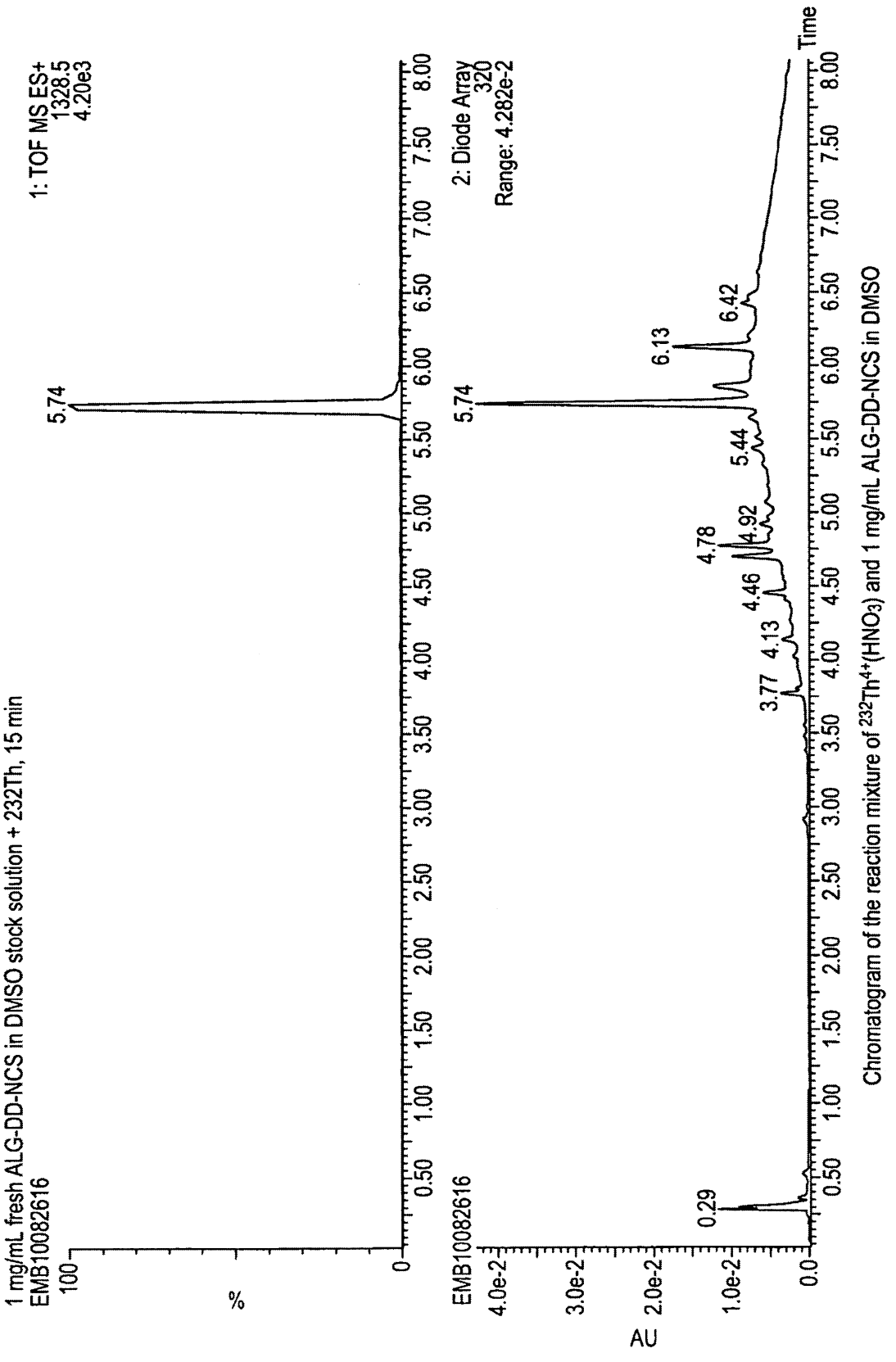
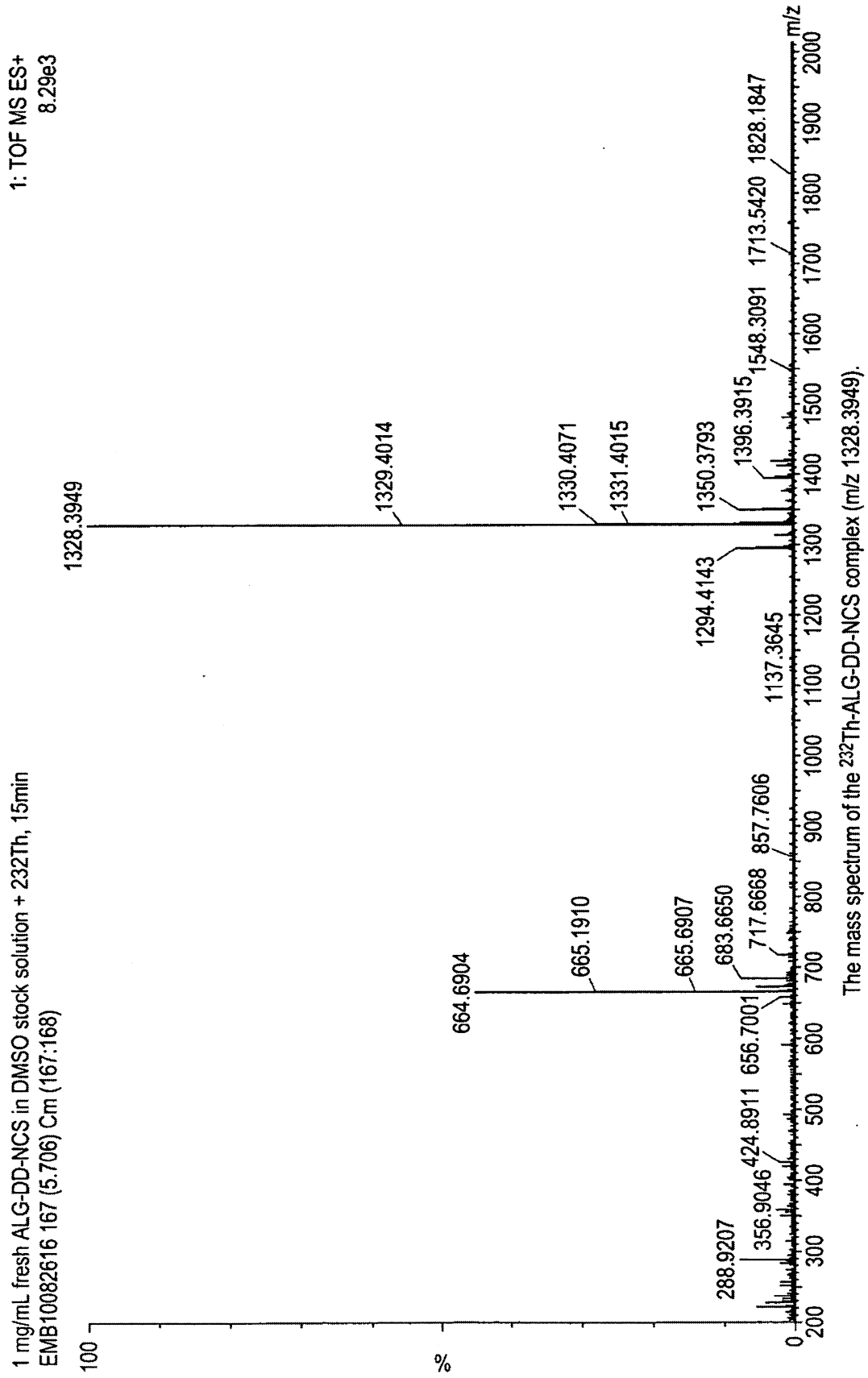

1 mg/mL fresh ALG-DD-NCS in DMSO stock solution + 232Th, 15 min
EMB10082616
1: TOF MS ES+
1328.5
4.20e3
100
%
0
5.74
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
EMB10082616
2: Diode Array
320
Range: 4.282e-2
4.0e-2
3.0e-2
2.0e-2
1.0e-2
0.0
AU
0.29
3.77
4.13
4.46
4.78
4.92
5.44
5.74
6.13
6.42
Time
Chromatogram of the reaction mixture of $^{232}Th^{4+}(HNO_3)$ and 1 mg/mL ALG-DD-NCS in DMSO

FIG. 1



The mass spectrum of the ^{232}Th-ALG-DD-NCS complex (m/z 1328.3949).

