Electronic Supplementary Material (ESI) for MedChemComm.

Novel peptidomimetics related to Gonadotropin releasing hormone (GnRH)

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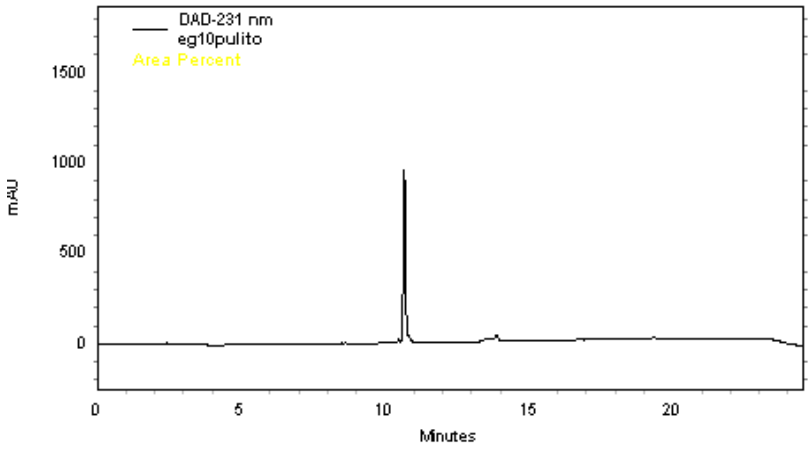
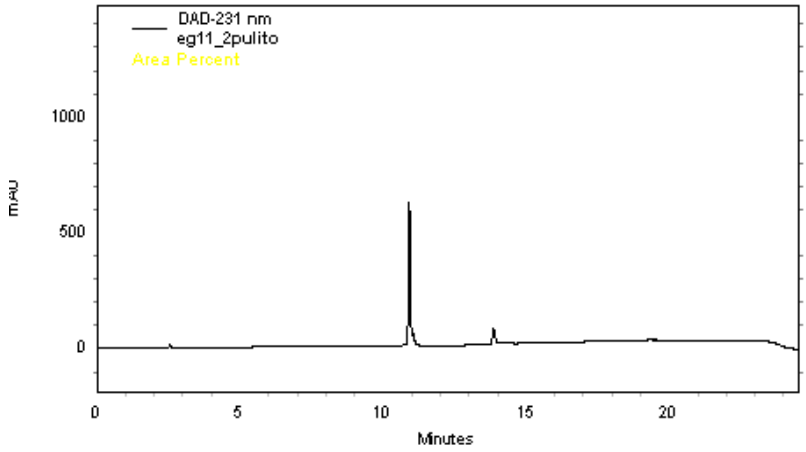
HPLC analysis

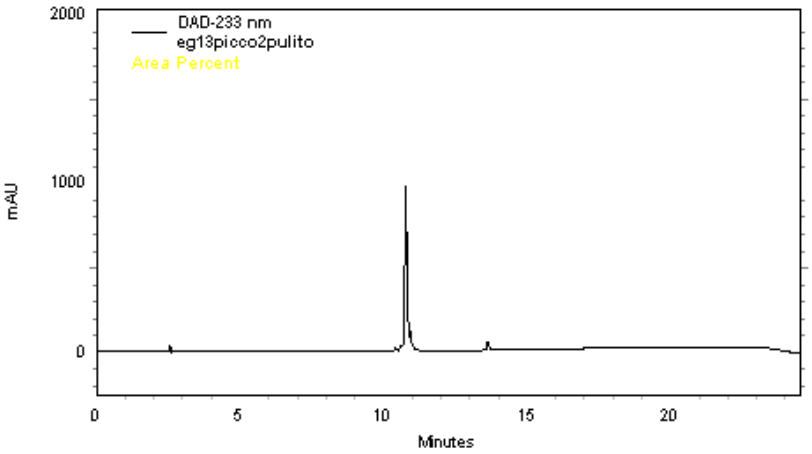
Ia



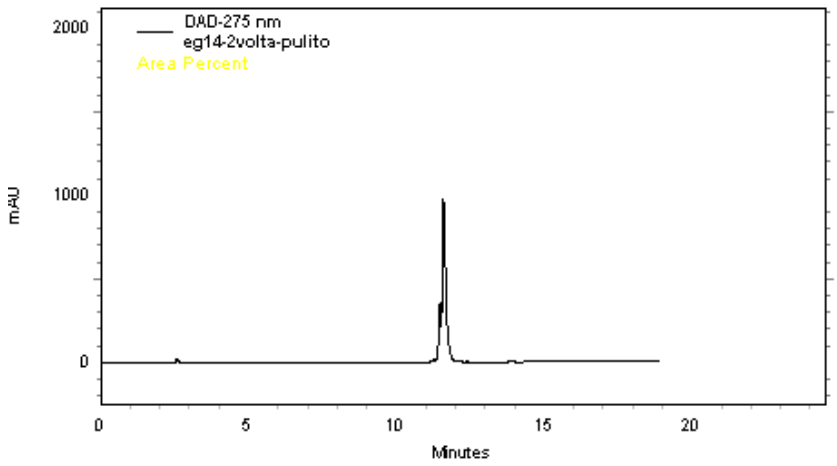
Ib



Id



Ie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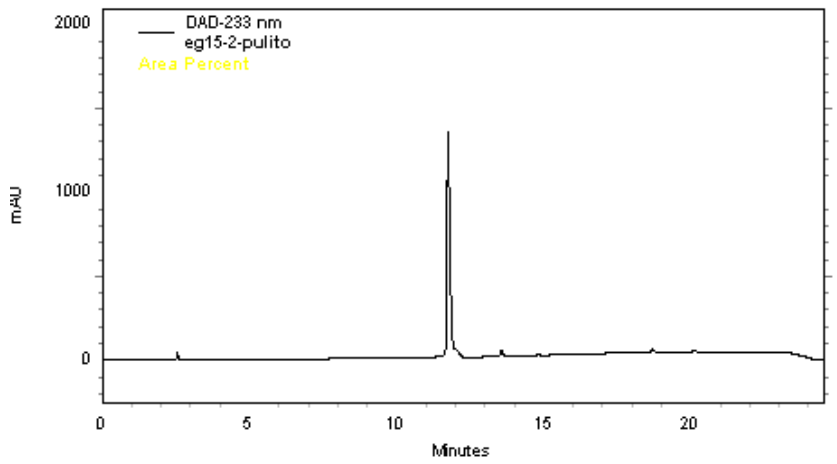
eg14-2volta-pulito
Area Percent
mAU
2000
1000
0
0
5
10
15
20
Minutes

If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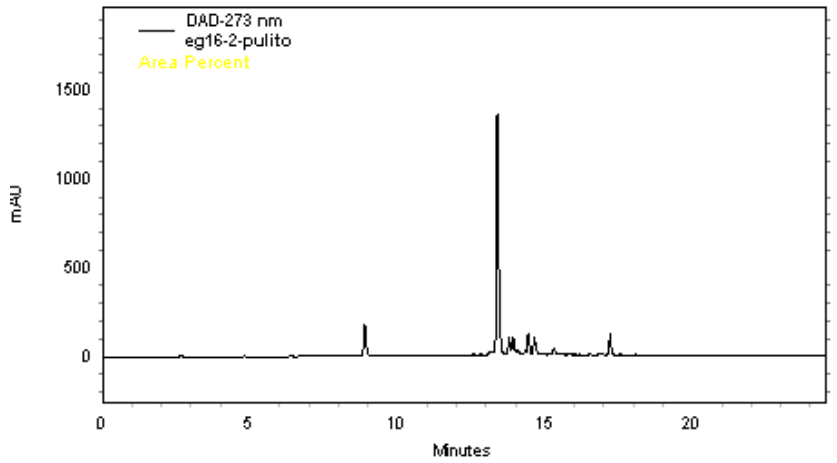
Minutes

Ig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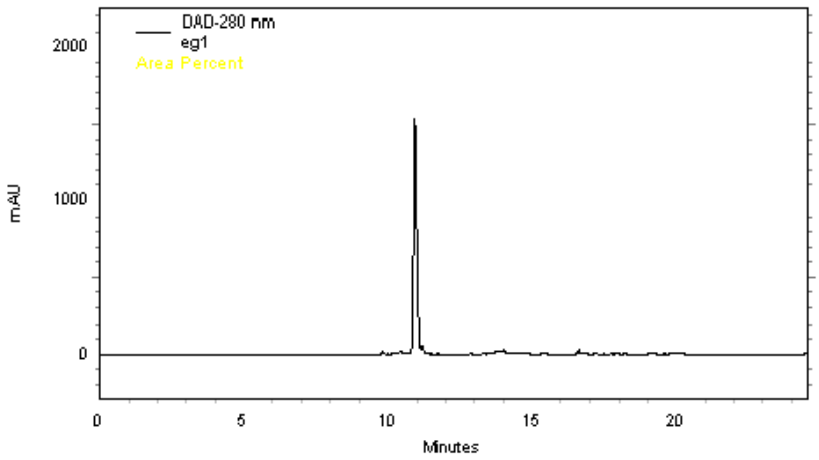
Minutes

IIa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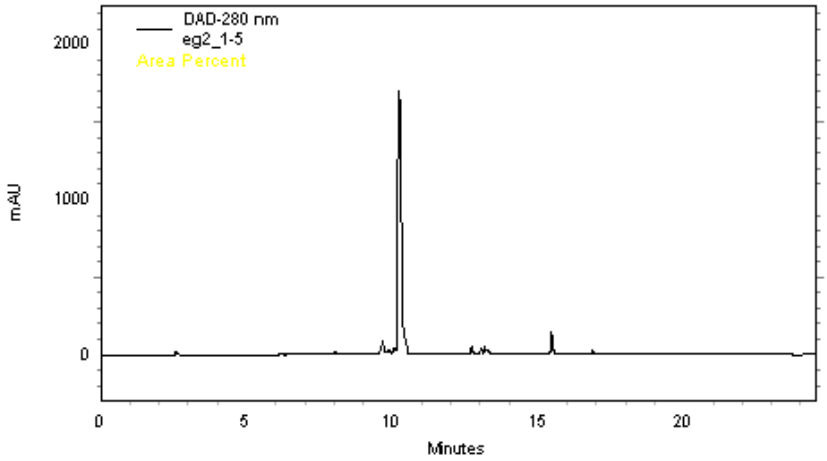
Minutes

