

Design, Synthesis, and Biological Evaluation of Stable Colchicine Binding Site Tubulin Inhibitors as Potential Anticancer Agents

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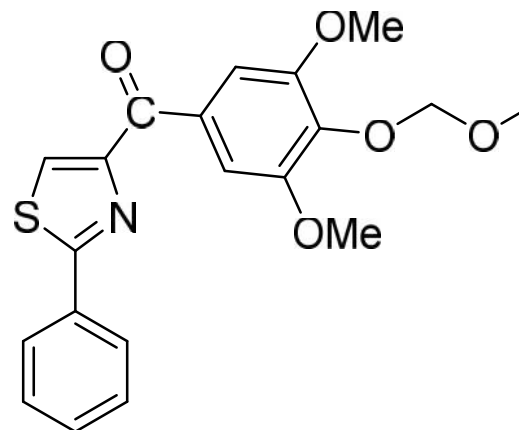
[‡] GTx Inc, Preclinical R&D, Memphis, TN, 38163

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S1 Mass and chromatograph spectrum of compounds **15**, **18**, **4**, **7**, and their metabolites.

Mass spectrum of Compound 15

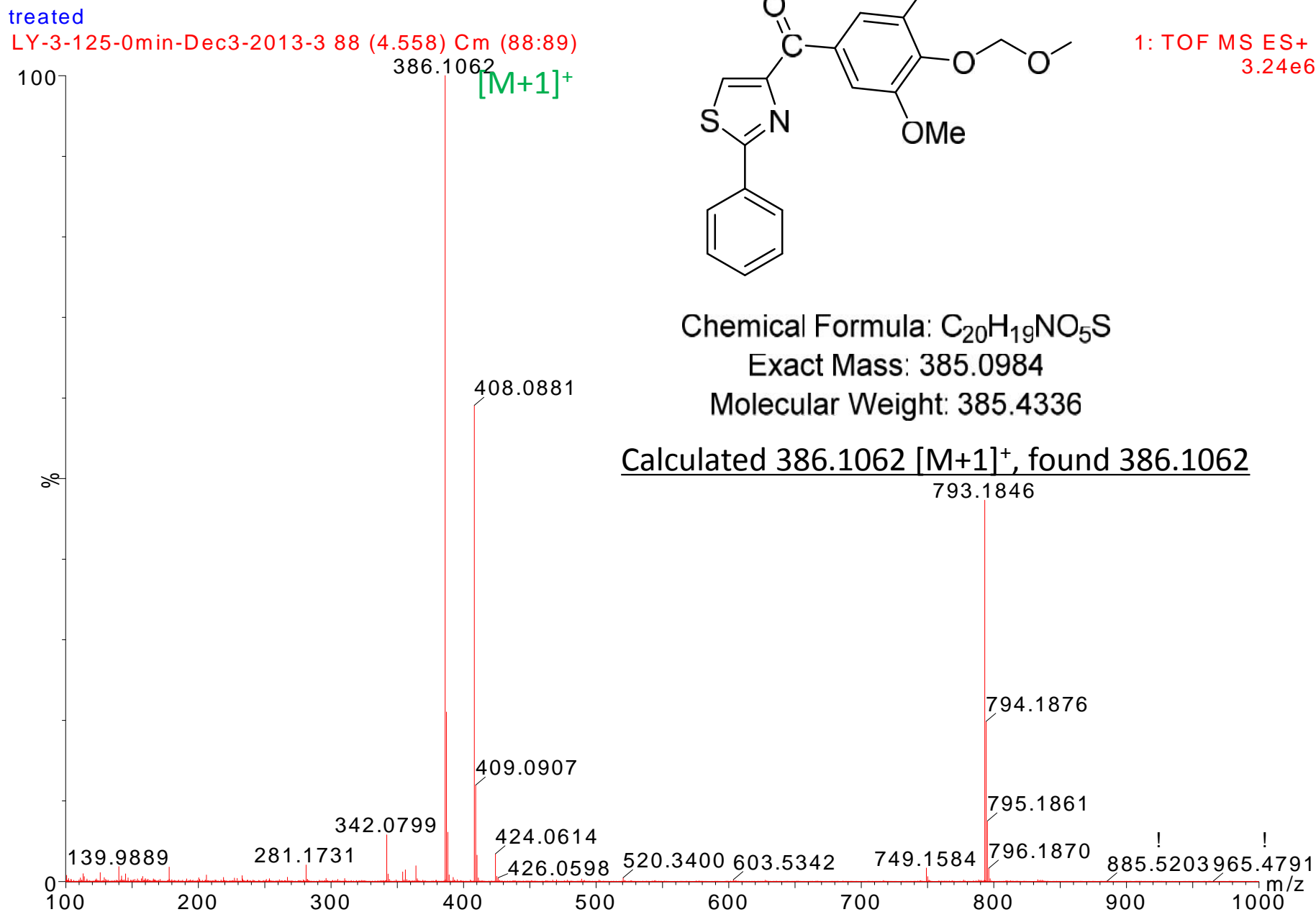


Chemical Formula: $C_{20}H_{19}NO_5S$

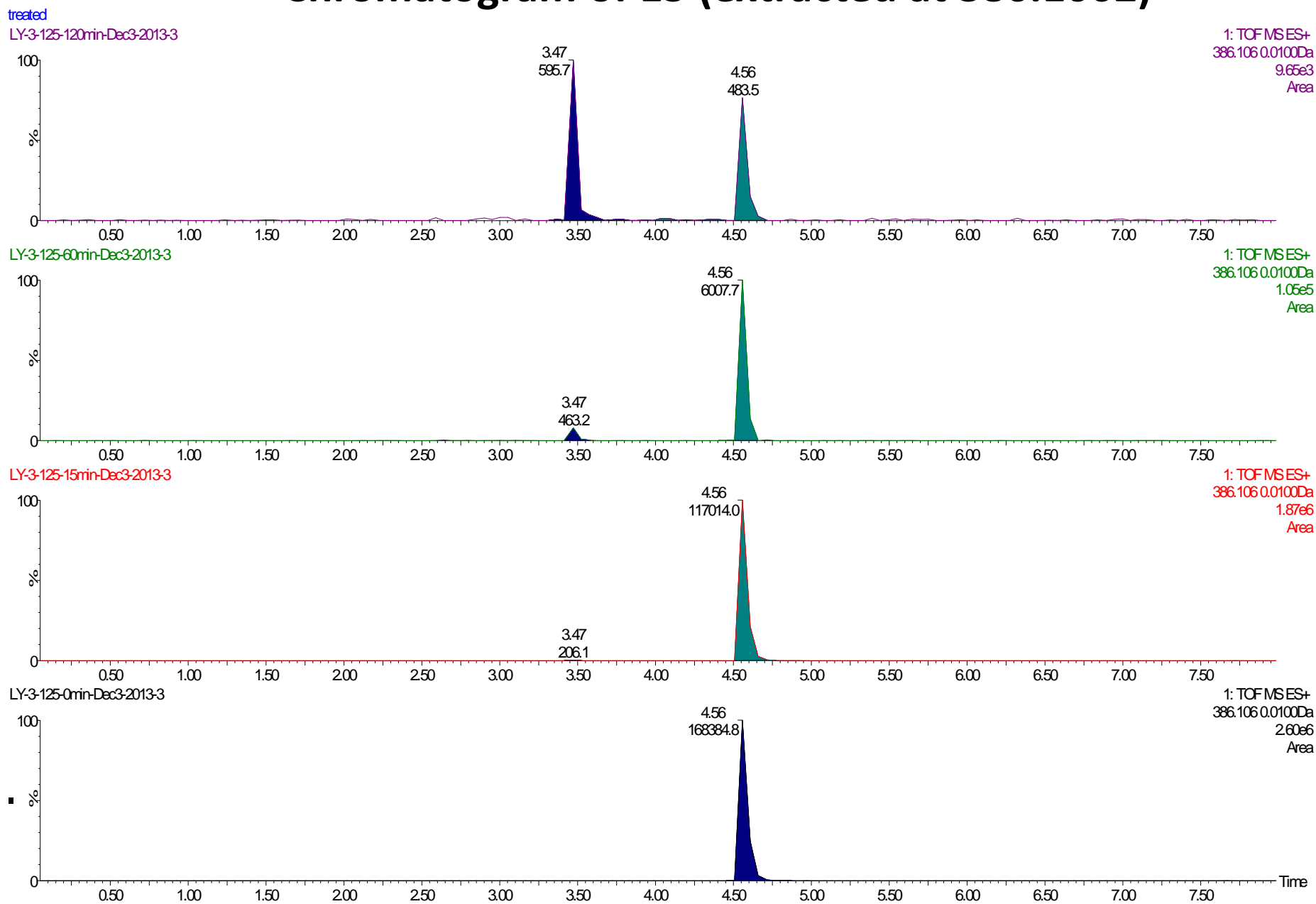
Exact Mass: 385.0984

Molecular Weight: 385.4336

Calculated 386.1062 [M+1]⁺, found 386.1062



Chromatogram of 15 (extracted at 386.1062)

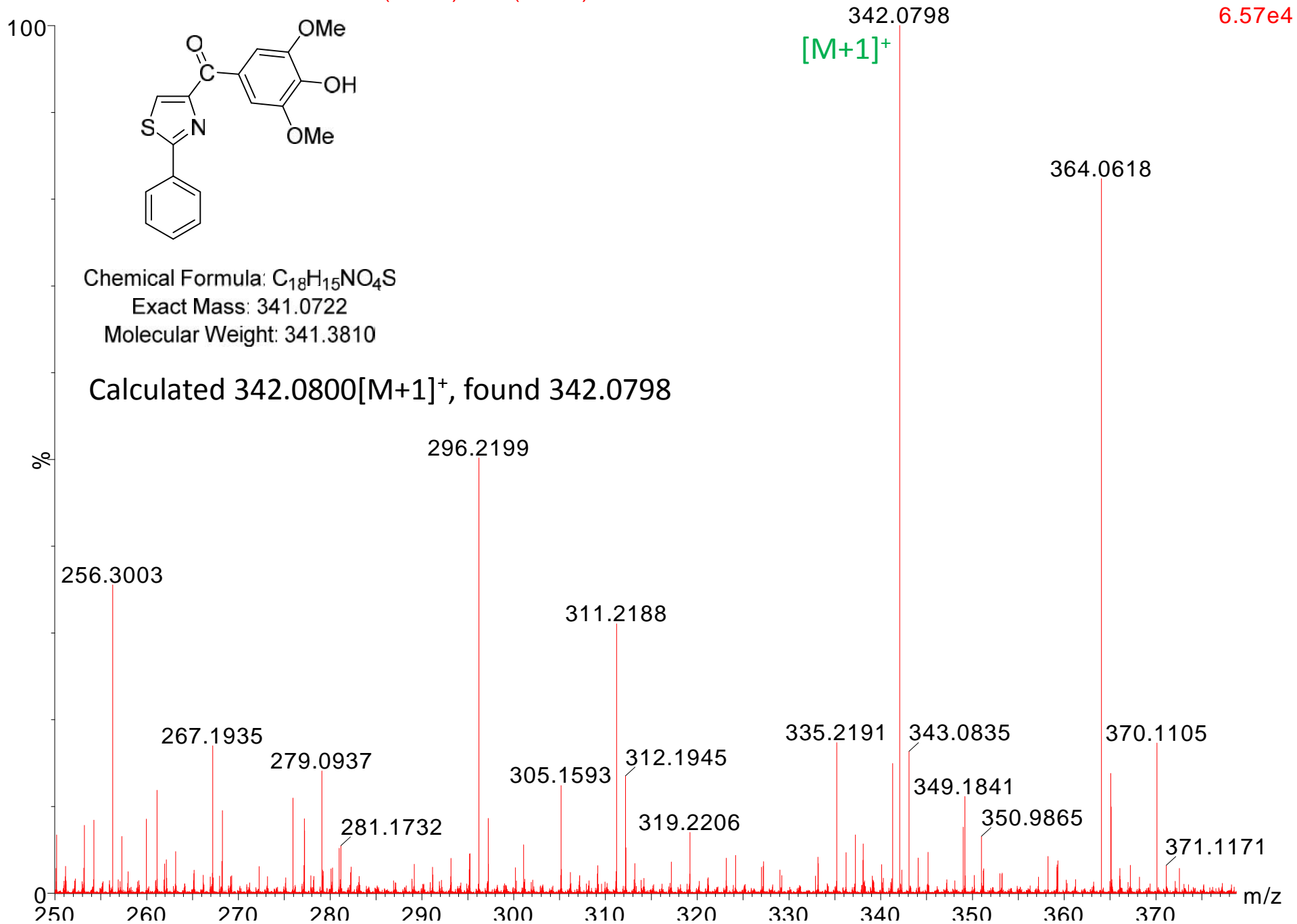


treated

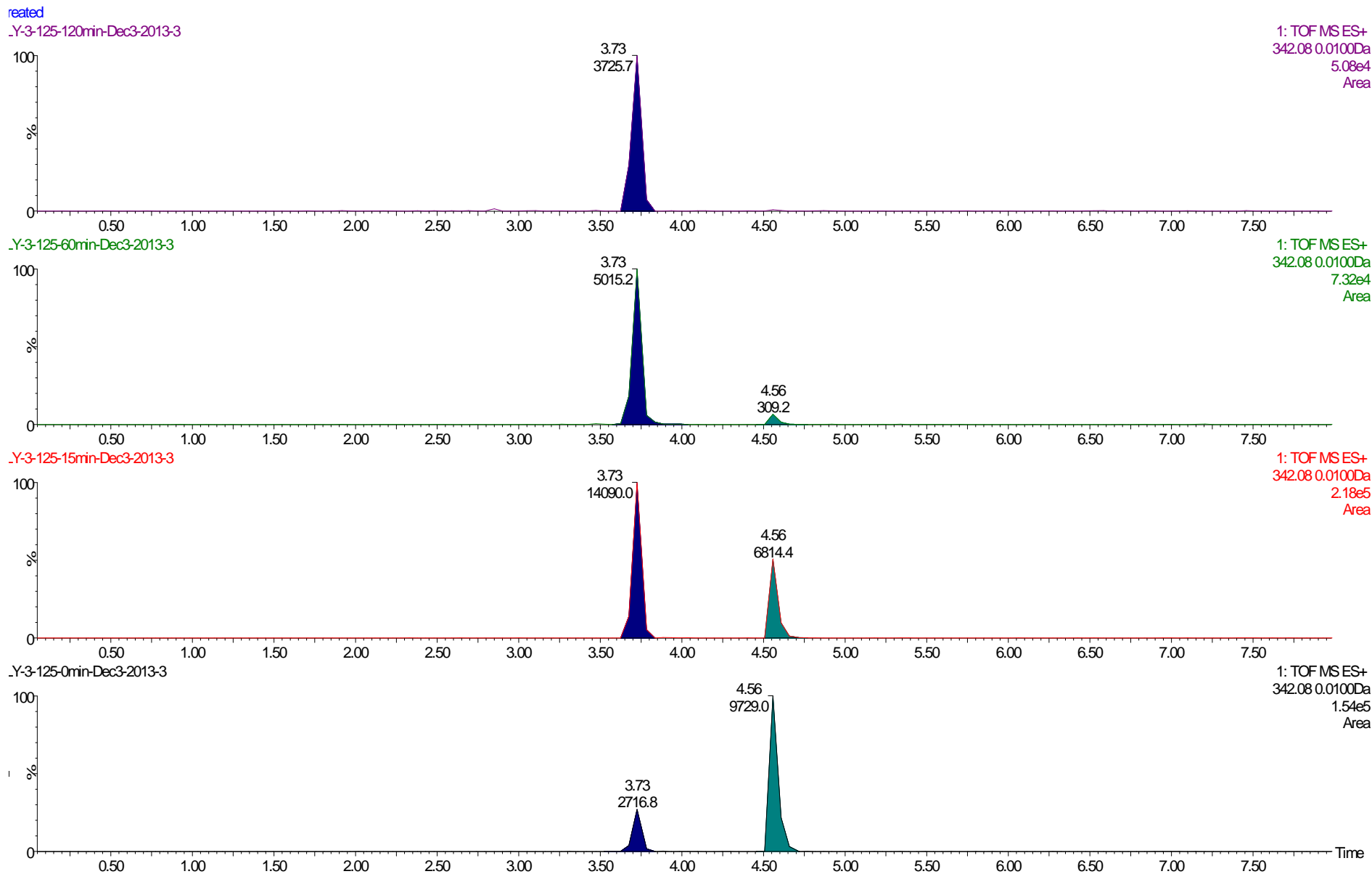
LY-3-125-120min-Dec3-2013-3 72 (3.725) Cm (71:72)

Mass spectrum of M1

1: TOF MS ES+
6.57e4



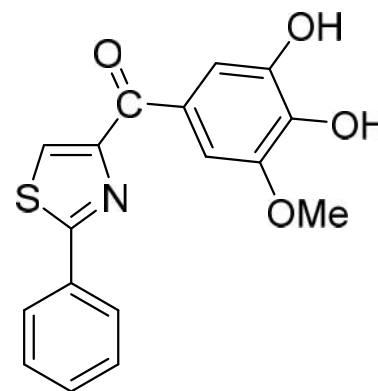
Chromatogram of M1 (extracted at 342.0800)



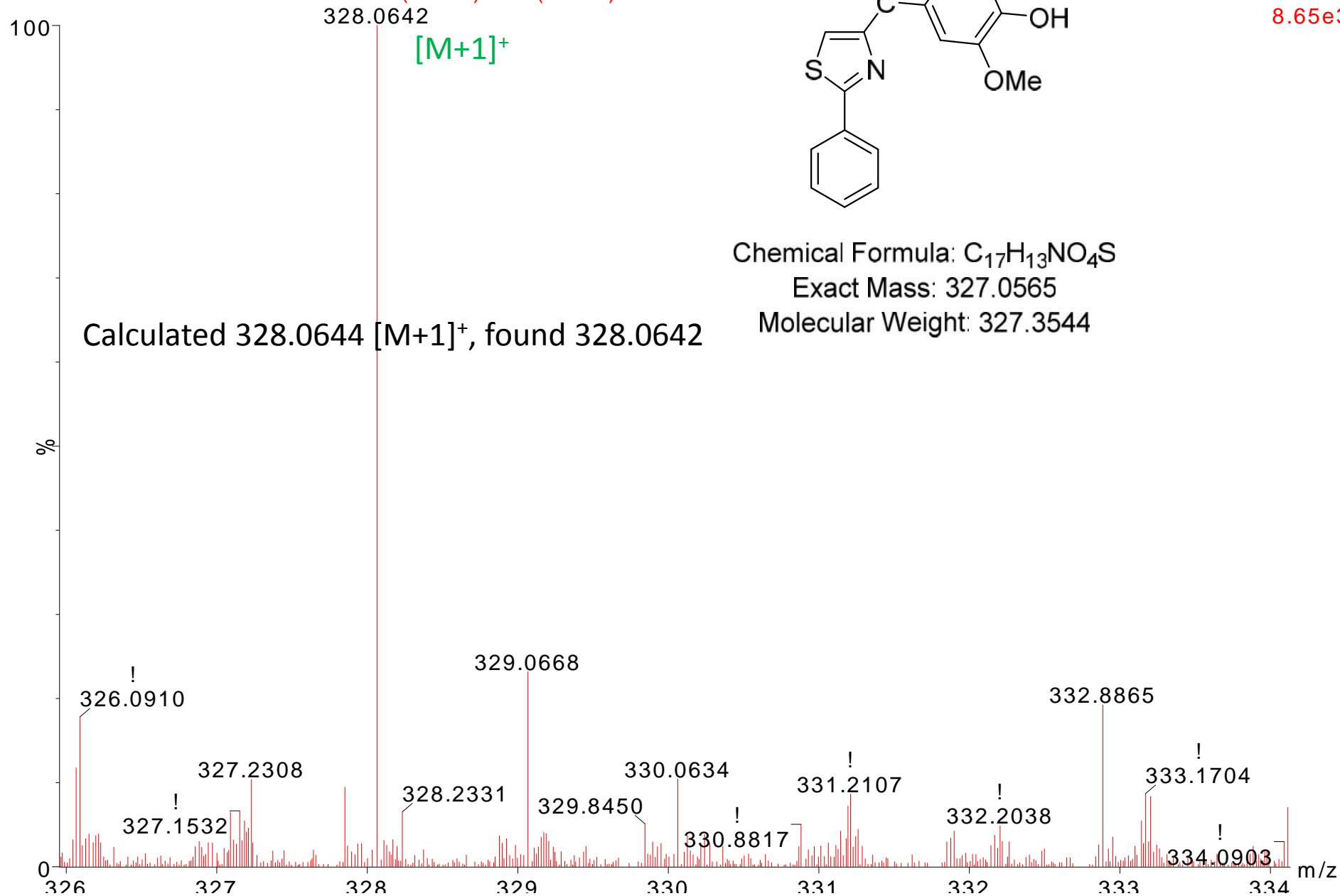
Mass spectrum of M2

treated

LY-3-125-120min-Dec3-2013-3 60 (3.103) Cm (60:61)



1: TOF MS ES+
8.65e3



Calculated 328.0644 [M+1]⁺, found 328.0642

Chemical Formula: C₁₇H₁₃NO₄S

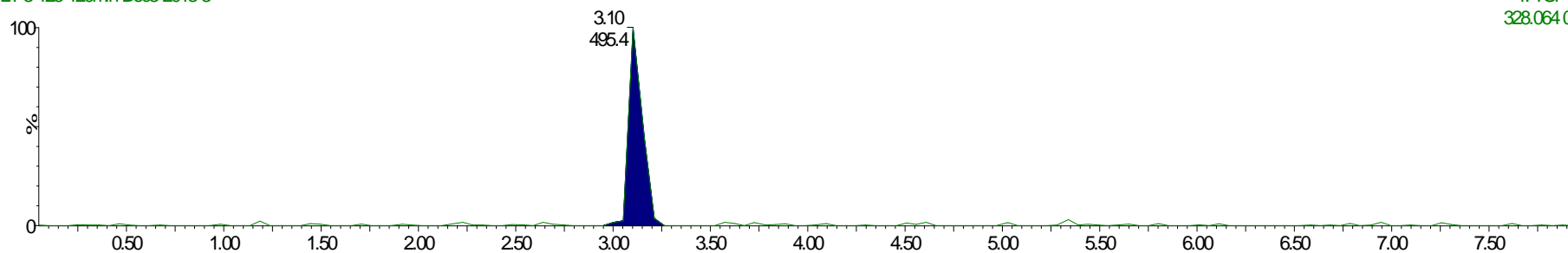
Exact Mass: 327.0565

Molecular Weight: 327.3544

Chromatogram of M2 (extracted at 328.0644)