FIG. 2

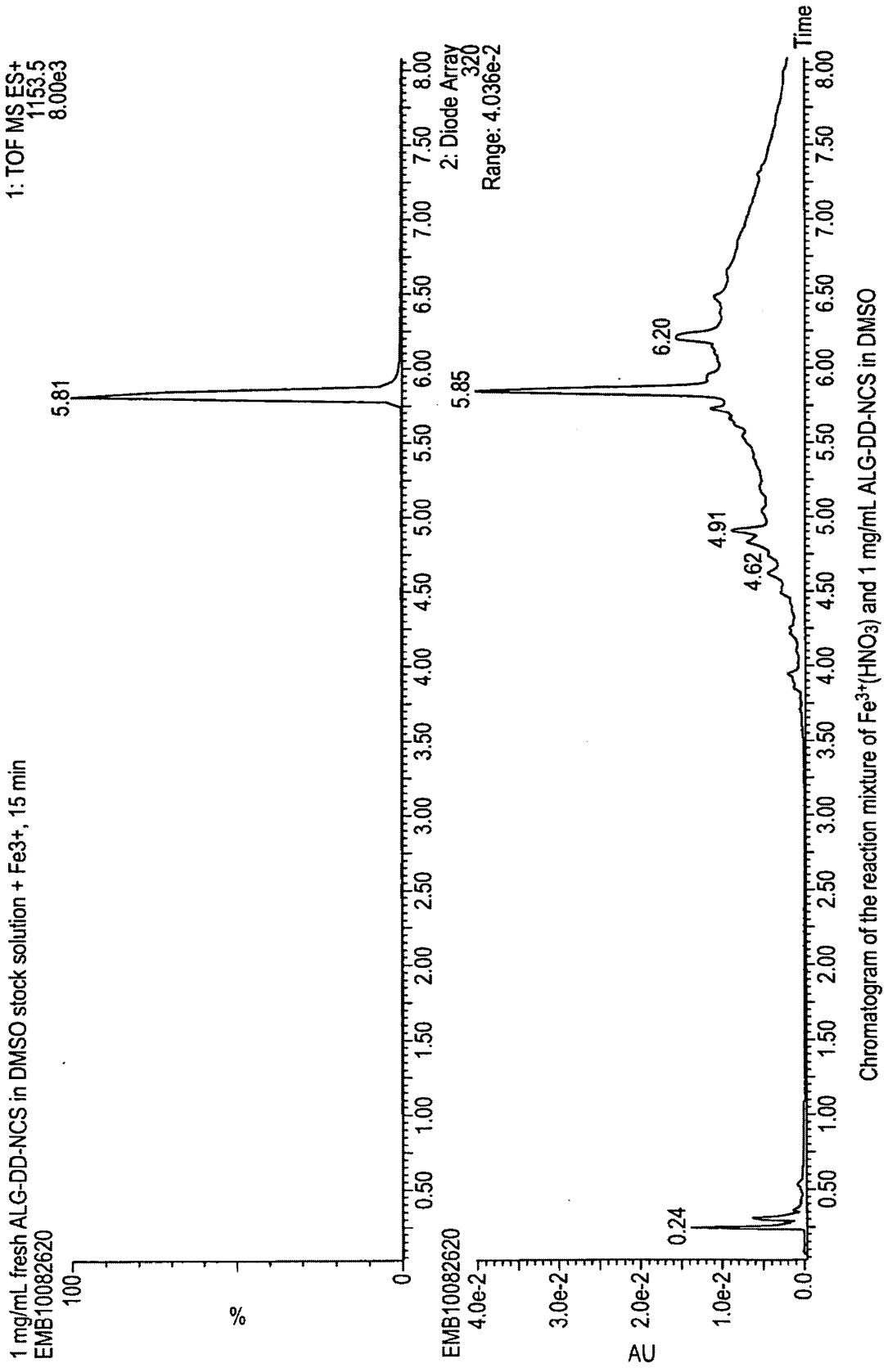

1 mg/mL fresh ALG-DD-NCS in DMSO stock solution + Fe3+, 15 min
EMB10082620
1: TOF MS ES+
1153.5
8.00e3
100
%
0
5.81
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
EMB10082620
2: Diode Array
320
Range: 4.036e-2
4.0e-2
3.0e-2
2.0e-2
1.0e-2
0.0
AU
5.85
6.20
4.91
4.62
0.24
Time
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
Chromatogram of the reaction mixture of $Fe^{3+}(HNO_3)$ and 1 mg/mL ALG-DD-NCS in DMSO

FIG. 3

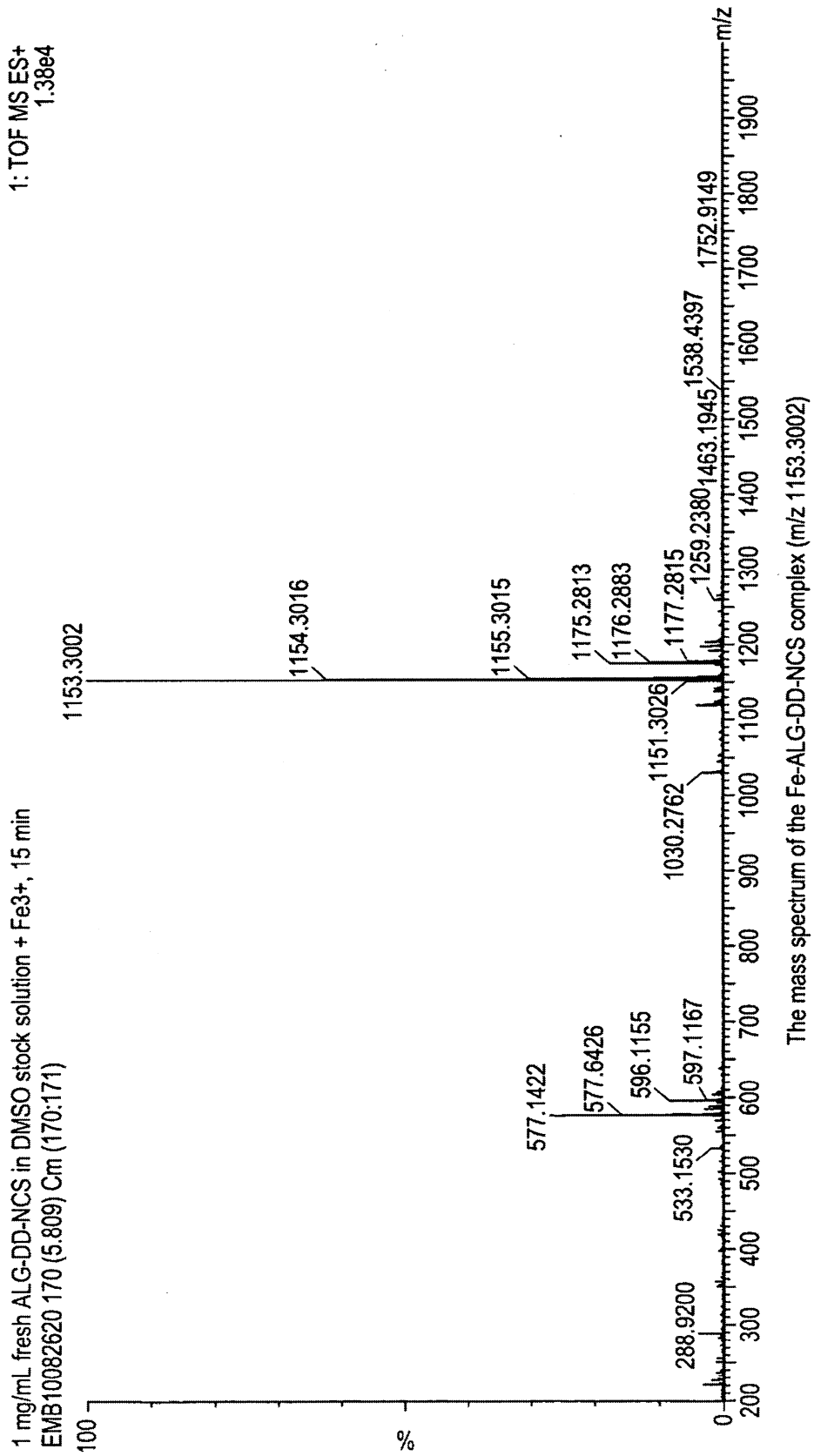

1: TOF MS ES+
1.38e4
1 mg/mL fresh ALG-DD-NCS in DMSO stock solution + Fe3+, 15 min
EMB10082620 170 (5.809) Cm (170:171)
100
%
0
288.9200
533.1530
577.1422
577.6426
596.1155
597.1167
1030.2762
1151.3026
1153.3002
1154.3016
1155.3015
1175.2813
1176.2883
1177.2815
1259.2380
1463.1945
1538.4397
1752.9149
200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900
m/z
The mass spectrum of the Fe-ALG-DD-NCS complex (m/z 1153.3002)

FIG. 4

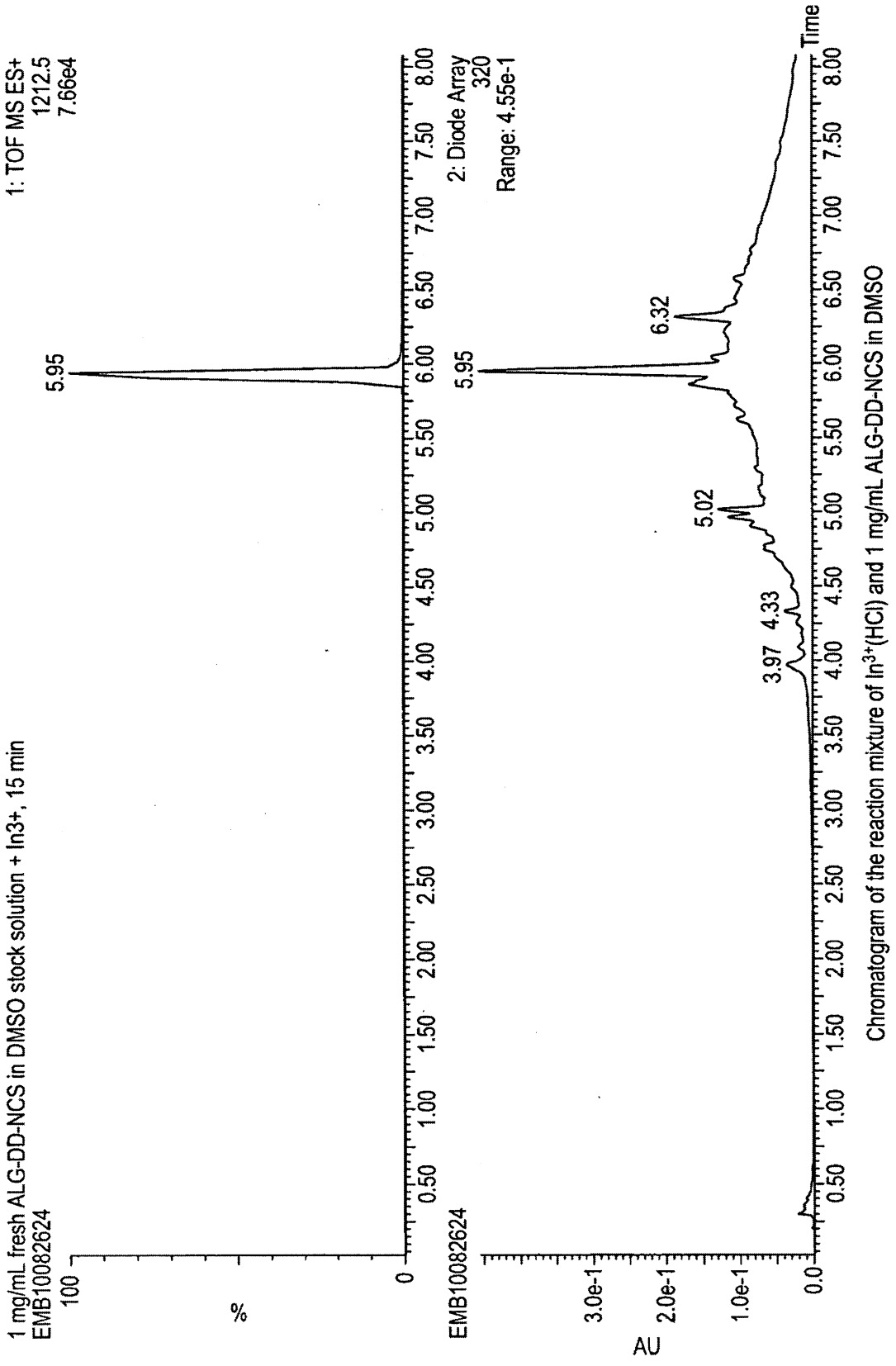

1 mg/mL fresh ALG-DD-NCS in DMSO stock solution + In3+, 15 min
EMB10082624
1: TOF MS ES+
1212.5
7.66e4
100
%
0
5.95
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
EMB10082624
2: Diode Array
320
Range: 4.55e-1
5.95
6.32
5.02
4.33
3.97
Time
AU
3.0e-1
2.0e-1
1.0e-1
0.0
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
Chromatogram of the reaction mixture of In3+(HCl) and 1 mg/mL ALG-DD-NCS in DMSO