IIb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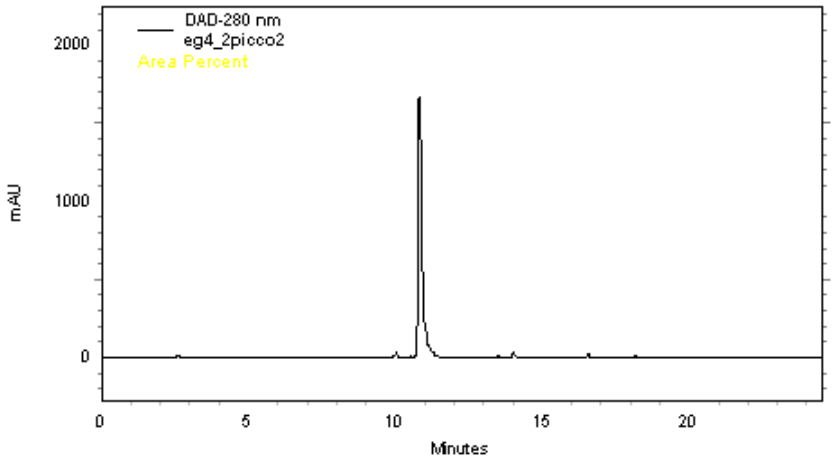
Minutes

IIc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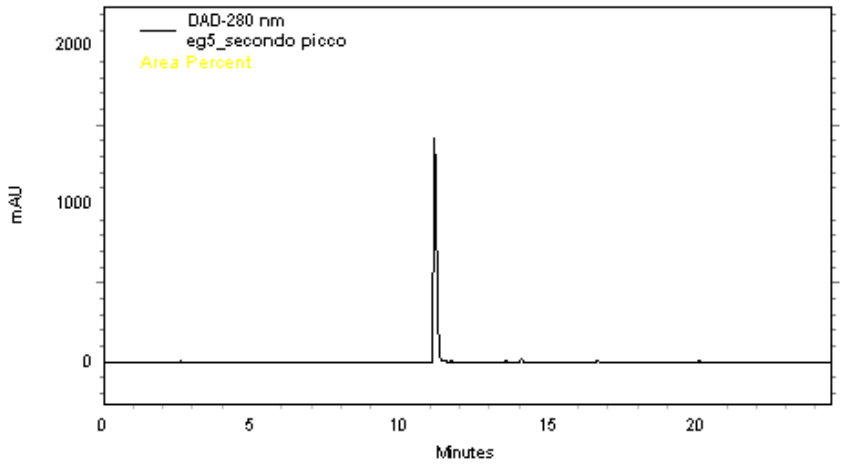
10
15
20
Minutes

IId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eg5_secondo picco
Area Percent
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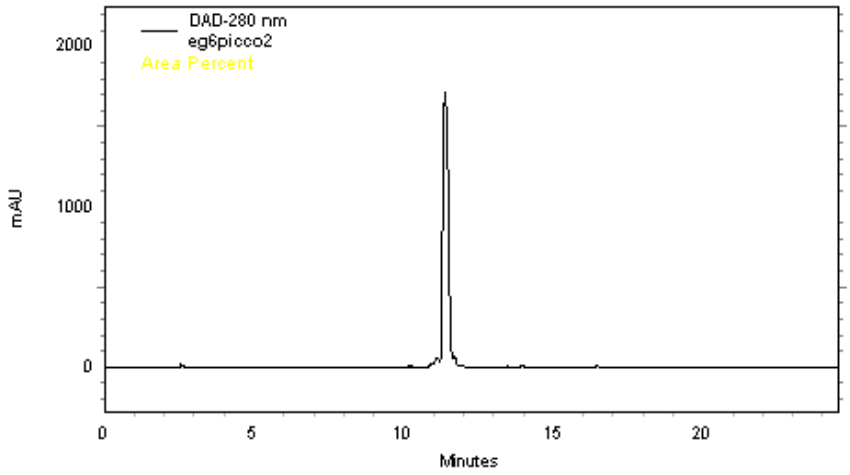
20
Minutes

IIe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Area Percent
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1000
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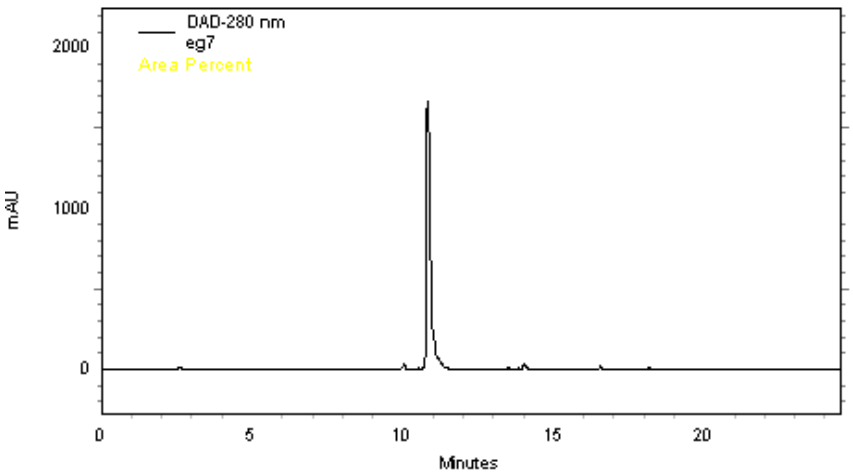
10
15
20
Minutes

IIf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Area Percent
mAU
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1000
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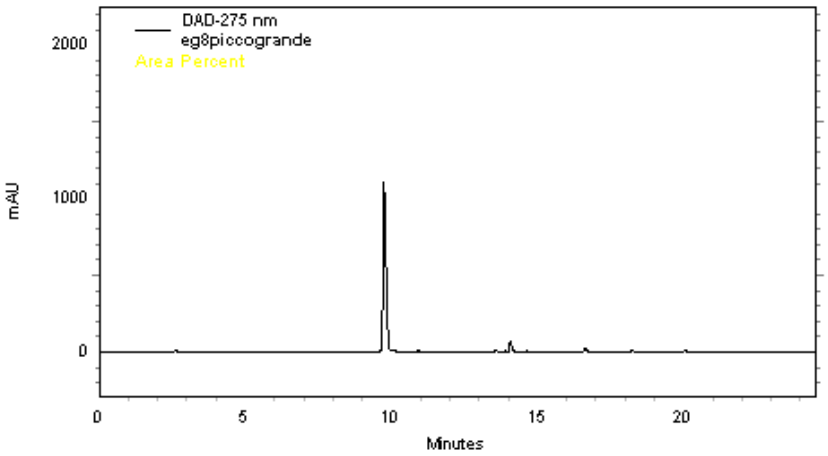
15
20
Minutes

IIg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1000
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mAU
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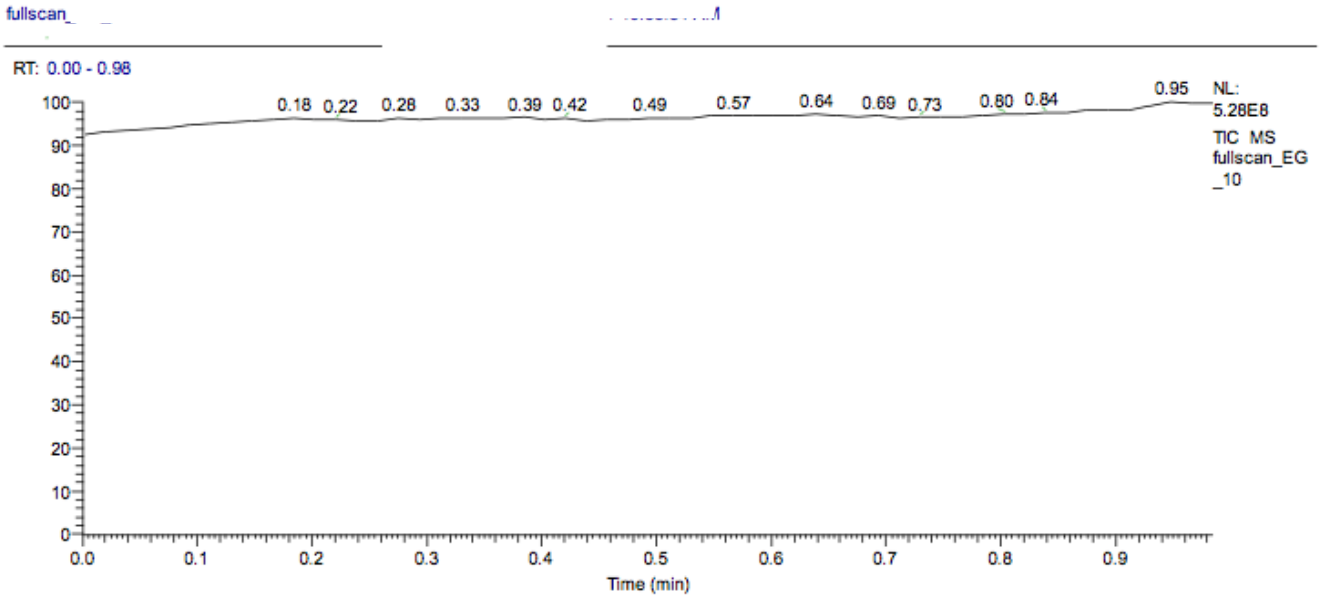
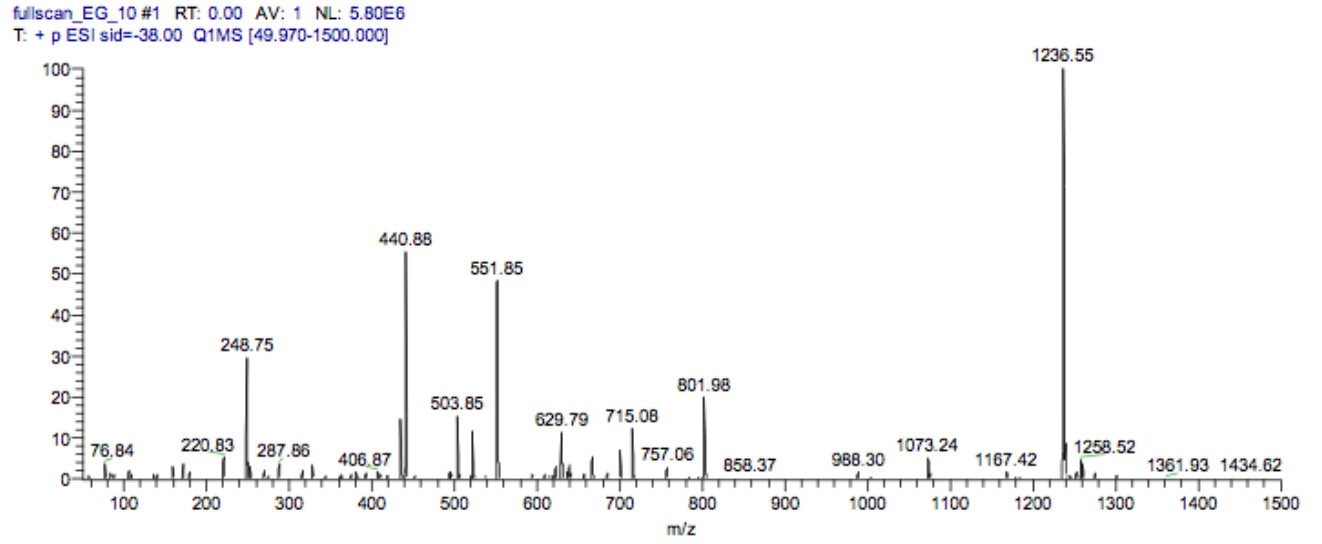
5
10
15
20
Minutes

