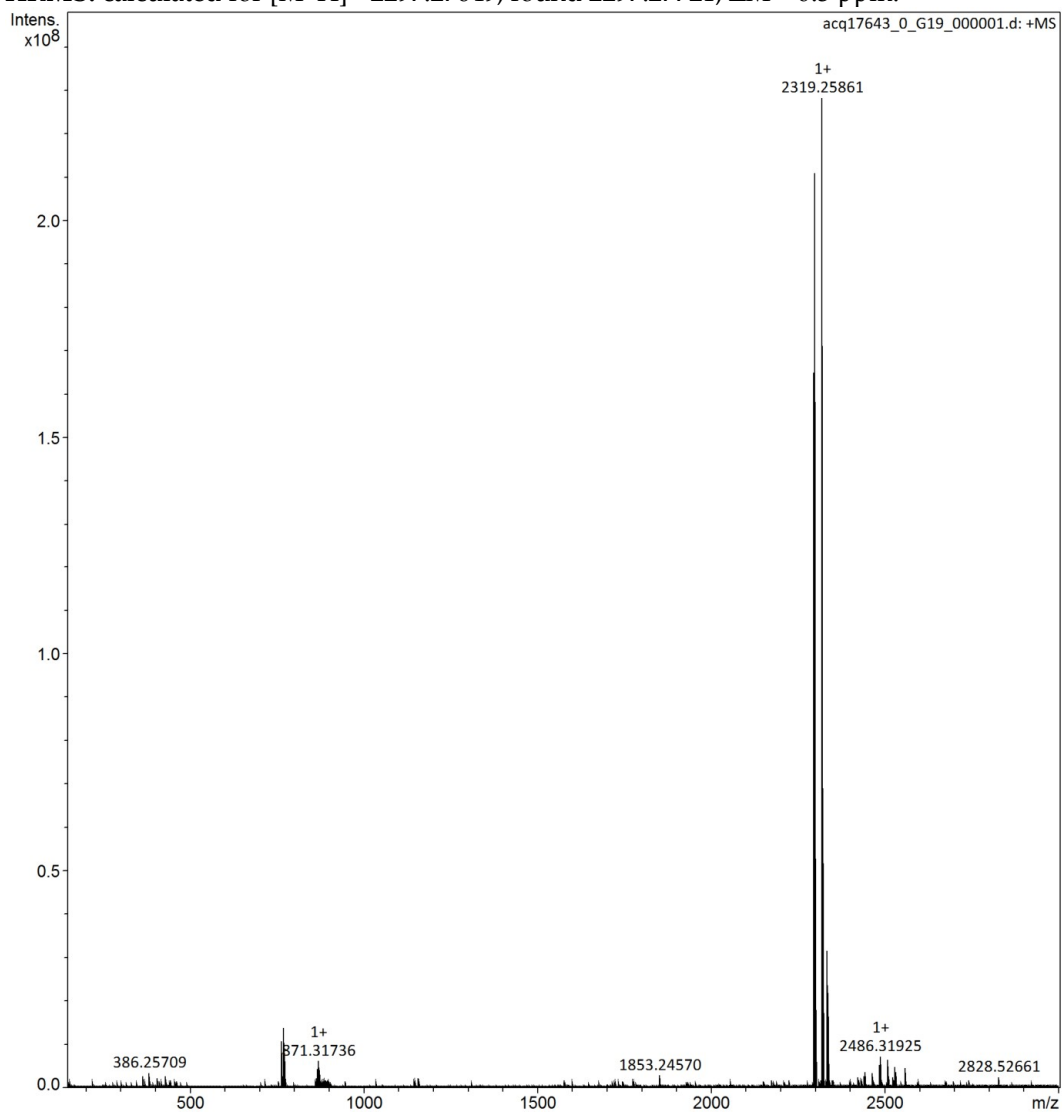
Compound 8

HRMS: calculated for $[M+H]^{1+}$ 2051.15492, found 2051.15671; $\Delta M = 0.9$ ppm.

HPLC: Charge: +7. t_R = 6.569 min, purity 99.294%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
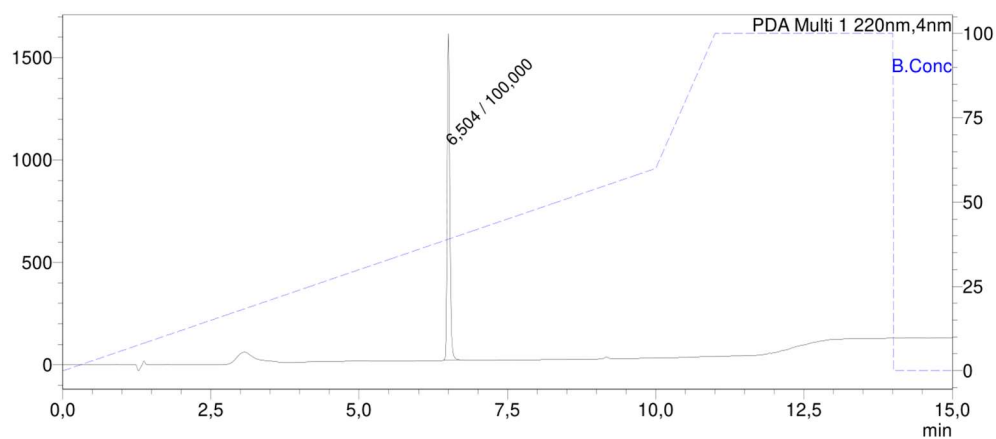
Compound 9