FIG. 5

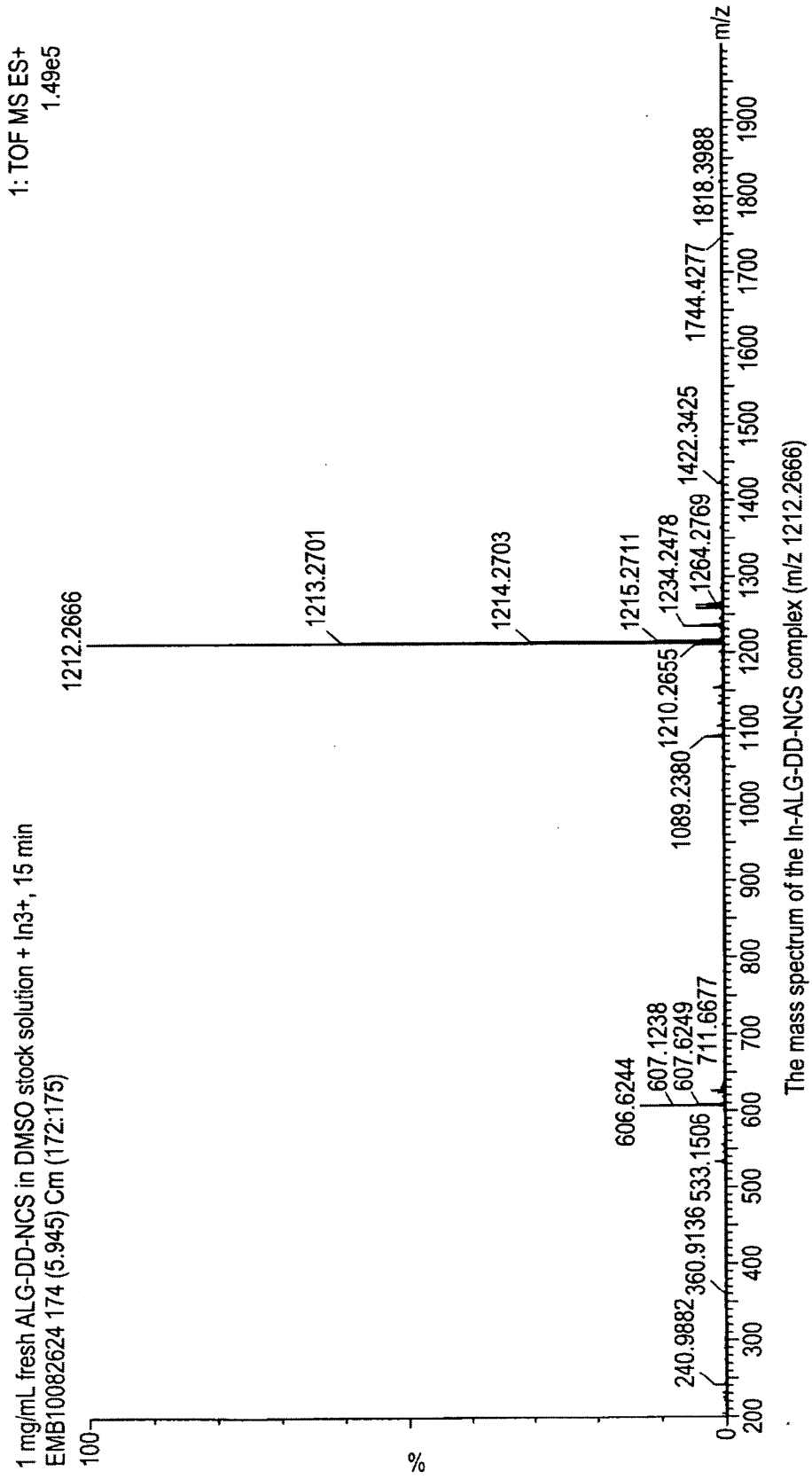
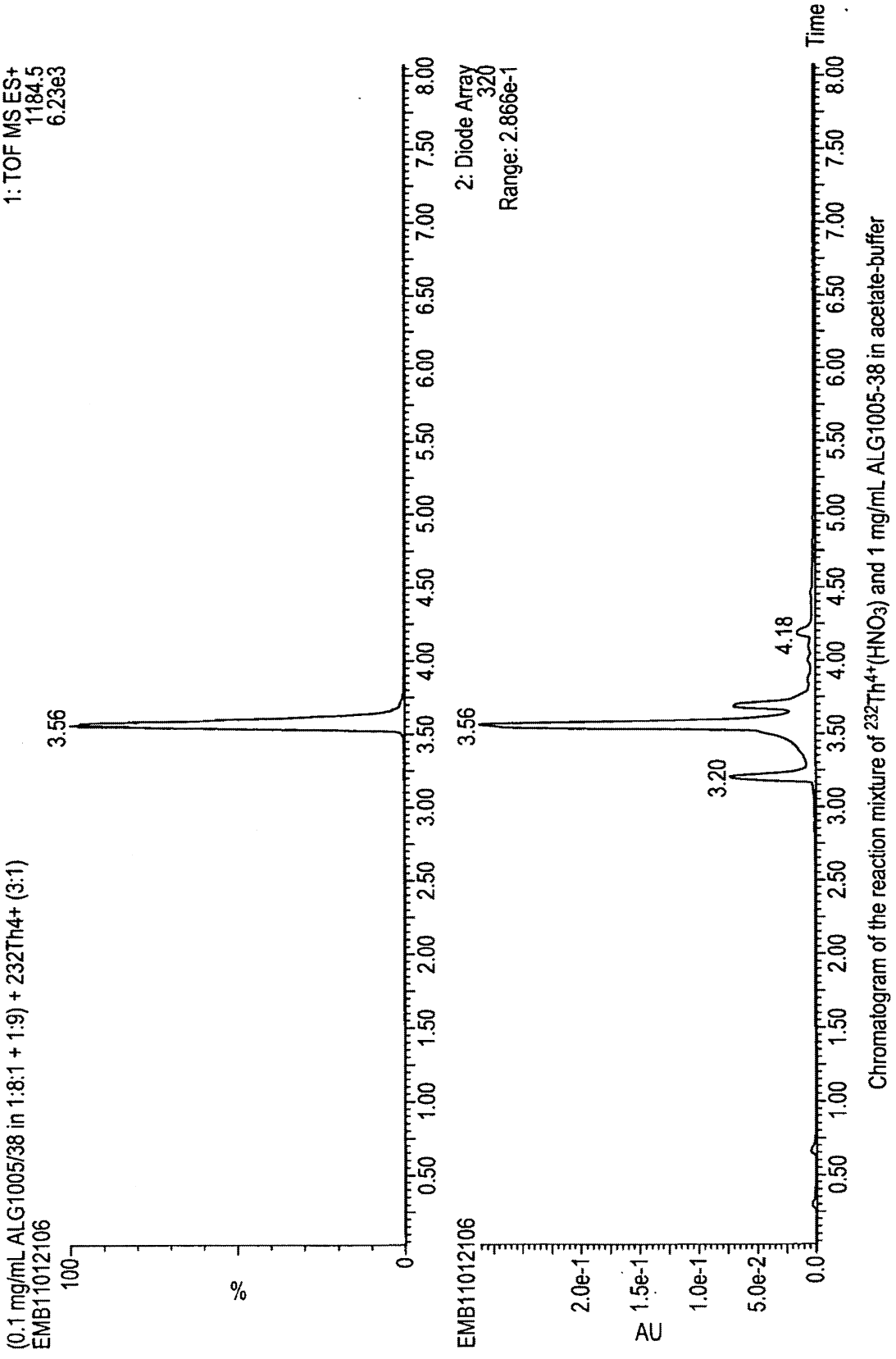

1: TOF MS ES+
1.49e5
1 mg/mL fresh ALG-DD-NCS in DMSO stock solution + In3+, 15 min
EMB10082624 174 (5.945) Cm (172:175)
100
%
0
1212.2666
1213.2701
1214.2703
1215.2711
1234.2478
1264.2769
1422.3425
1744.4277
1818.3988
1210.2655
1089.2380
606.6244
607.1238
607.6249
711.6677
240.9882
360.9136
533.1506
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
m/z
The mass spectrum of the In-ALG-DD-NCS complex (m/z 1212.2666)

FIG. 6



Chromatogram of the reaction mixture of $^{232}Th^{4+}(HNO_3)$ and 1 mg/mL ALG1005-38 in acetate-buffer

