Supplemental Material

Metabolism and Disposition of Lesinurad, a Uric Acid Reabsorption Inhibitor, in Humans

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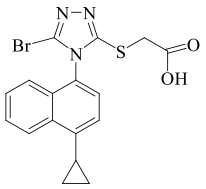
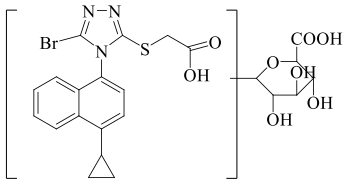
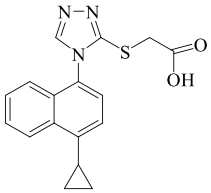
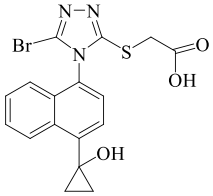
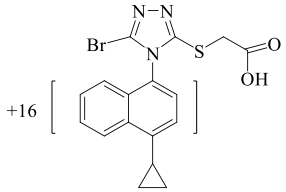
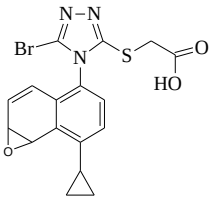
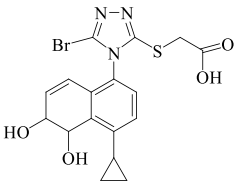
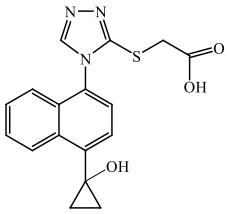
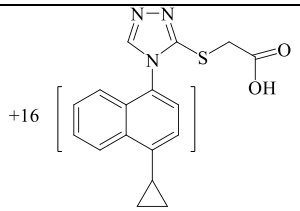
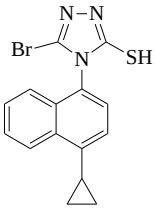
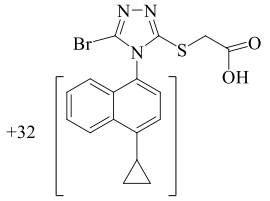
Supplemental File A

Table 1 Chemical Names and Structures for Lesinurad and its Proposed Metabolites

Name of Compound	Structure and Name
Lesinurad Molecular formula: $C_{17}H_{14}BrN_3O_2S$	 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4H-1,2,4-triazol-3-ylthio)acetic acid
M1 Molecular formula: $C_{23}H_{22}BrN_3O_8S$	 6-(2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4H-1,2,4-triazol-3-ylthio)acetoxy)-3,4,5-trihydroxytetrahydro-2H-pyran-2-carboxylic acid
M2 Molecular formula: $C_{17}H_{15}N_3O_2S$	 2-(4-(4-cyclopropylnaphthalen-1-yl)-4H-1,2,4-triazol-3-ylthio)acetic acid
M3 Molecular formula: $C_{17}H_{14}BrN_3O_3S$	

	2-(5-bromo-4-(4-(1-hydroxycyclopropyl)naphthalene-1-yl)-4H-1,2,4-tryazol-3-ylthio)acetic acid
M3b Molecular formula: $C_{17}H_{14}BrN_3O_3S$	
M3c Molecular formula: $C_{17}H_{14}BrN_3O_3S$	
M4 Molecular formula: $C_{17}H_{16}BrN_3O_4S$	 2-(5-bromo-4-(4-cyclopropyl-5,6-dihydroxy-5,6-dihydronaphthalene-1-yl)-4H-1,2,4-tryazol-3-ylthio)acetic acid
M5 Molecular formula: $C_{17}H_{15}N_3O_3S$	 2-(4-(4-(1-hydroxycyclopropyl)naphthalene-1-yl)-4H-1,2,4-tryazol-3-ylthio)acetic acid
M5b Molecular formula: $C_{17}H_{15}N_3O_3S$	

	
M15 Molecular formula: $C_{15}H_{12}BrN_3S$	
M16 Molecular formula: $C_{17}H_{14}BrN_3O_4S$	