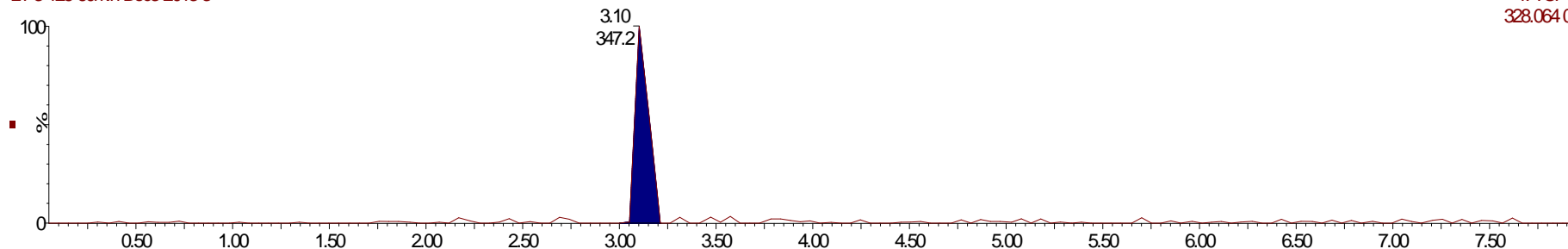
treated

LY-3-125-120min-Dec3-2013-3



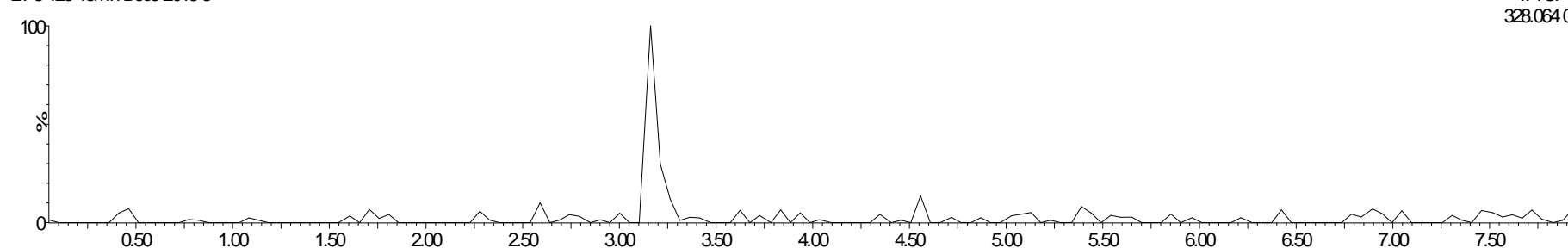
1: TOF MS ES+
328.064 0.0100Da
6.02e3
Area

LY-3-125-60min-Dec3-2013-3



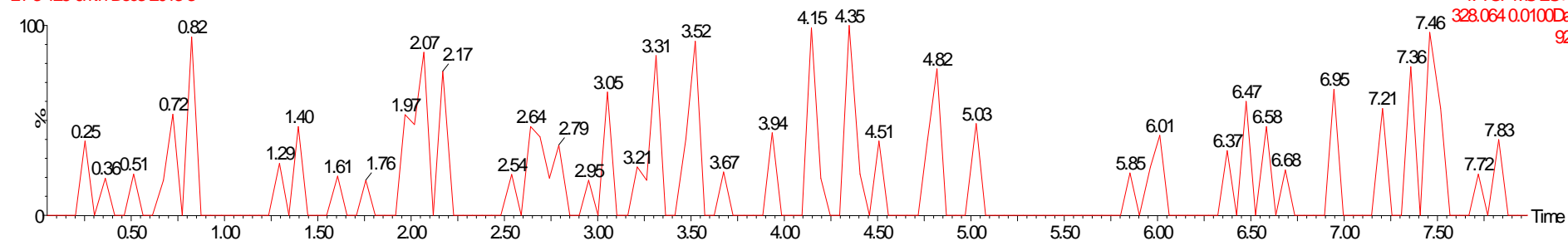
1: TOF MS ES+
328.064 0.0100Da
4.30e3
Area

LY-3-125-15min-Dec3-2013-3



1: TOF MS ES+
328.064 0.0100Da
1.39e3
Area

LY-3-125-0min-Dec3-2013-3

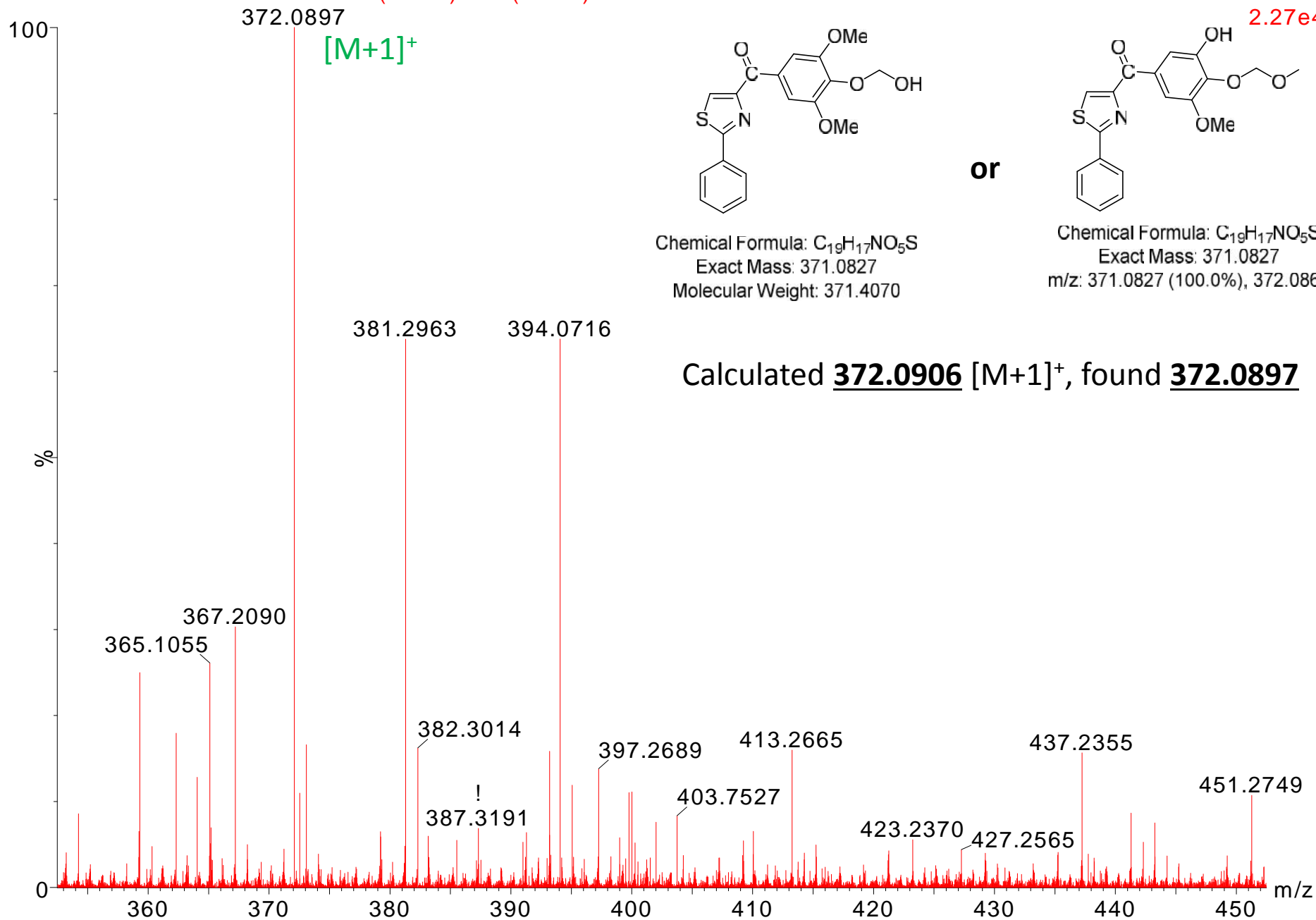


1: TOF MS ES+
328.064 0.0100Da
92

Mass spectrum of M3

treated

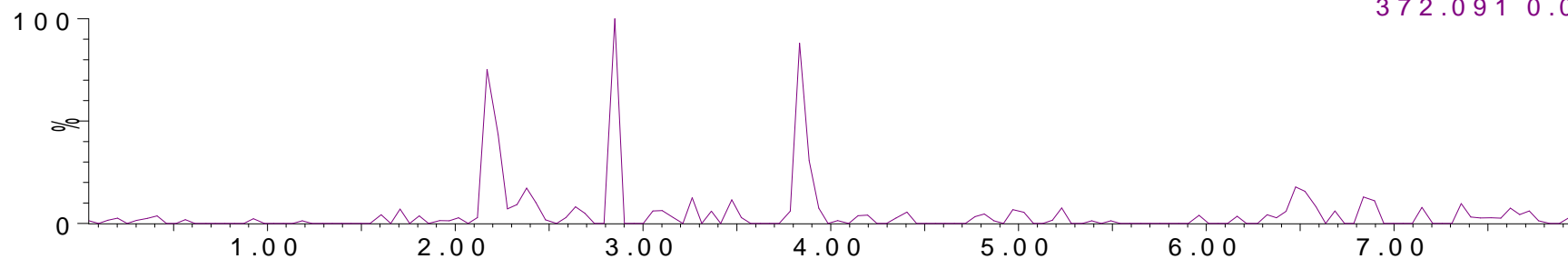
LY-3-125-15min-Dec3-2013-3 74 (3.834) Cm (74:75)



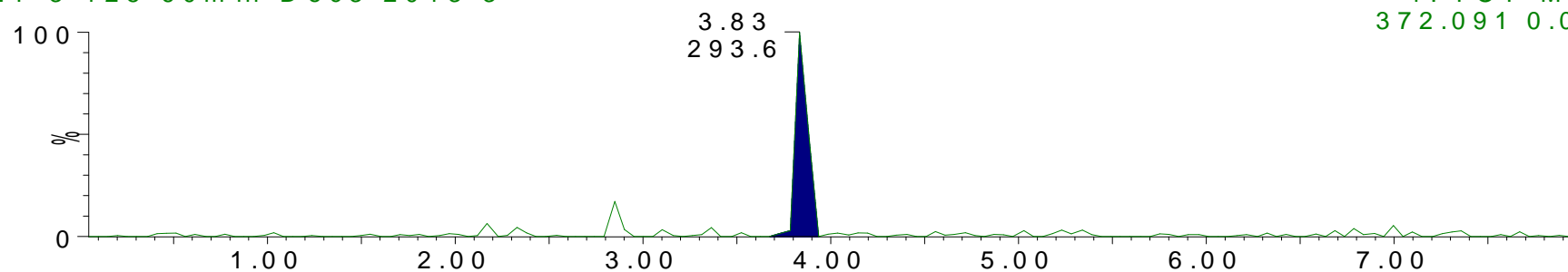
Chromatogram of M3 (extracted at 372.0906)

treated

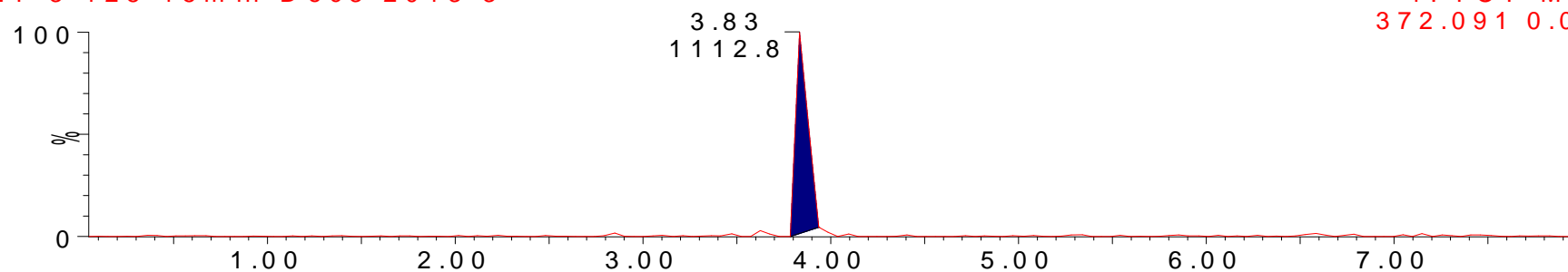
LY-3-125-120min-Dec3-2013-3



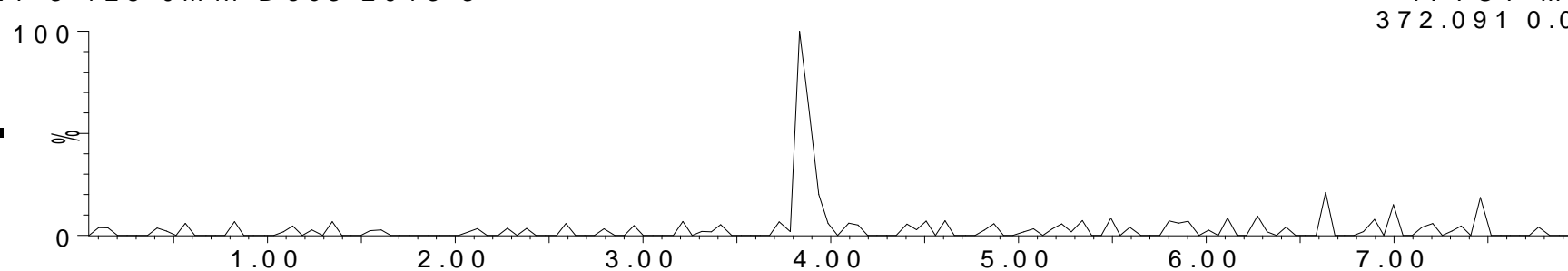
LY-3-125-60min-Dec3-2013-3



LY-3-125-15min-Dec3-2013-3



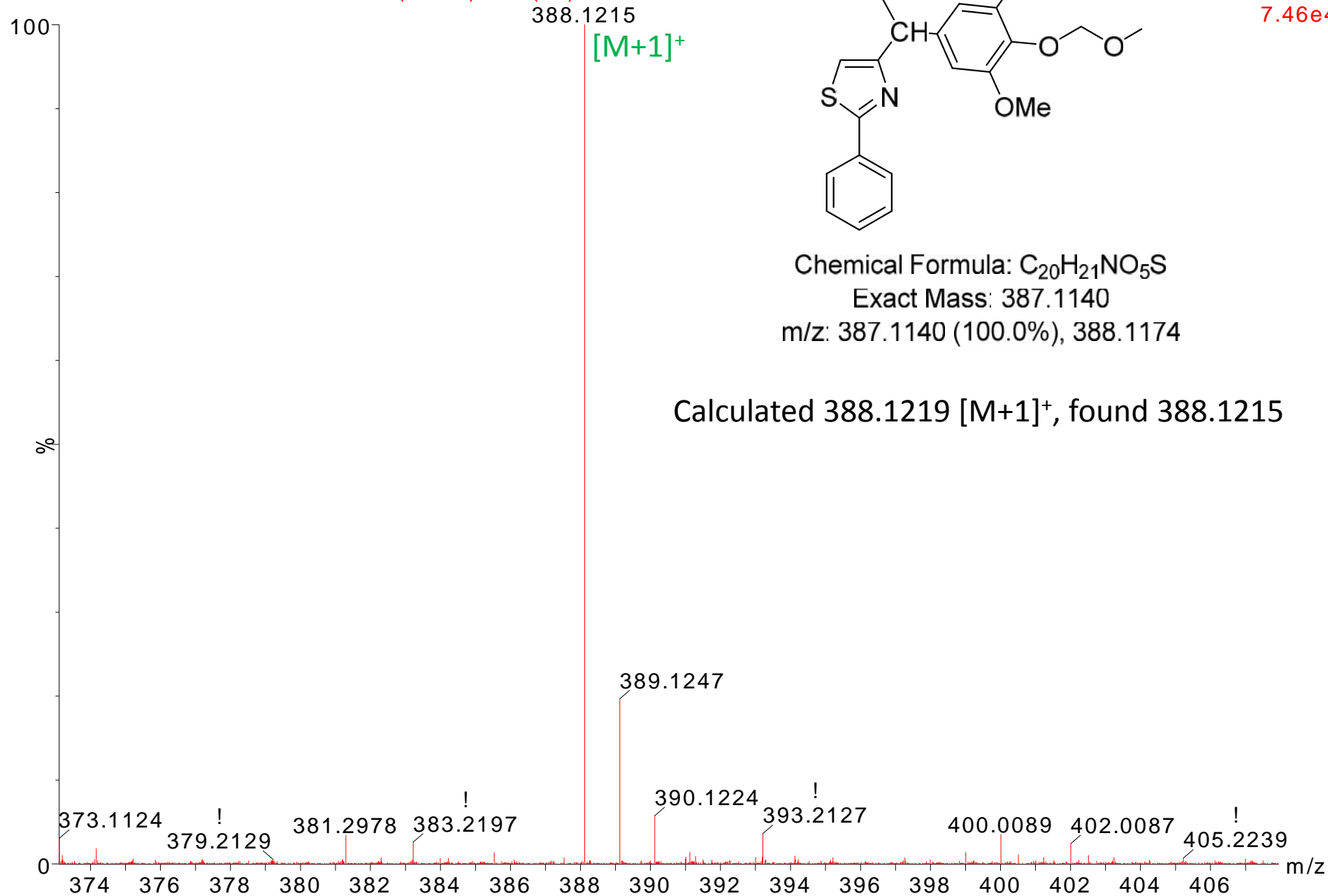
LY-3-125-0min-Dec3-2013-3



Mass spectrum of M4

treated

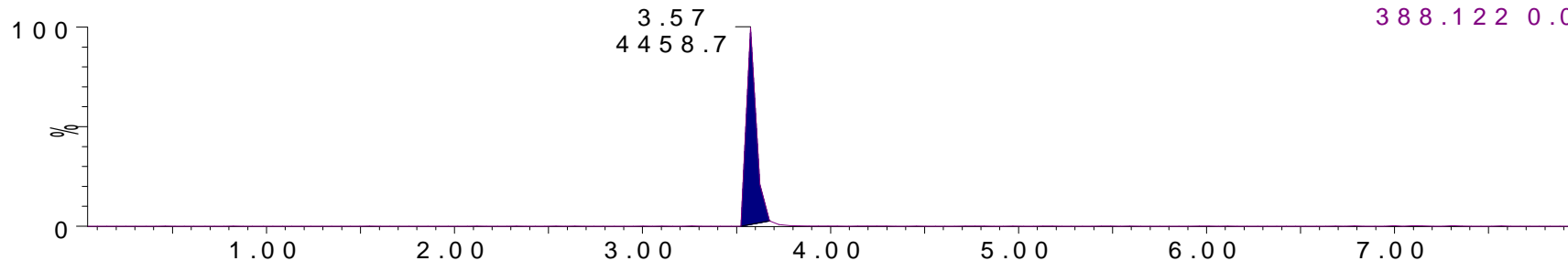
LY-3-125-120min-Dec3-2013-3 69 (3.574) Cm (69)



Chromatogram of M4 (extracted at 388.1219)

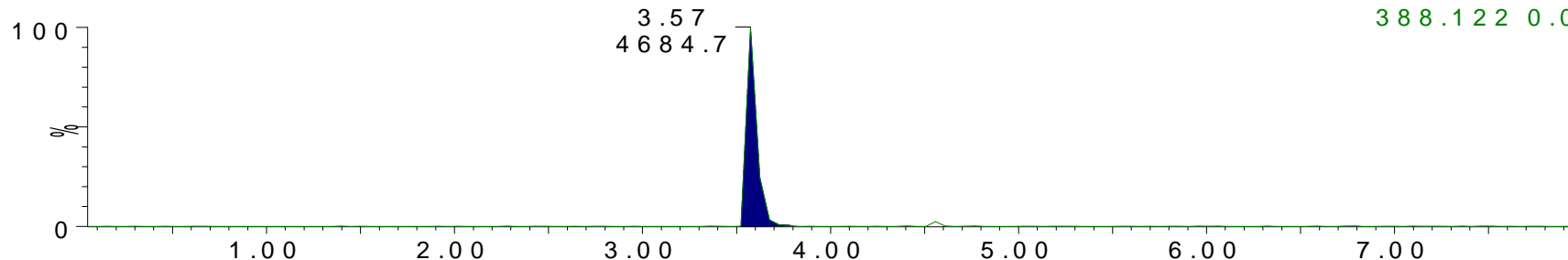
treated

LY-3-125-120min-Dec3-2013-3



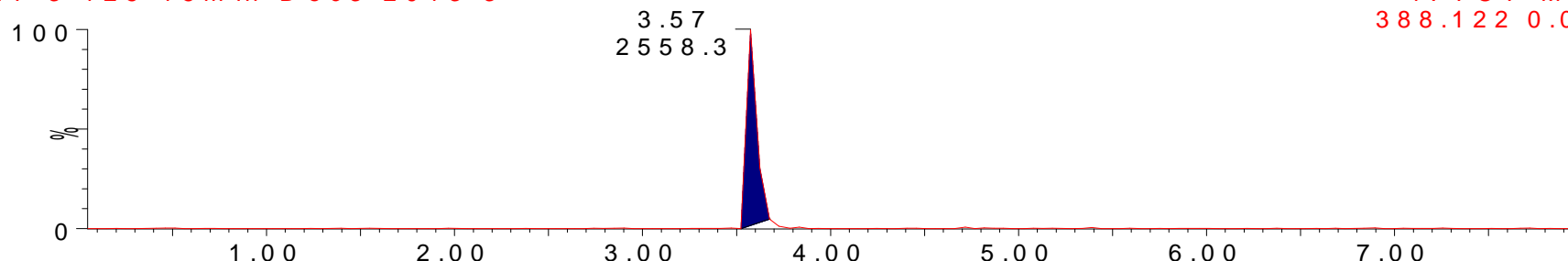
1: TOF MS ES+
388.122 0.0100Da
7.46e4
Area