FIG. 7

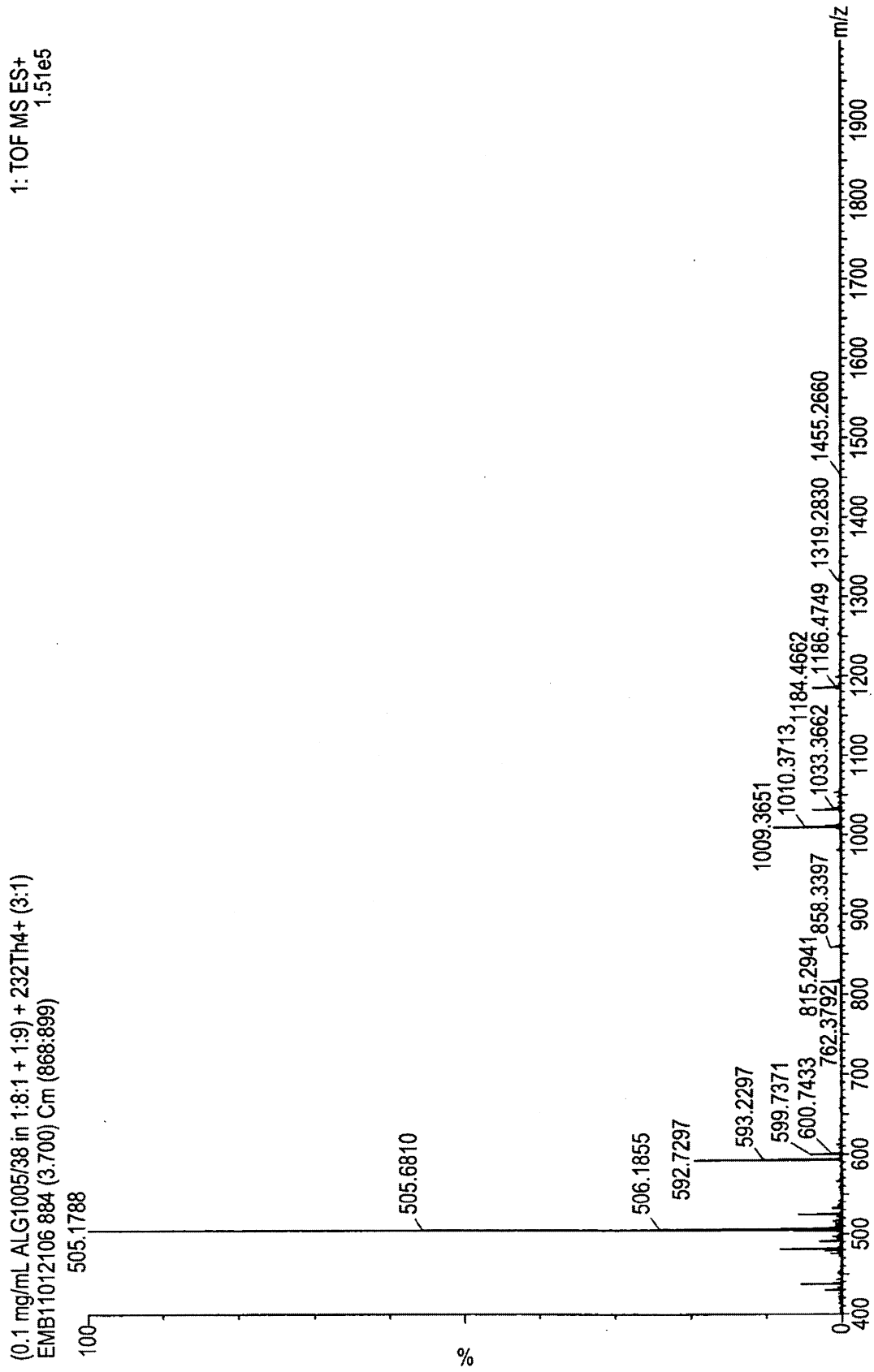

1: TOF MS ES+
1.51e5
(0.1 mg/mL ALG1005/38 in 1:8:1 + 1:9) + 232Th4+ (3:1)
EMB11012106 884 (3.700) Cm (868:899)
505.1788
505.6810
506.1855
592.7297
593.2297
599.7371
600.7433
762.3792
815.2941
858.3397
1009.3651
1010.3713
1033.3662
1184.4662
1186.4749
1319.2830
1455.2660
100
%
0
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
m/z
The mass spectrum of the 232Th-ALG1005-38 complex (m/z 1184.4662)

FIG. 8

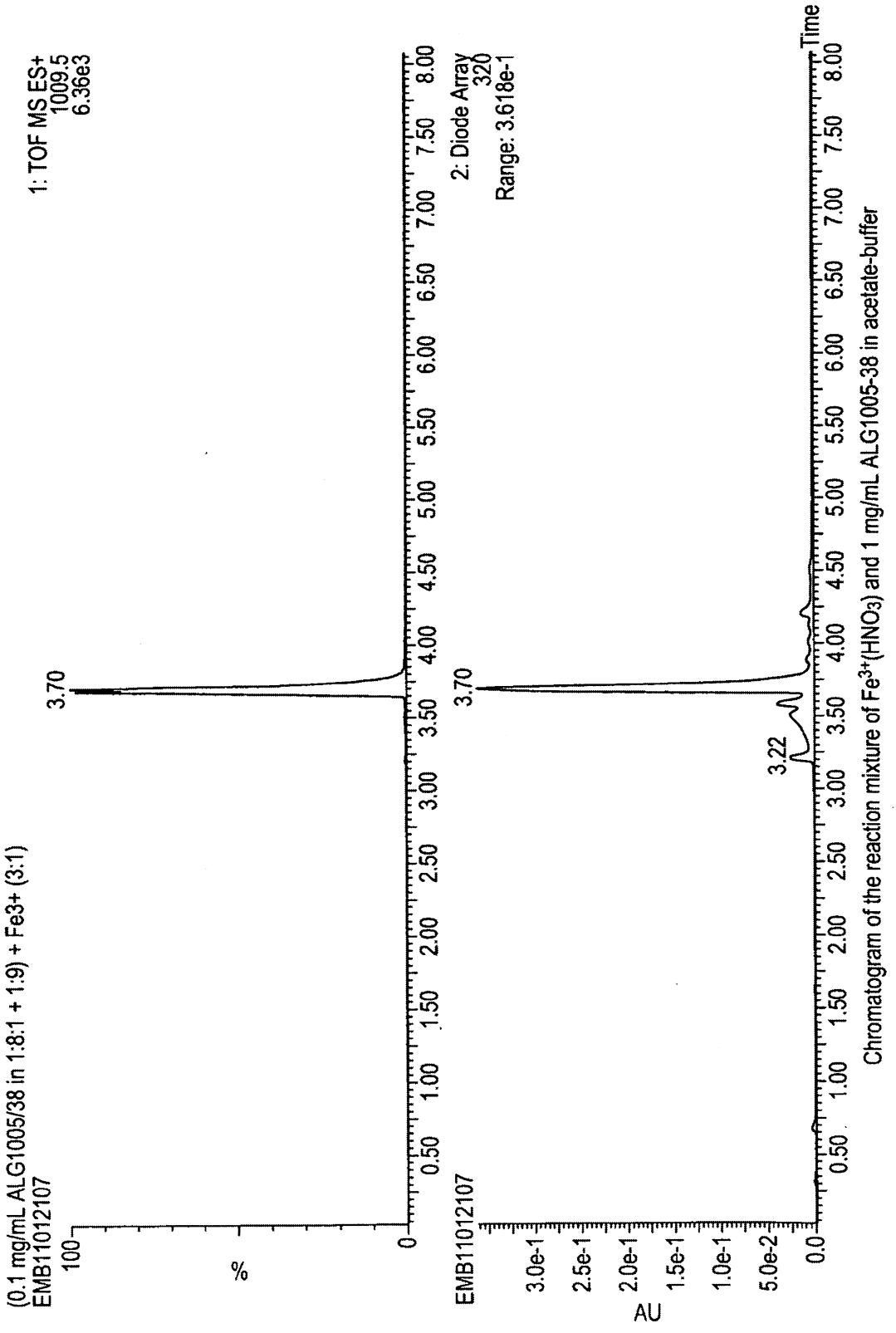
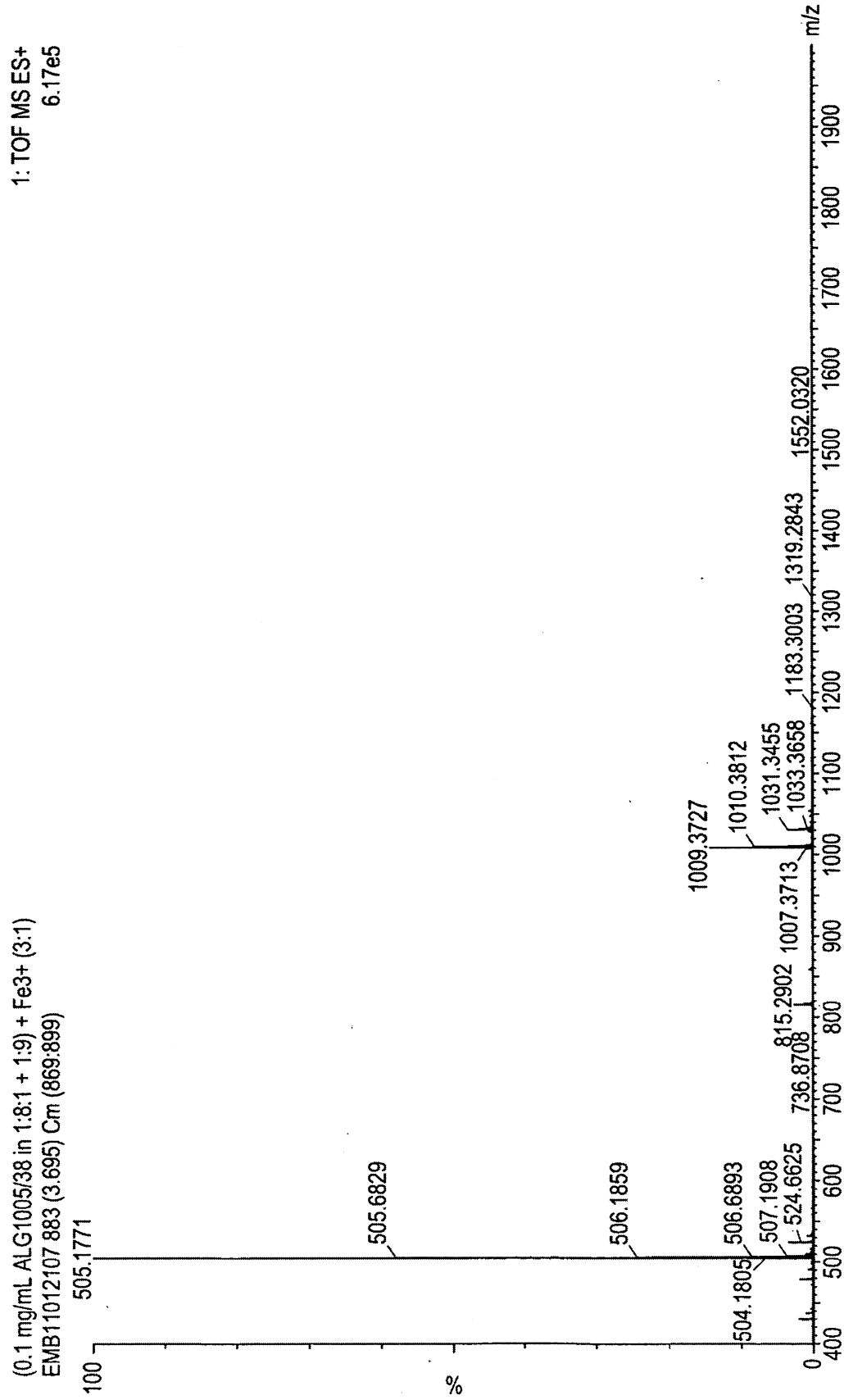

(0.1 mg/mL ALG1005/38 in 1:8:1 + 1:9) + Fe3+ (3:1)
EMB11012107
1: TOF MS ES+
1009.5
6.36e3
100
%
0
3.70
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
EMB11012107
2: Diode Array
320
Range: 3.618e-1
3.70
3.22
3.0e-1
2.5e-1
2.0e-1
1.5e-1
1.0e-1
5.0e-2
0.0
AU
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
Time
Chromatogram of the reaction mixture of $Fe^{3+}(HNO_3)$ and 1 mg/mL ALG1005-38 in acetate-buffer

FIG. 9



The mass spectrum of the Fe-ALG1005-38 complex (m/z 1009.3727)