Supplemental Figures

Fig. 1 Proton NMR Spectrum of M4

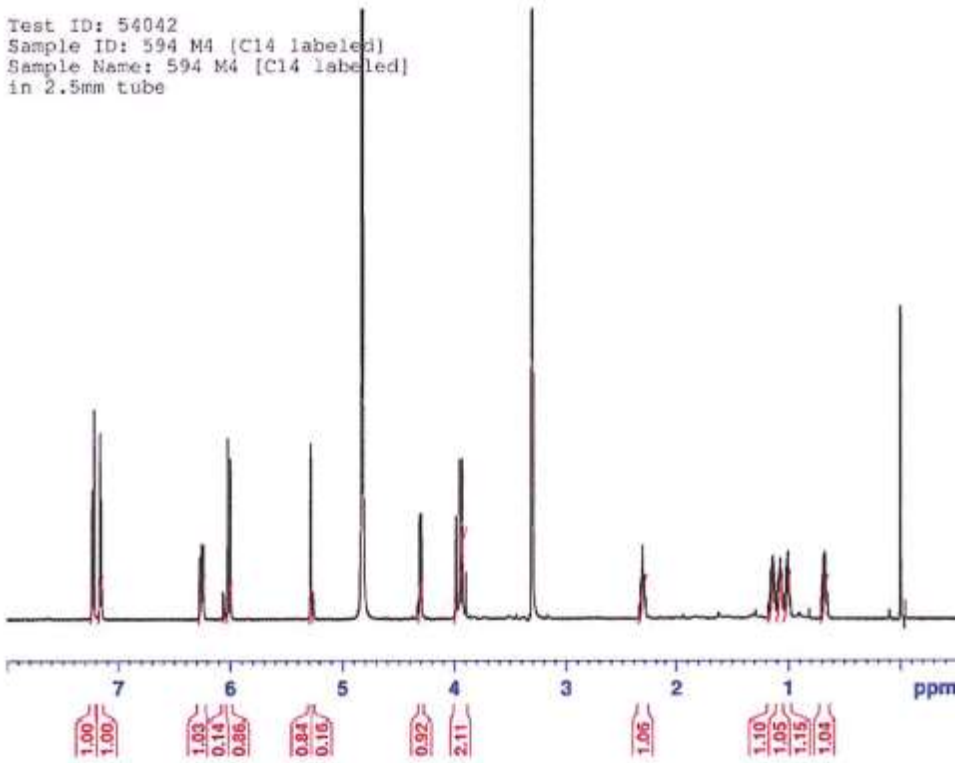


Fig. 2 Carbon NMR of M4

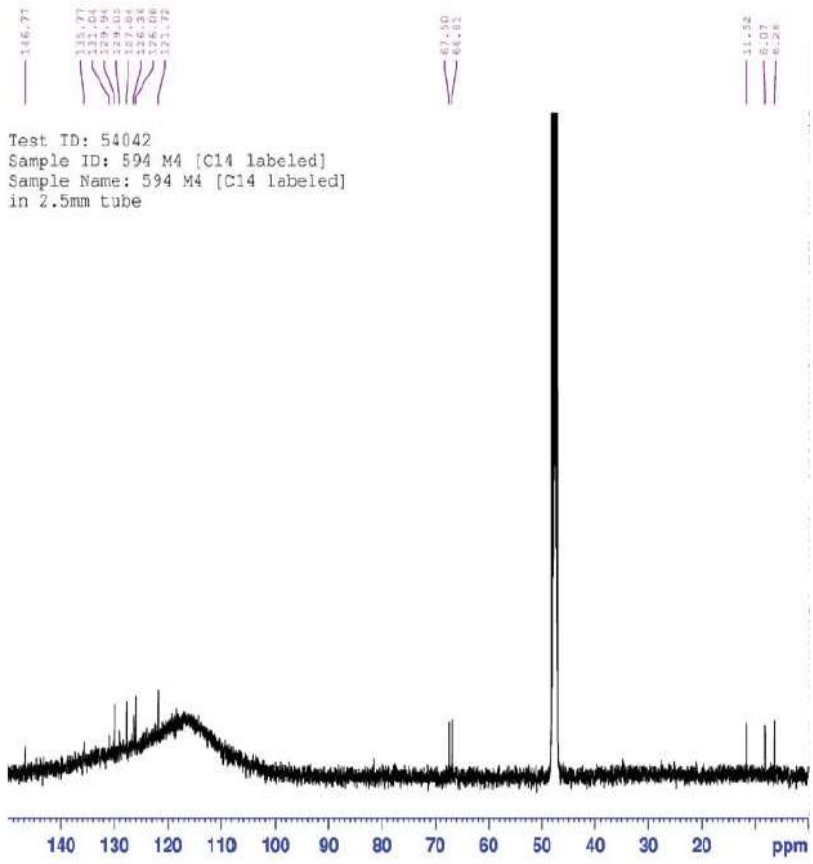


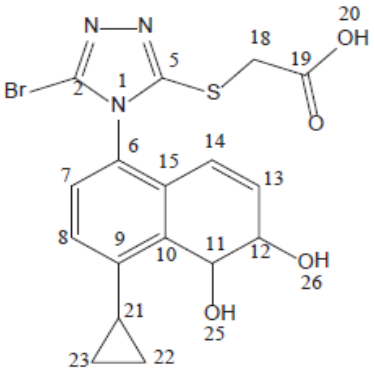
Fig. 3 NMR Chemical shifts of M4

Proton chemical shifts of M4

Atom	Chemical Shift (ppm)	Multiplicity	No of Protons	Coupling Constants (Hz)
7	7.23	d	1	8.2
8	7.16	d	1	8.2
13	6.26	ddd	1	9.9, 5.5, 0.6
14	6.01	d	1	9.9
11	5.28	dd	1	1.8, 0.6
12	4.30	dd	1	5.5, 1.8
18	3.97	d	1	15.9
18	3.92	d	1	15.9
21	2.32	m	1	
22 or 23	1.14	m	1	
23 or 22	1.08	m	1	
23 or 22	1.01	m	1	
22 or 23	0.68	m	1	

Carbon chemical shifts of M4

Atom	Chemical Shift (ppm)	Multiplicity
19	170.5	s
5	154.9	s
9	146.8	s
10	135.8	s
2	131.0	s
13	129.9	s
15	129.1	s
7	127.8	s
6	126.4	s
8	126.0	s
14	121.7	s
12	67.5	s
11	66.8	s
18	35.0	s
21	11.5	s
23 or 22	8.1	s
22 or 23	6.3	s



Chemical Formula: $C_{17}H_{16}BrN_3O_4S$
Molecular Weight: 438.30
Exact mass: 437 and 439