LY-3-125-60min-Dec3-2013-3



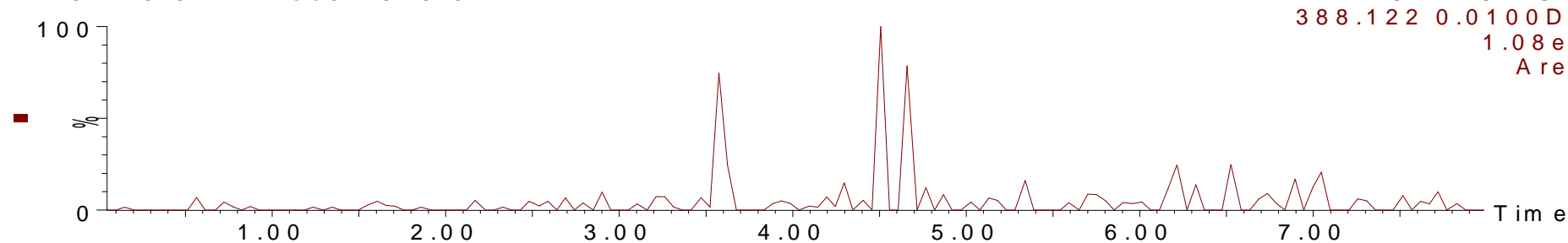
1: TOF MS ES+
388.122 0.0100Da
7.28e4
Area

LY-3-125-15min-Dec3-2013-3



1: TOF MS ES+
388.122 0.0100Da
4.04e4
Area

LY-3-125-0min-Dec3-2013-3

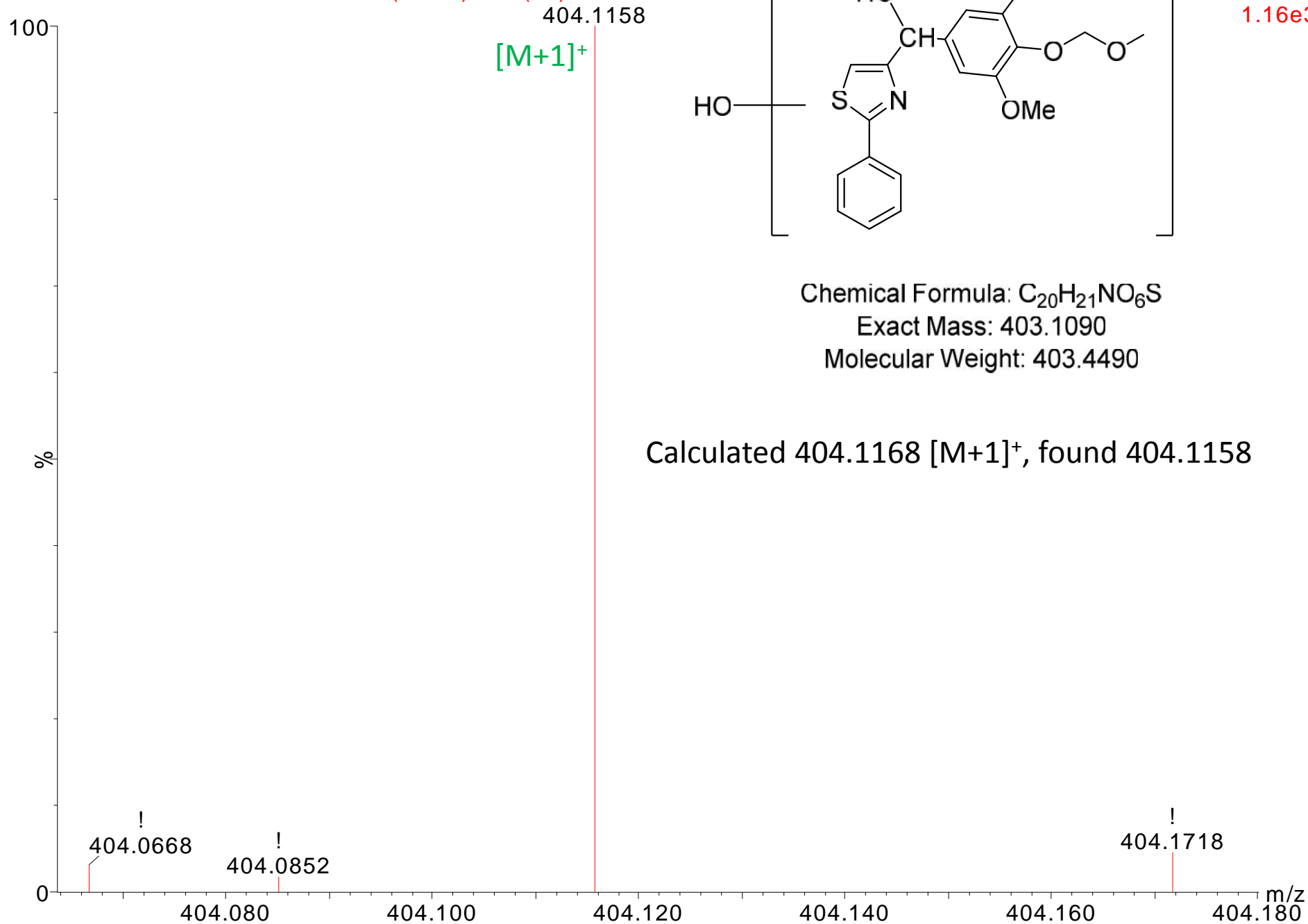


1: TOF MS ES+
388.122 0.0100Da
1.08e3
Area

treated

LY-3-125-120min-Dec3-2013-3 32 (1.656) Cm (32)

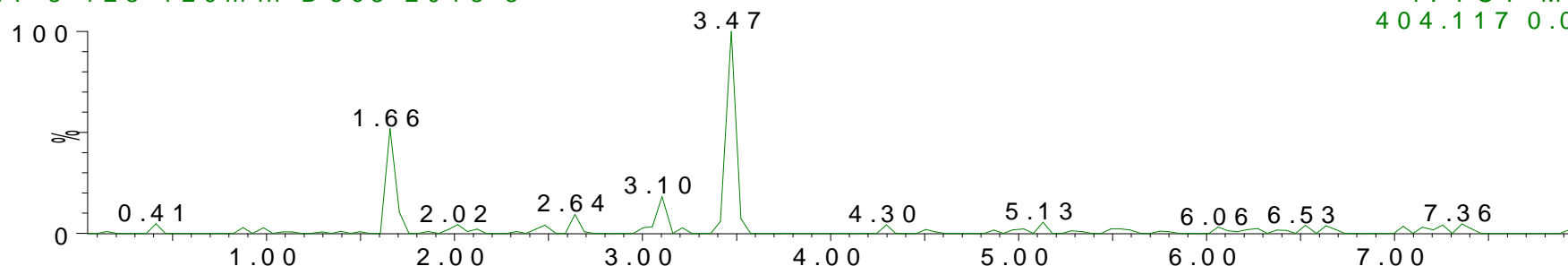
Mass spectrum of M5



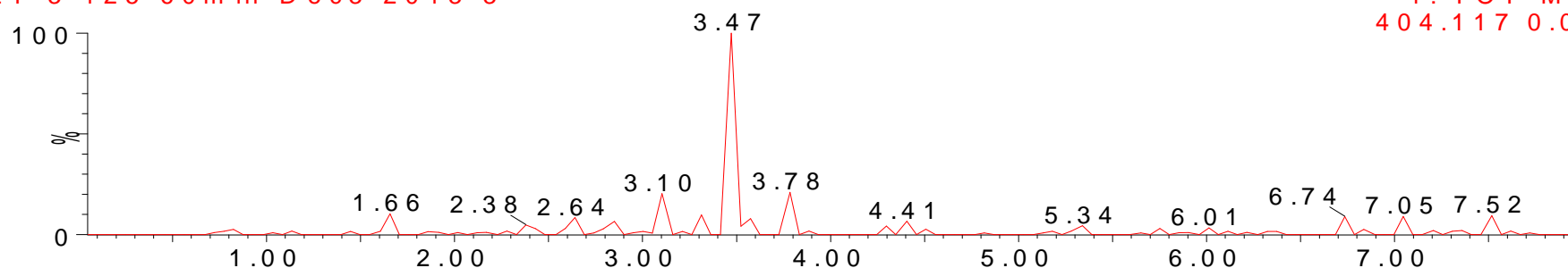
Chromatogram of M5 (extracted at 404.1168)

treated

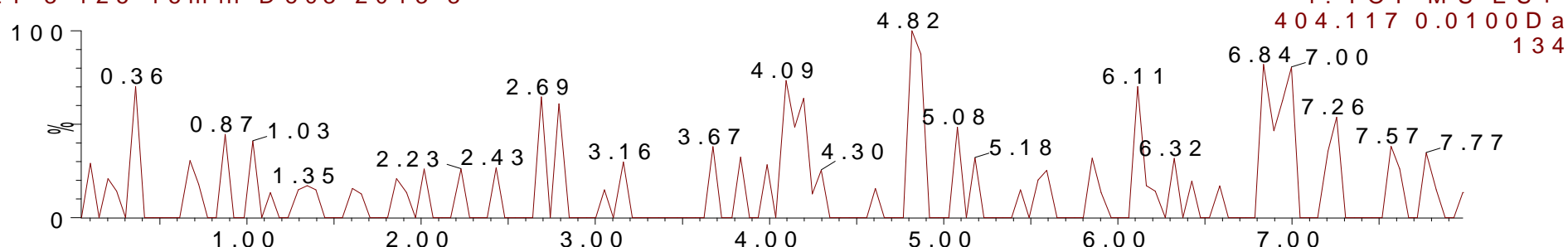
LY-3-125-120m in-Dec3-2013-3



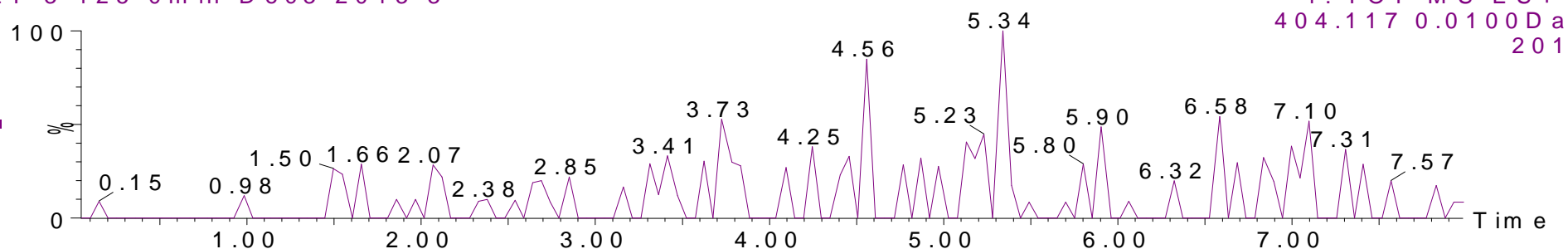
LY-3-125-60m in-Dec3-2013-3



LY-3-125-15m in-Dec3-2013-3



LY-3-125-0m in-Dec3-2013-3

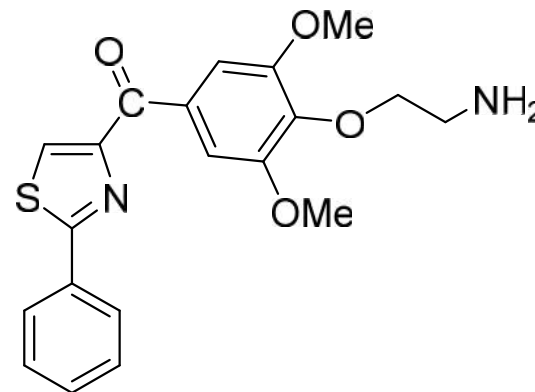
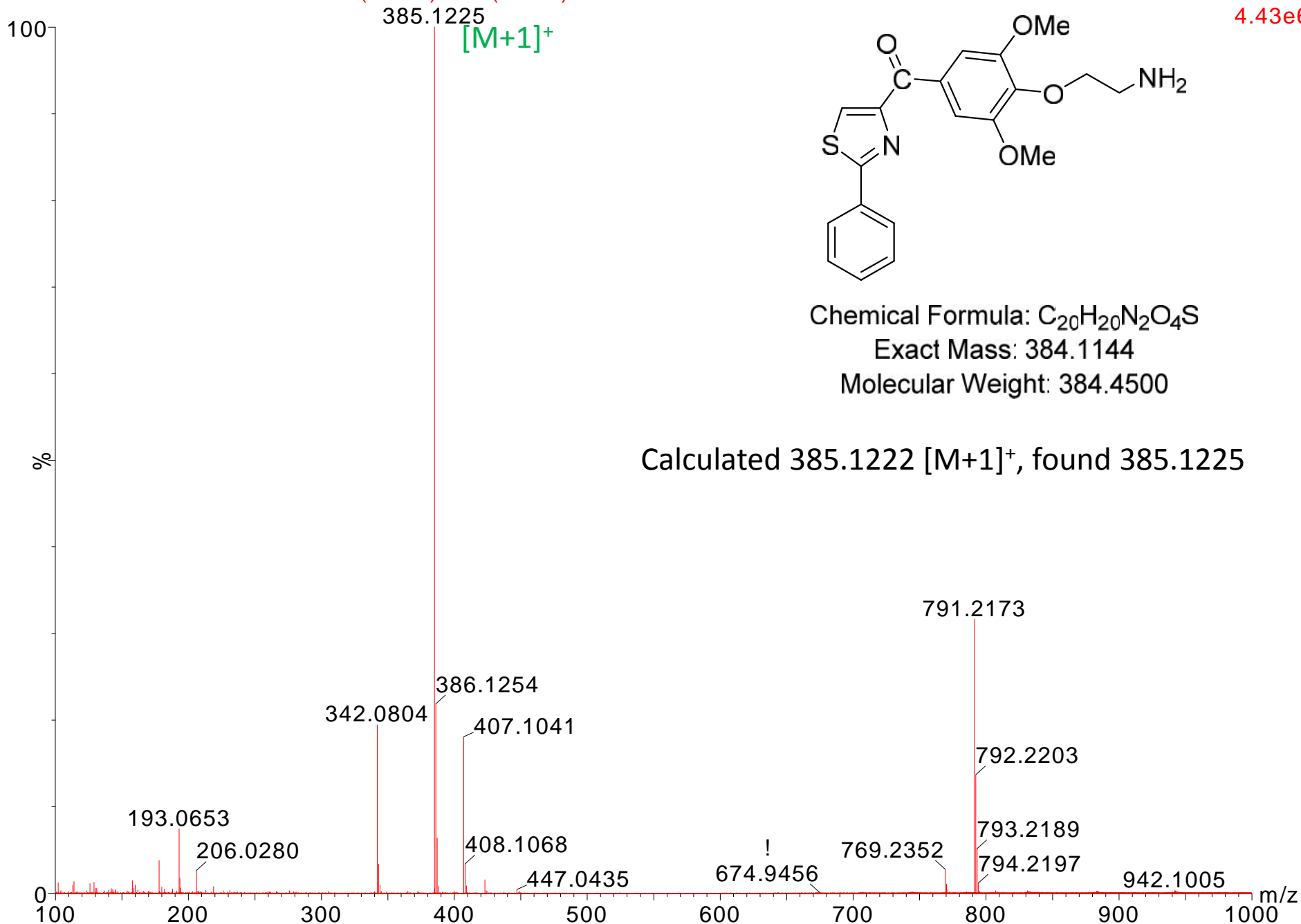


treated

Mass spectrum of 18

LY-3-128-0min-Dec3-2013-3 49 (2.539) Cm (48:49)

1: TOF MS ES+
4.43e6



Chemical Formula: C₂₀H₂₀N₂O₄S
Exact Mass: 384.1144
Molecular Weight: 384.4500

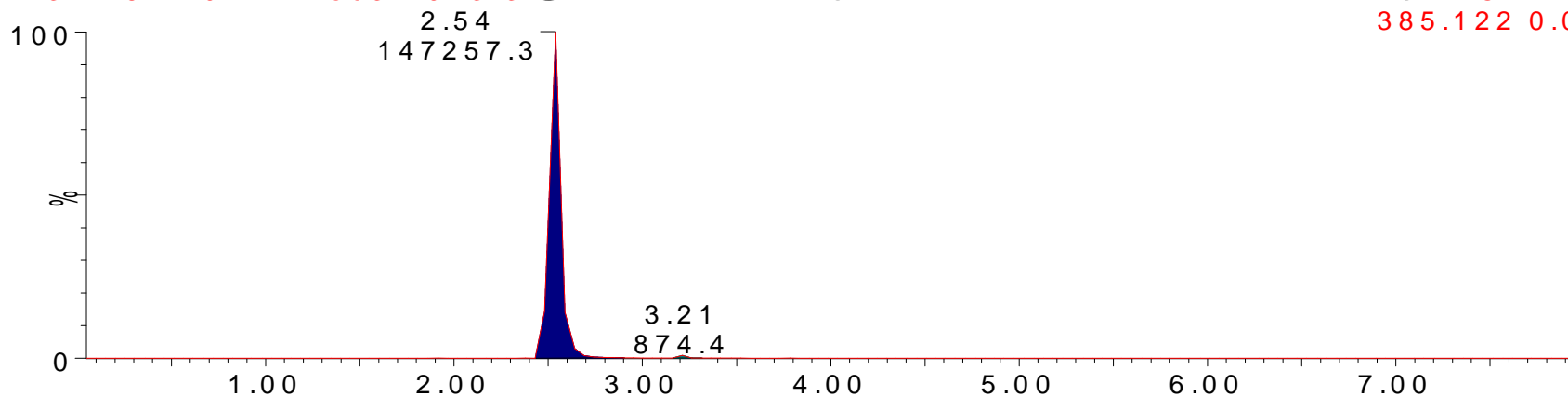
Calculated 385.1222 [M+1]⁺, found 385.1225