HRMS: calculated for [M+H]$^{1+}$ 2109.19678, found 2109.19733; ΔM = 0.3 ppm.
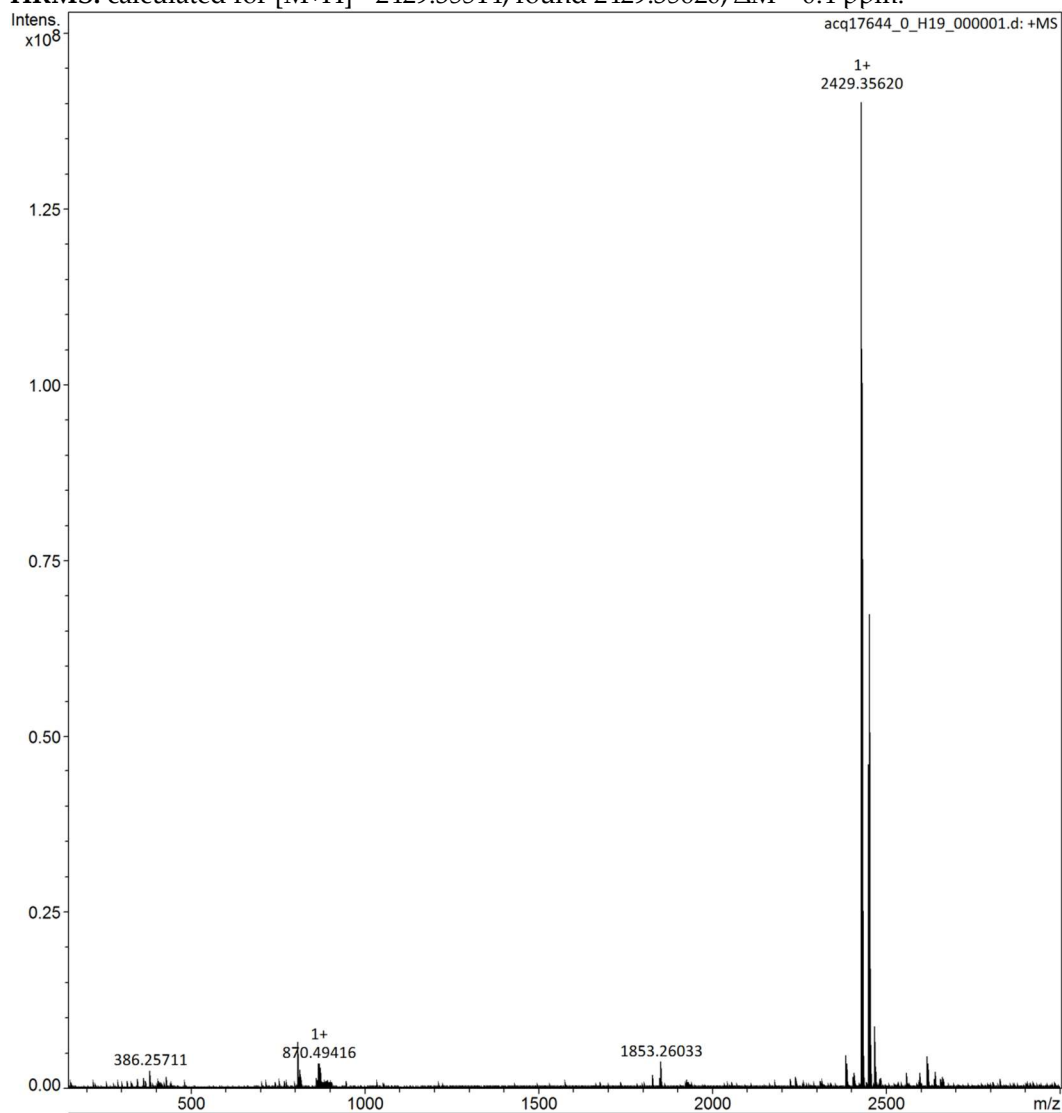

HPLC: Charge: +7. t_R = 6.588 min, purity 99.198%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 10

HRMS: calculated for [M+H]$^{1+}$ 2197.24921, found 2197.25033; $\Delta M = 0.5$ ppm.