Fig 4. COSY Data of M4

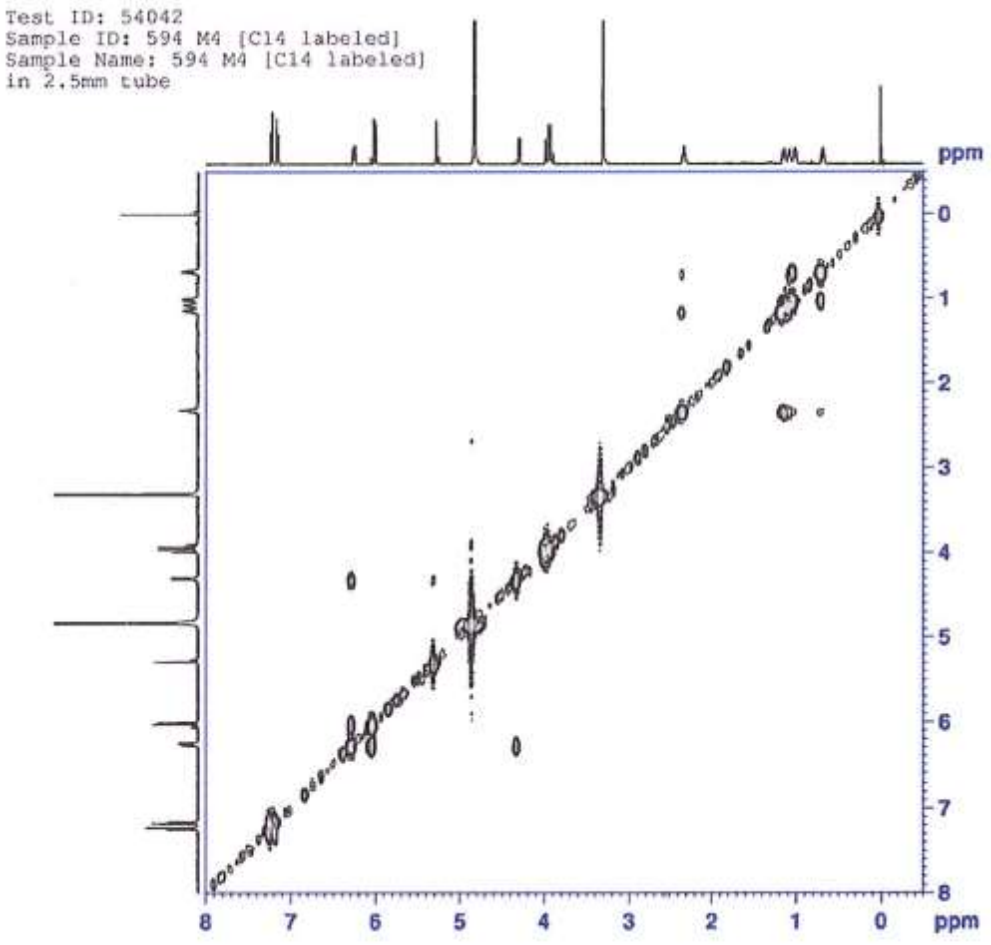


Fig 5. HSQC Data of M4

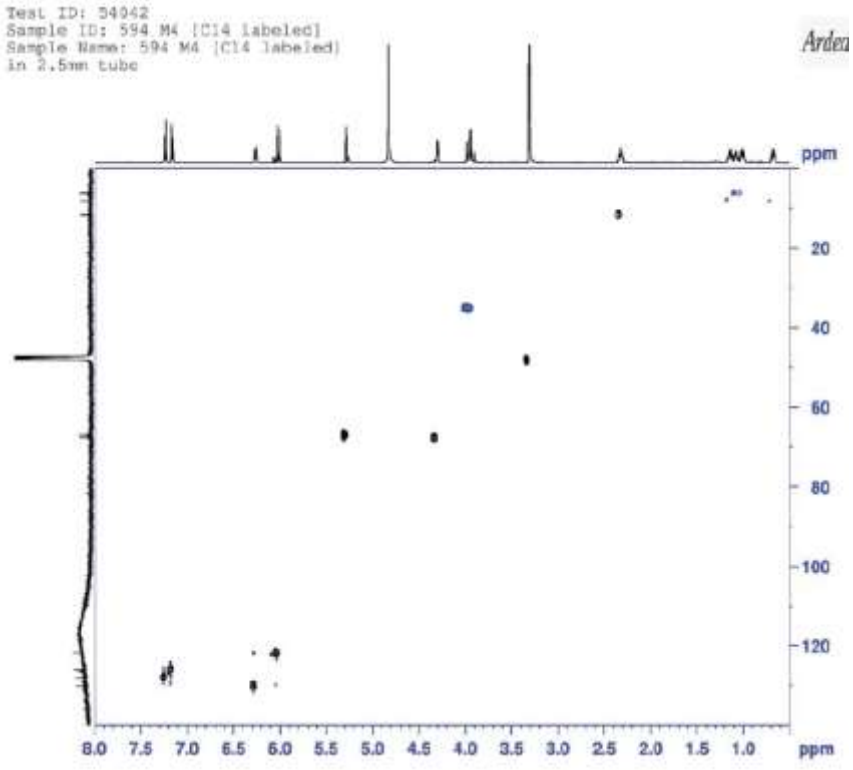


Fig. 6 HMBC Data of M4

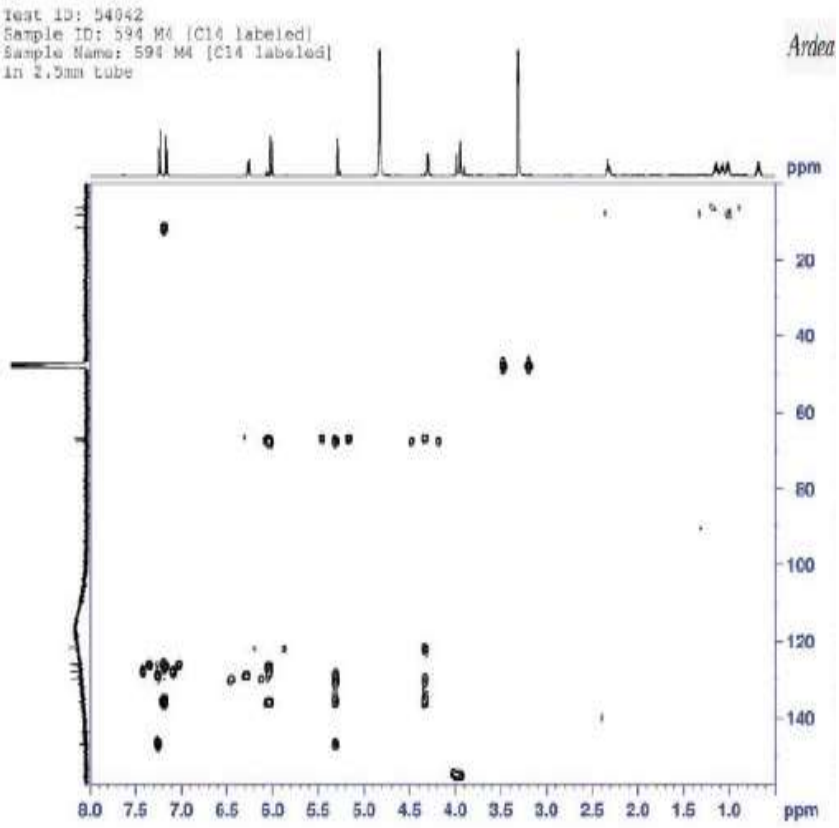
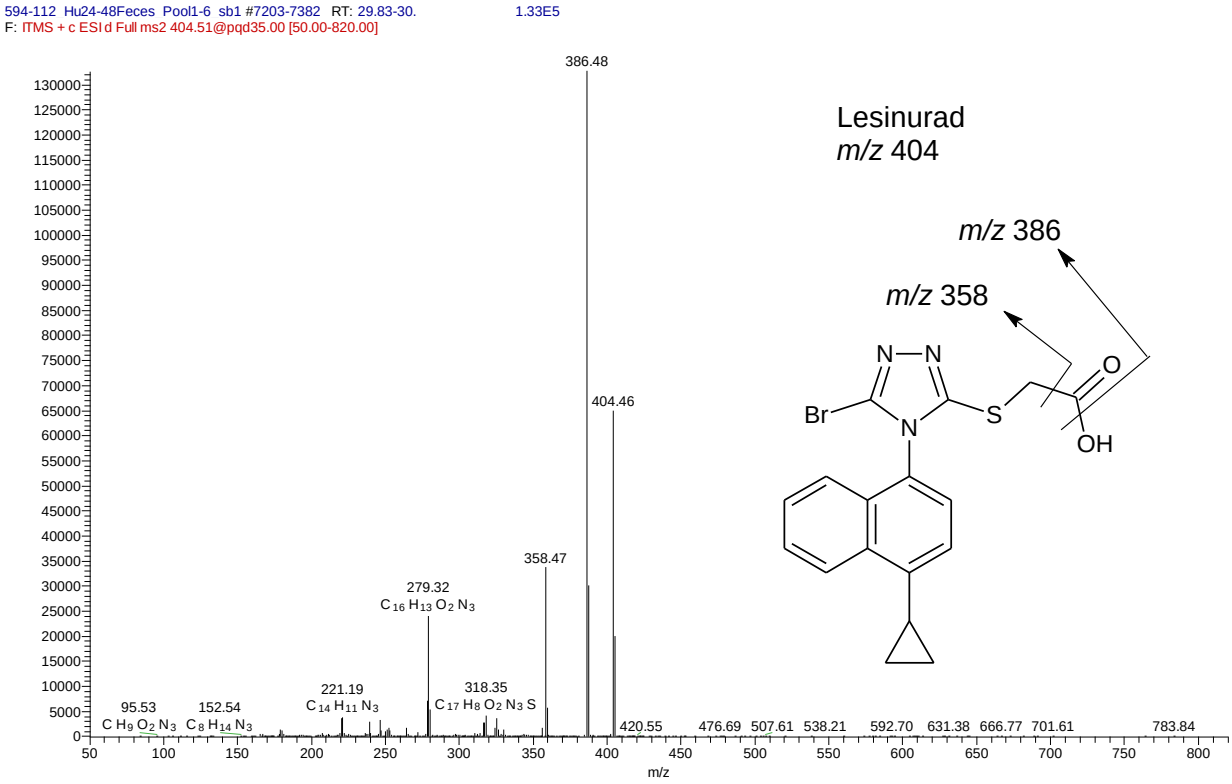
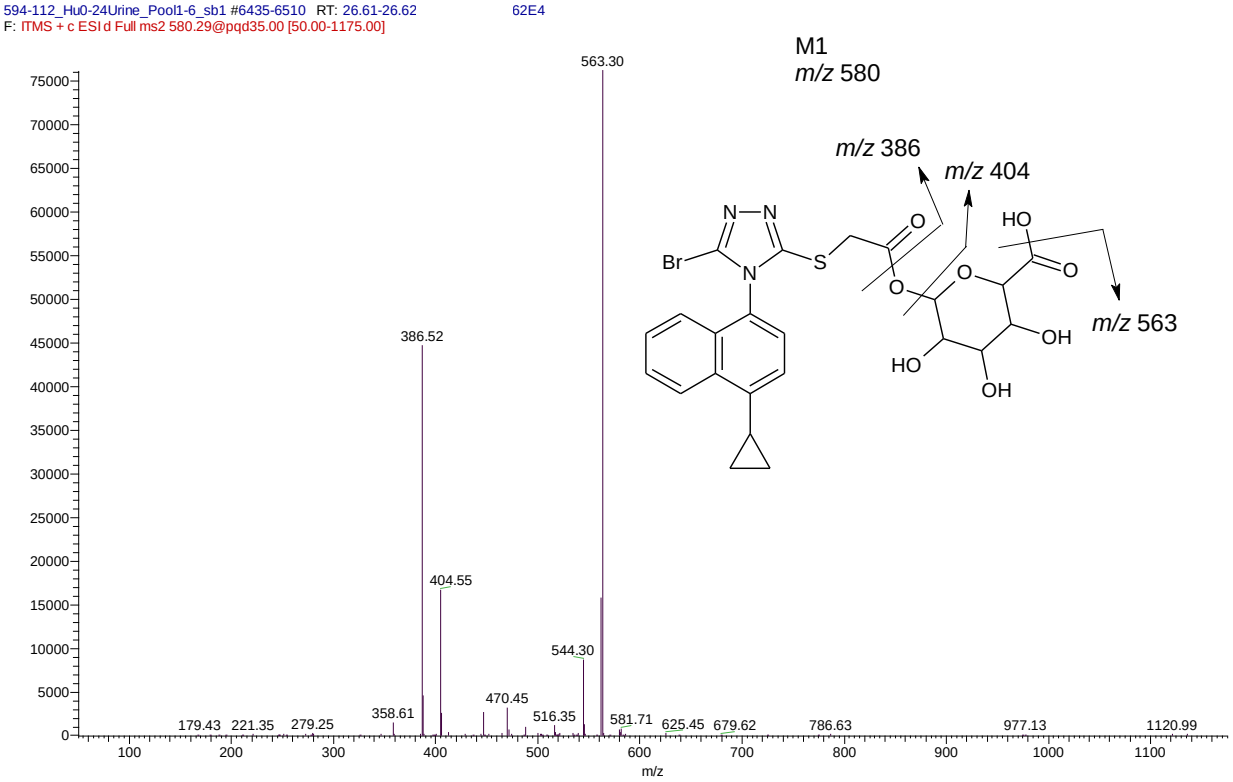