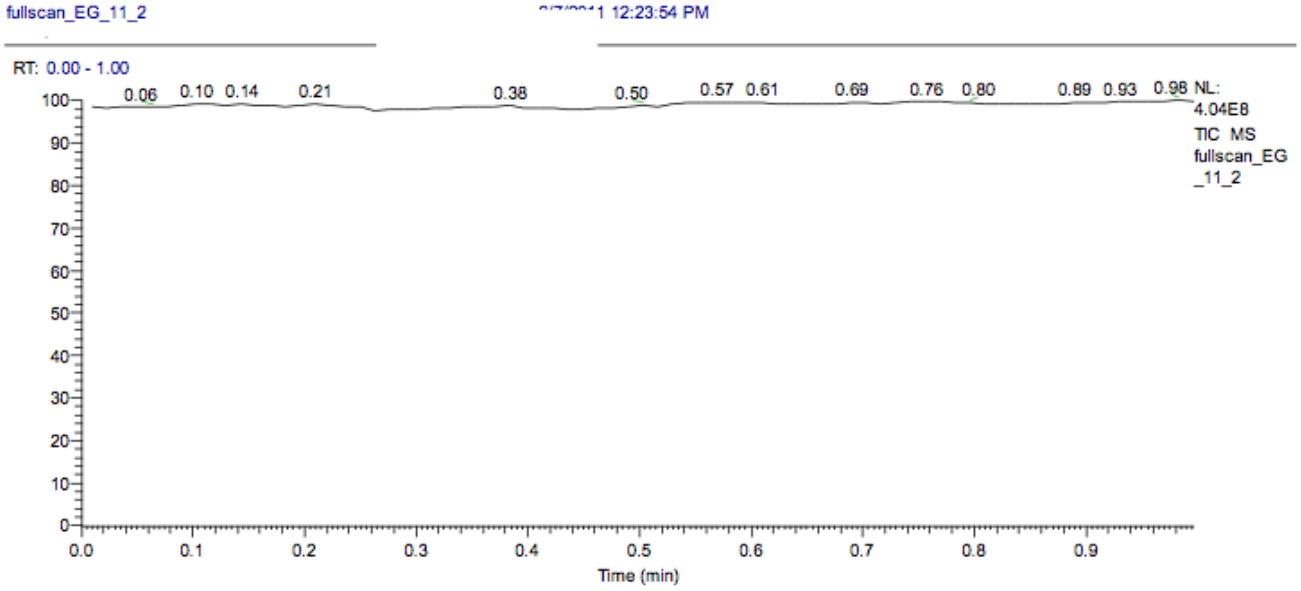
MS analysis

Ia





Ib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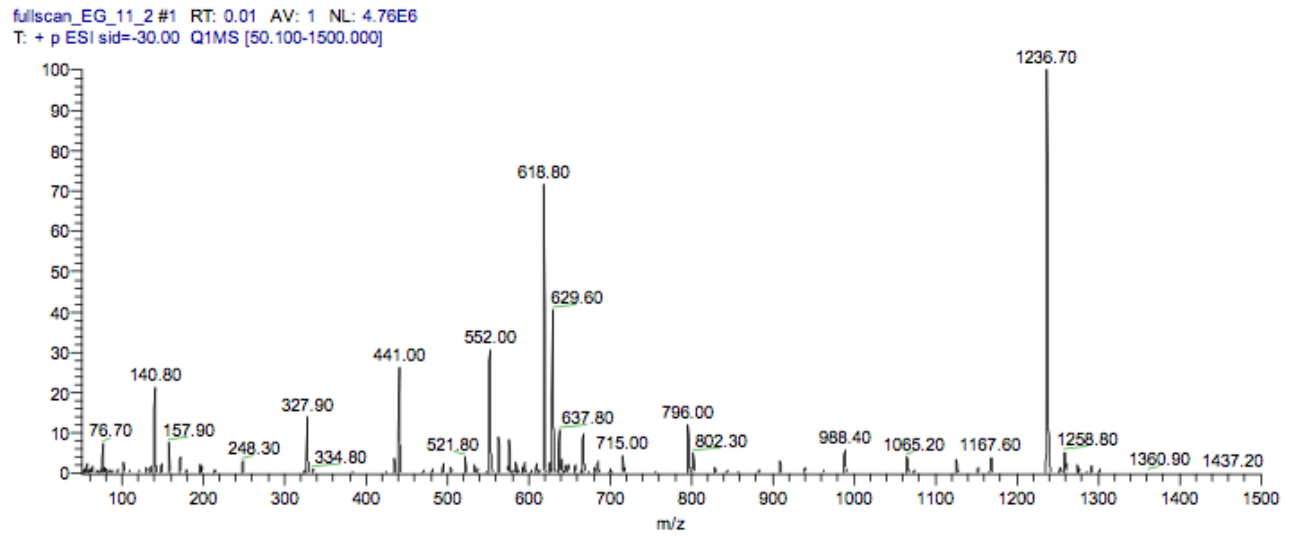
RT: 0.00 - 1.00
0.06 0.10 0.14 0.21 0.38 0.50 0.57 0.61 0.69 0.76 0.80 0.89 0.93 0.98
NL: 4.04E8
TIC MS fullscan_EG_11_2
Time (min)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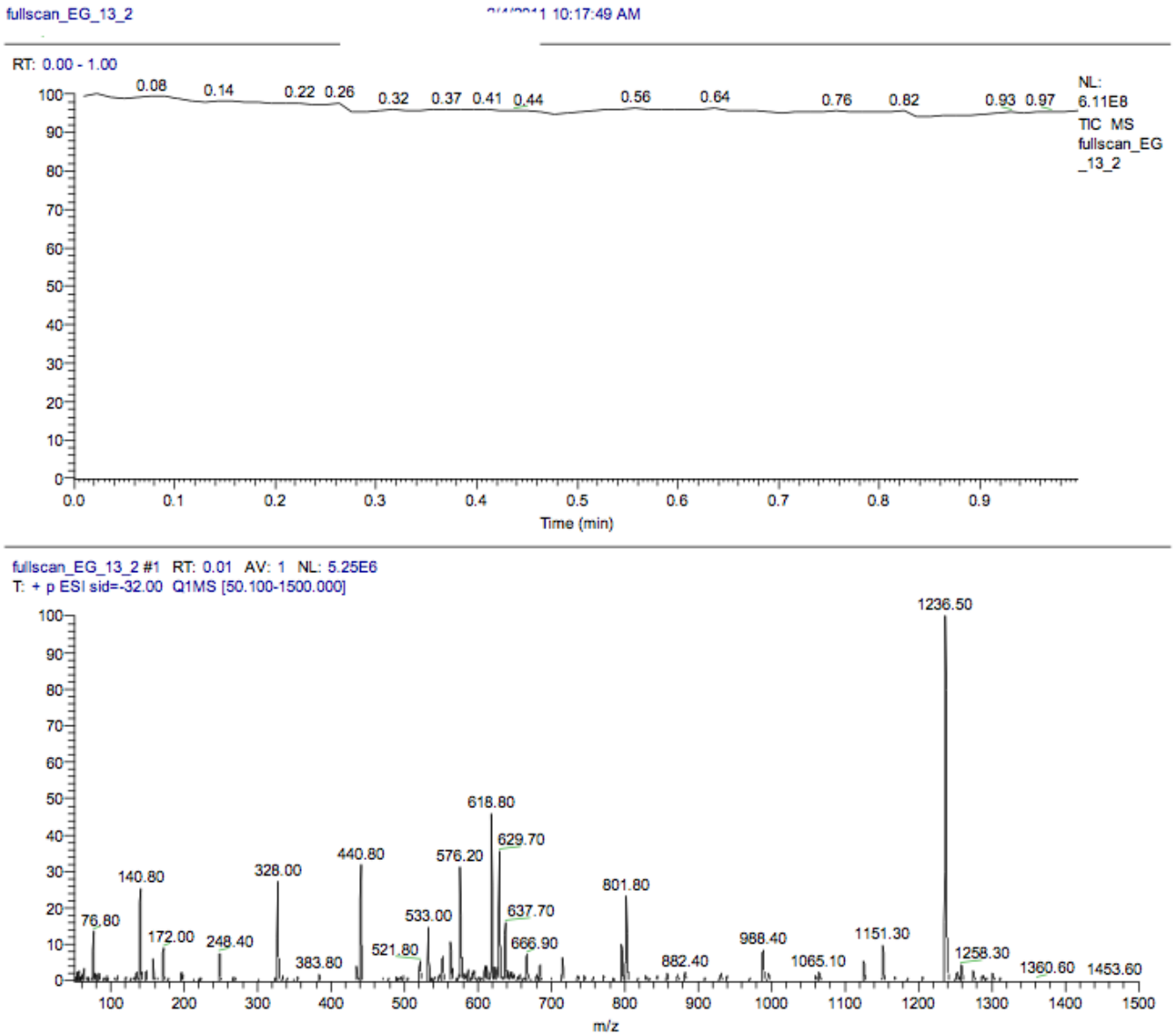
618.80
629.60
552.00
441.00
140.80
327.90
637.80
796.00
76.70
157.90
248.30
334.80
521.80
715.00
802.30
988.40
1065.20
1167.60
1258.80
1360.90
1437.20
m/z