HPLC: Charge: +7. t_R = 6.664 min, purity 99.251%. Gradient: 0–60% B during 10 min. B = 95% MeCN + 0.1% TFA.
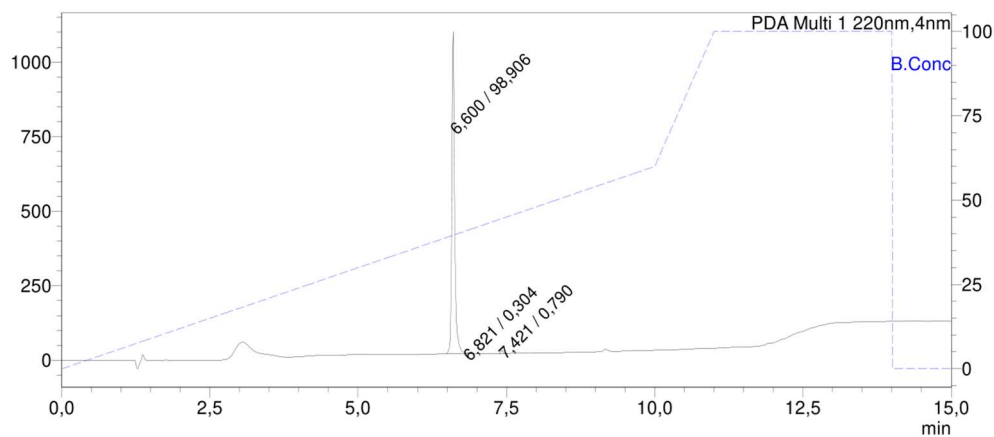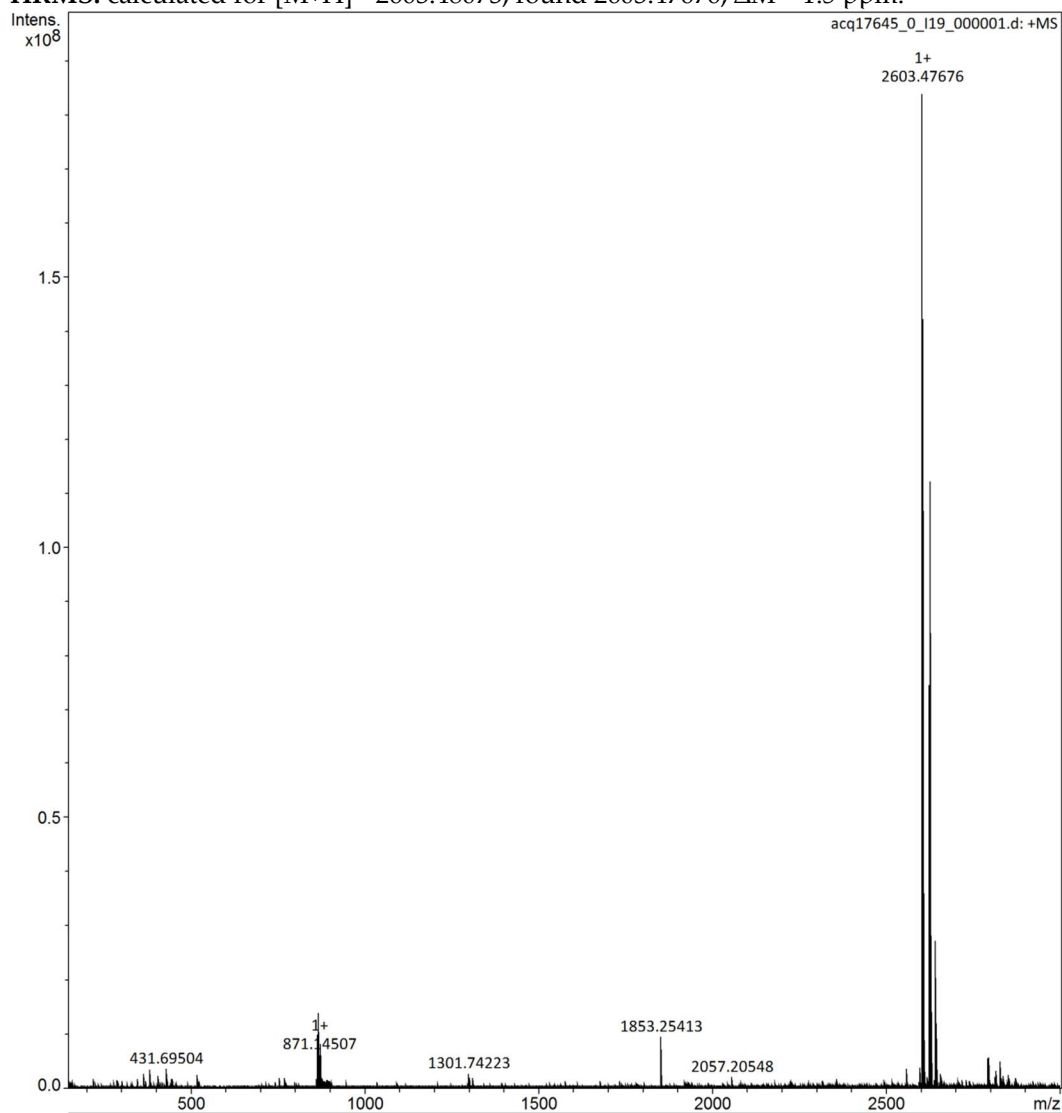
Compound 11

HRMS: calculated for $[M+H]^{1+}$ 2165.19785, found 2165.19755; $\Delta M = 0.1$ ppm.

HPLC: Charge: +7. t_R = 6.422 min, purity 100.000%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 12

HRMS: calculated for [M+H]$^{1+}$ 2297.27649, found 2297.27721; ΔM = 0.3 ppm.

HPLC: Charge: +7. t_R = 6.504 min, purity 100.000%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 13

HRMS: calculated for $[M+H]^{1+}$ 2429.35514, found 2429.35620; ΔM = 0.4 ppm.