Fig. 7 Mass spectral fragmentations of lesinurad and metabolites

Lesinurad



M1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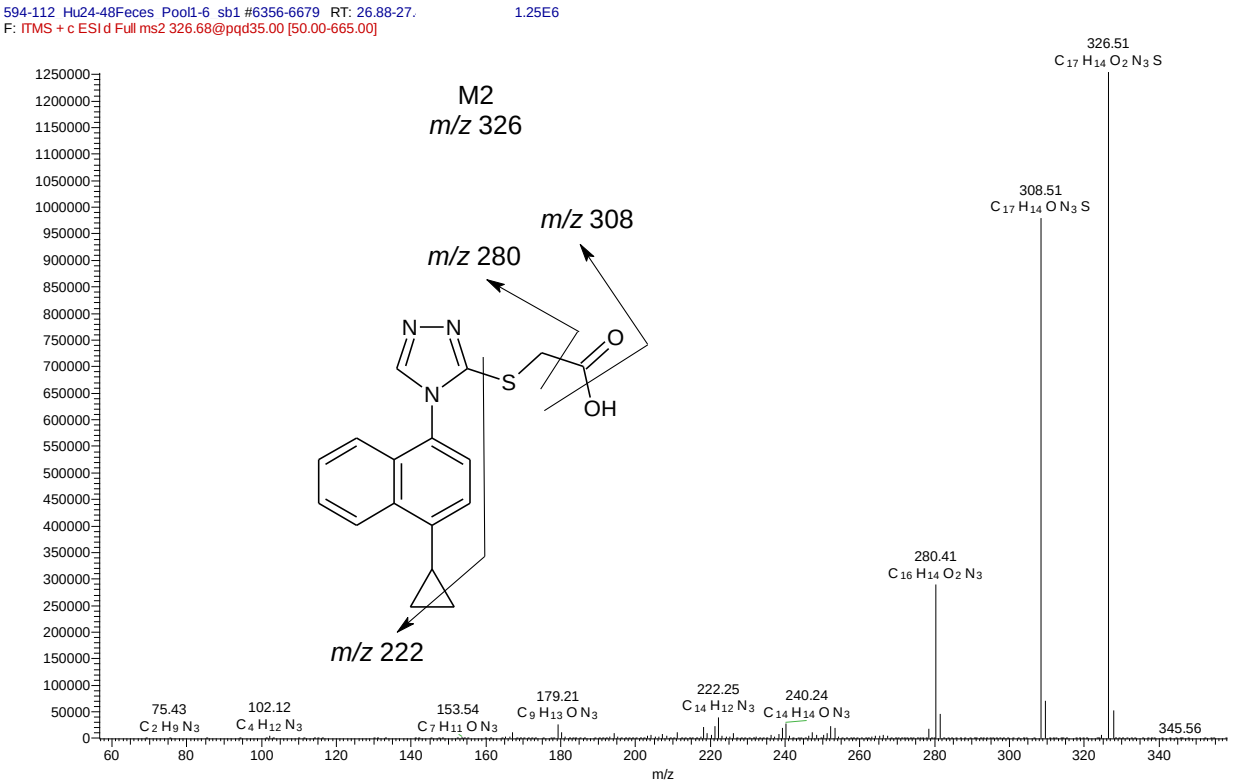
M1
m/z 580
m/z 386
m/z 404
m/z 563
563.30
386.52
404.55
544.30
470.45
358.61
516.35
581.71
179.43
221.35
279.25
625.45
679.62
786.63
977.13
1120.99
m/z