Id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RT: 0.00 - 1.00
NL:
6.11E8
TIC MS
fullscan_EG
_13_2
Time (min)
fullscan_EG_13_2 #1 RT: 0.01 AV: 1 NL: 5.25E6
T: + p ESI sid=-32.00 Q1MS [50.100-1500.000]
m/z
1236.50
618.80
629.70
576.20
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533.00
666.90
76.80
172.00
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882.40
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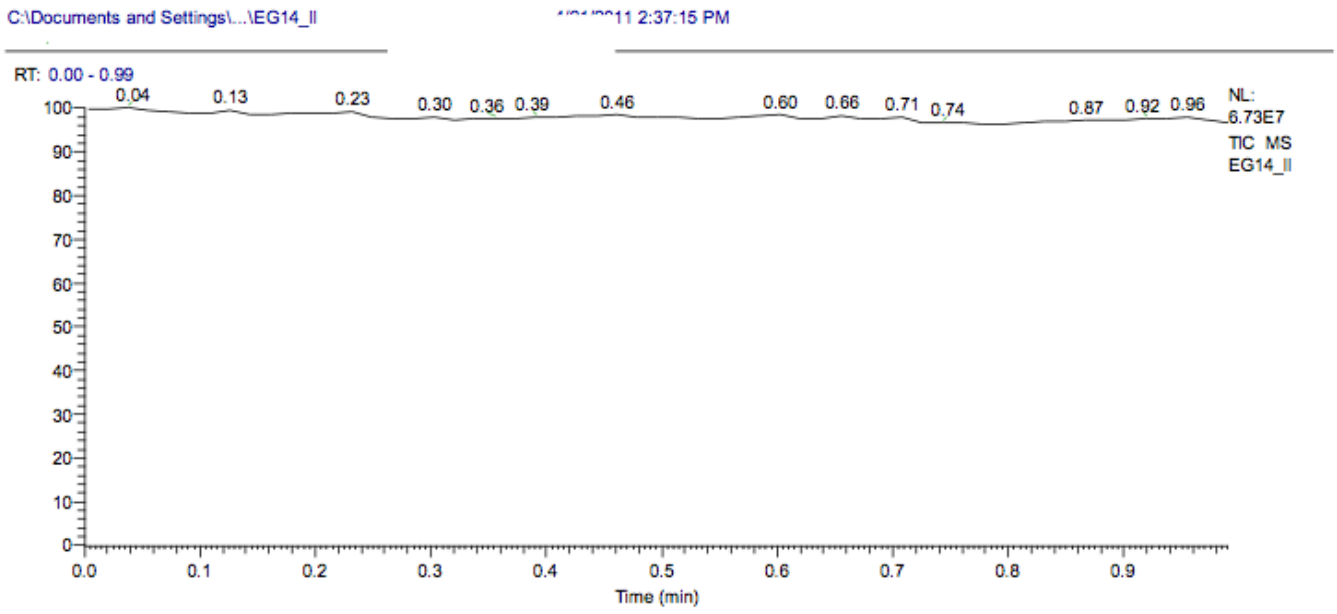
1258.30
1360.60
1453.60

Ie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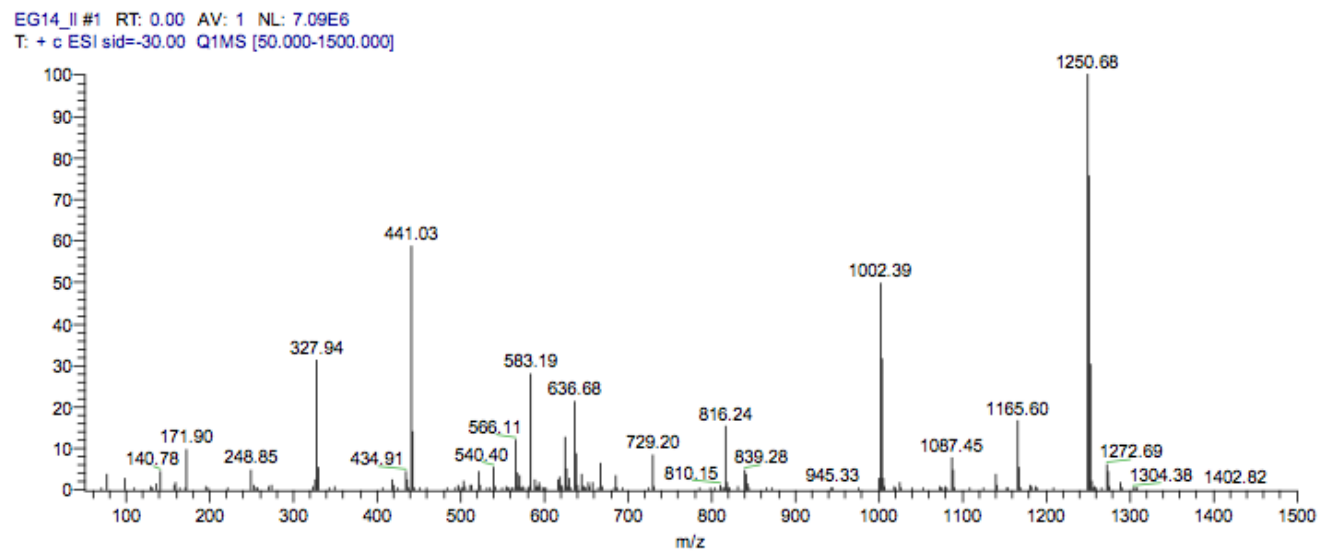
RT: 0.00 - 0.99
0.04
0.13
0.23
0.30
0.36
0.39
0.46
0.60
0.66
0.71
0.74
0.87
0.92
0.96
NL:
6.73E7
TIC MS
EG14_II
Time (min)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441.03
1002.39
327.94
583.19
636.68
816.24
1165.60
171.90
566.11
729.20
1087.45
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540.40
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810.15
945.33
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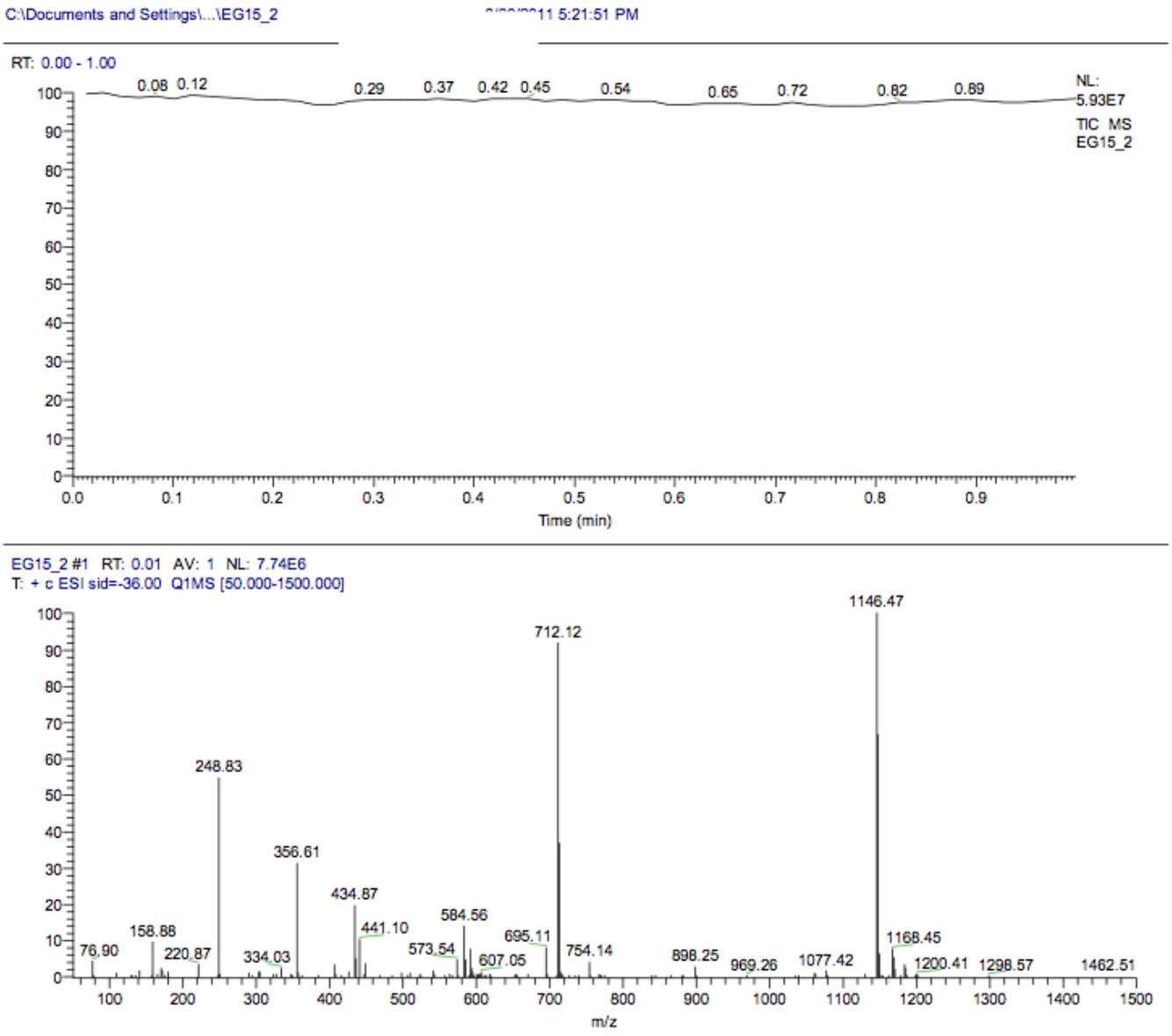
1402.82
m/z