HPLC: Charge: +7. t_R = 6.600 min, purity 98.906%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
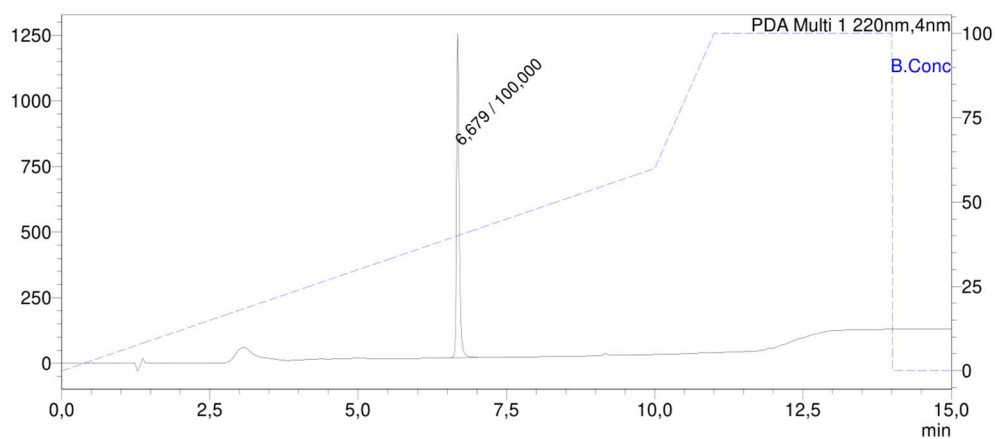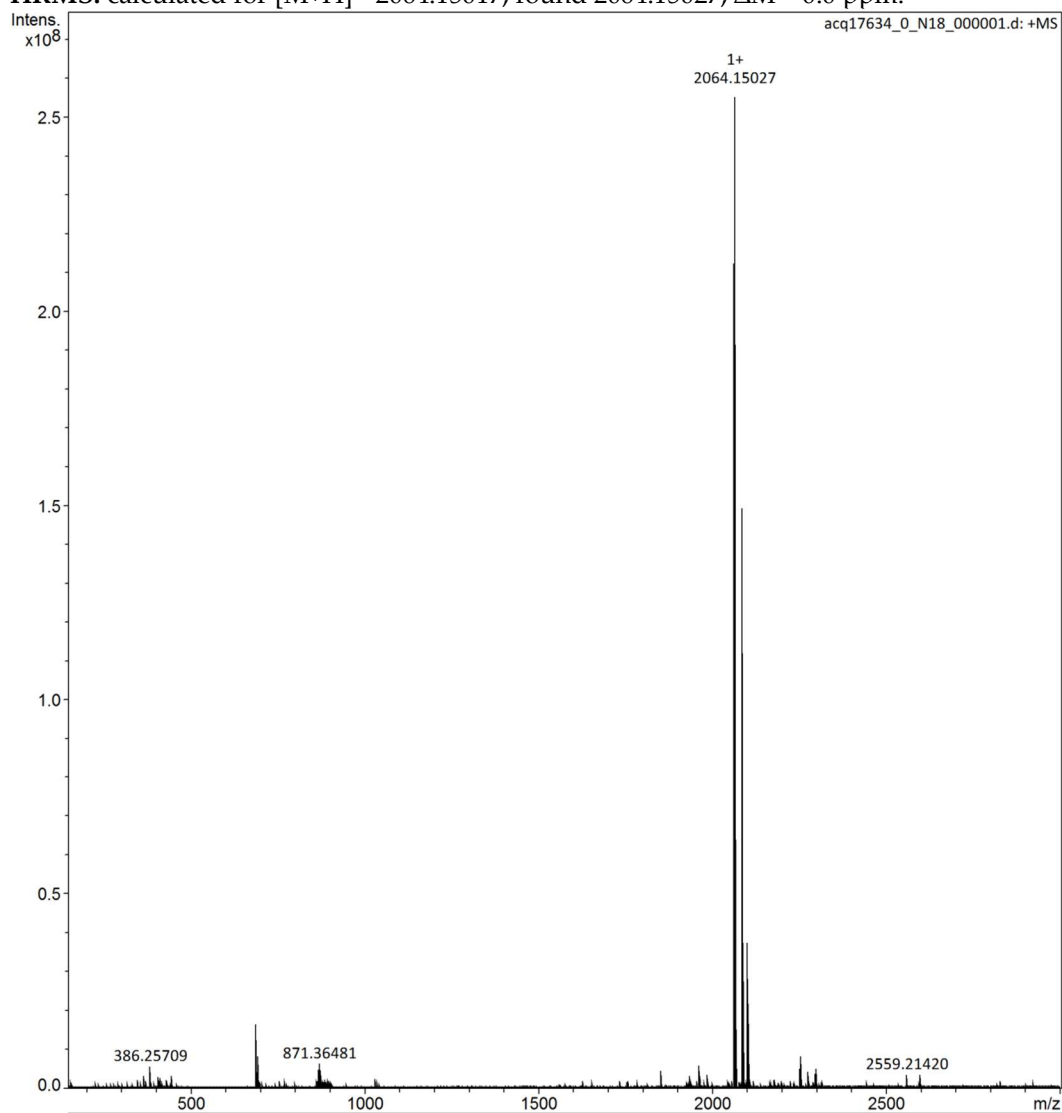
Compound 14

HRMS: calculated for [M+H]$^{1+}$ 2603.48073, found 2603.47676; ΔM = 1.5 ppm.

HPLC: Charge: +7. t_R = 6.679 min, purity 100.000%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
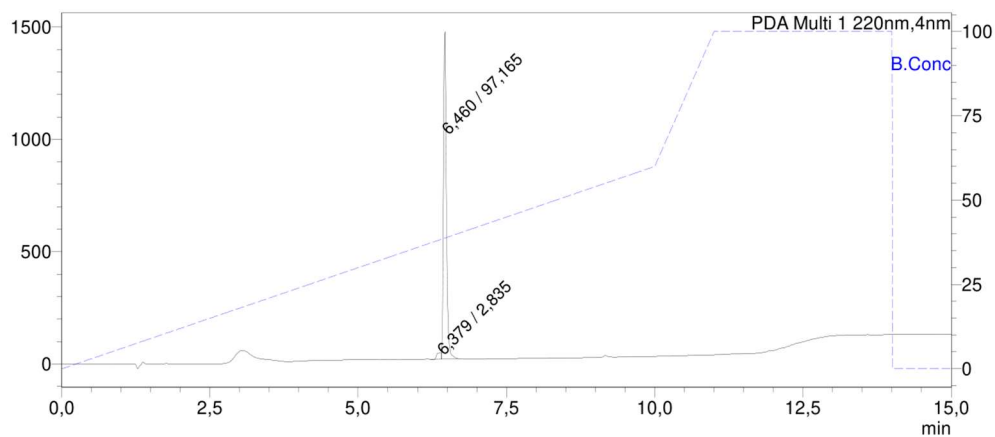
Compound 15