M2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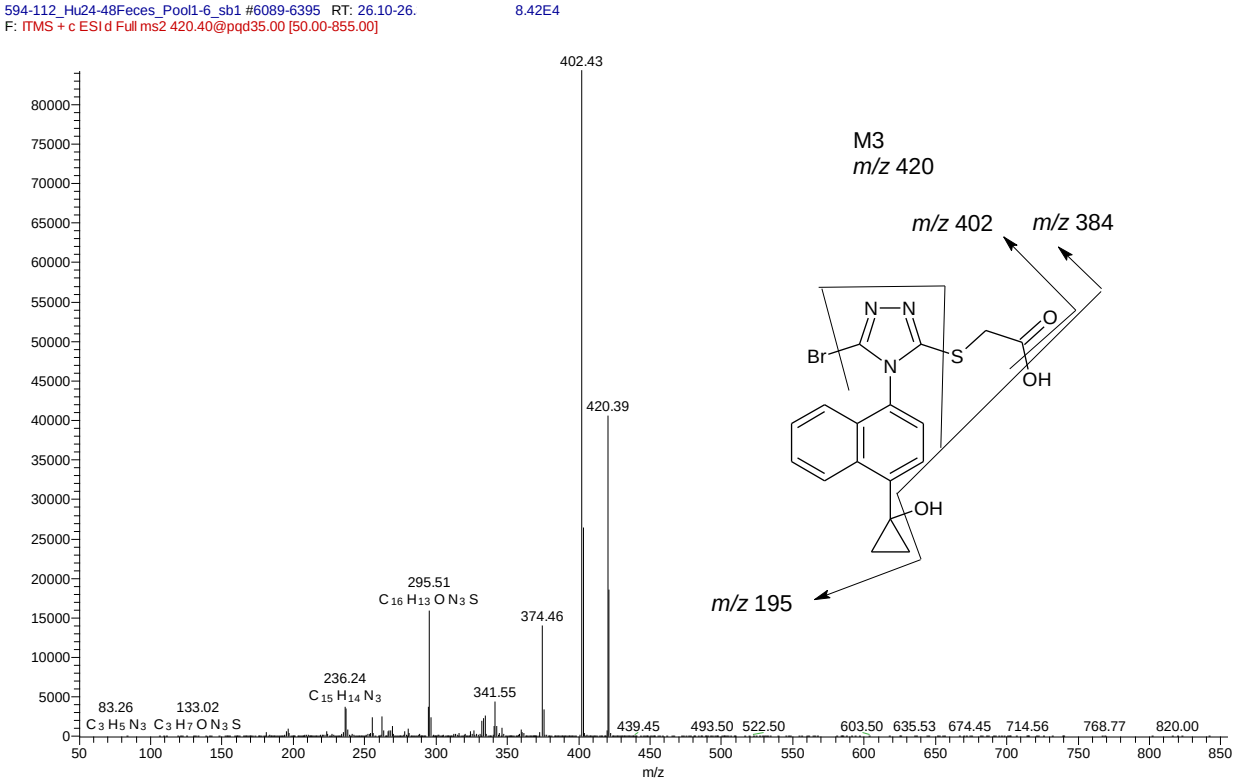
M2
m/z 326
m/z 308
m/z 280
m/z 222
326.51
C17 H14 O2 N3 S
308.51
C17 H14 O N3 S
280.41
C16 H14 O2 N3
75.43
C2 H9 N3
102.12
C4 H12 N3
153.54
C7 H11 O N3
179.21
C9 H13 O N3
222.25
C14 H12 N3
240.24
C14 H14 O N3
345.56
m/z