Chromatogram of 18 (extracted at 385.1222)

treated

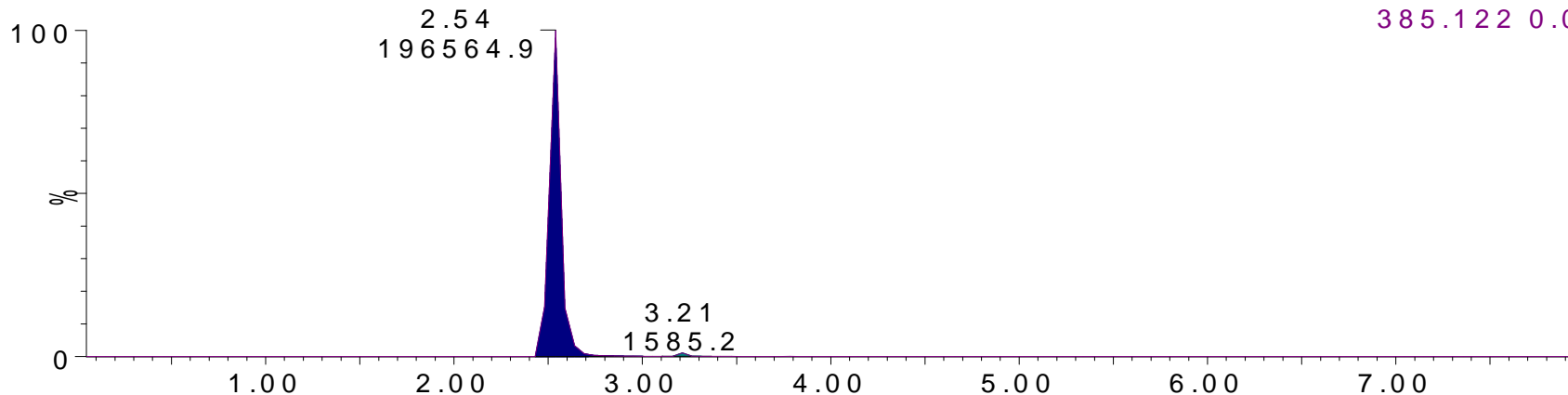
LY-3-128-120min-Dec3-2013-3

1: TOF MS ES+
385.122 0.0100Da
2.06e6
Area



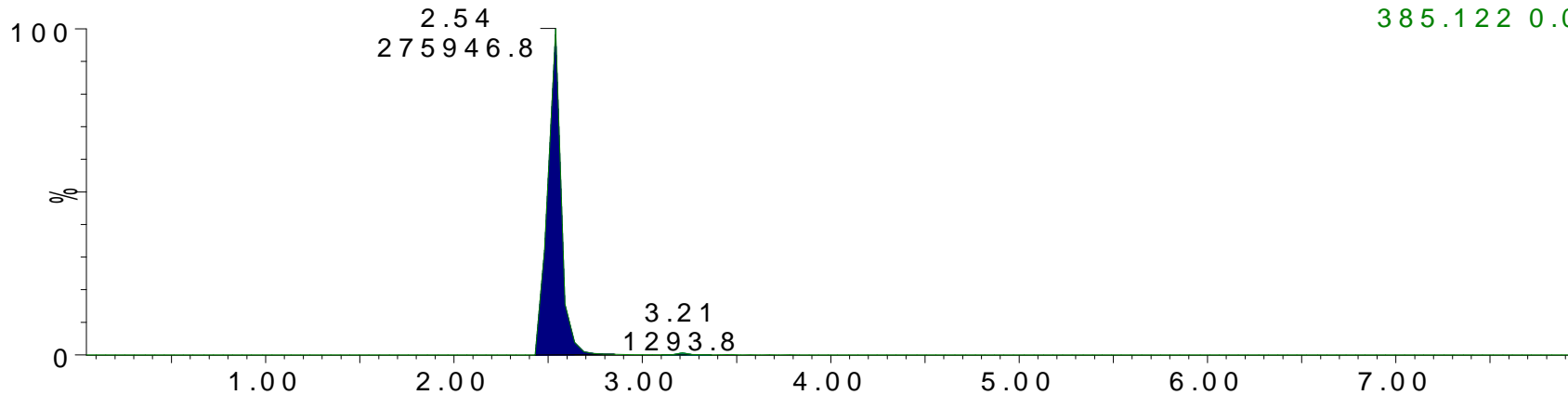
LY-3-128-60min-Dec3-2013-3

1: TOF MS ES+
385.122 0.0100Da
2.71e6
Area



LY-3-128-0min-Dec3-2013-3

1: TOF MS ES+
385.122 0.0100Da
3.35e6
Area



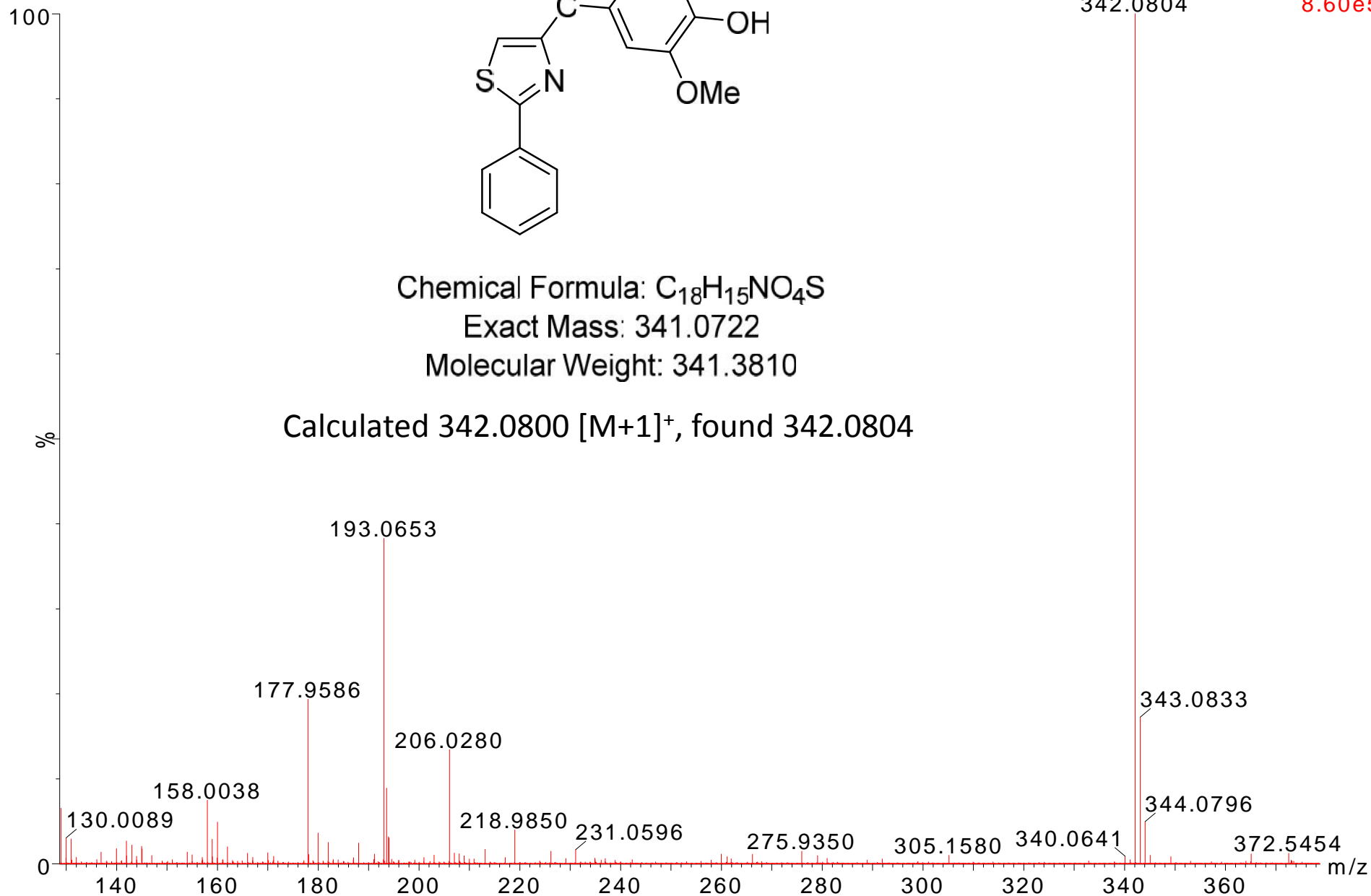
Time

Mass spectrum of M6

treated

LY-3-128-0min-Dec3-2013-3 49 (2.539) Cm (48,49)

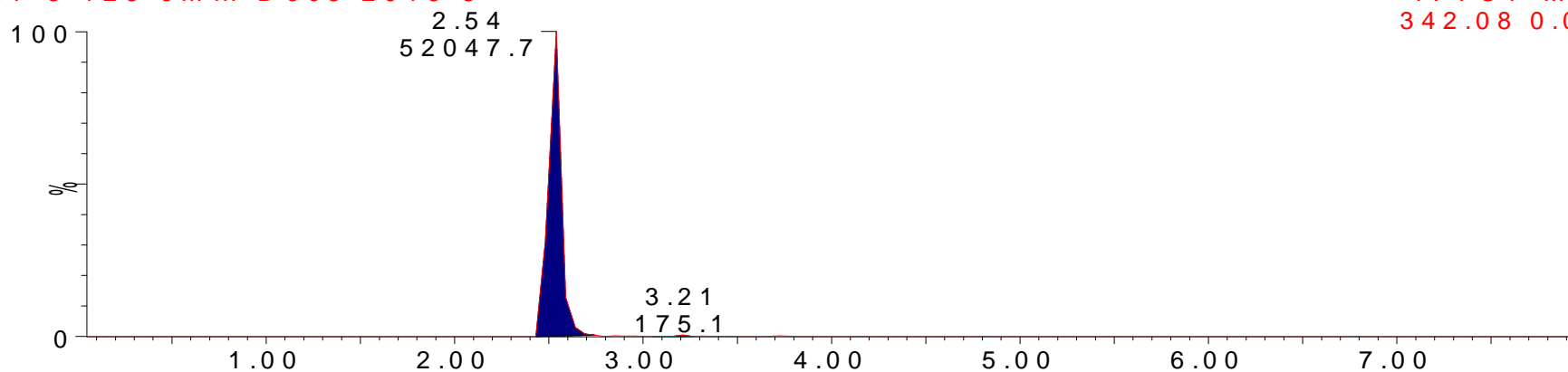
[M+1]⁺ 1: TOF MS ES+
342.0804 8.60e5



Chromatogram of M6 (extracted at 342.0800)

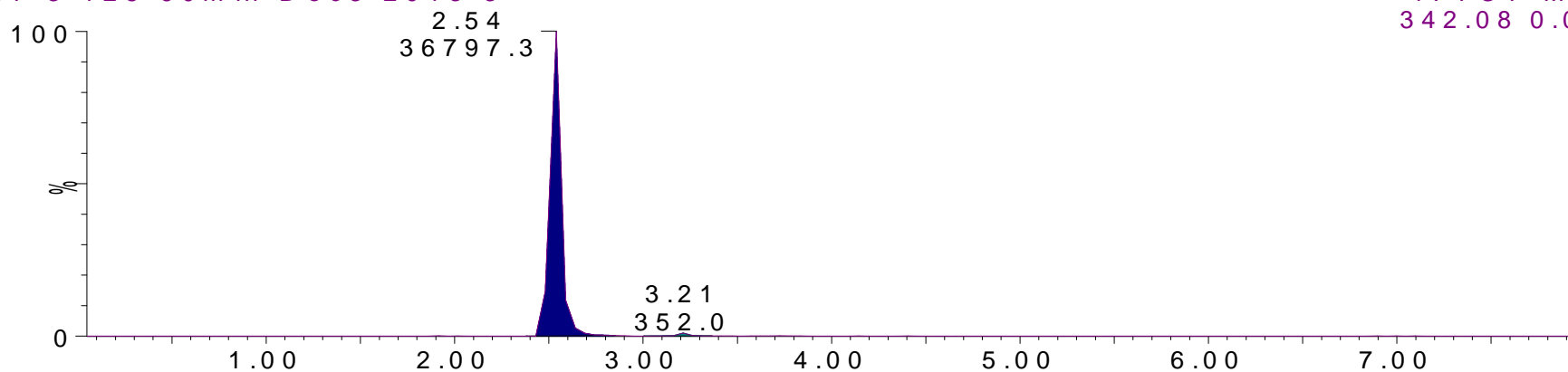
treated

LY-3-128-0 min-Dec3-2013-3



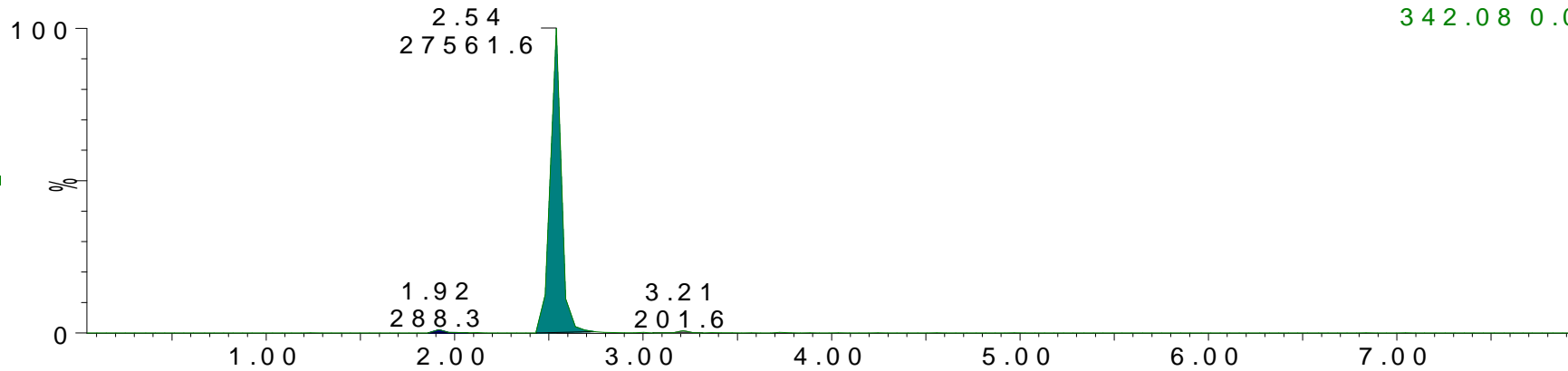
1: TOF MS ES+
342.08 0.0100Da
6.59e5
Area

LY-3-128-60 min-Dec3-2013-3



1: TOF MS ES+
342.08 0.0100Da
5.24e5
Area

LY-3-128-120 min-Dec3-2013-3



1: TOF MS ES+
342.08 0.0100Da
4.06e5
Area

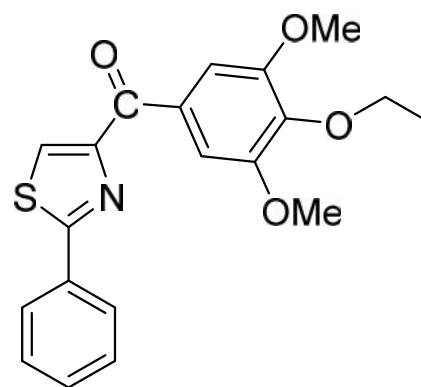
■

Time

treated

LY-3-128-120min-Dec3-2013-3 56 (2.901) Cm (56)

Mass spectrum of M7

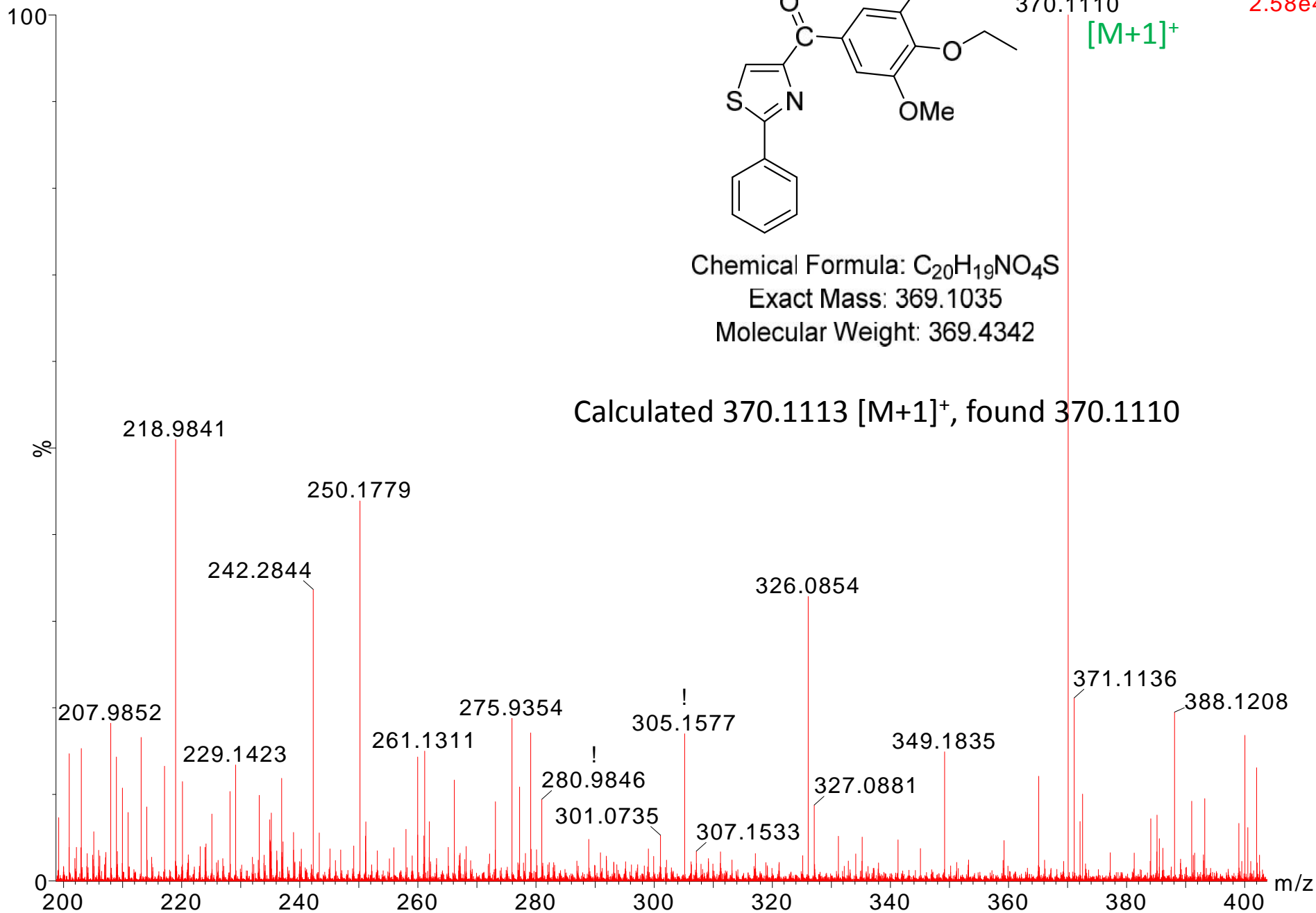


Chemical Formula: C₂₀H₁₉NO₄S

Exact Mass: 369.1035

Molecular Weight: 369.4342

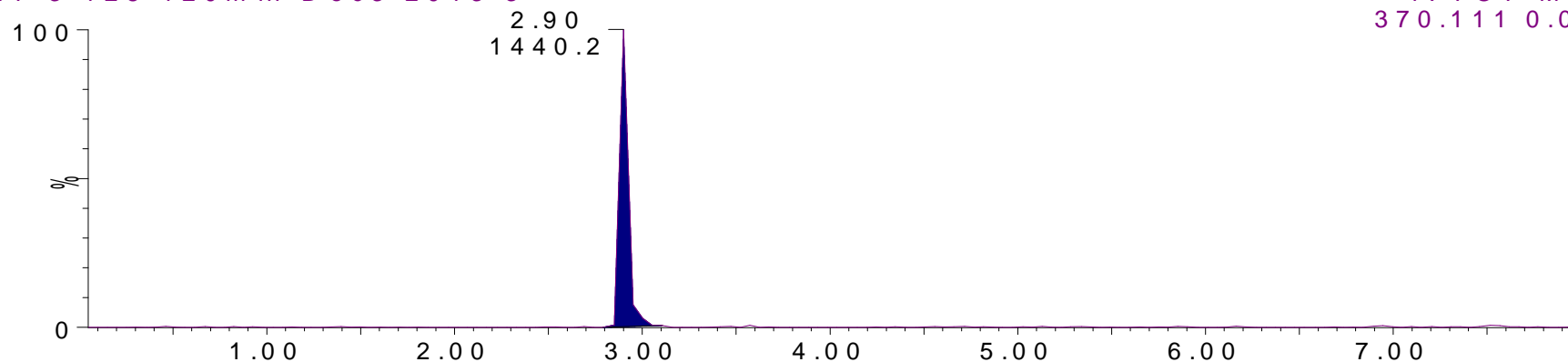
Calculated 370.1113 [M+1]⁺, found 370.1110



Chromatogram of M7 (extracted at 370.1113)

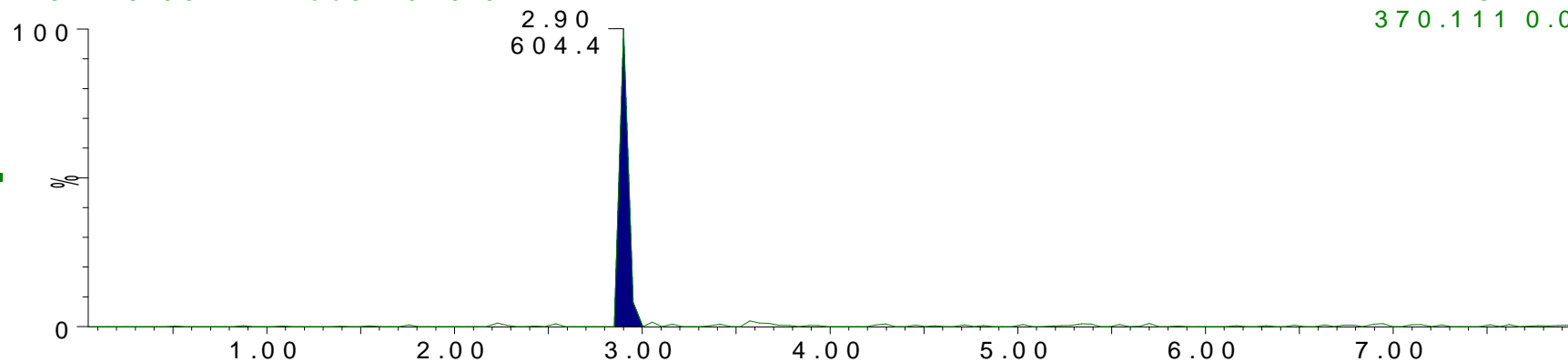
treated

LY-3-128-120m in-Dec3-2013-3



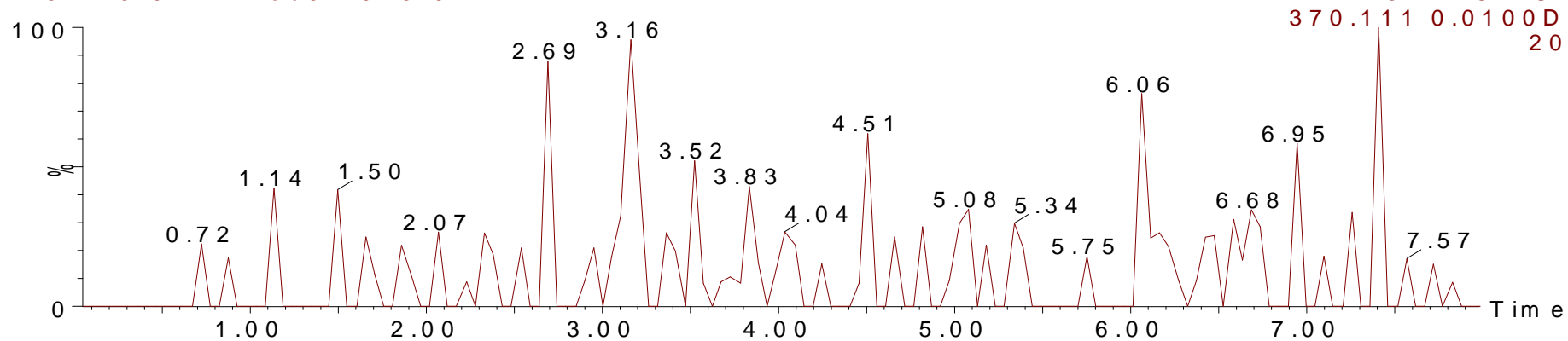
1: TOF MS ES+
370.111 0.0100Da
2.58e4
Area