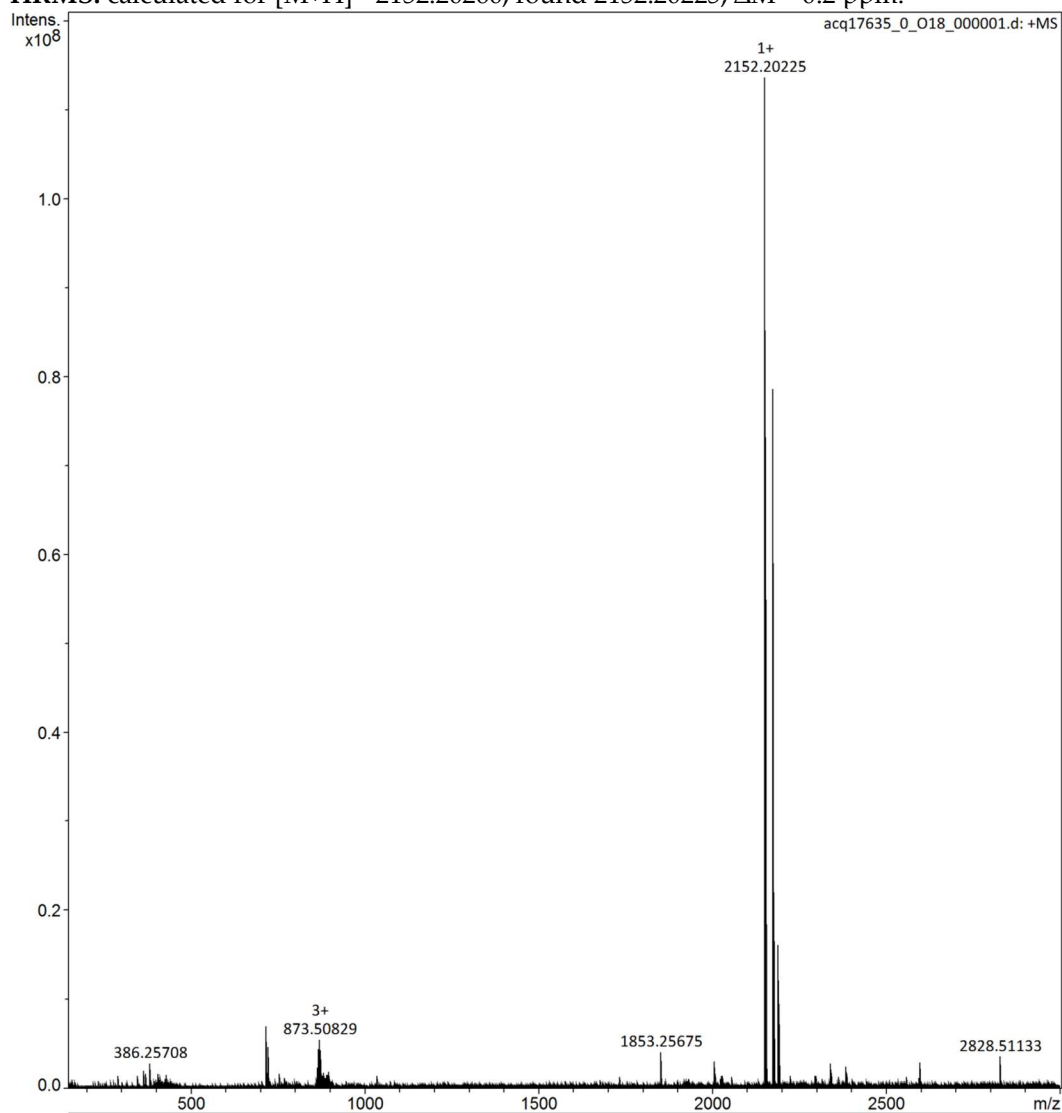**HRMS:** calculated for $[M+H]^{1+}$ 2064.15017, found 2064.15027; $\Delta M = 0.0$ ppm.

HPLC: Charge: +7. t_R = 6.460 min, purity 97.165%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
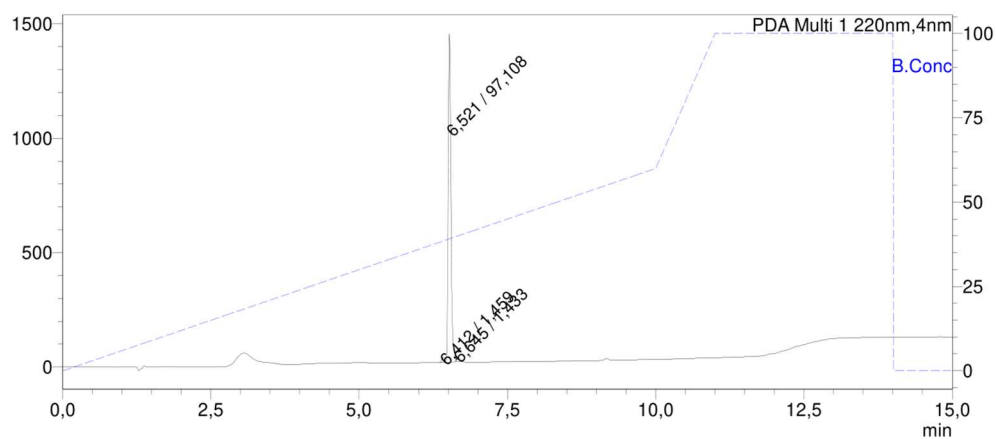
Compound 16