M3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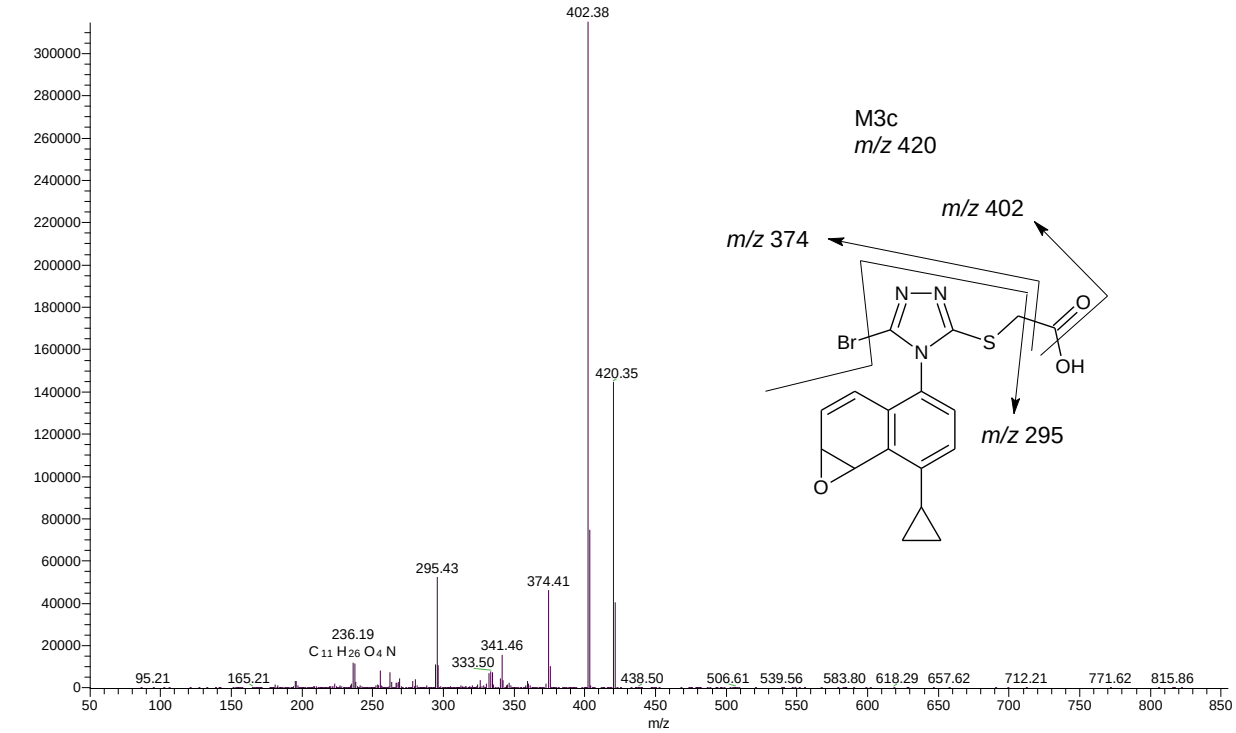
402.43
420.39
295.51
C16 H13 O N3 S
374.46
236.24
C15 H14 N3
341.55
83.26
C3 H5 N3
133.02
C3 H7 O N3 S
439.45
493.50
522.50
603.50
635.53
674.45
714.56
768.77
820.00
m/z
M3
m/z 420
m/z 402
m/z 384
m/z 195
Br
N
S
O
OH

M3c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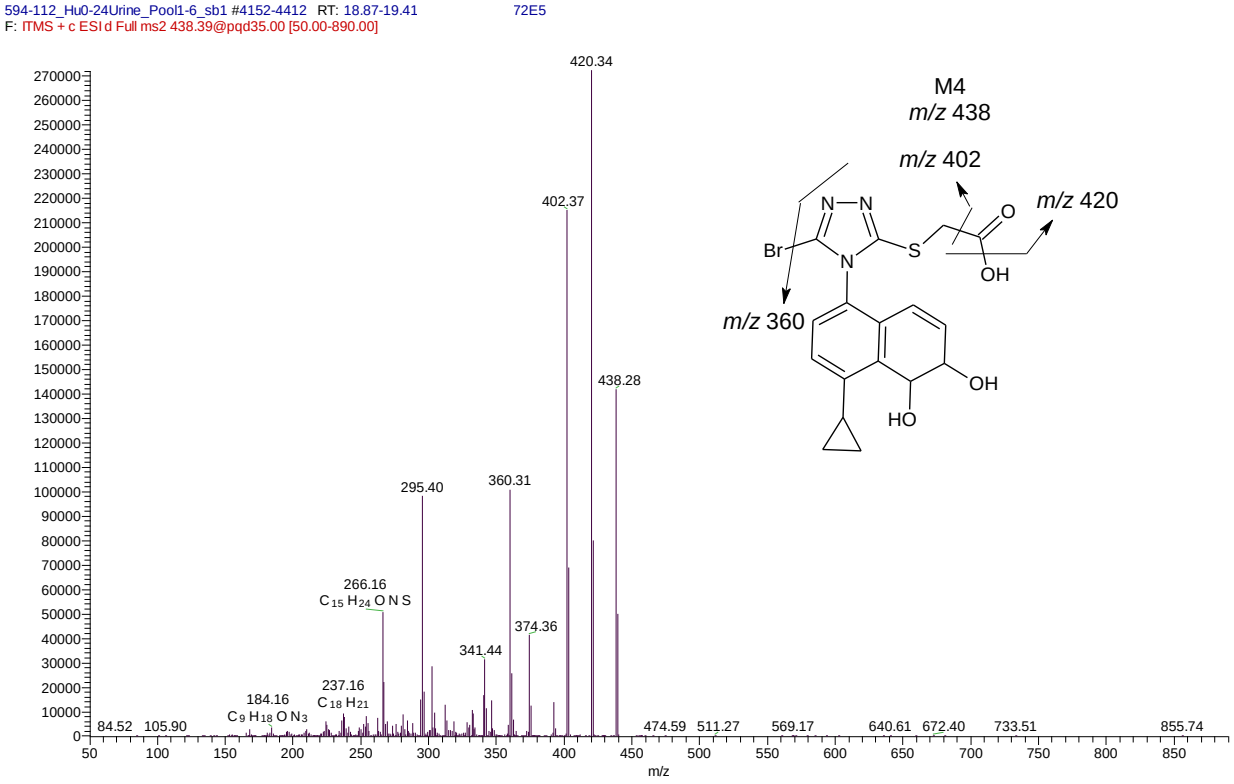
F: ITMS + c ESI d Full ms2 420.47@pqd35.00 [50.00-855.00]
402.38
420.35
295.43
374.41
236.19
C11 H26 O4 N
341.46
333.50
95.21
165.21
438.50
506.61
539.56
583.80
618.29
657.62
712.21
771.62
815.86
m/z
M3c
m/z 420
m/z 402
m/z 374
m/z 295
Br
N
S
O
OH