FIG. 10

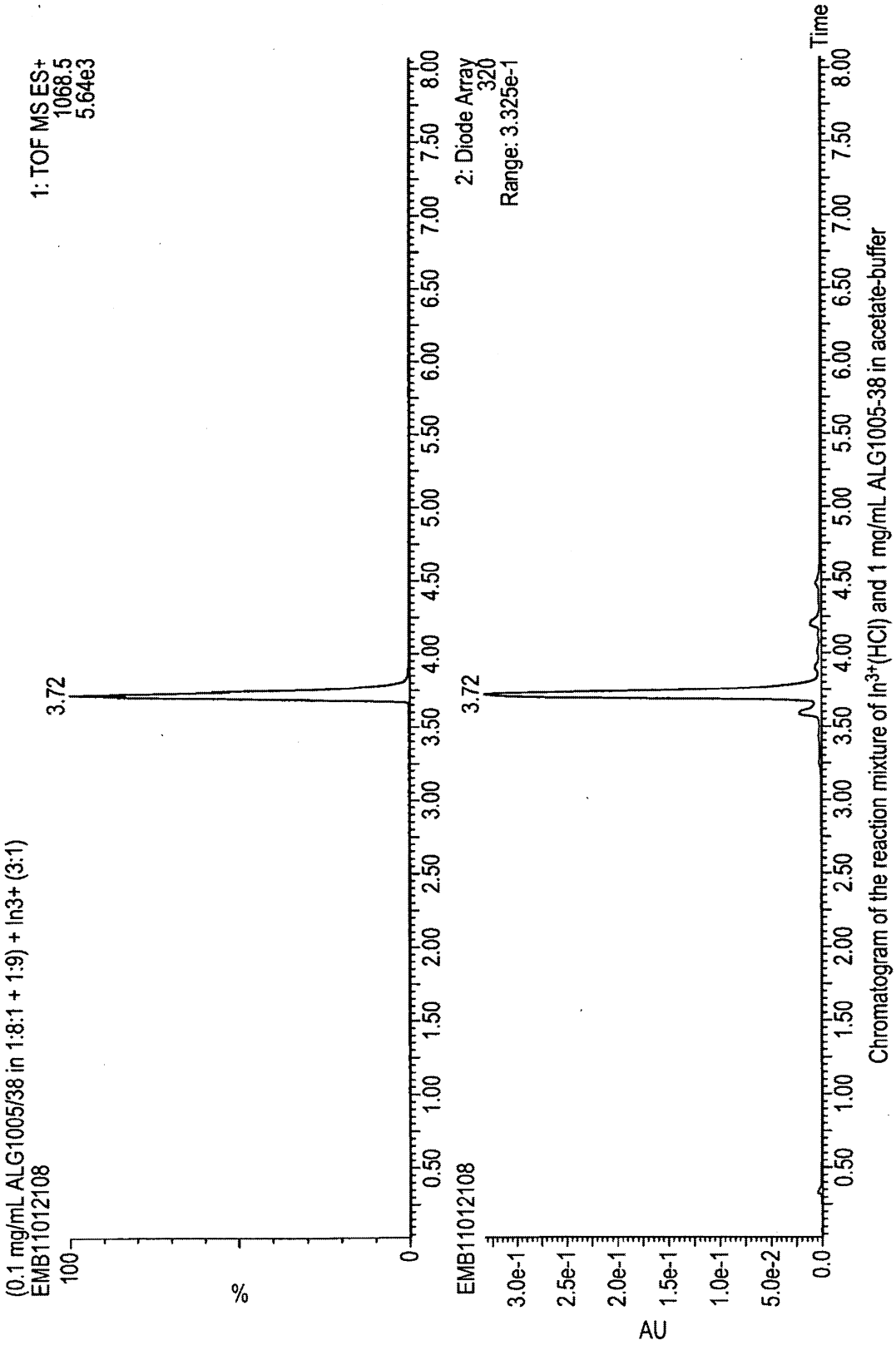

(0.1 mg/mL ALG1005/38 in 1:8:1 + 1:9) + In3+ (3:1)
EMB11012108
1: TOF MS ES+
1068.5
5.64e3
100
%
0
3.72
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
EMB11012108
2: Diode Array
320
Range: 3.325e-1
3.72
3.0e-1
2.5e-1
2.0e-1
1.5e-1
1.0e-1
5.0e-2
0.0
AU
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
Time
Chromatogram of the reaction mixture of In3+(HCl) and 1 mg/mL ALG1005-38 in acetate-buffer

FIG. 11

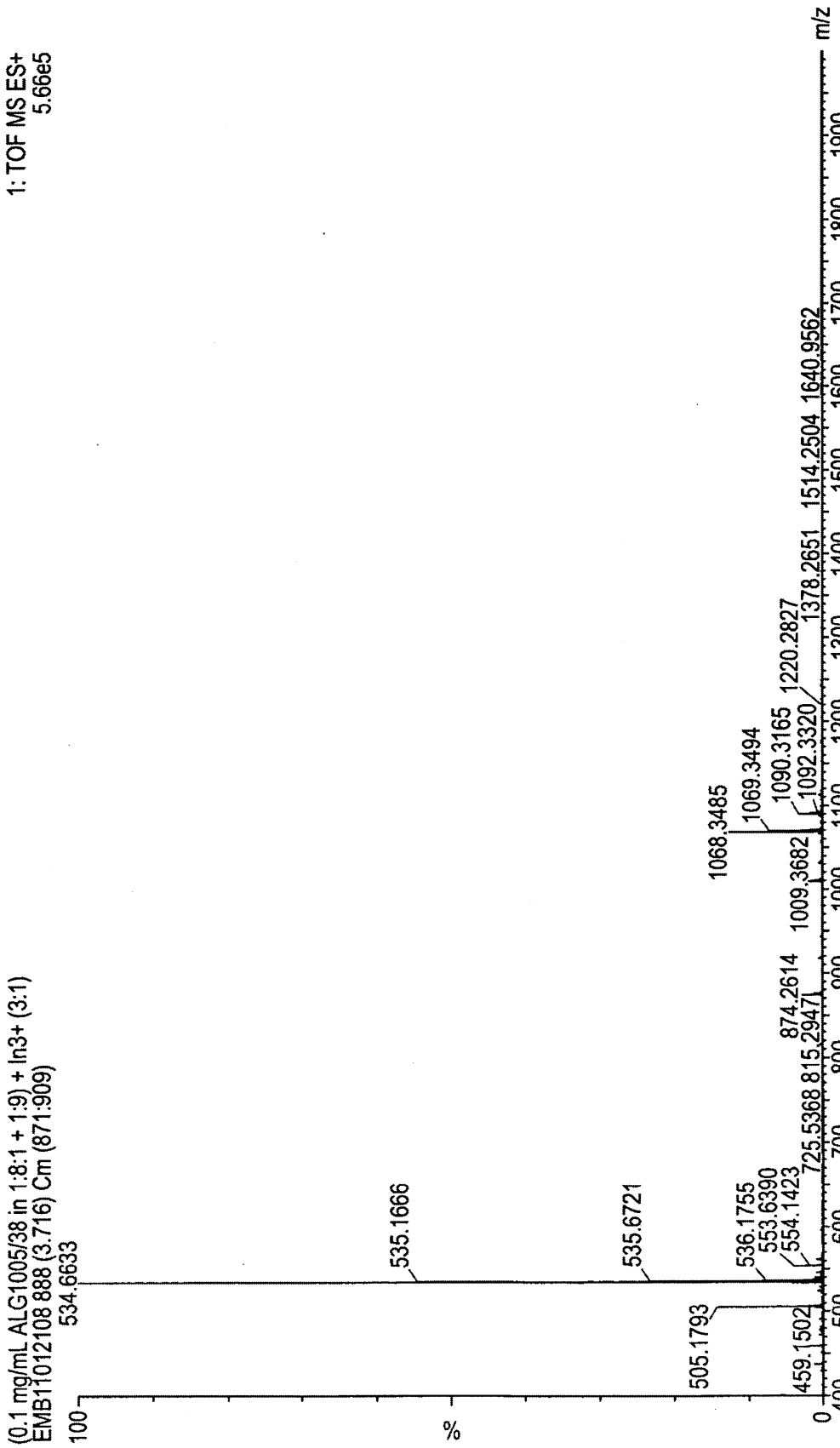

1: TOF MS ES+
5.66e5
(0.1 mg/mL ALG1005/38 in 1:8:1 + 1:9) + In3+ (3:1)
EMB11012108 888 (3.716) Cm (871:909)
100
%
0
534.6633
535.1666
535.6721
536.1755
553.6390
554.1423
725.5368
815.2947
874.2614
1009.3682
1068.3485
1069.3494
1090.3165
1092.3320
1220.2827
1378.2651
1514.2504
1640.9562
505.1793
459.1502
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
m/z
The mass spectrum of the In-ALG1005-38 complex (m/z 1068.3485)