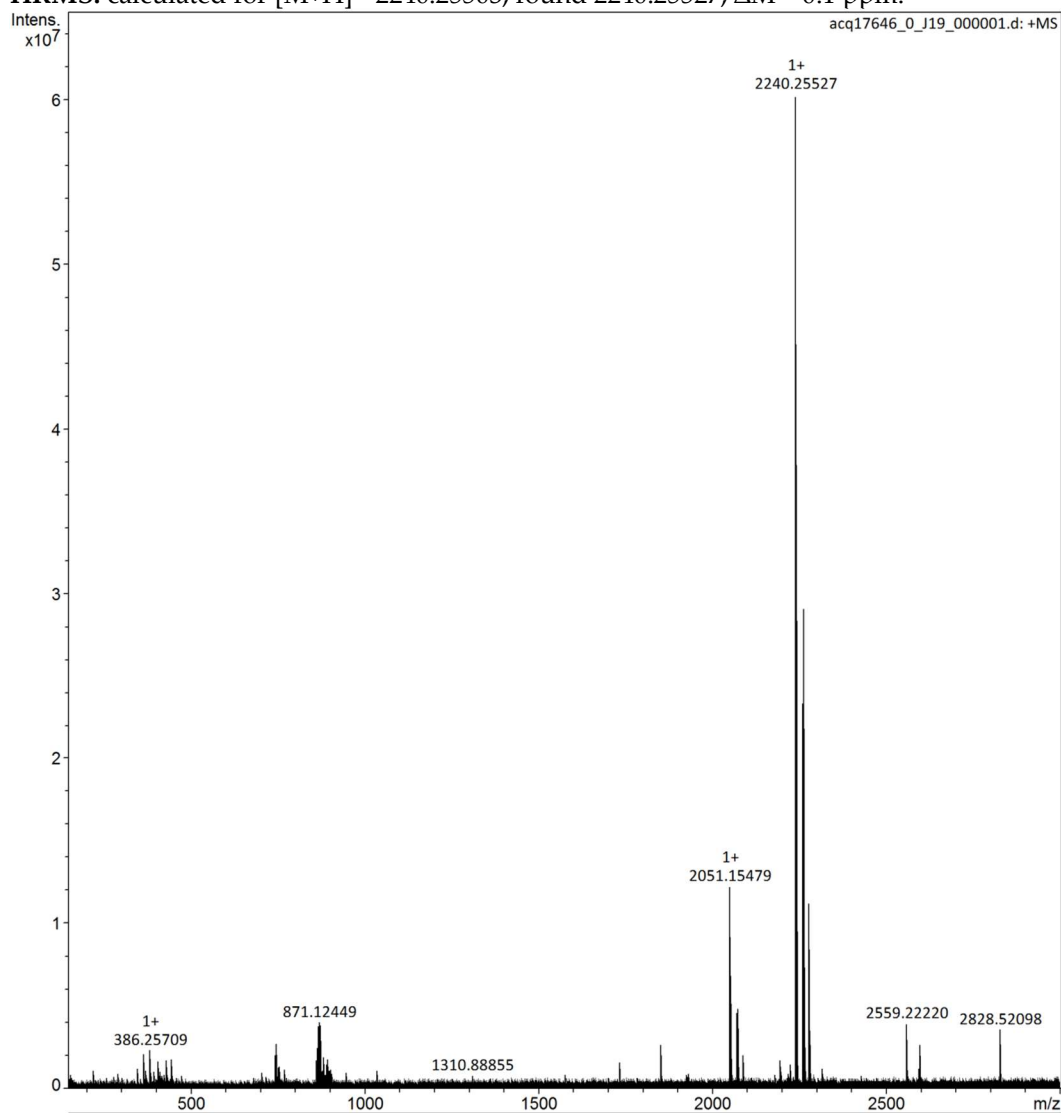**HRMS:** calculated for $[M+H]^{1+}$ 2152.20260, found 2152.20225; $\Delta M = 0.2$ ppm.

HPLC: Charge: +7. $t_R = 6.521$ min, purity 97.108%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
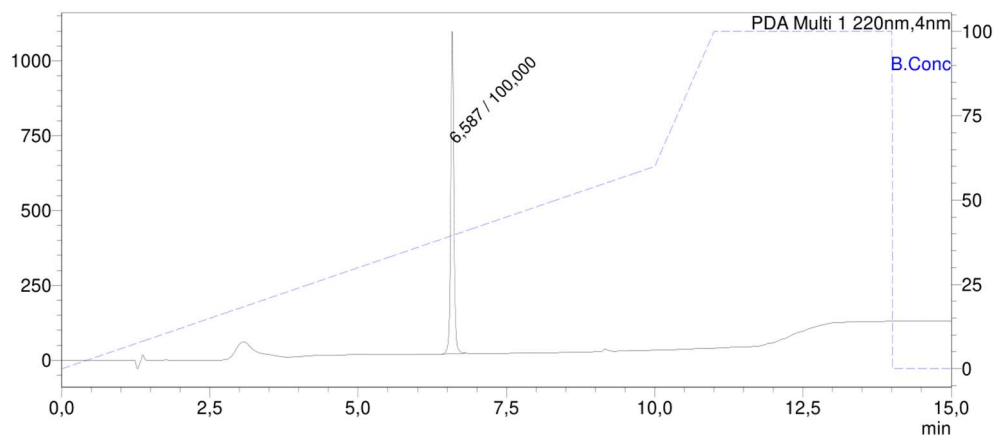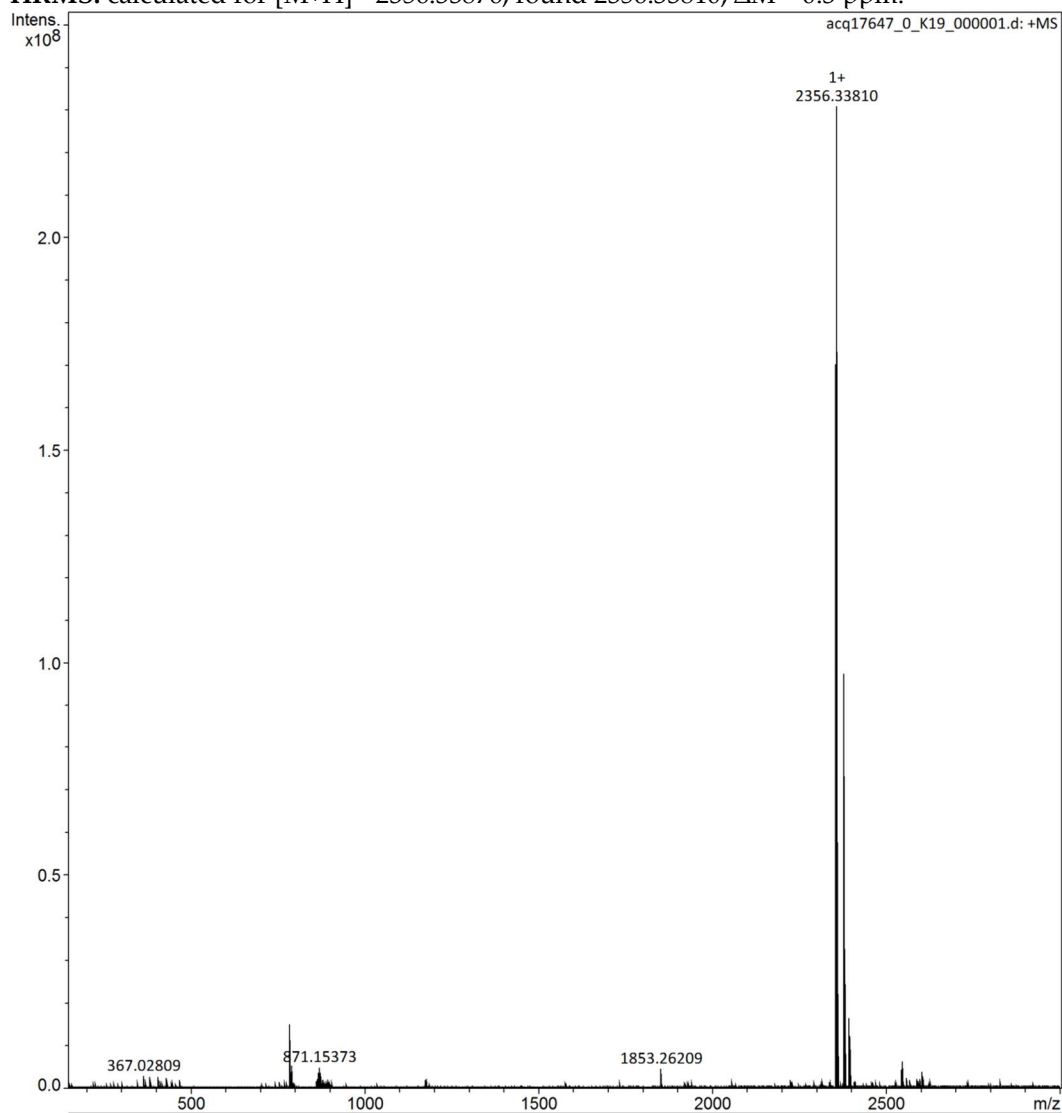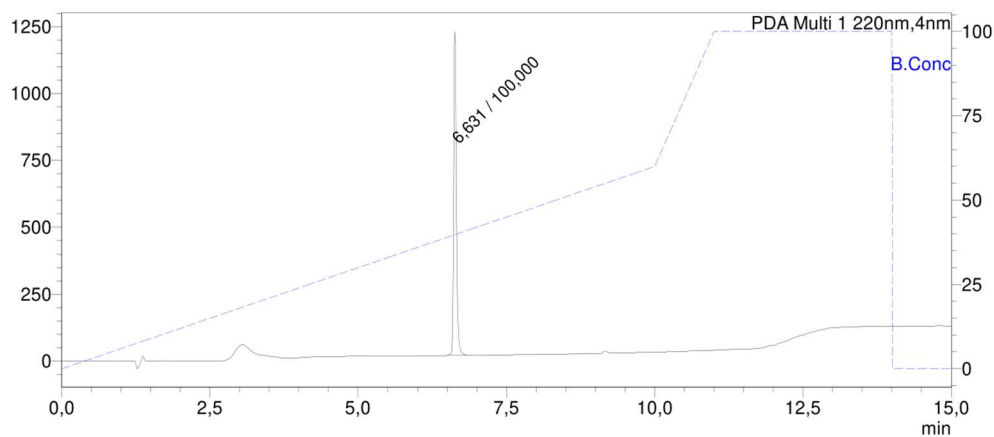
Compound 17