M4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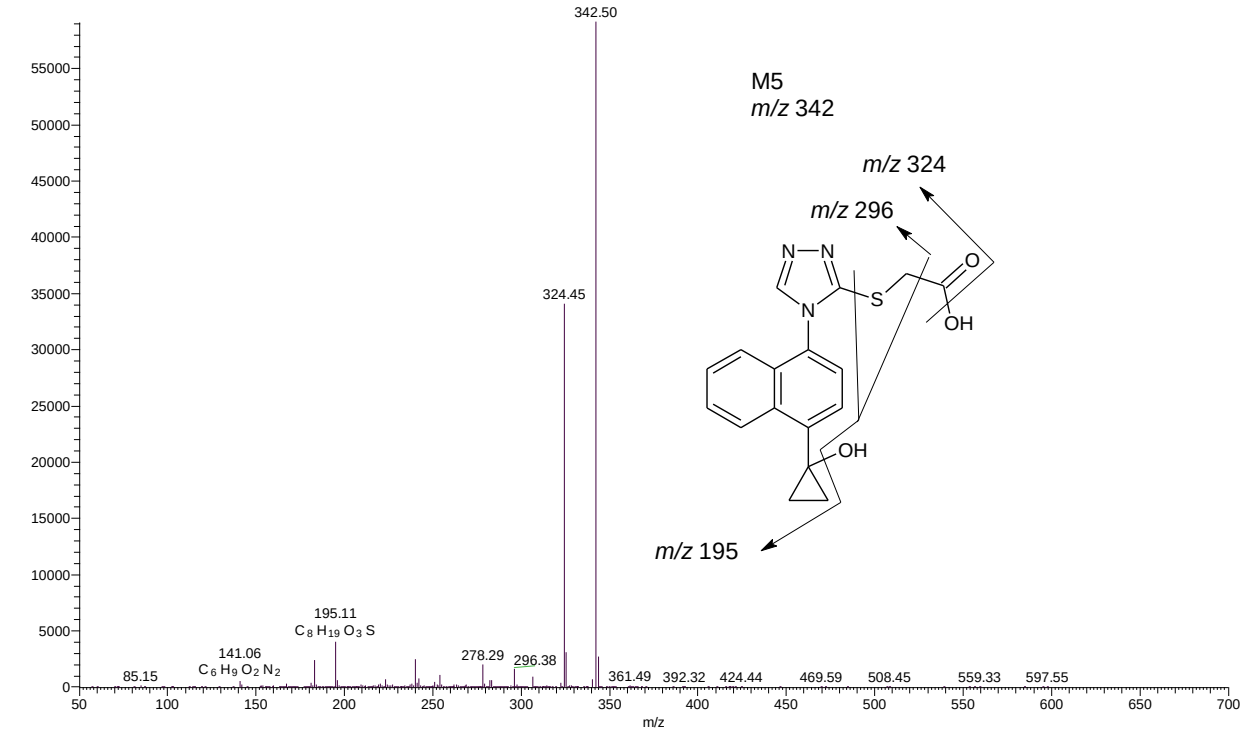
420.34
402.37
438.28
295.40
360.31
266.16
C15 H24 O N S
374.36
341.44
237.16
C18 H21
184.16
C9 H18 O N3
84.52
105.90
474.59
511.27
569.17
640.61
672.40
733.51
855.74
m/z
M4
m/z 438
m/z 402
m/z 420
m/z 360
Br
N
S
O
OH
HO

M5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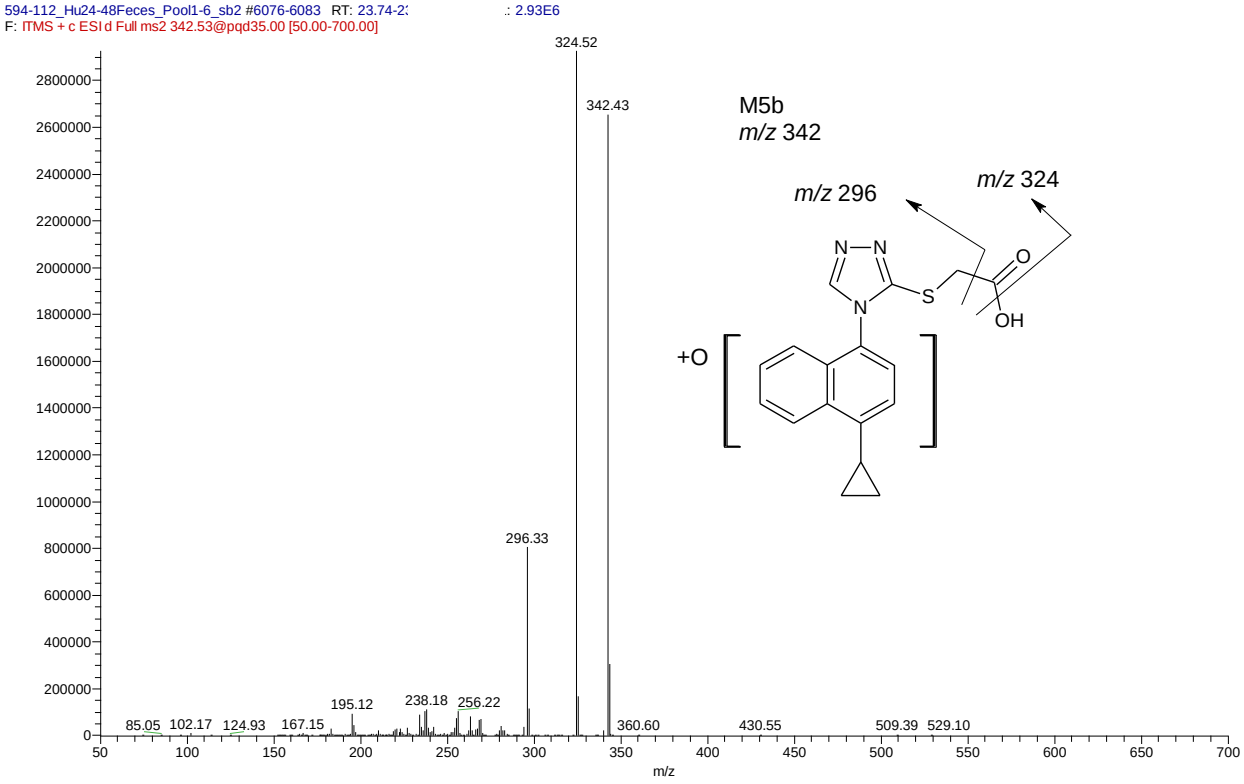
342.50
324.45
195.11
C8 H19 O3 S
141.06
C6 H9 O2 N2
85.15
278.29
296.38
361.49
392.32
424.44
469.59
508.45
559.33
597.55
m/z
M5
m/z 342
m/z 324
m/z 296
m/z 195
N
S
O
OH