FIG. 12

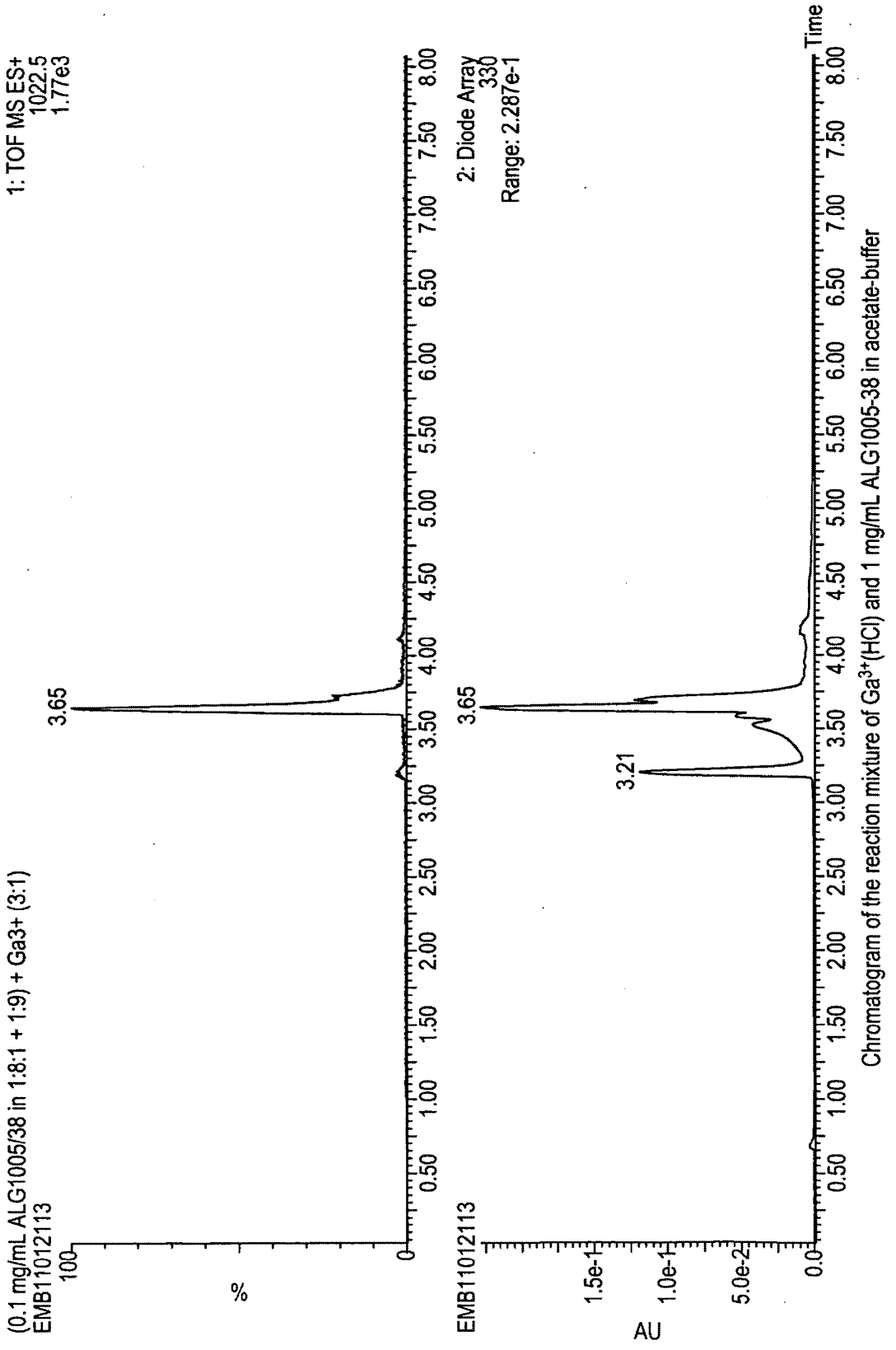

1: TOF MS ES+
1022.5
1.77e3
(0.1 mg/mL ALG1005/38 in 1:8:1 + 1:9) + Ga3+ (3:1)
EMB11012113
100
%
0
3.65
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
2: Diode Array
330
Range: 2.287e-1
EMB11012113
1.5e-1
1.0e-1
5.0e-2
0.0
AU
3.65
3.21
0.50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00
Time
Chromatogram of the reaction mixture of Ga^{3+}(HCl) and 1 mg/mL ALG1005-38 in acetate-buffer

FIG. 13

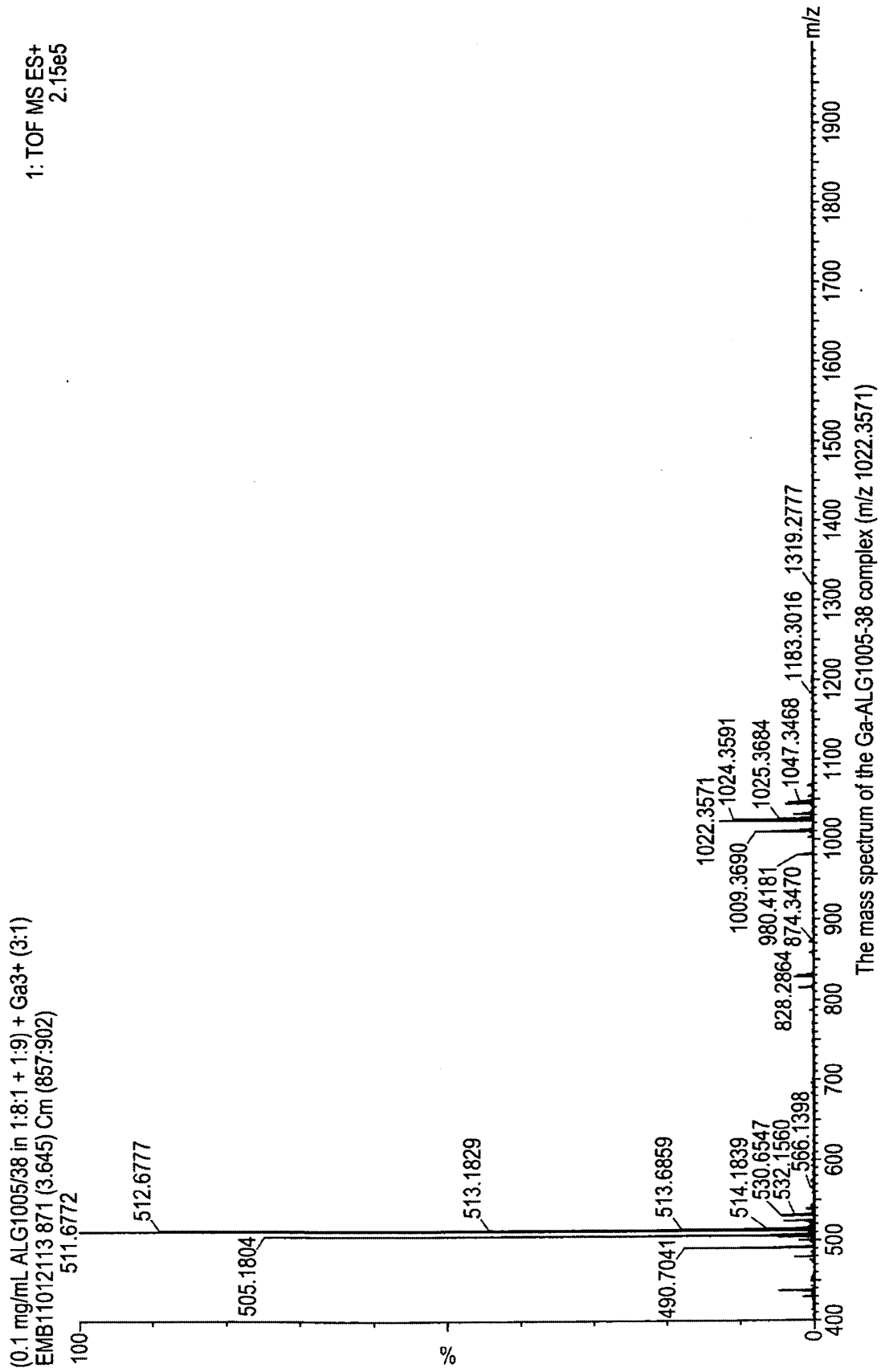
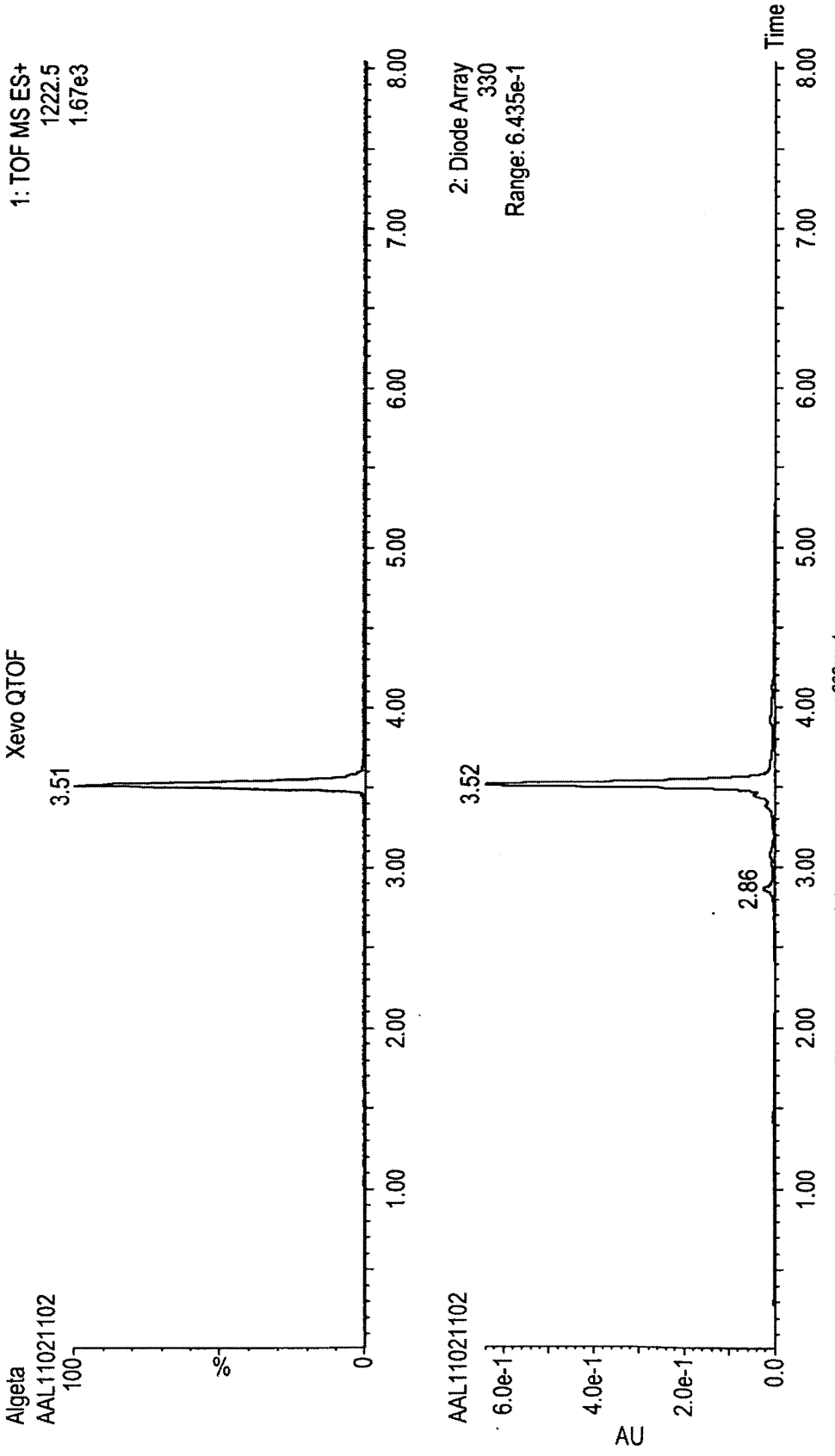
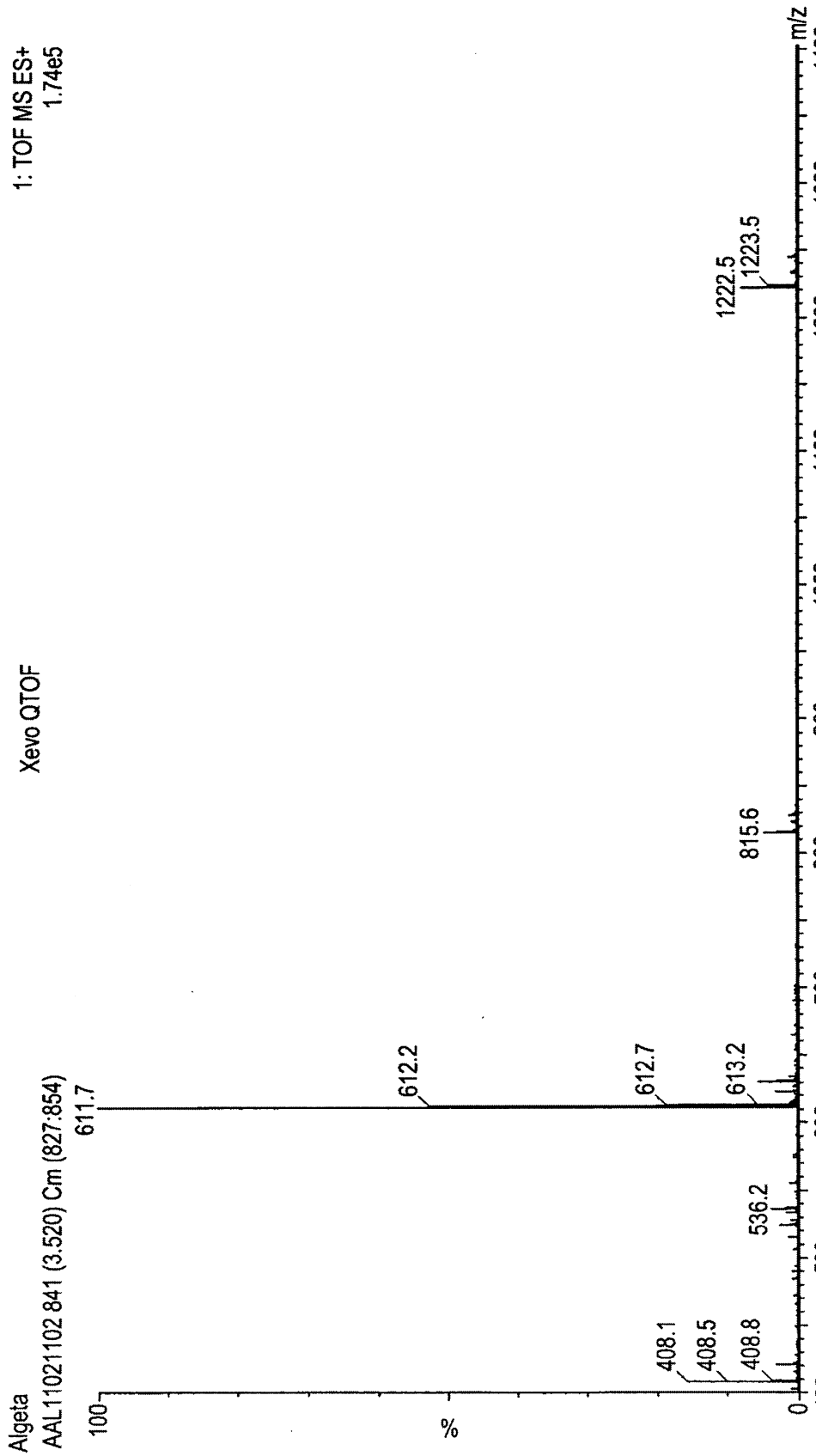