If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TIC MS
EG15_2
Time (min)
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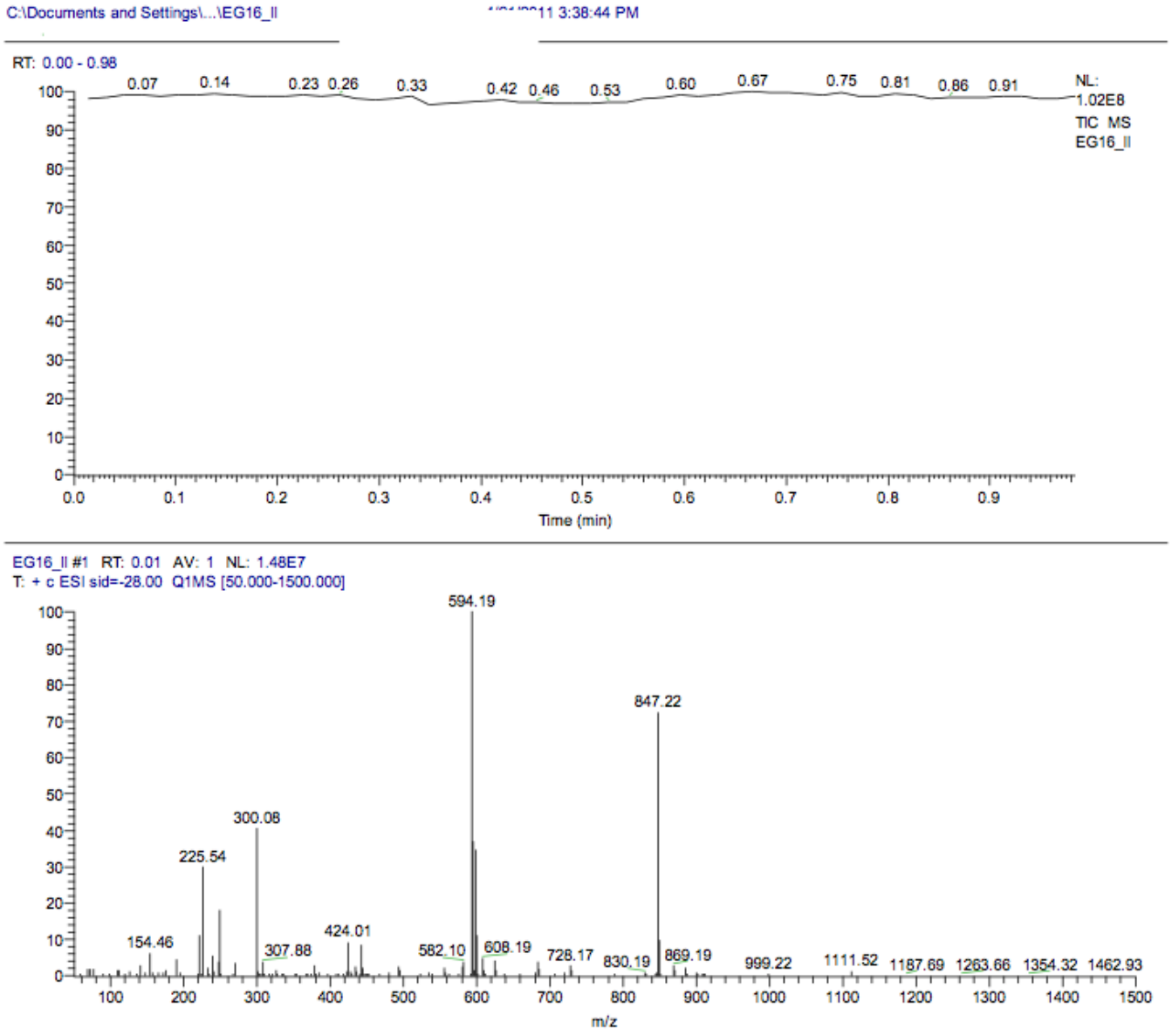
1146.47
712.12
248.83
356.61
434.87
584.56
441.10
695.11
158.88
76.90
220.87
334.03
573.54
607.05
754.14
898.25
969.26
1077.42
1168.45
1200.41
1298.57
1462.51
m/z

Ig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11 3:38:44 PM
RT: 0.00 - 0.98
NL:
1.02E8
TIC MS
EG16_II
Time (min)
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T: + c ESI sid=-28.00 Q1MS [50.000-1500.000]
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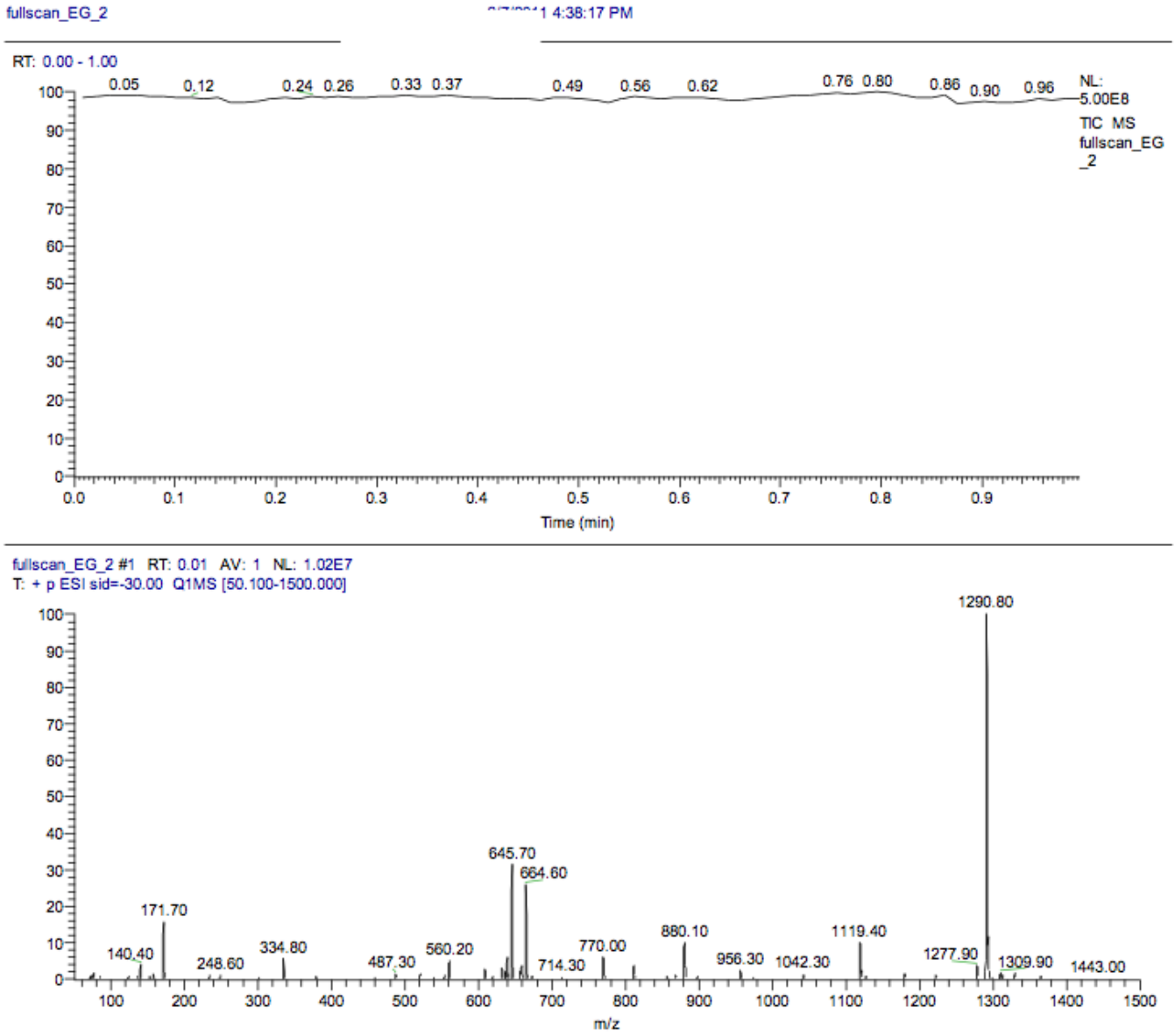
847.22
300.08
225.54
154.46
307.88
424.01
582.10
608.19
728.17
830.19
869.19
999.22
1111.52
1187.69
1263.66
1354.32
1462.93
m/z

IIa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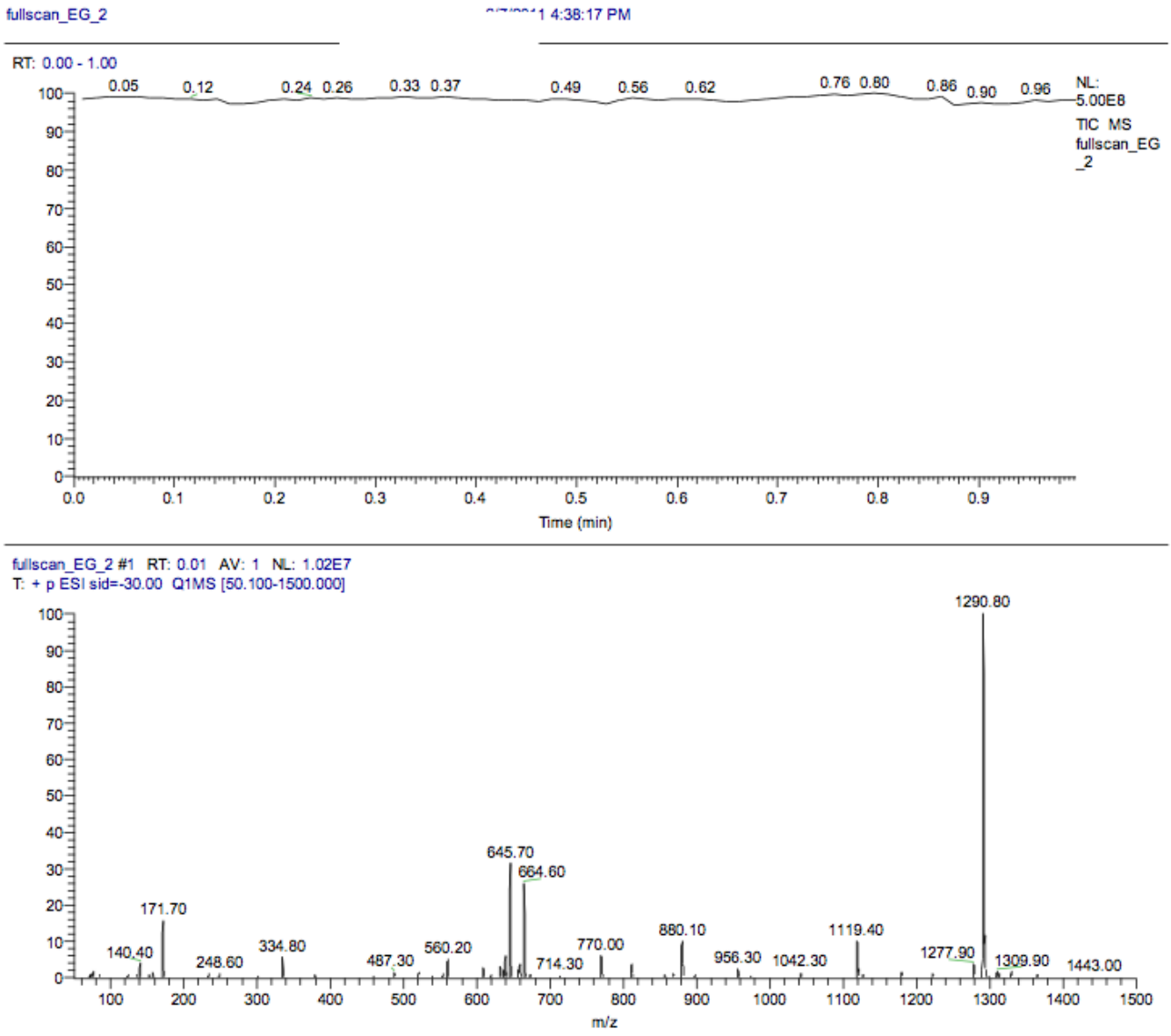
1 4:38:17 PM
RT: 0.00 - 1.00
NL:
5.00E8
TIC MS
fullscan_EG
_2
Time (min)
fullscan_EG_2 #1 RT: 0.01 AV: 1 NL: 1.02E7
T: + p ESI sid=-30.00 Q1MS [50.100-1500.000]
m/z
1290.80
645.70
664.60
171.70
140.40
248.60
334.80
487.30
560.20
714.30
770.00
880.10
956.30
1042.30
1119.40
1277.90
1309.90
1443.00