M5b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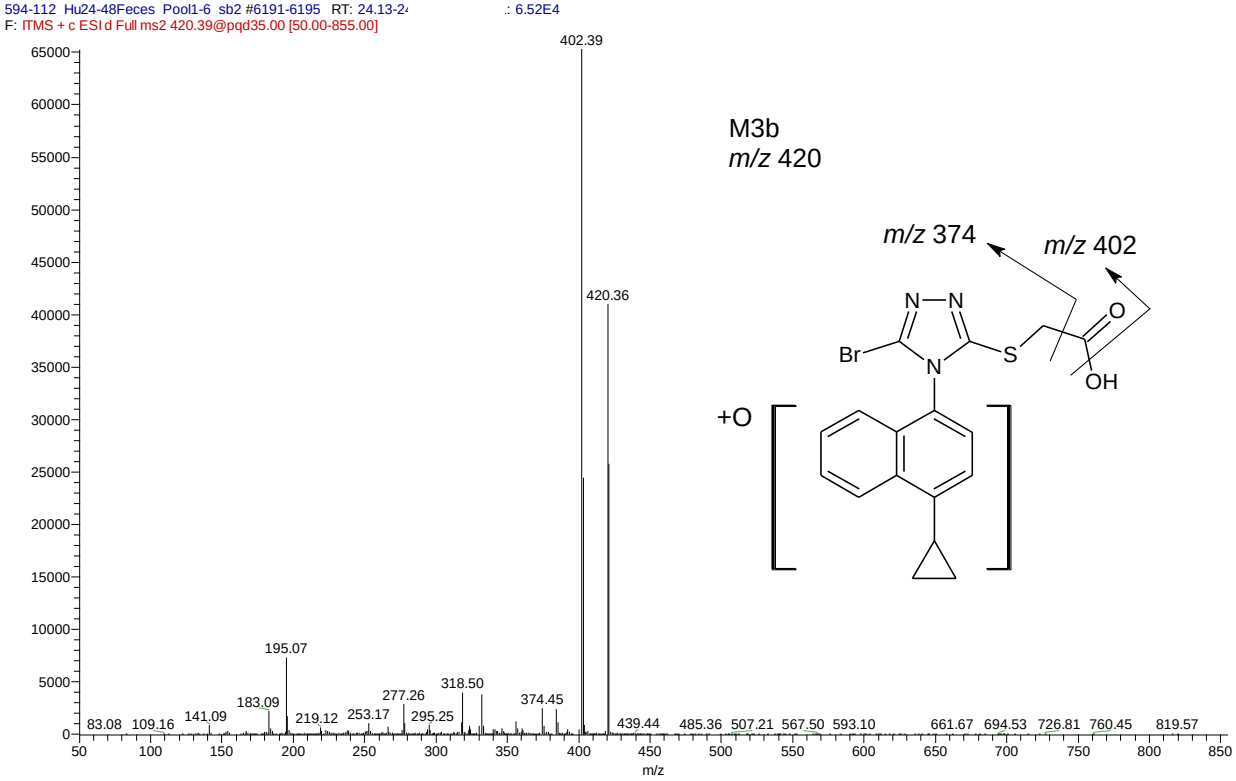
324.52
342.43
296.33
195.12
238.18
256.22
85.05
102.17
124.93
167.15
360.60
430.55
509.39
529.10
m/z
M5b
m/z 342
m/z 296
m/z 324
+O

M3b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.: 6.52E4
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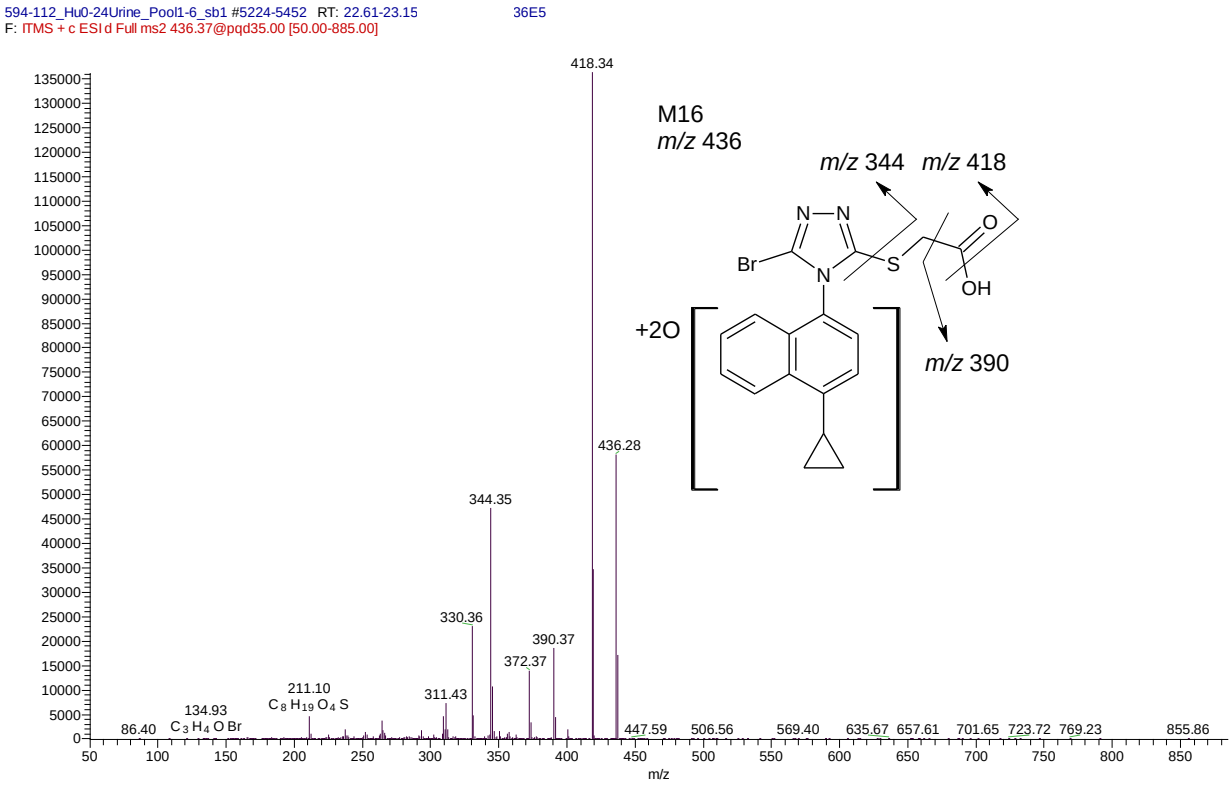
318.50
374.45
83.08
109.16
141.09
219.12
253.17
295.25
439.44
485.36
507.21
567.50
593.10
661.67
694.53
726.81
760.45
819.57
m/z
M3b
m/z 420
m/z 374
m/z 402
+O

M16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418.34
436.28
344.35
330.36
390.37
372.37
211.10
C8 H19 O4 S
311.43
134.93
C3 H4 O Br
86.40
447.59
506.56
569.40
635.67
657.61
701.65
723.72
769.23
855.86
m/z
M16
m/z 436
m/z 344
m/z 418
m/z 390
+2O
Br
N
S
O
OH