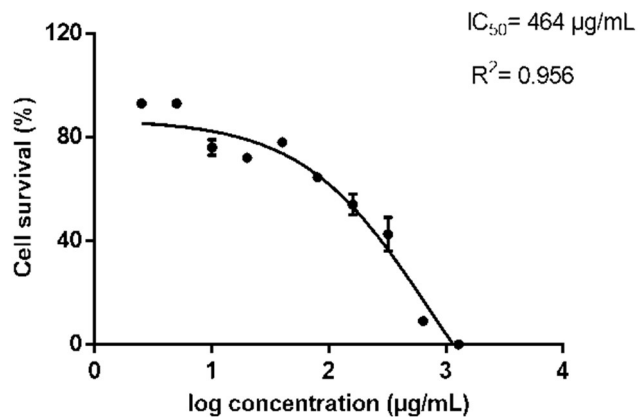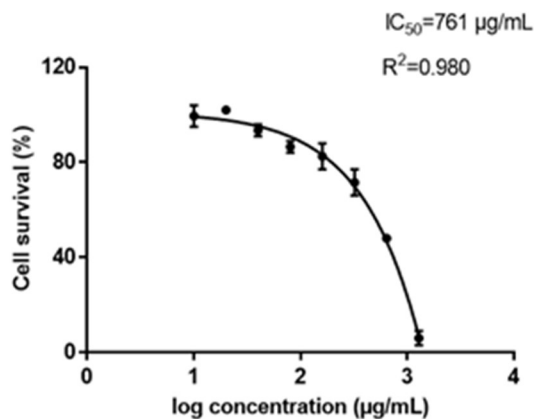**HRMS:** calculated for [M+H]$^{1+}$ 2240.25503, found 2240.25527; ΔM = 0.1 ppm.
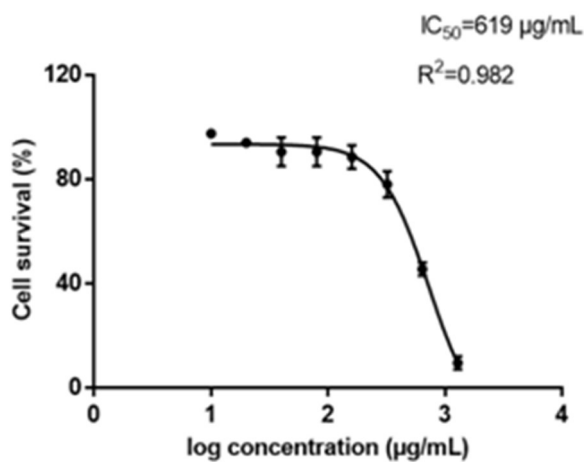

HPLC: Charge: +7. t_R = 6.587 min, purity 100.000%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.