LY-3-128-60m in-Dec3-2013-3



1: TOF MS ES+
370.111 0.0100Da
1.11e4
Area

LY-3-128-0m in-Dec3-2013-3

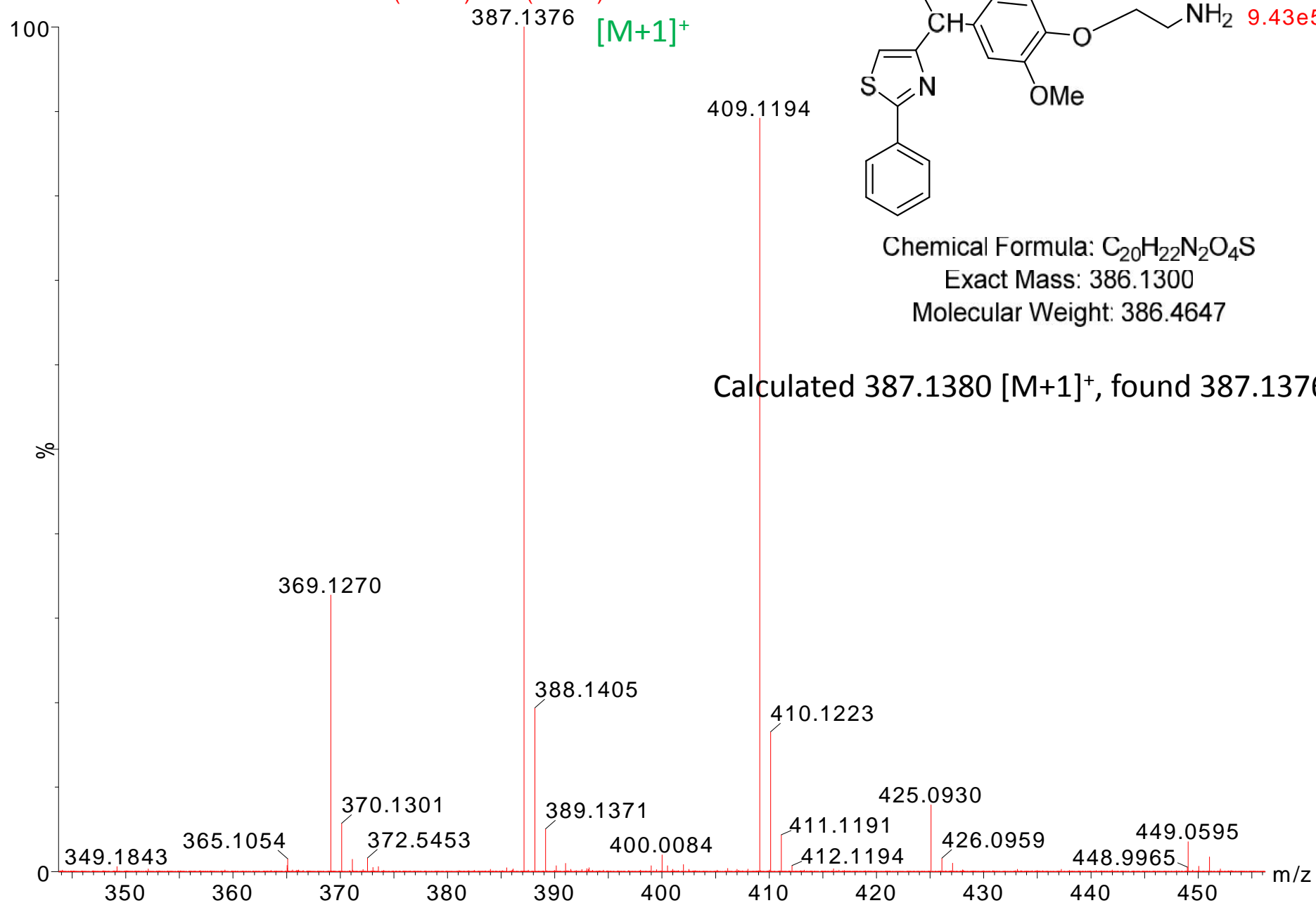


1: TOF MS ES+
370.111 0.0100Da
205

Mass spectrum of M8

treated

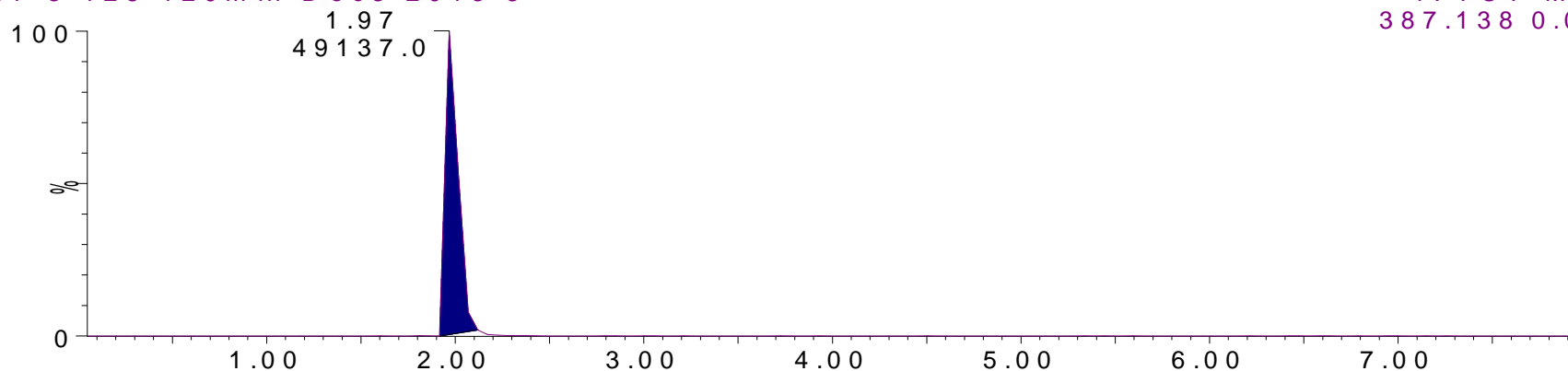
LY-3-128-120min-Dec3-2013-3 38 (1.968) Cm (38:39)



Chromatogram of M8 (extracted at 387.1380)

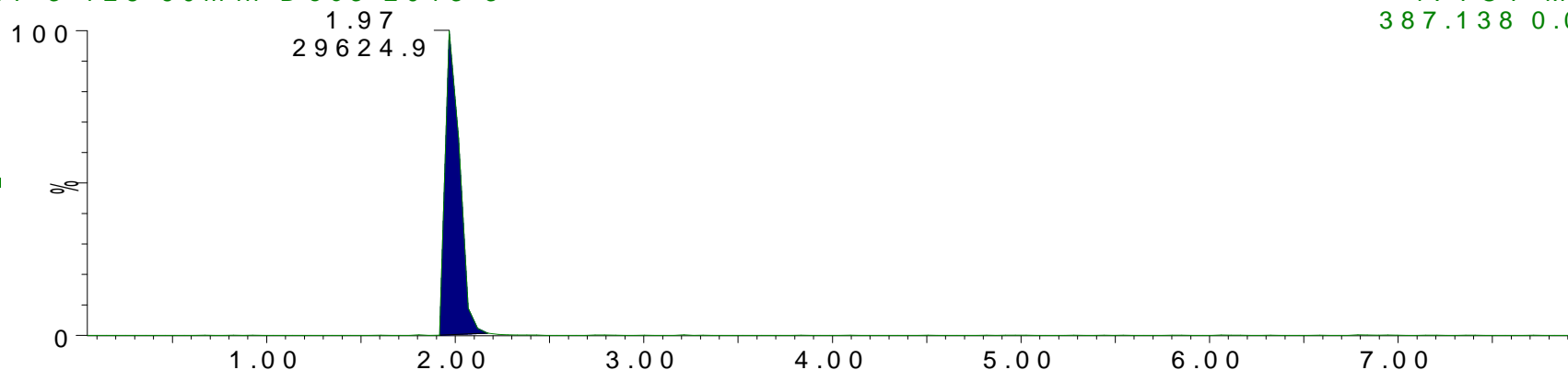
treated

LY-3-128-120m in-Dec3-2013-3



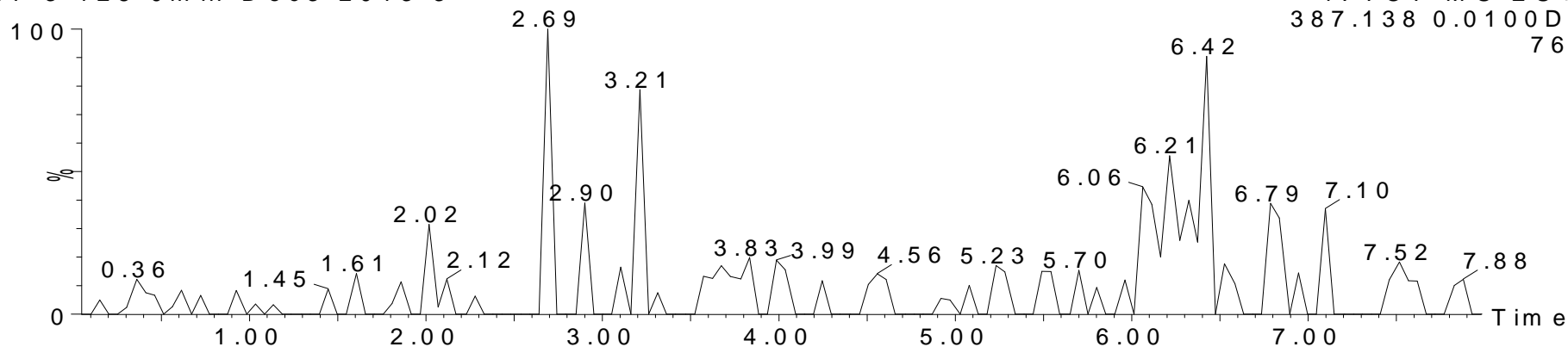
1: TOF MS ES+
387.138 0.0100Da
6.19e5
Area

LY-3-128-60m in-Dec3-2013-3



1: TOF MS ES+
387.138 0.0100Da
3.36e5
Area

LY-3-128-0m in-Dec3-2013-3



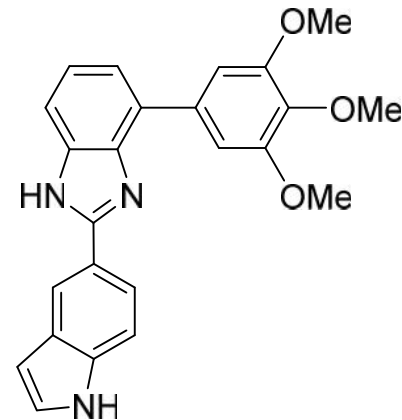
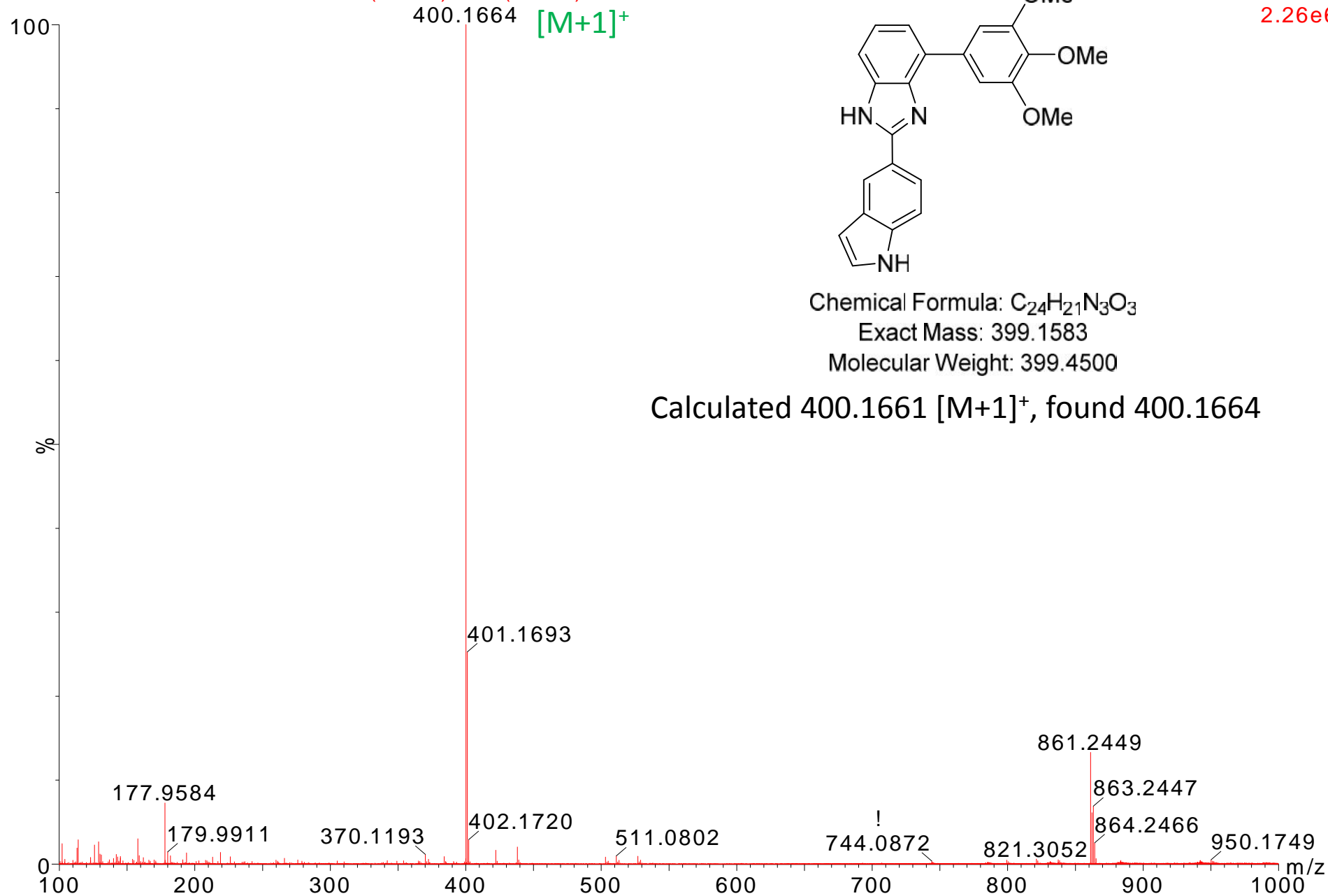
1: TOF MS ES+
387.138 0.0100Da
762

Mass spectrum of 4

treated

LY-3-286-0min-Dec3-2013-3 49 (2.539) Cm (49:50)

1: TOF MS ES+
2.26e6



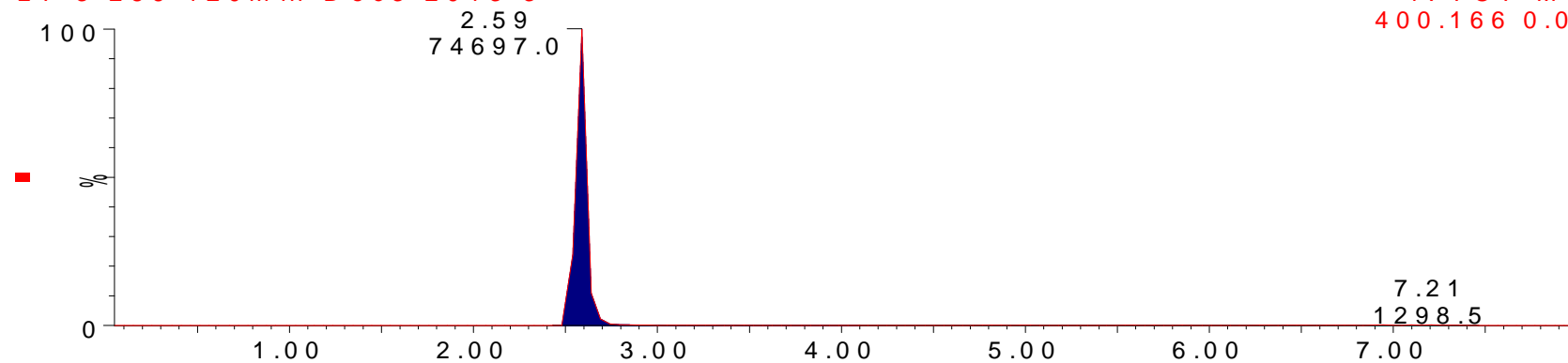
Chemical Formula: C₂₄H₂₁N₃O₃
Exact Mass: 399.1583
Molecular Weight: 399.4500

Calculated 400.1661 [M+1]⁺, found 400.1664

Chromatogram of 4 (extracted at 400.1661)

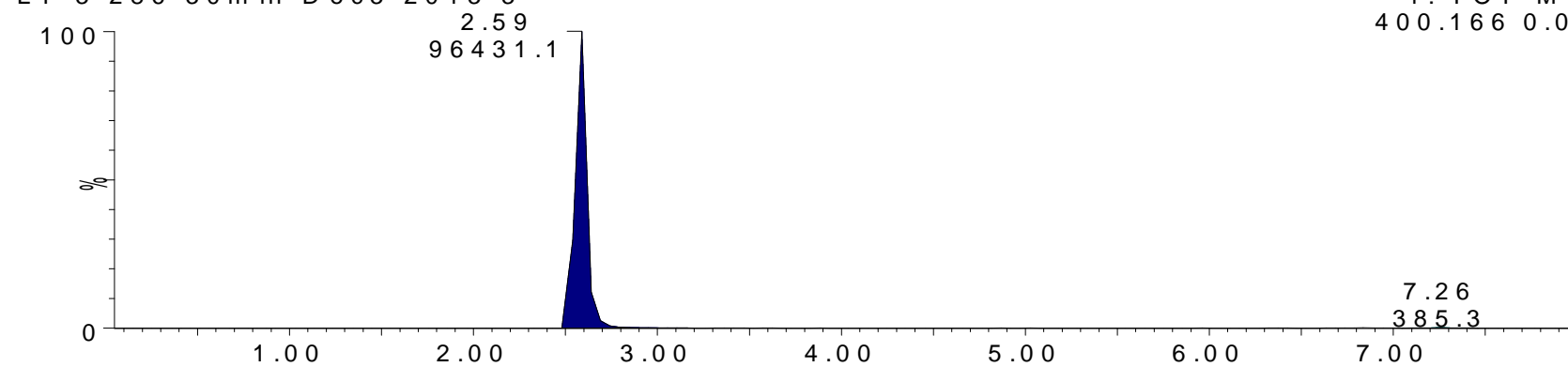
treated

LY-3-286-120min-Dec3-2013-3



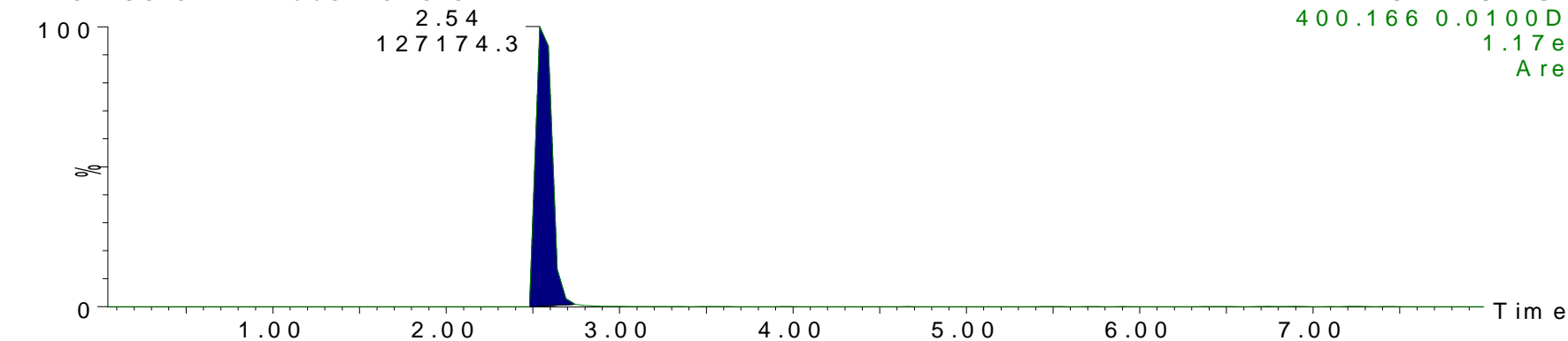
1: TOF MS ES+
400.166 0.0100Da
1.05e6
Area