1: TOF MS ES+
2.15e5
(0.1 mg/mL ALG1005/38 in 1:8:1 + 1:9) + Ga3+ (3:1)
EMB11012113 871 (3.645) Cm (857:902)
100
%
0
m/z
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
511.6772
512.6777
505.1804
513.1829
490.7041
513.6859
514.1839
530.6547
532.1560
566.1398
828.2864
874.3470
980.4181
1009.3690
1022.3571
1024.3591
1025.3684
1047.3468
1183.3016
1319.2777
The mass spectrum of the Ga-ALG1005-38 complex (m/z 1022.3571)

FIG. 14



Chromatogram of the reaction mixture of $^{232}Th^{4+}$(HCl) and Bb-1-HOPO-1-DEBN

FIG. 15



The mass spectrum of the ^{232}Th-Bb-1-HOPO-1-DEBN complex (*m/z* 1222.5)

FIG. 16

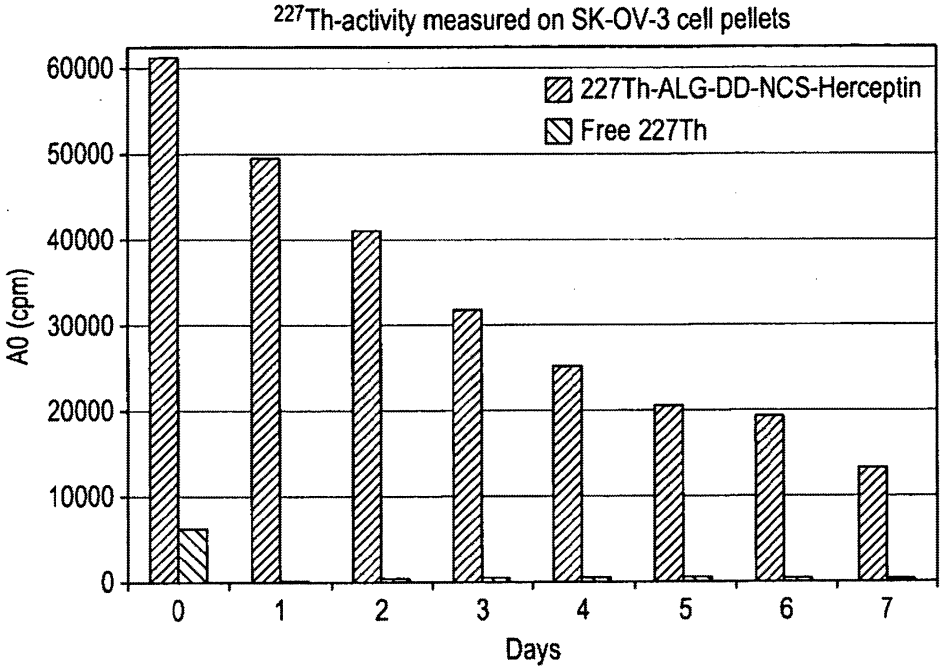

227Th-activity measured on SK-OV-3 cell pellets
227Th-ALG-DD-NCS-Herceptin
Free 227Th
A0 (cpm)
60000
50000
40000
30000
20000
10000
0
0
1
2
3
4
5
6
7
Days

FIG. 17

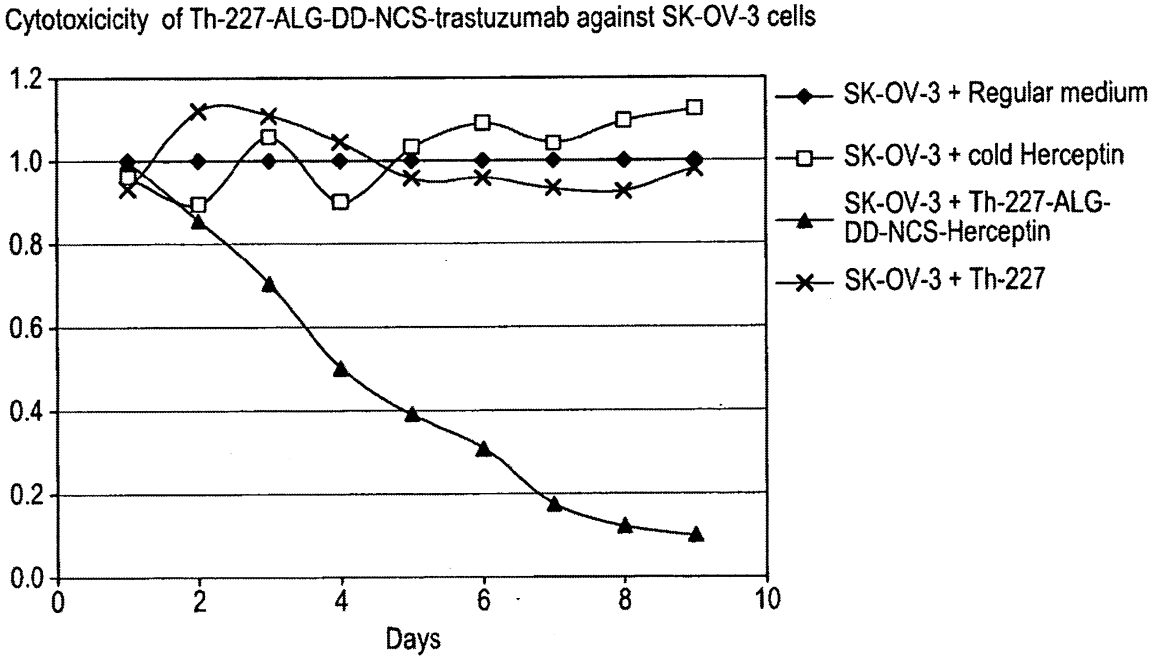

Cytotoxicity of Th-227-ALG-DD-NCS-trastuzumab against SK-OV-3 cells
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
2
4
6
8
10
Days
SK-OV-3 + Regular medium
SK-OV-3 + cold Herceptin
SK-OV-3 + Th-227-ALG-DD-NCS-Herceptin
SK-OV-3 + Th-227
Luminescence values for treated SK-OV-3 cells