Compound 18

HRMS: calculated for [M+H]$^{1+}$ 2356.33876, found 2356.33810; ΔM = 0.3 ppm.

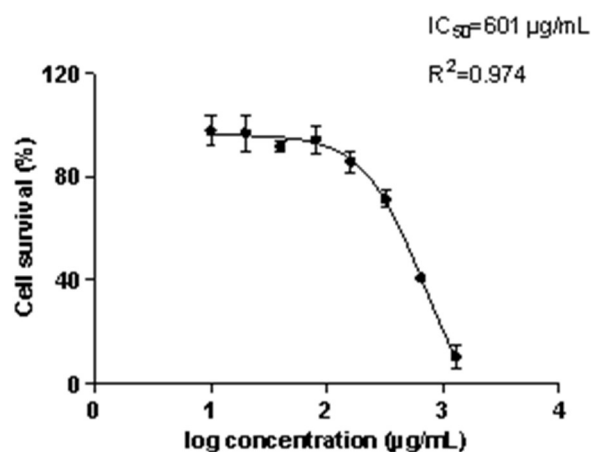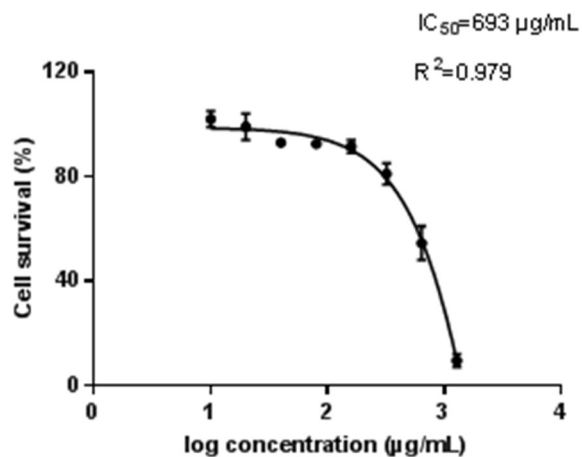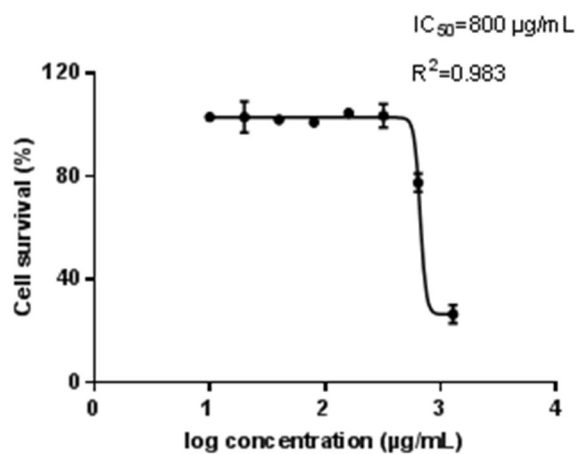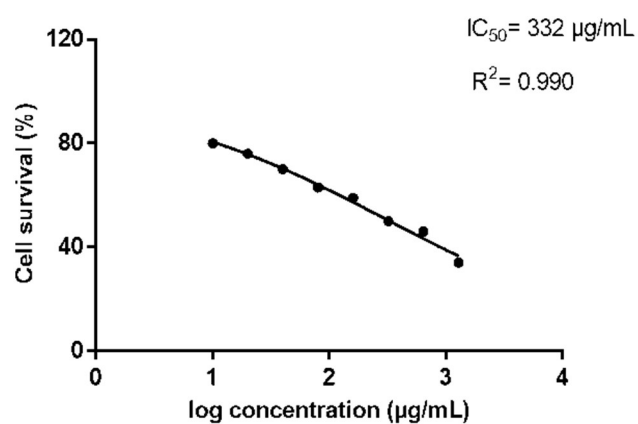**HPLC:** Charge: +7. t_R = 6.631 min, purity 100.000%. Gradient: 0-60% B during 10 min. B = 95% MeCN + 0.1% TFA.
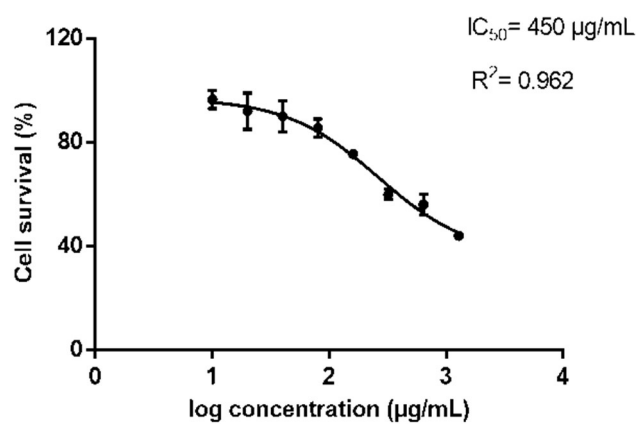
HepG2 IC$_{50}$ curves

Curves only drawn for compounds diplaying IC$_{50}$ < 1280 µg/mL, i.e., **1**, **6-10**, **12**, **14-16**.

Compound 1

IC$_{50}$= 464 µg/mL

R^2= 0.956

Compound 6

IC$_{50}$=761 µg/mL

R^2=0.980

Compound 7

IC$_{50}$=619 µg/mL

R^2=0.982

Compound 8

IC$_{50}$=601 µg/mL

R^2=0.974

Compound 9

IC$_{50}$=693 µg/mL

R^2=0.979

Compound 10

IC$_{50}$=800 µg/mL

R^2=0.983

Compound 12

IC_{50} = 332 µg/mL

R^2 = 0.990

Compound 14

IC_{50} = 450 µg/mL

R^2 = 0.962

Compound 15

IC_{50} = 568 µg/mL

R^2 = 0.965

Compound 16

IC_{50} = 687 µg/mL

R^2 = 0.973