IIb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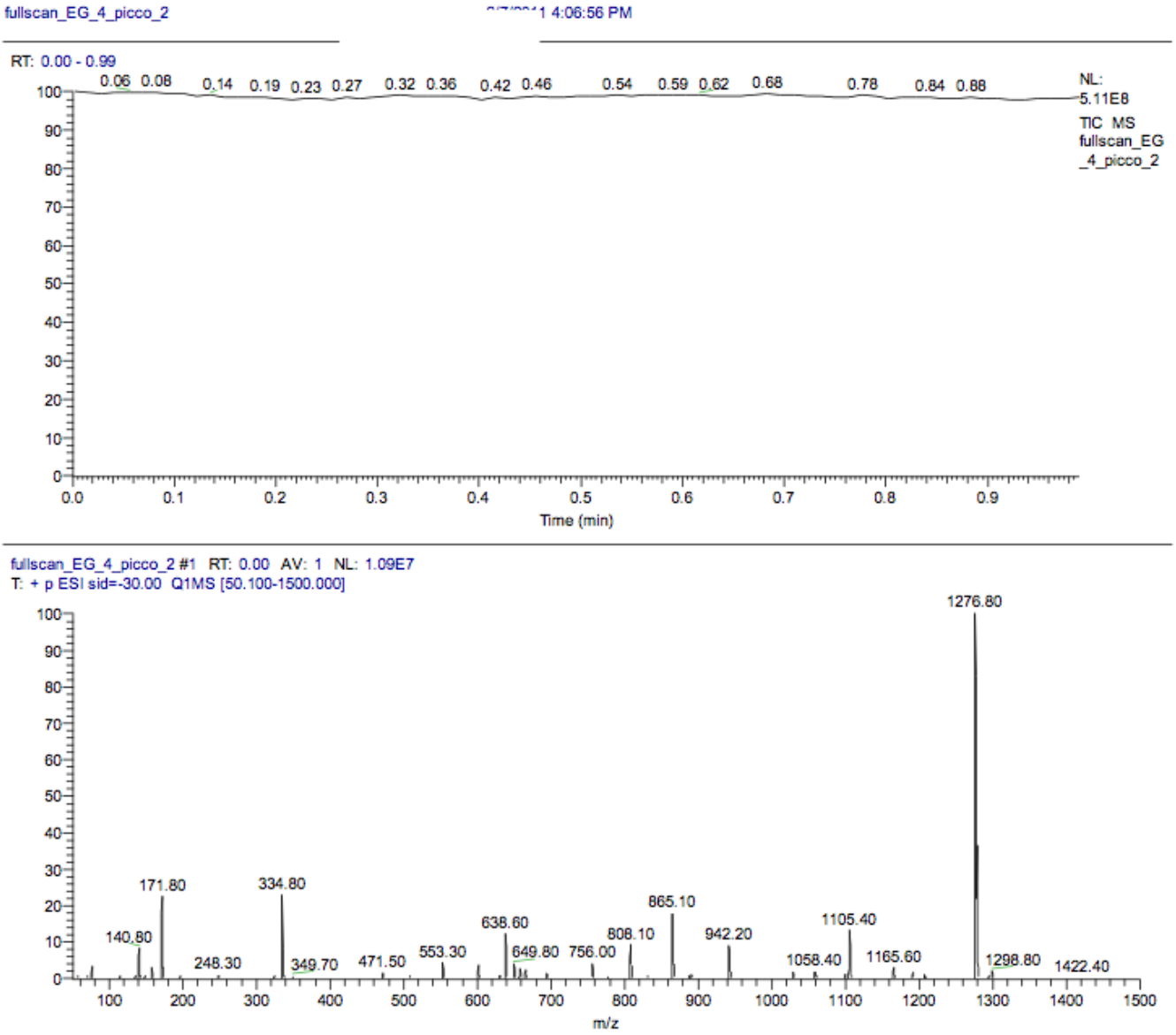
NL:
5.00E8
TIC MS
fullscan_EG
_2
Time (min)
fullscan_EG_2 #1 RT: 0.01 AV: 1 NL: 1.02E7
T: + p ESI sid=-30.00 Q1MS [50.100-1500.000]
m/z
1290.80
645.70
664.60
171.70
140.40
248.60
334.80
487.30
560.20
714.30
770.00
880.10
956.30
1042.30
1119.40
1277.90
1309.90
1443.00

IIc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RT: 0.00 - 0.99
NL:
5.11E8
TIC MS
fullscan_EG
_4_picco_2
Time (min)
fullscan_EG_4_picco_2 #1 RT: 0.00 AV: 1 NL: 1.09E7
T: + p ESI sid=-30.00 Q1MS [50.100-1500.000]
m/z
1276.80
865.10
638.60
1105.40
334.80
171.80
140.80
248.30
349.70
471.50
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756.00
808.10
942.20
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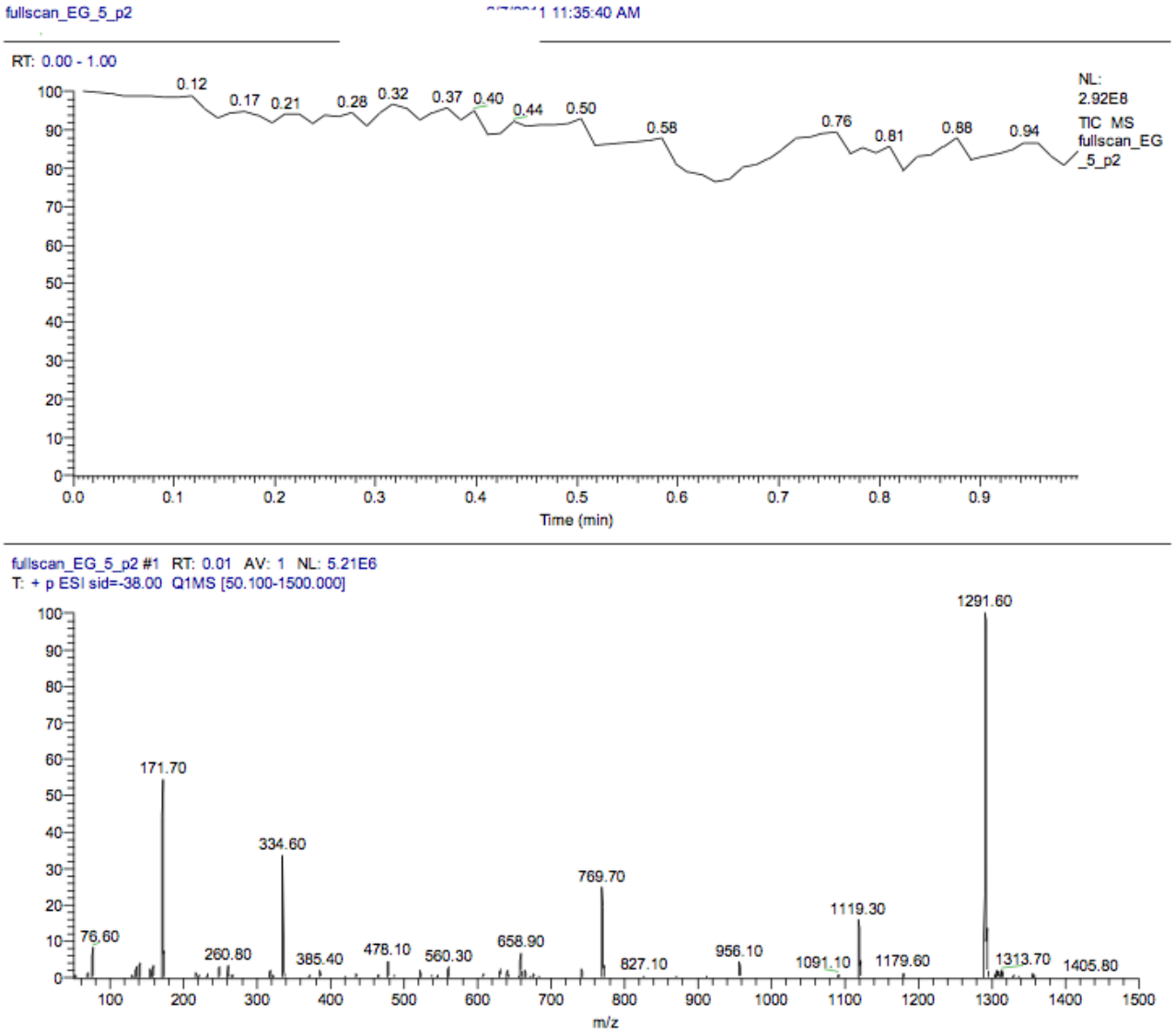
1422.40