LY-3-286-30min-Dec3-2013-3



1: TOF MS ES+
400.166 0.0100Da
1.29e6
Area

LY-3-286-0min-Dec3-2013-3



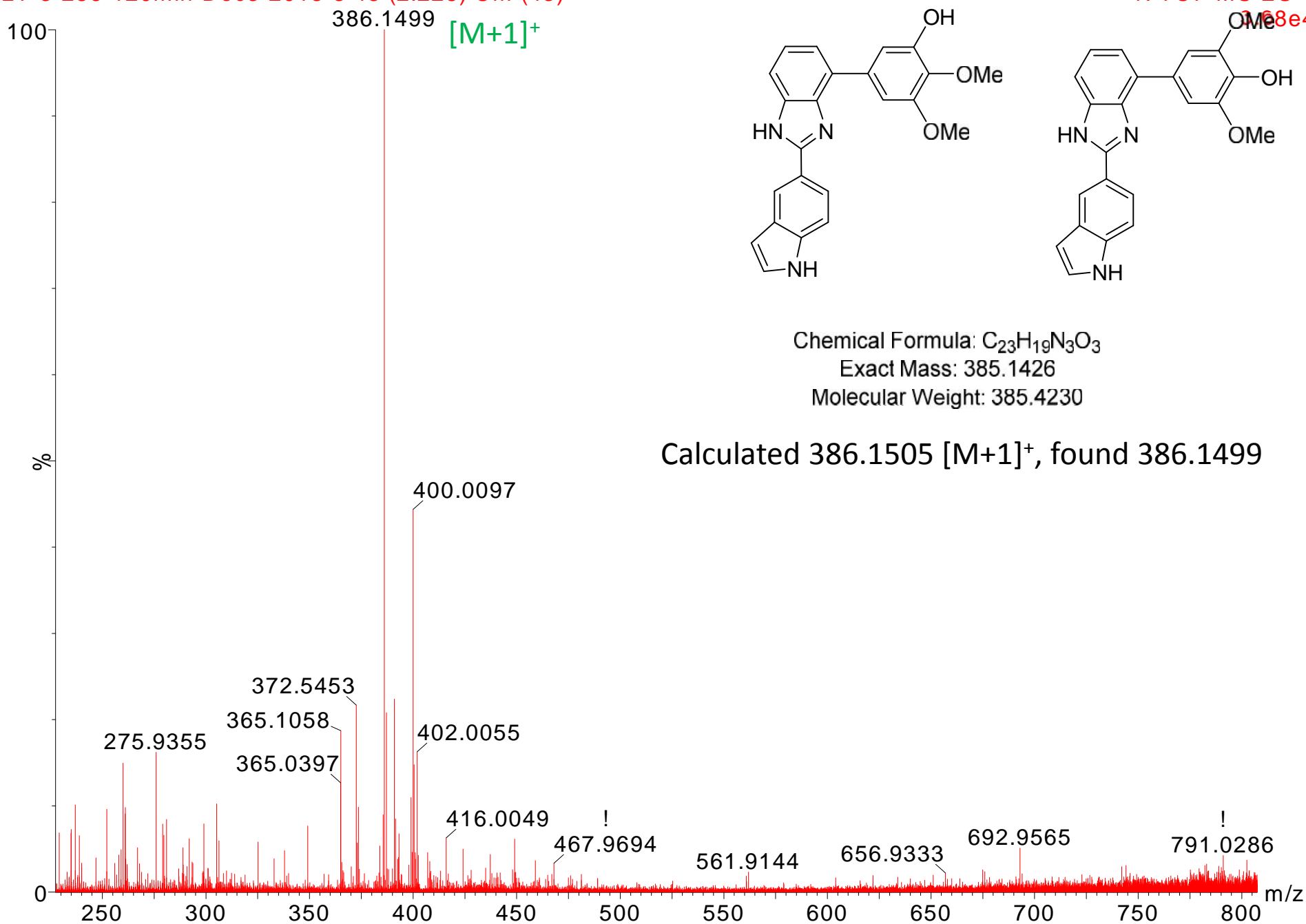
1: TOF MS ES+
400.166 0.0100Da
1.17e6
Area

treated

LY-3-286-120min-Dec3-2013-3 43 (2.228) Cm (43)

Mass spectrum of M9

1: TOF MS ES+
1.68e4

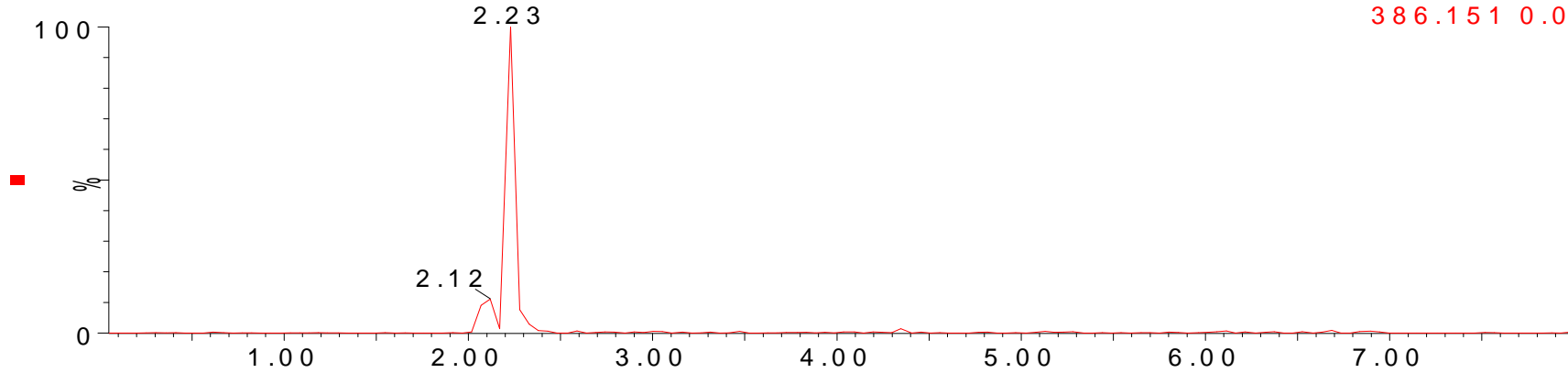


Chromatogram of M9 (extracted at 386.1505)

treated

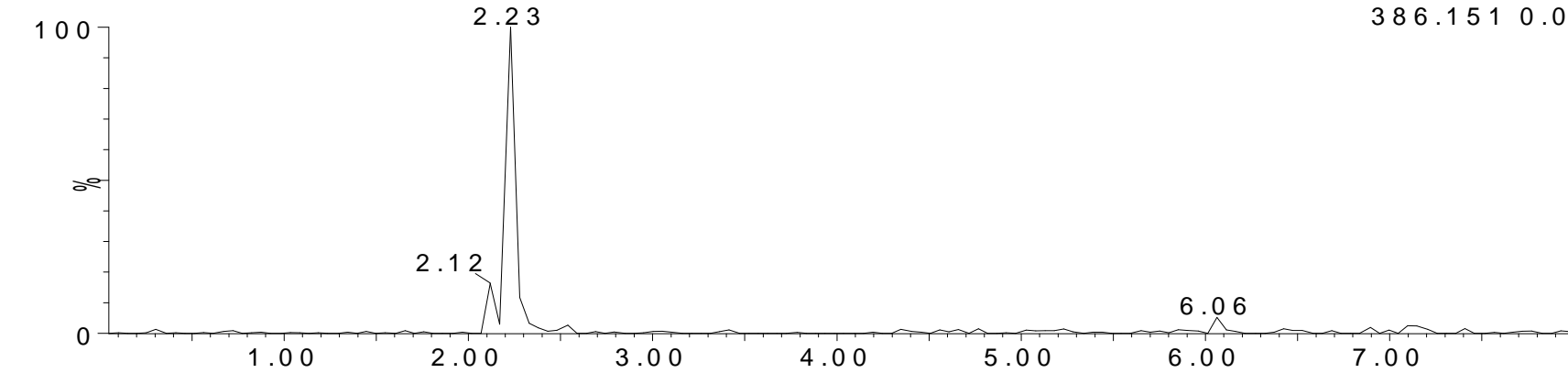
LY-3-286-120m in-Dec3-2013-3

1: TOF MS ES+
386.151 0.0100Da
3.68e4



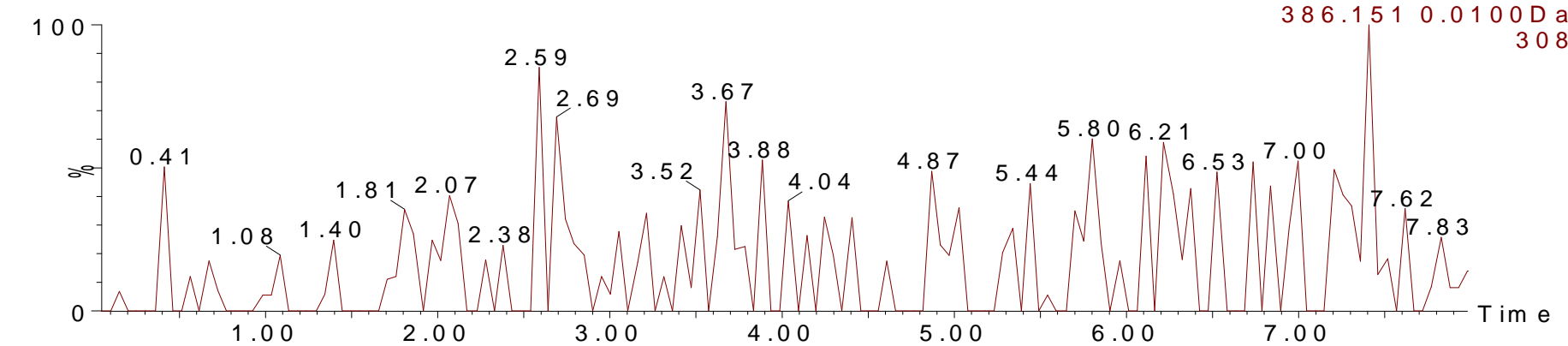
LY-3-286-30m in-Dec3-2013-3

1: TOF MS ES+
386.151 0.0100Da
1.01e4



LY-3-286-0m in-Dec3-2013-3

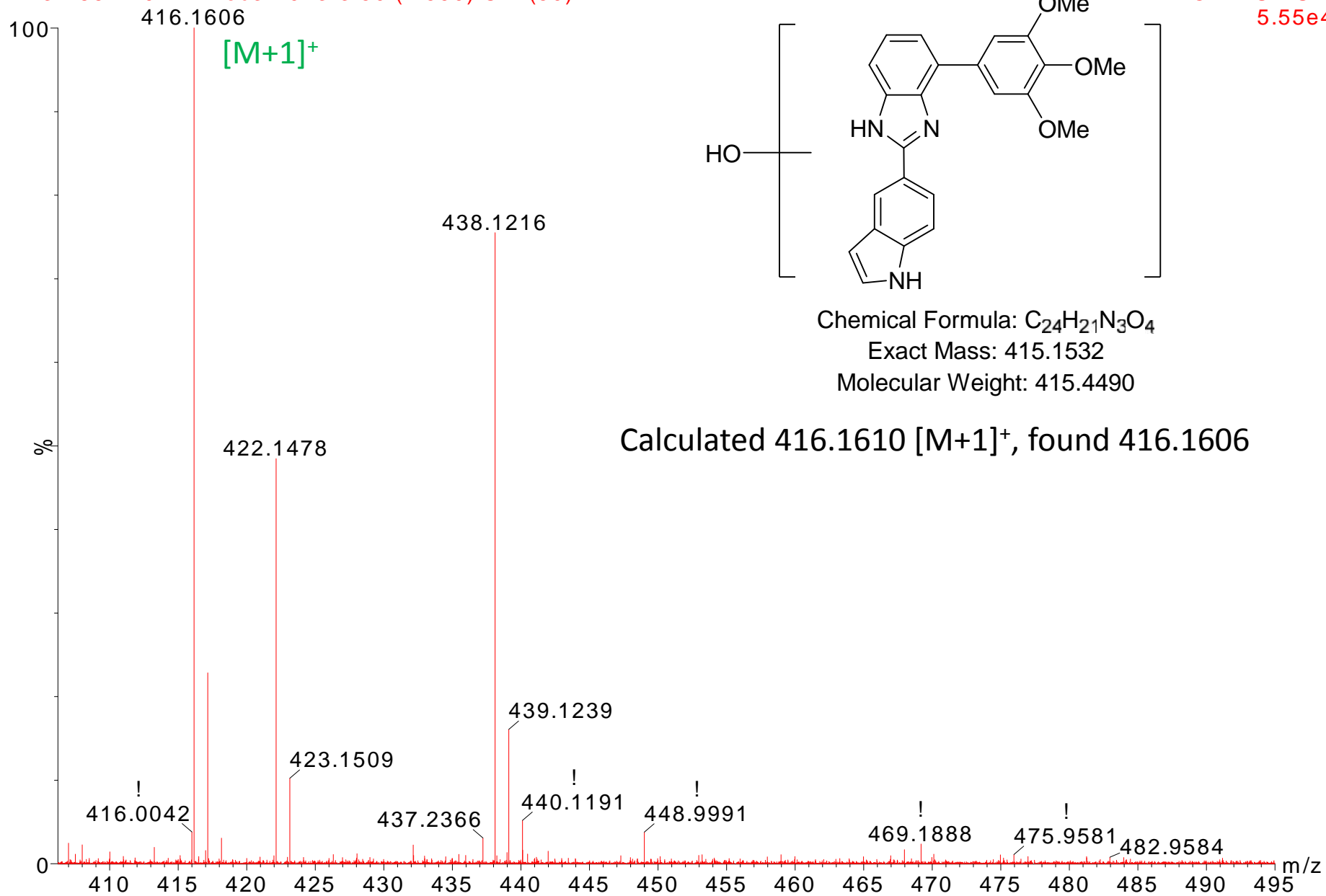
1: TOF MS ES+
386.151 0.0100Da
308



Mass spectrum of M10

treated

LY-3-286-120min-Dec3-2013-3 50 (2.590) Cm (50)

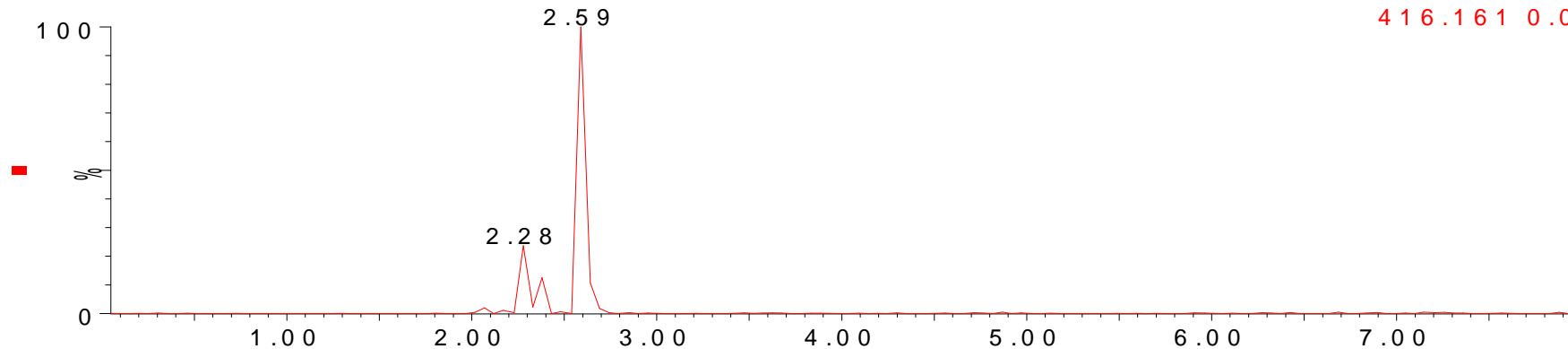


Chromatogram of M10 (extracted at 416.1610)

treated

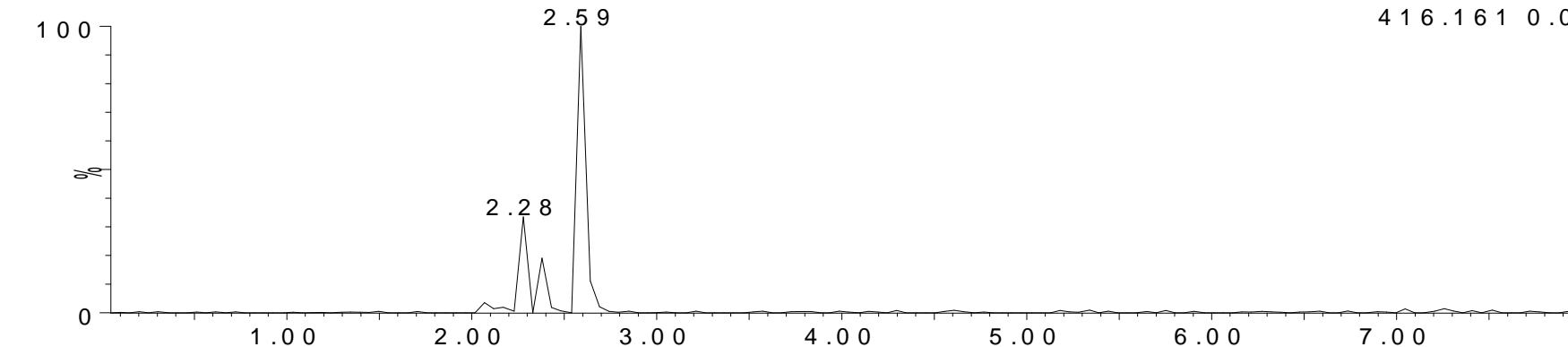
LY-3-286-120 min-Dec3-2013-3

1: TOF MS ES+
416.161 0.0100 Da
5.55e4



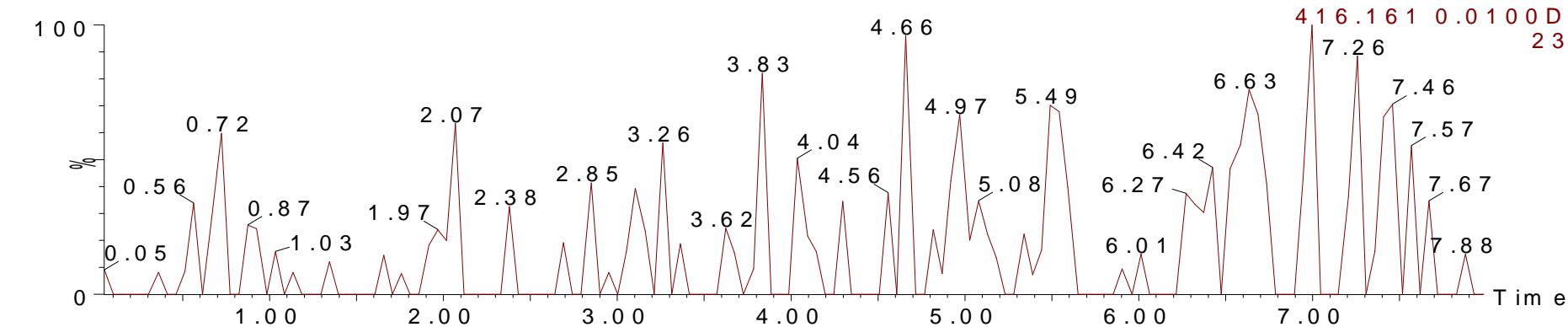
LY-3-286-30 min-Dec3-2013-3

1: TOF MS ES+
416.161 0.0100 Da
1.90e4



LY-3-286-0 min-Dec3-2013-3

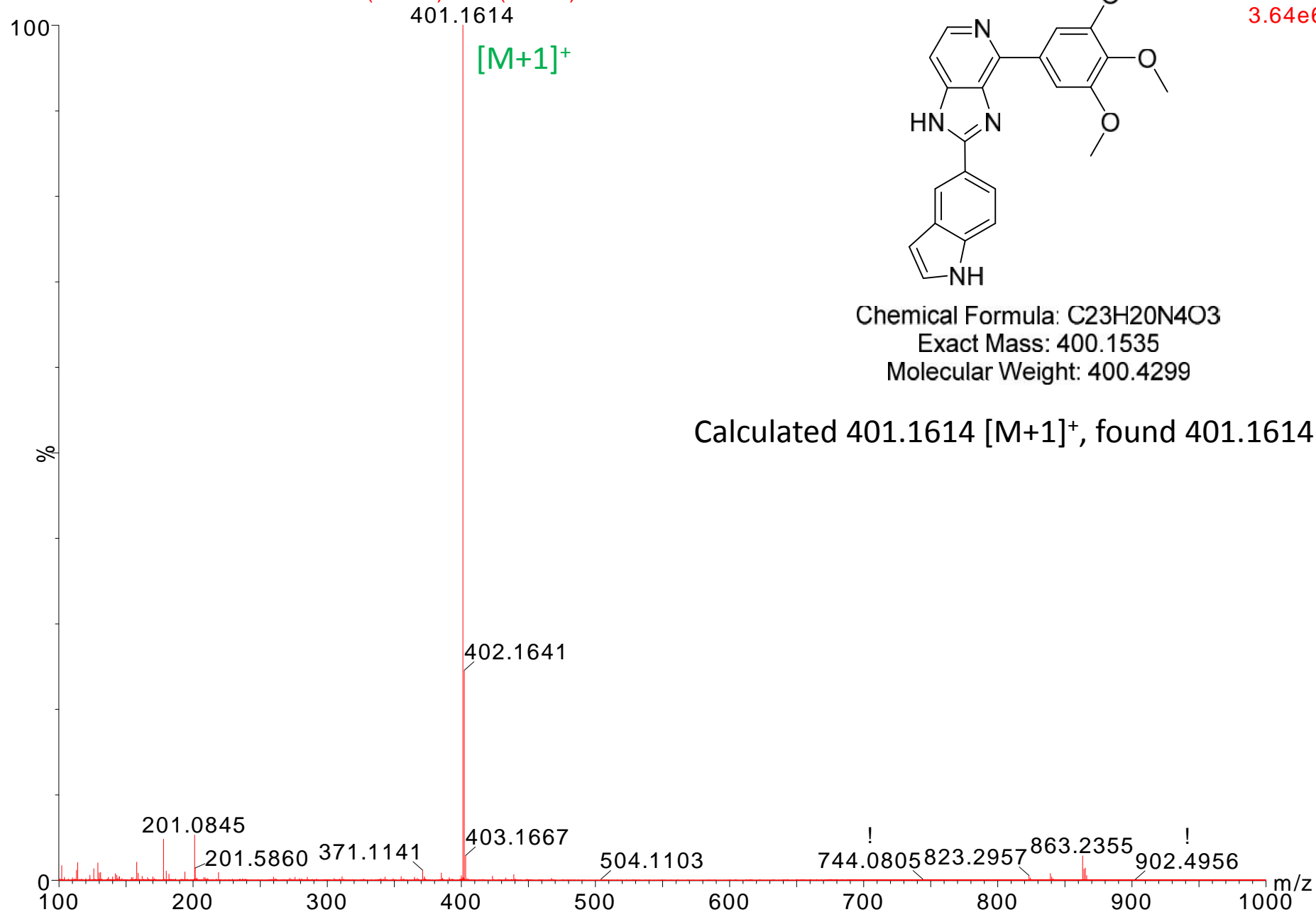
1: TOF MS ES+
416.161 0.0100 Da
234



Mass spectrum of 7

treated

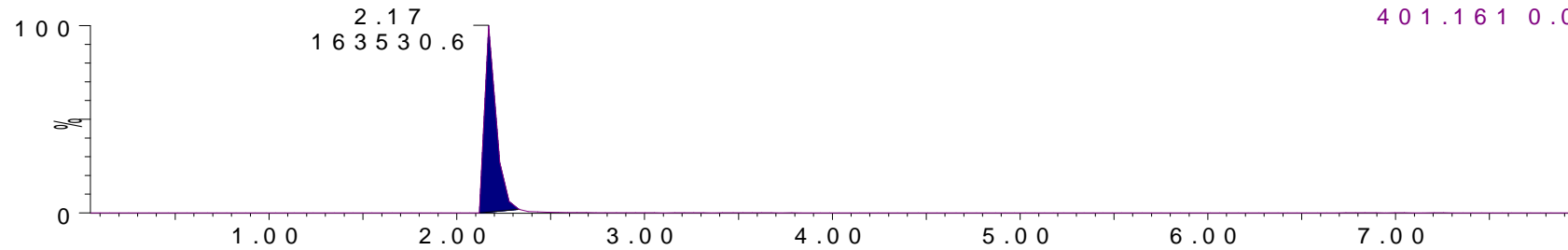
LY-3-296-0min-Dec3-2013-3 42 (2.170) Cm (42:43)