FIG. 18

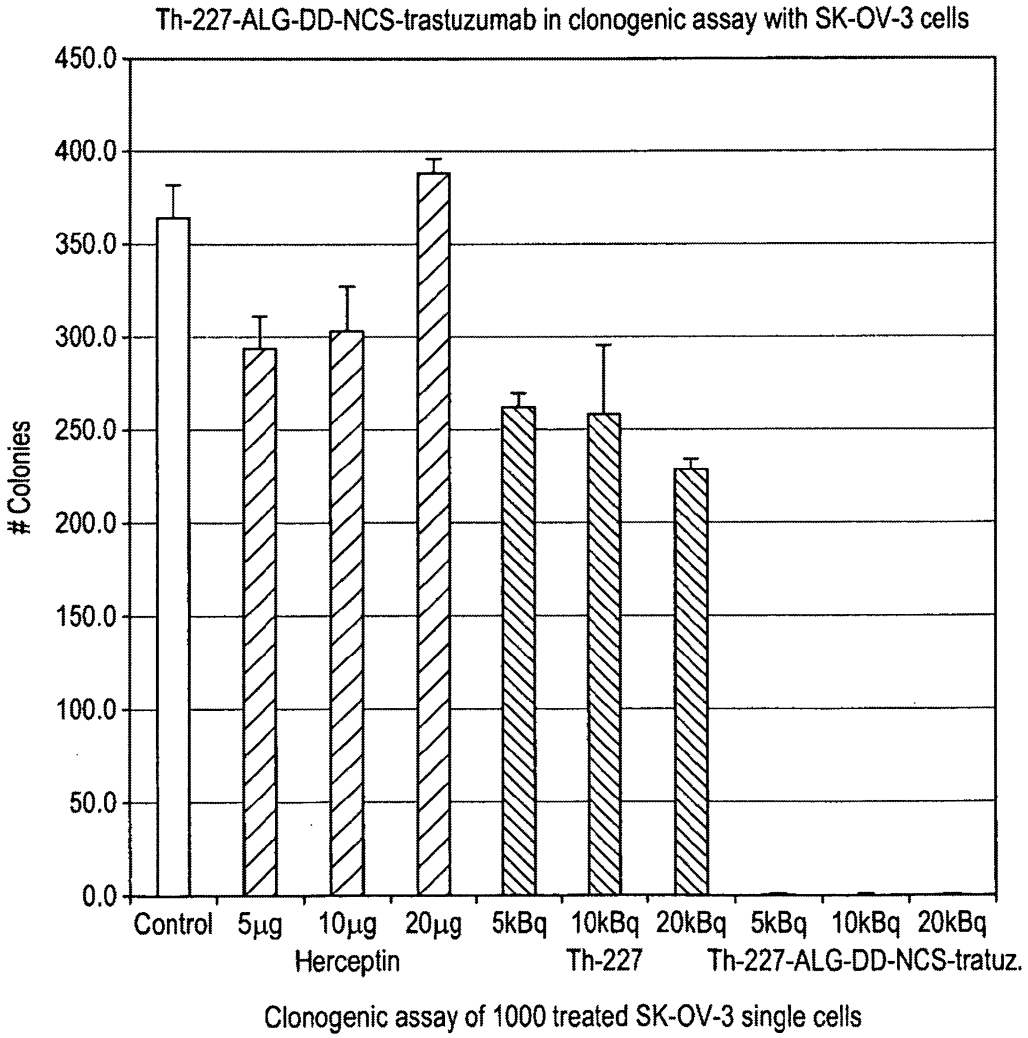

Th-227-ALG-DD-NCS-trastuzumab in clonogenic assay with SK-OV-3 cells
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
Colonies
Control
5µg
10µg
20µg
5kBq
10kBq
20kBq
5kBq
10kBq
20kBq
Herceptin
Th-227
Th-227-ALG-DD-NCS-tratuz.
Clonogenic assay of 1000 treated SK-OV-3 single cells

FIG. 19

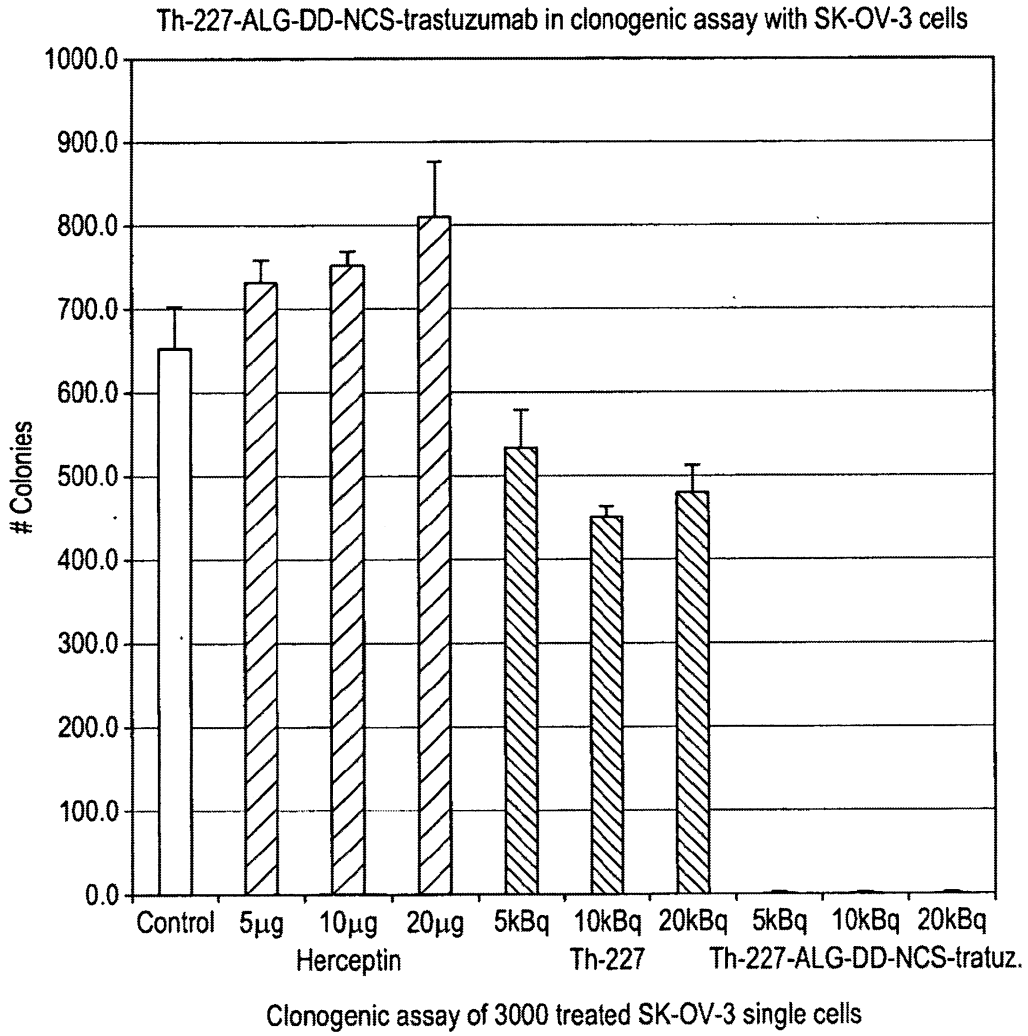

Th-227-ALG-DD-NCS-trastuzumab in clonogenic assay with SK-OV-3 cells
Colonies
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
Control
5µg
10µg
20µg
5kBq
10kBq
20kBq
5kBq
10kBq
20kBq
Herceptin
Th-227
Th-227-ALG-DD-NCS-tratuz.
Clonogenic assay of 3000 treated SK-OV-3 single cells

FIG. 20

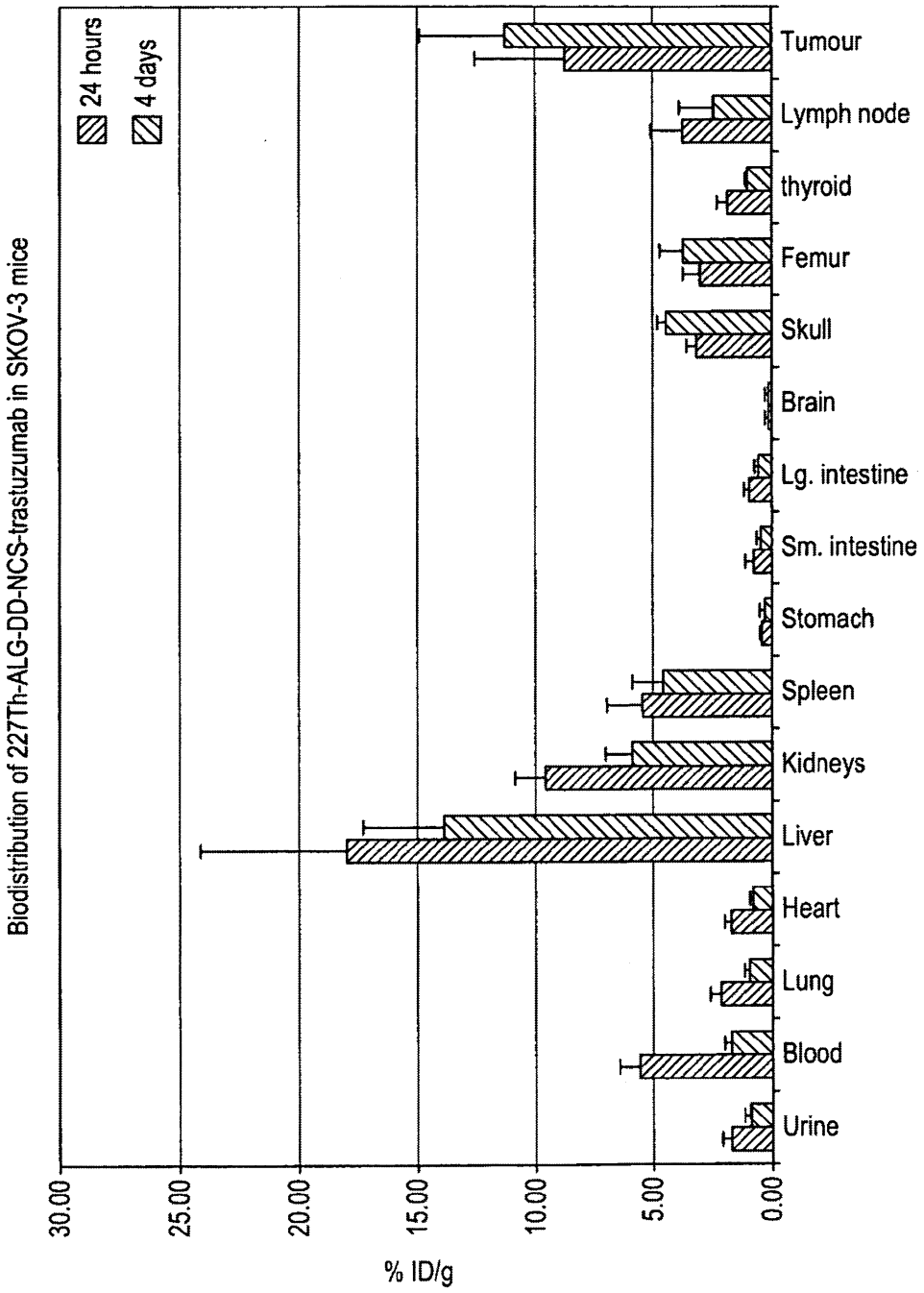

Biodistribution of 227Th-ALG-DD-NCS-trastuzumab in SKOV-3 mice
24 hours
4 days
Tumour
Lymph node
thyroid
Femur
Skull
Brain
Lg. intestine
Sm. intestine
Stomach
Spleen
Kidneys
Liver
Heart
Lung
Blood
Urine
30.00
25.00
20.00
15.00
10.00
5.00
0.00
% ID/g
Organ distribution of 227Th-ALG-DD-NCS-trastuzumab (2700 Bq(µg) in Balb/c nude mice with SK-OV-3 xenografts

FIG. 21