IId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fullscan_EG
_5_p2
Time (min)
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m/z
1291.60
171.70
334.60
769.70
1119.30
76.60
260.80
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478.10
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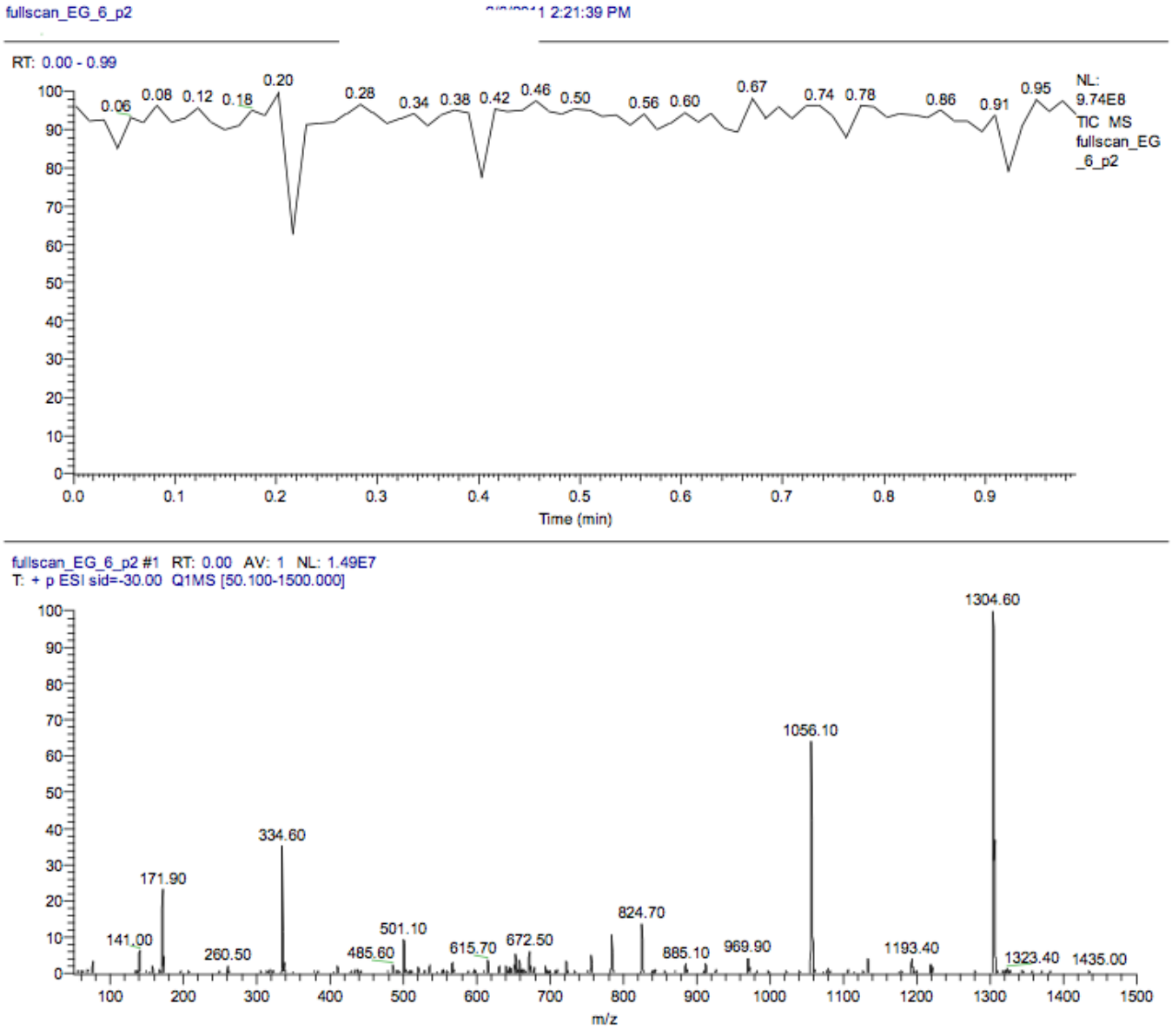
658.90
827.10
956.10
1091.10
1179.60
1313.70
1405.80

IIe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NL:
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_6_p2
Time (min)
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T: + p ESI sid=-30.00 Q1MS [50.100-1500.000]
m/z
1304.60
1056.10
334.60
171.90
824.70
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969.90
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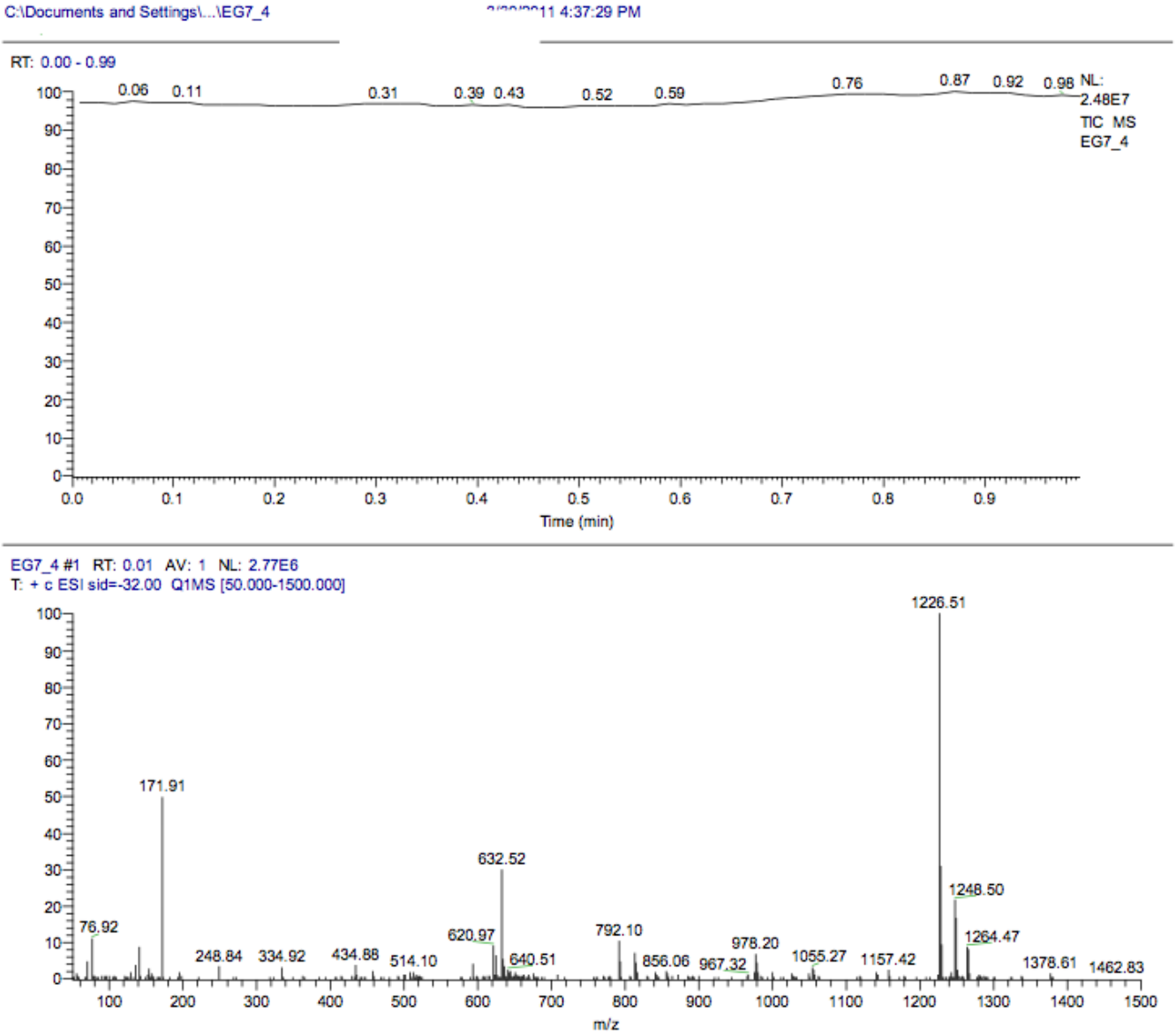
1435.00

IIf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0.11
0.31
0.39
0.43
0.52
0.59
0.76
0.87
0.92
0.98
NL:
2.48E7
TIC MS
EG7_4
Time (min)
EG7_4 #1 RT: 0.01 AV: 1 NL: 2.77E6
T: + c ESI sid=-32.00 Q1MS [50.000-1500.000]
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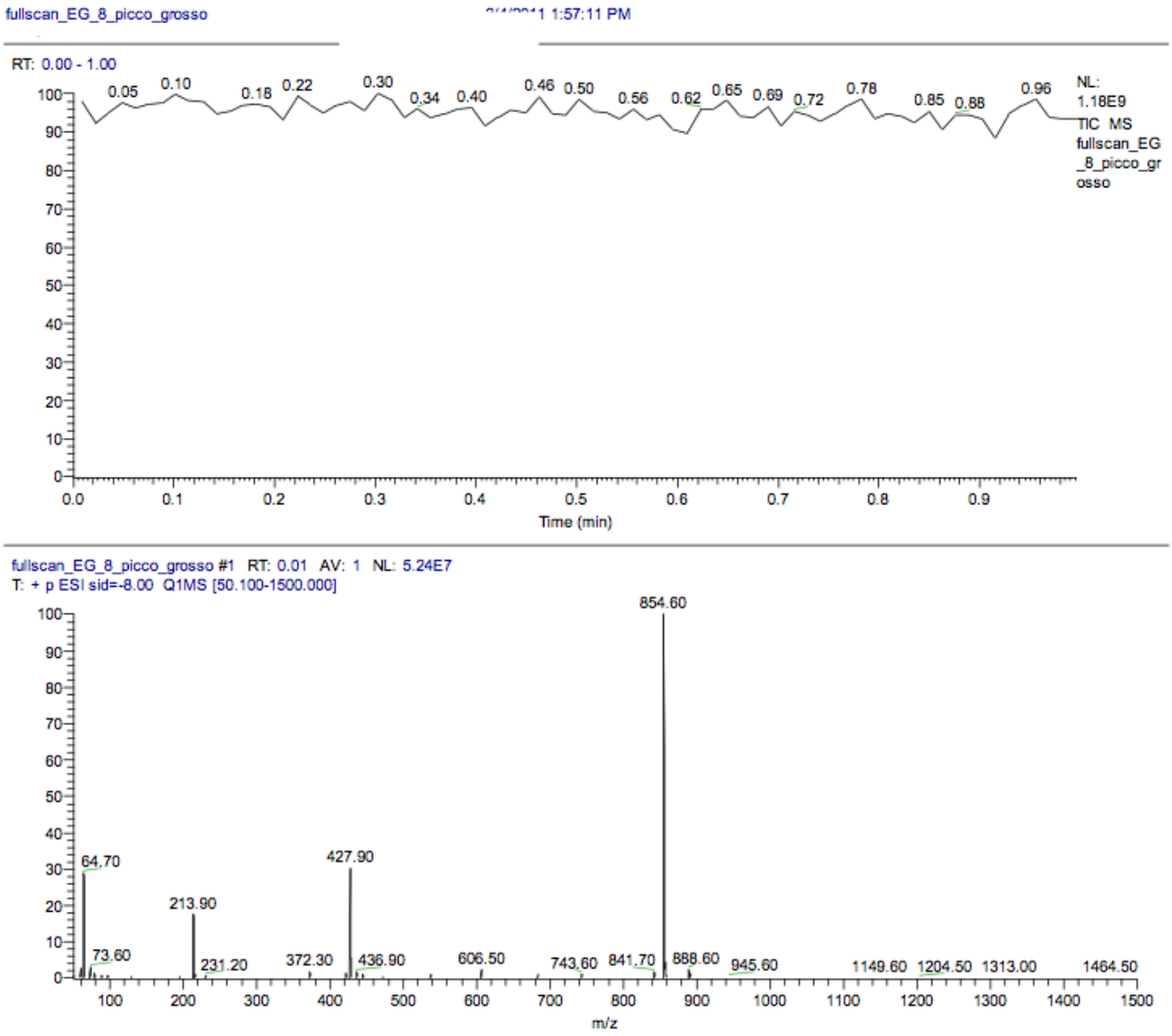
171.91
632.52
1248.50
76.92
620.97
792.10
978.20
1264.47
248.84
334.92
434.88
514.10
640.51
856.06
967.32
1055.27
1157.42
1378.61
1462.83
m/z