Chromatogram of 7 (extracted at 401.1614)

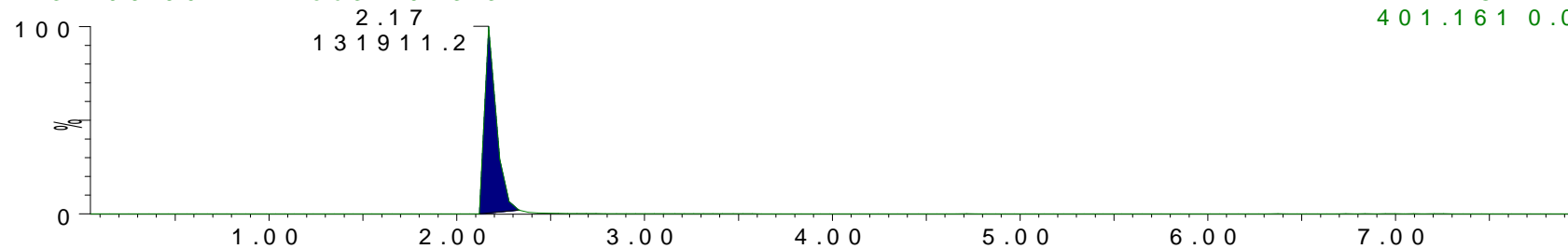
treated

LY-3-296-120 min-Dec3-2013-3



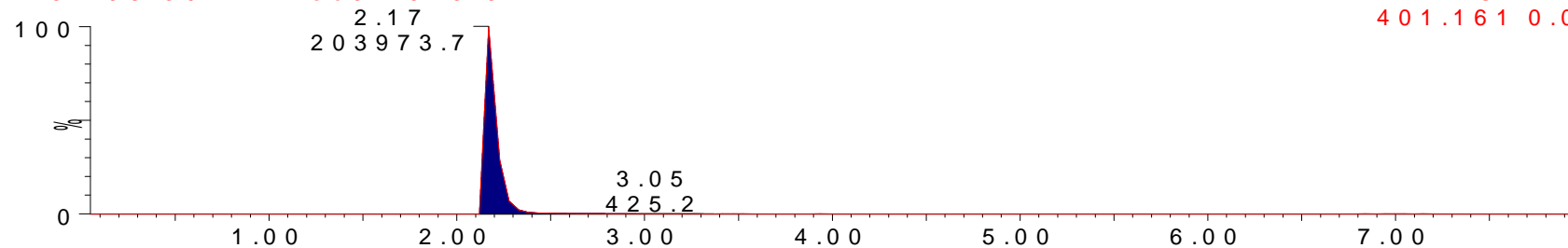
1: TOF MS ES+
401.161 0.0100 Da
2.31e6
Area

LY-3-296-60 min-Dec3-2013-3



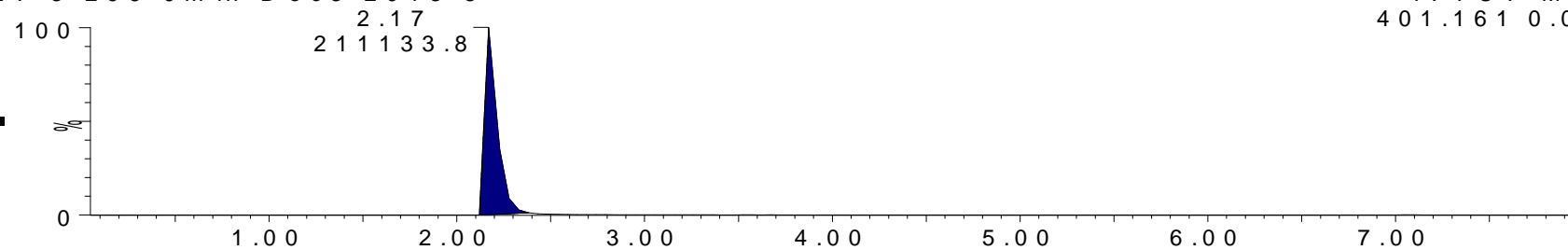
1: TOF MS ES+
401.161 0.0100 Da
1.83e6
Area

LY-3-296-30 min-Dec3-2013-3



1: TOF MS ES+
401.161 0.0100 Da
2.68e6
Area

LY-3-296-0 min-Dec3-2013-3



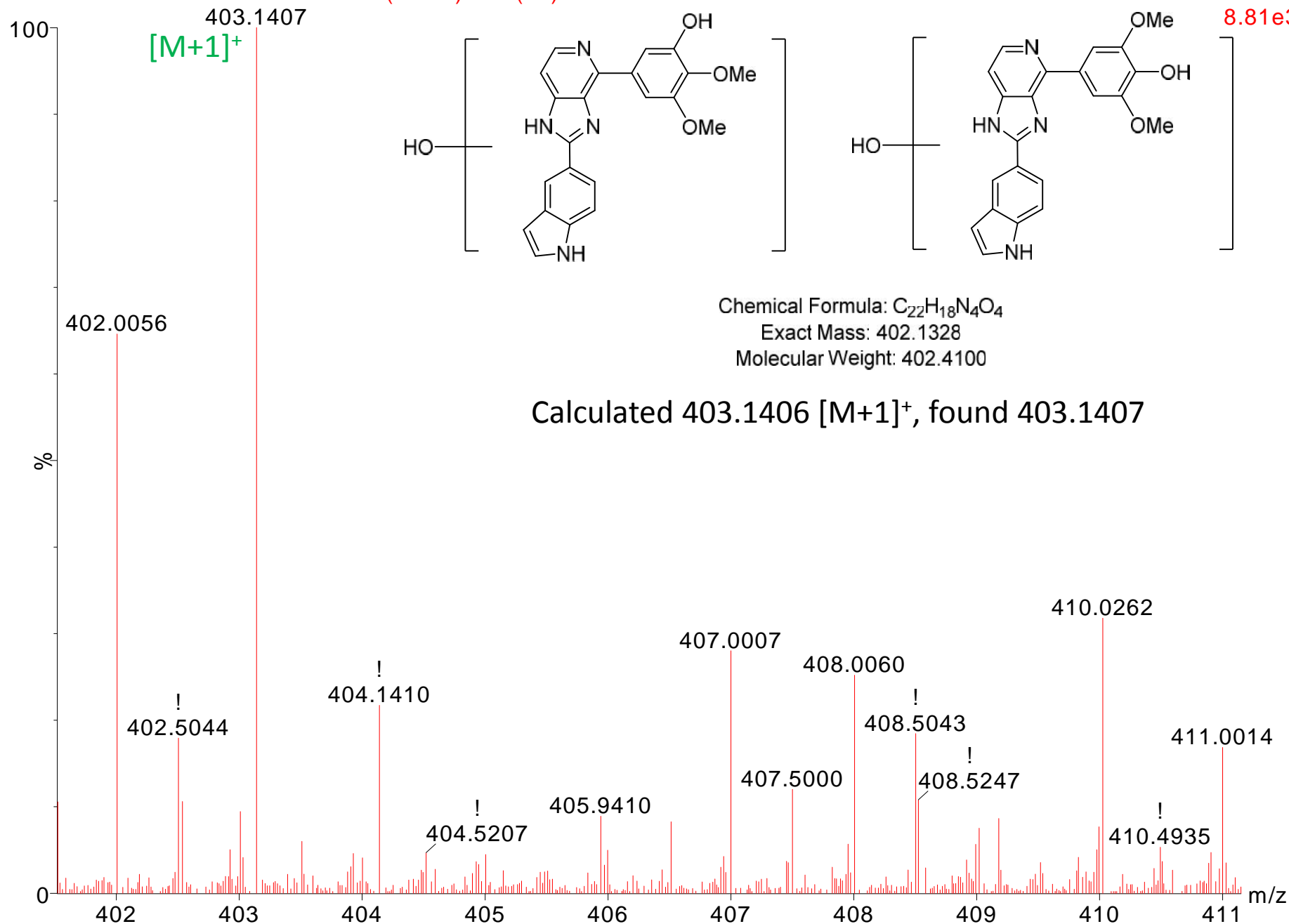
1: TOF MS ES+
401.161 0.0100 Da
2.70e6
Area

Mass spectrum of M11

treated

LY-3-296-120min-Dec3-2013-3 18 (0.925) Cm (18)

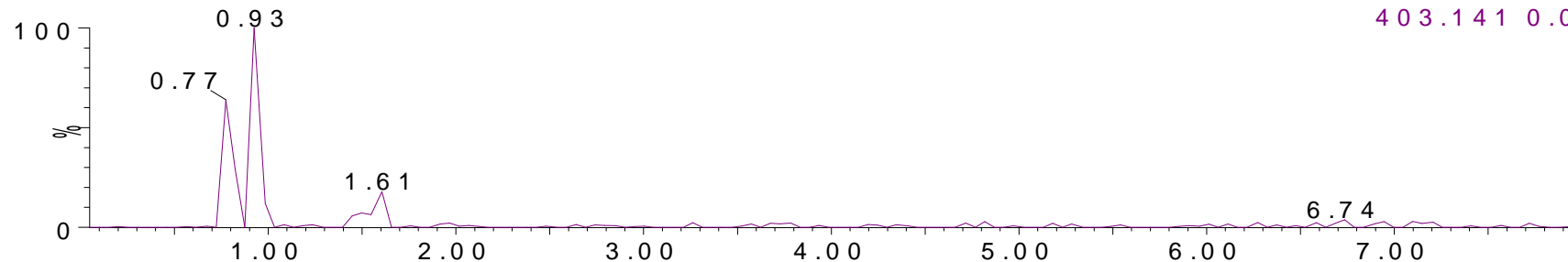
1: TOF MS ES+
8.81e3



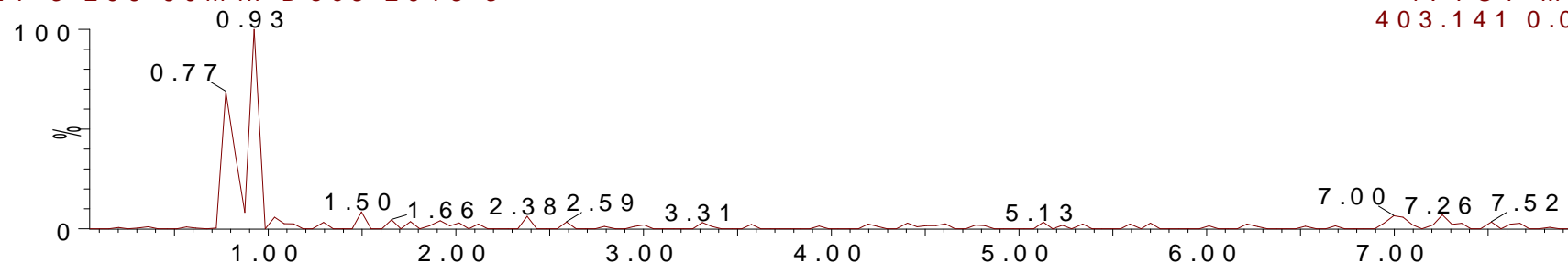
Chromatogram of M11 (extracted at 403.1406)

treated

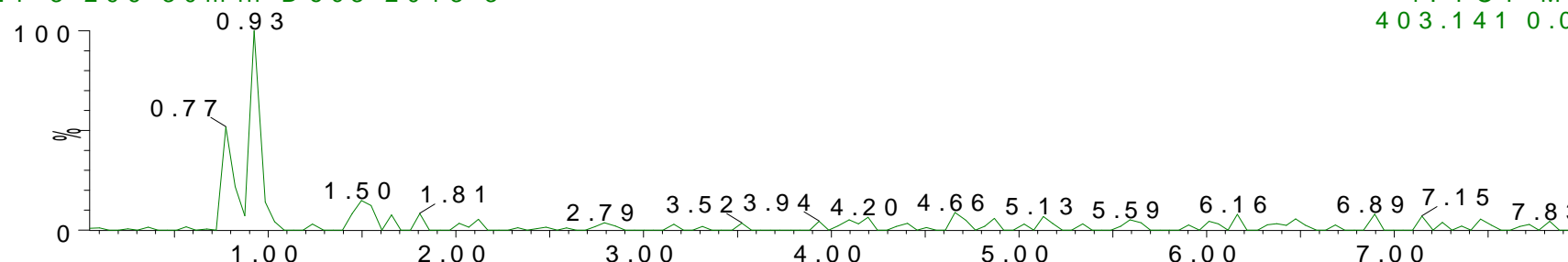
LY-3-296-120min-Dec3-2013-3



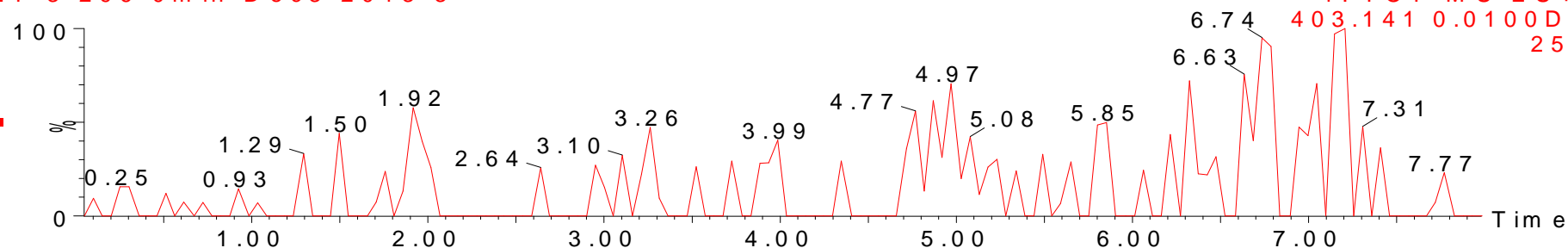
LY-3-296-60min-Dec3-2013-3



LY-3-296-30min-Dec3-2013-3



LY-3-296-0min-Dec3-2013-3



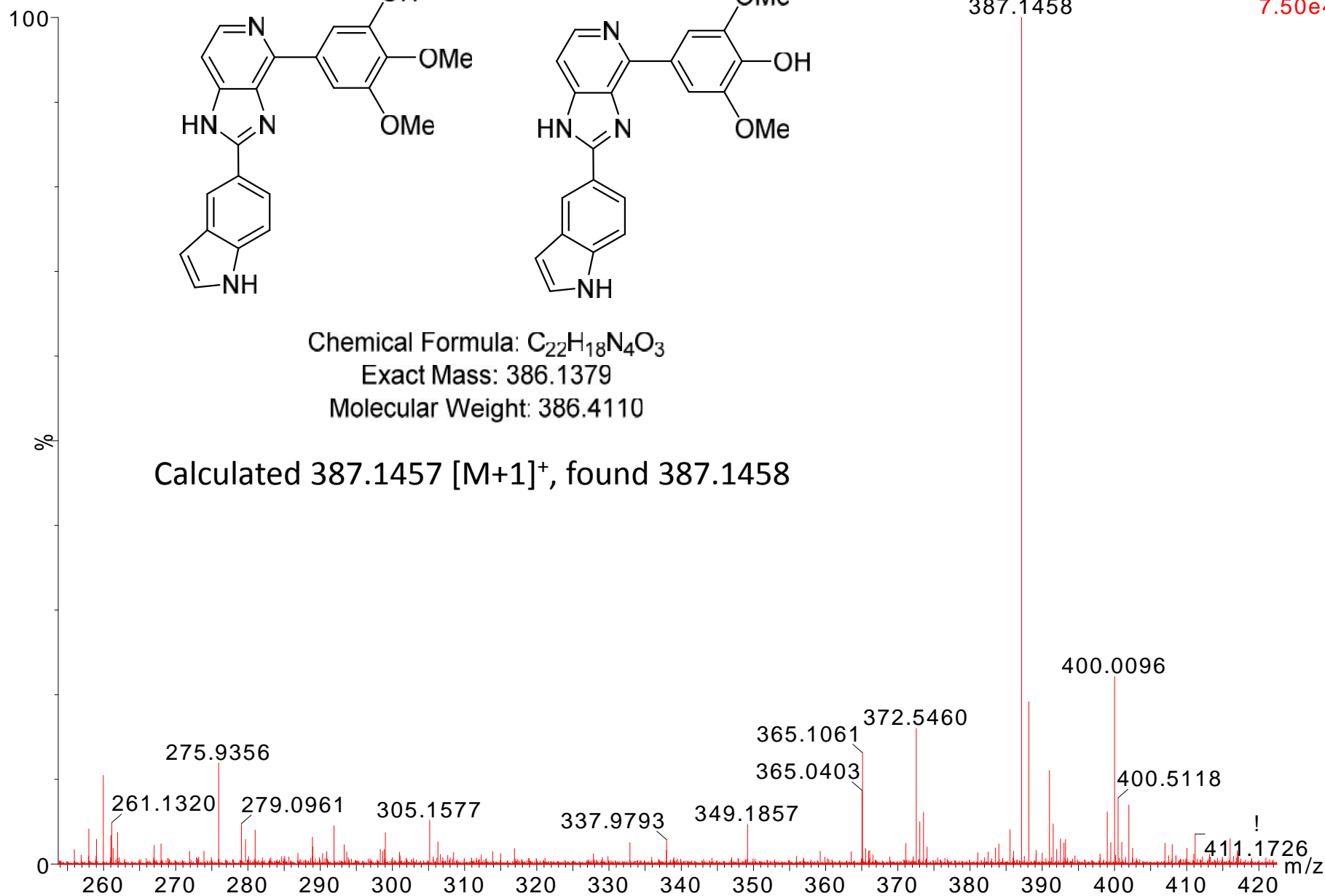
Mass spectrum of M12

treated

LY-3-296-120min-Dec3-2013-3 32 (1.656) Cm (32)