IIg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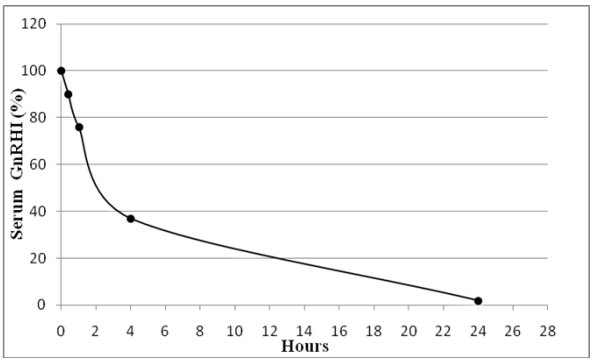
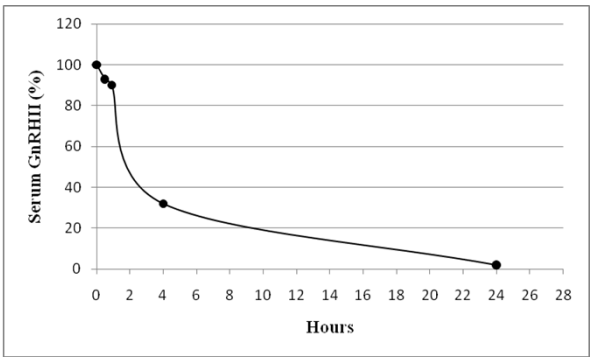
1:57:11 PM
RT: 0.00 - 1.00
NL:
1.18E9
TIC MS
fullscan_EG
_8_picco_gr
osso
Time (min)
fullscan_EG_8_picco_grosso #1 RT: 0.01 AV: 1 NL: 5.24E7
T: + p ESI sid=-8.00 Q1MS [50.100-1500.000]
854.60
64.70
427.90
213.90
73.60
231.20
372.30
436.90
606.50
743.60
841.70
888.60
945.60
1149.60
1204.50
1313.00
1464.50
m/z

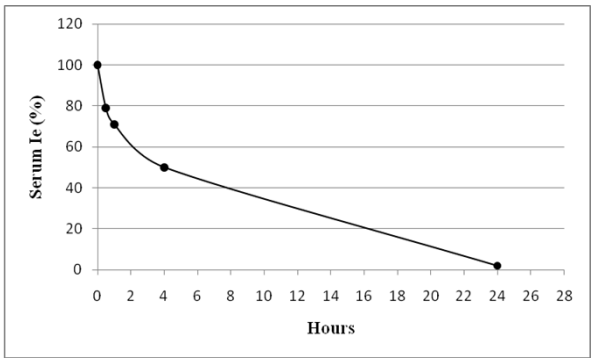
Model equation: Y=(Y0 - Plateau)*exp(-K*X) + Plateau

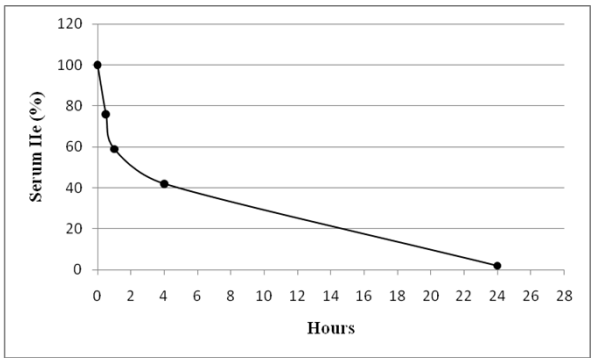
	GnRHI	GnRHII	Ie	IIe
One phase decay				
Best-fit values				
Y0	99.81	105.2	91.38	89.56
PLATEAU	2.026	0.7945	1.224	3.553
K	0.2636	0.2706	0.1751	0.2553
Half Life	2.630	2.562	3.959	2.715
Tau	3.794	3.696	5.712	3.918
Span	97.78	104.4	90.16	86.01
Std. Error				
Y0	2.155	5.432	6.616	9.957
PLATEAU	2.876	7.195	10.38	13.41
K	0.02557	0.06155	0.06813	0.1312
Span	3.429	8.594	11.50	15.95
95% Confidence Intervals				
Y0	90.53 to 109.1	81.84 to 128.6	62.91 to 119.9	46.72 to 132.4
PLATEAU	-10.35 to 14.40	-30.16 to 31.75	-43.44 to 45.88	-54.17 to 61.28
K	0.1536 to 0.3736	0.005720 to 0.5354	0.0 to 0.4682	0.0 to 0.8197
Half Life	1.855 to 4.514	1.295 to 121.2		
Tau	2.677 to 6.512	1.868 to 174.8		
Span	83.03 to 112.5	67.44 to 141.4	40.65 to 139.7	17.38 to 154.6
Goodness of Fit				
Degrees of Freedom	2	2	2	2
R^2	0.9976	0.9869	0.9700	0.9368
Absolute Sum of Squares	16.00	100.8	166.4	344.9
Sy.x	2.828	7.099	9.122	13.13
Constraints				
K	K > 0.0	K > 0.0	K > 0.0	K > 0.0
Number of points				
Analyzed	5	5	5	5

Metabolic stability of GnRHI-II and their derivatives **Ie** and **IIe**



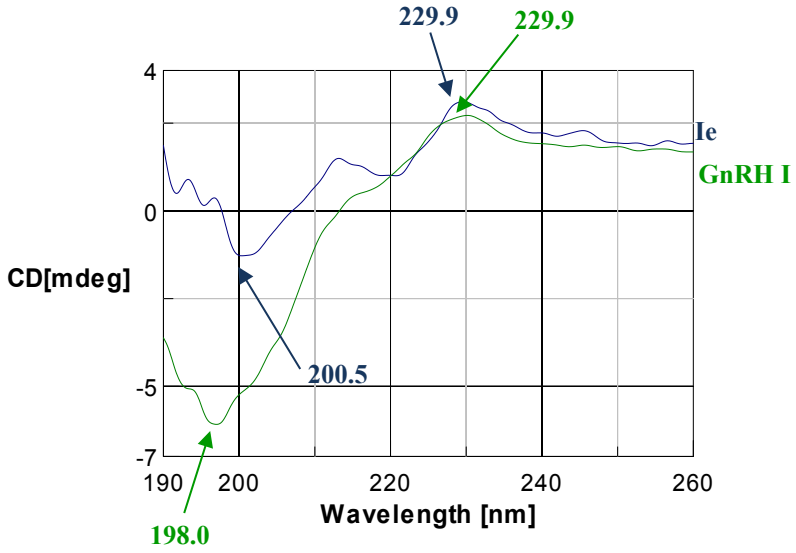




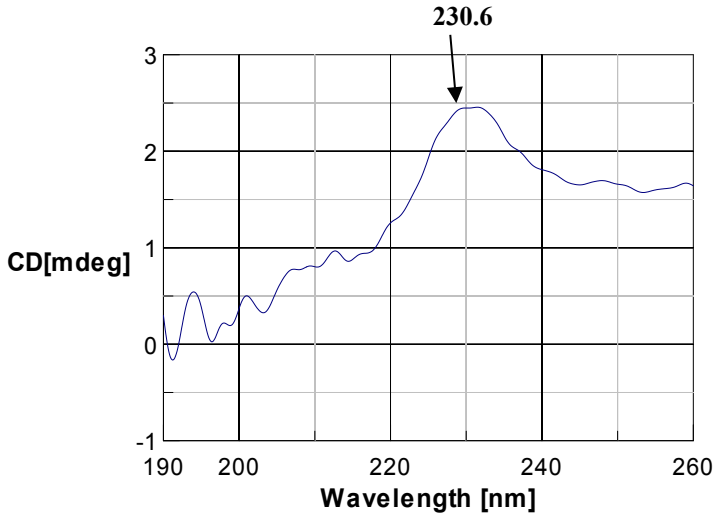


CD Spectra

Overlay **GnRH I-Ie**



IIe



Circular Dichroism: Milli-Q H_2O was used to prepare phosphate buffer at pH 7 with $Na_2HPO_4 \cdot 2H_2O$ and NaH_2PO_4. Firstly, the samples were dissolved in 200 µL of milli-Q H_2O (solution A). 10 µL of solution A were diluited in 2 mL of phosphate buffer (solution B) and then 500 µL (for **Ie**) and 300 µL (for **IIe**) of solution B were diluited in 2 mL of phosphate buffer giving the stock solutions. Aliquots of these stock solutions were taken to prepare the cuvette samples for spectrophotometric analyses. The CD spectra of the solutions were recorded with a Jasco J-710 spectropolarimeter from 190 to 260 nm in a 1 cm quartz cuvette through 10 accumulations.