$[M+1]^+$
387.1458

1: TOF MS ES+
7.50e4

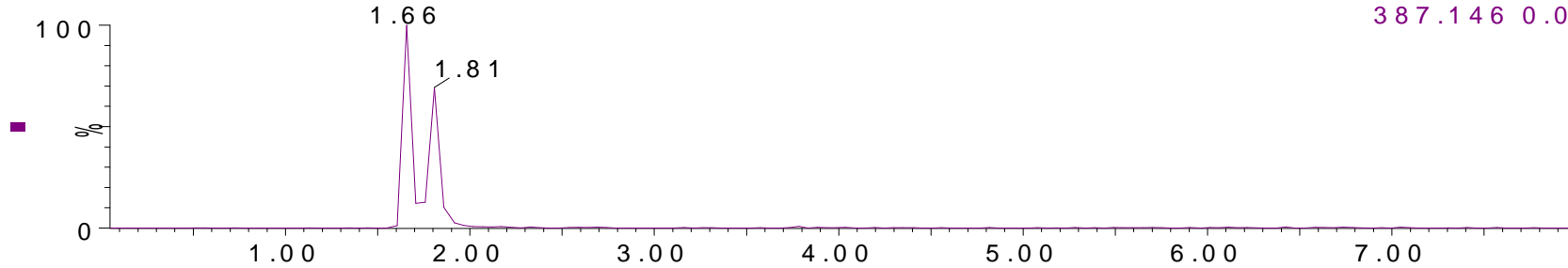


Chromatogram of M12 (extracted at 387.1457)

treated

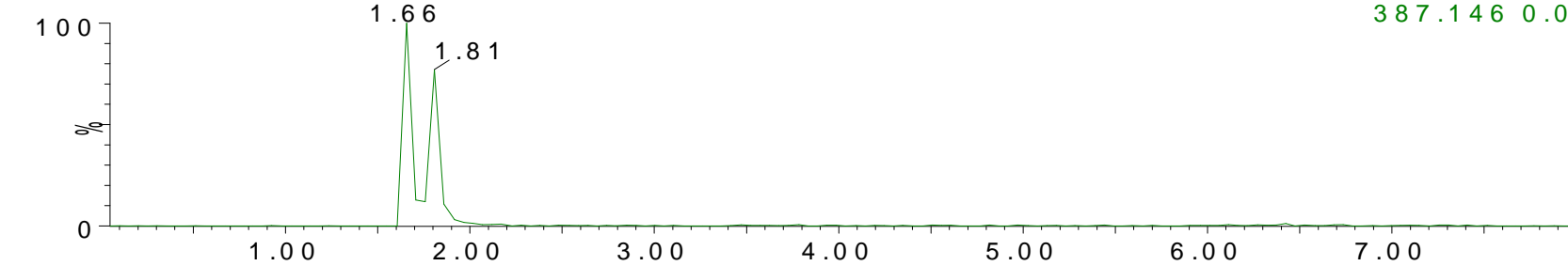
LY-3-296-120m in-Dec3-2013-3

1: TOF MS ES+
387.146 0.0100Da
7.50e4



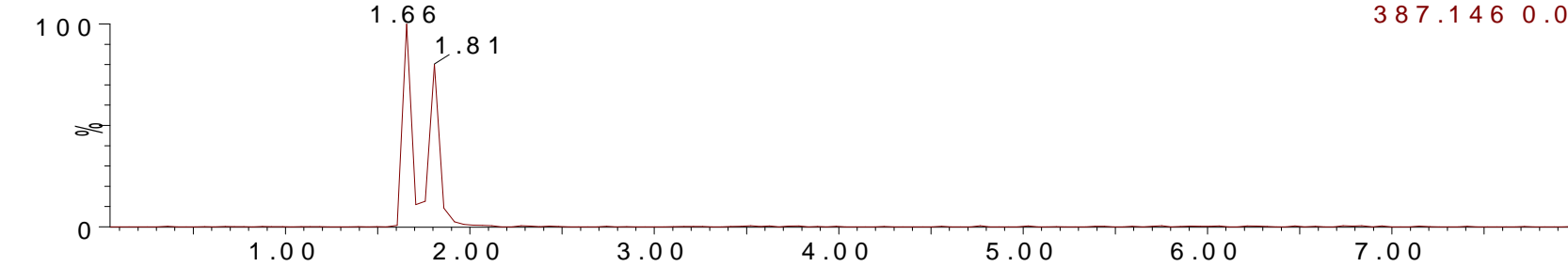
LY-3-296-60m in-Dec3-2013-3

1: TOF MS ES+
387.146 0.0100Da
5.03e4



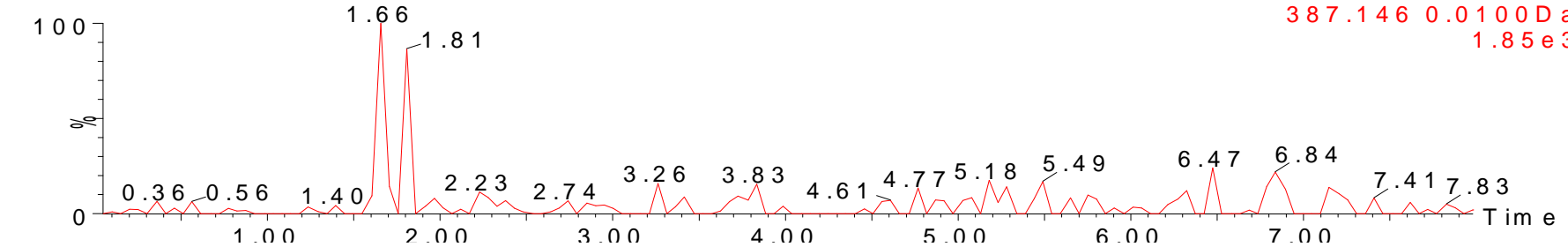
LY-3-296-30m in-Dec3-2013-3

1: TOF MS ES+
387.146 0.0100Da
5.46e4



LY-3-296-0m in-Dec3-2013-3

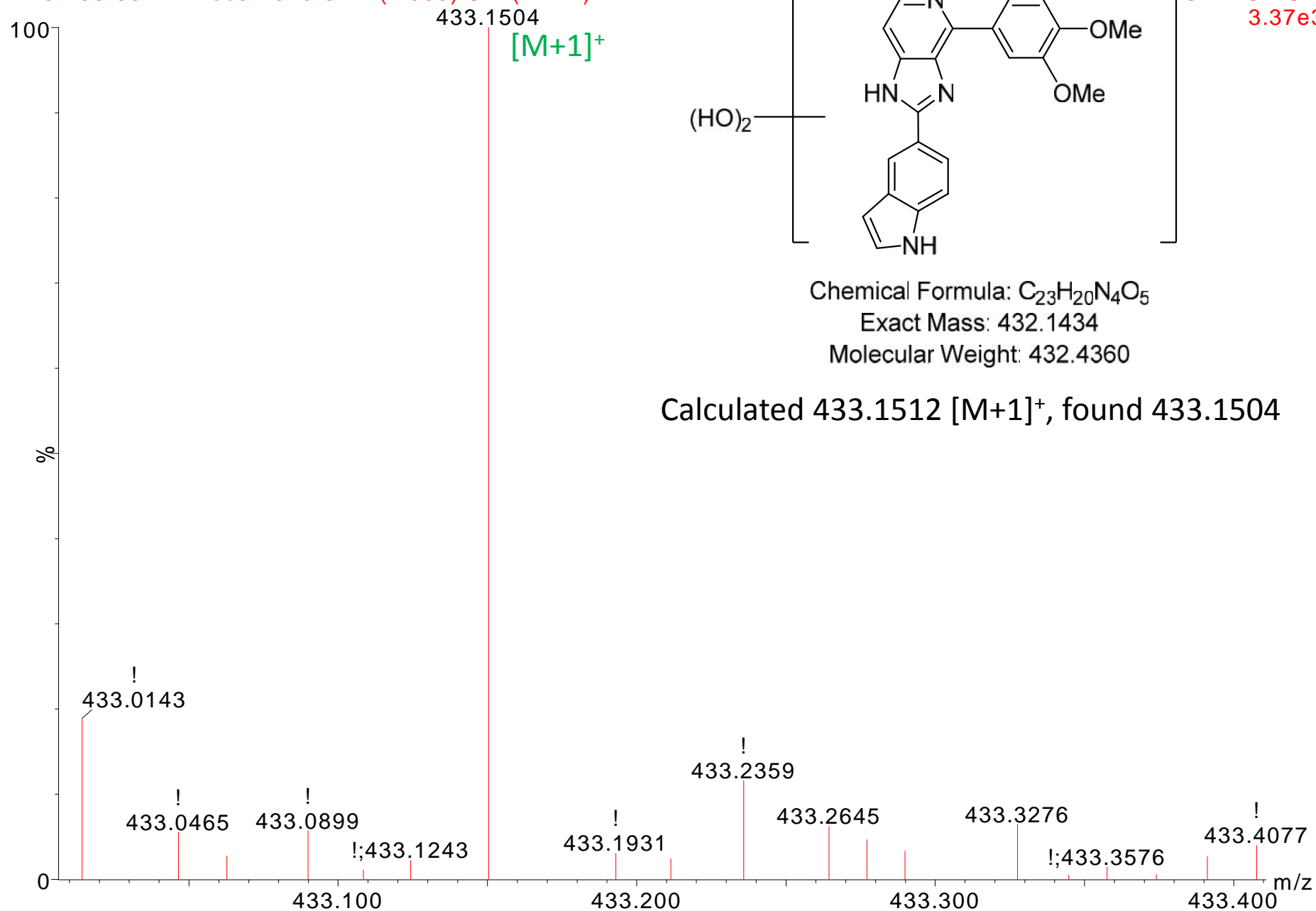
1: TOF MS ES+
387.146 0.0100Da
1.85e3



Mass spectrum of M13

treated

LY-3-296-60min-Dec3-2013-3 21 (1.085) Cm (21:22)

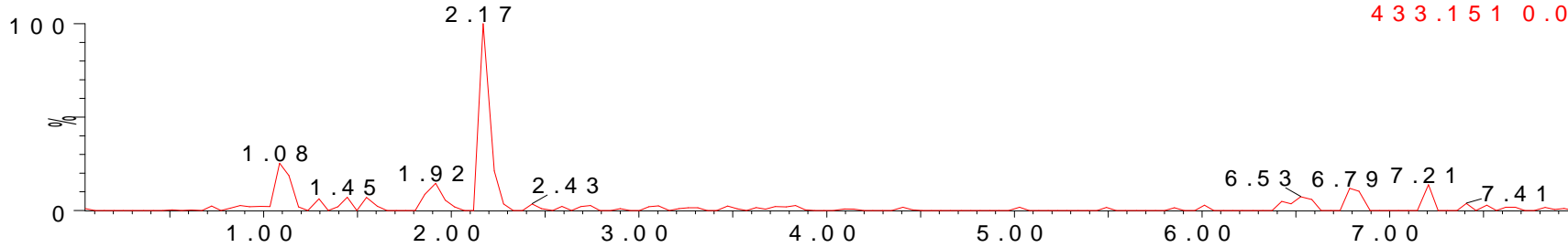


Chromatogram of M13 (extracted at 433.1512)

treated

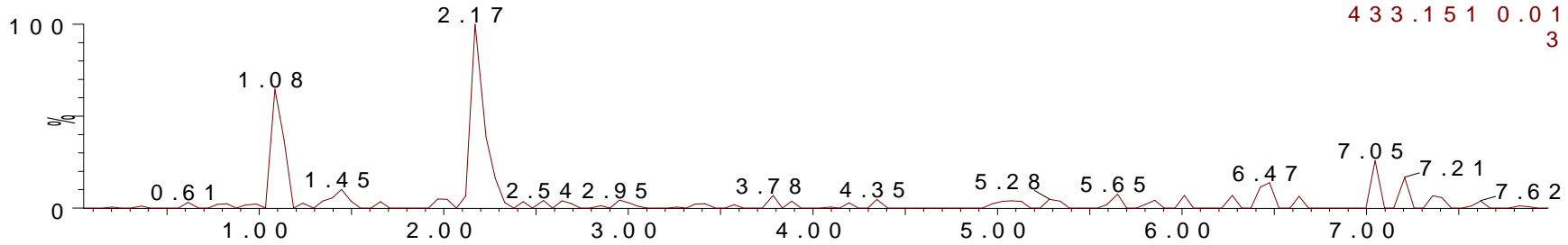
LY-3-296-120min-Dec3-2013-3

1: TOF MS ES+
433.151 0.0100 Da
5.41e3



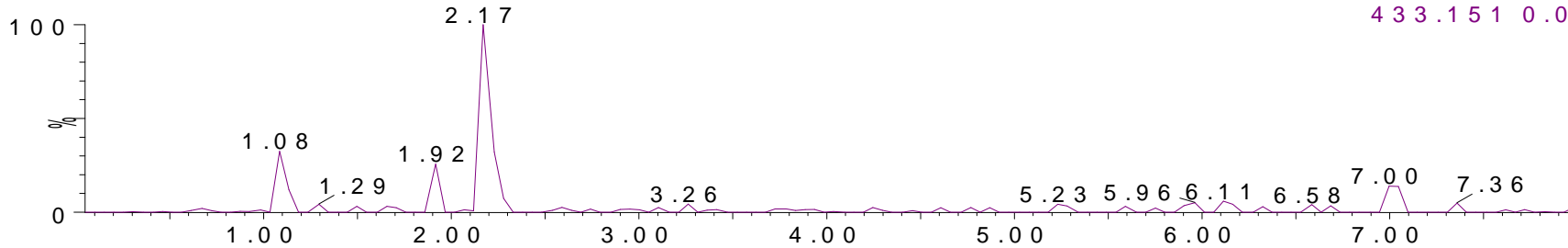
LY-3-296-60min-Dec3-2013-3

1: TOF MS ES+
433.151 0.0100 Da
3.31e3



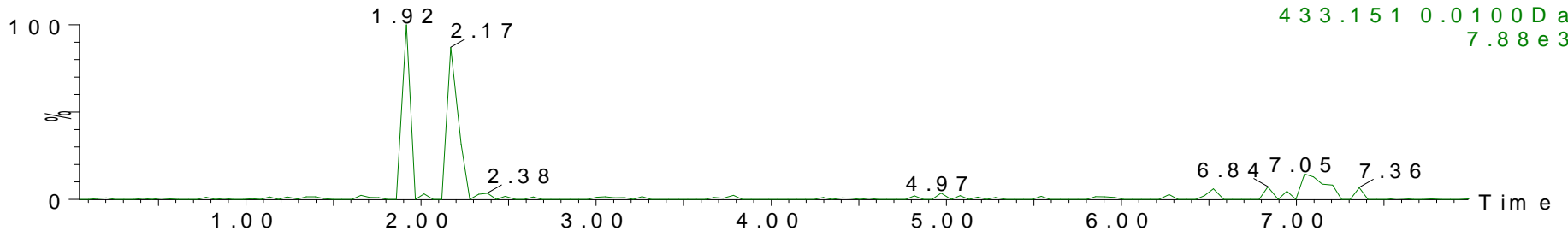
LY-3-296-30min-Dec3-2013-3

1: TOF MS ES+
433.151 0.0100 Da
5.90e3



LY-3-296-0min-Dec3-2013-3

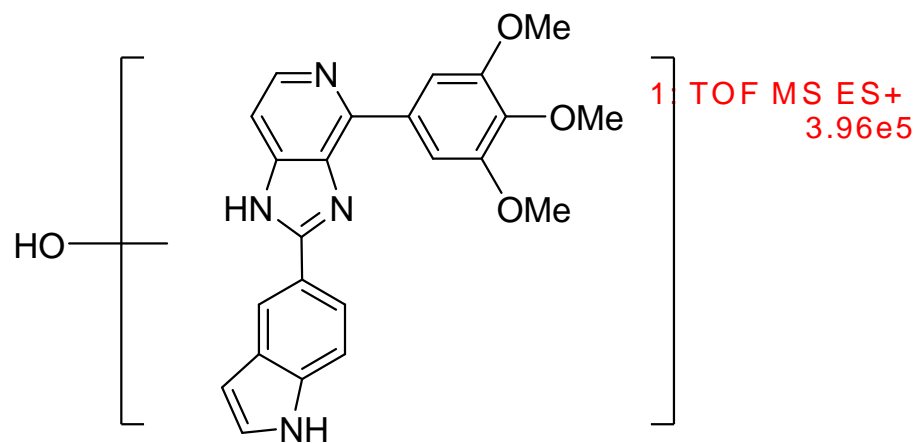
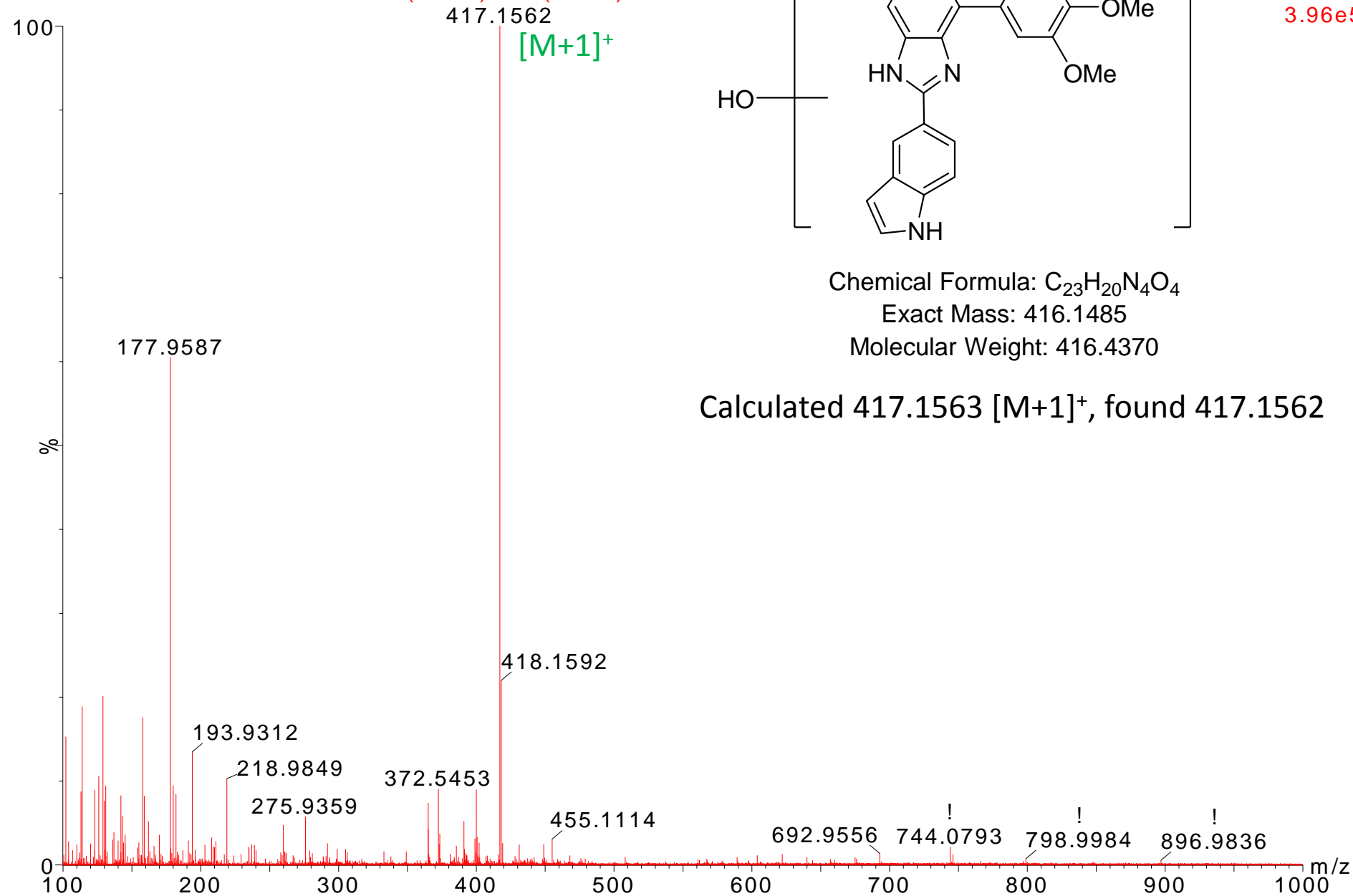
1: TOF MS ES+
433.151 0.0100 Da
7.88e3



Mass spectrum of M14

treated

LY-3-296-120min-Dec3-2013-3 28 (1.446) Cm (28:29)



Chemical Formula: C₂₃H₂₀N₄O₄

Exact Mass: 416.1485

Molecular Weight: 416.4370

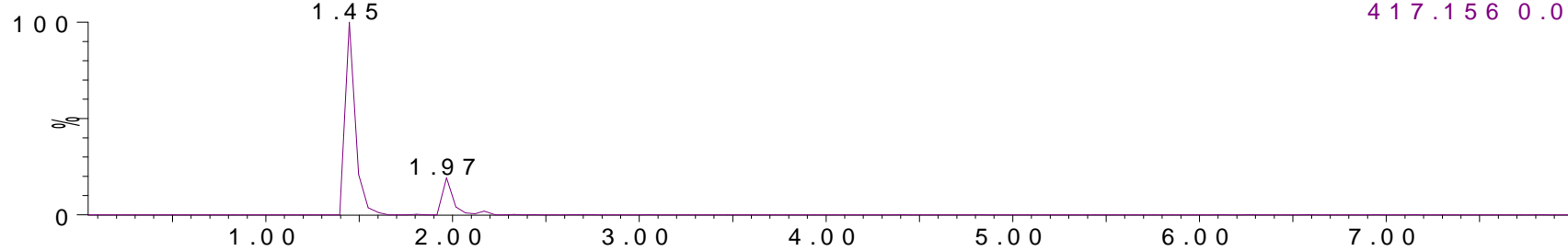
Calculated 417.1563 [M+1]⁺, found 417.1562

Chromatogram of M14 (extracted at 417.1563)

treated

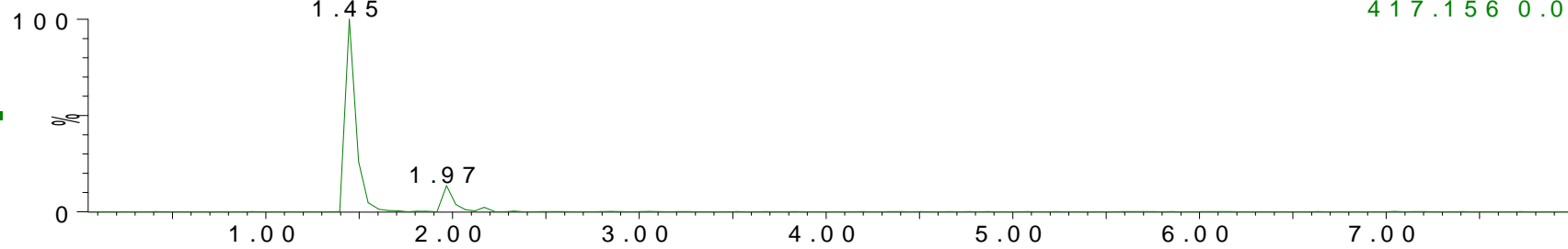
LY-3-296-120 m in - Dec 3 - 2013 - 3

1: TOF MS ES+
417.156 0.0100 Da
3.28 e5



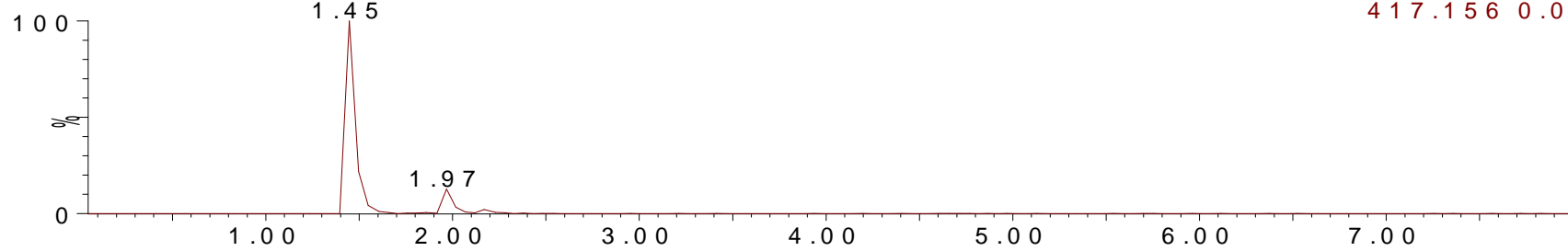
LY-3-296-60 m in - Dec 3 - 2013 - 3

1: TOF MS ES+
417.156 0.0100 Da
1.99 e5



LY-3-296-30 m in - Dec 3 - 2013 - 3

1: TOF MS ES+
417.156 0.0100 Da
1.81 e5



LY-3-296-0 m in - Dec 3 - 2013 - 3

1: TOF MS ES+
417.156 0.0100 Da
1.12 e3

