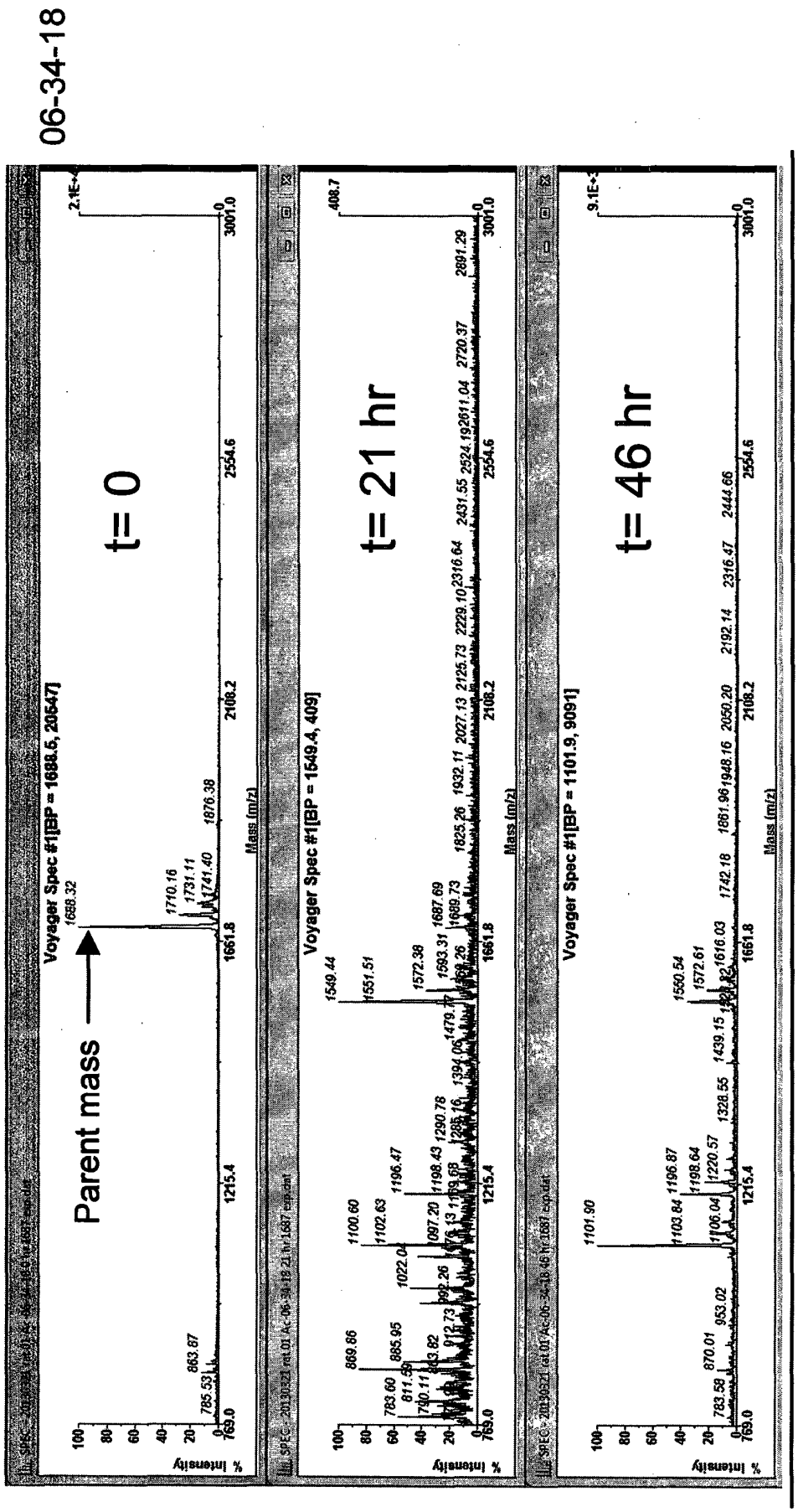

06-34-18
Voyager Spec #1[BP = 1688.6, 20547]
Parent mass
t= 0
Voyager Spec #1[BP = 1549.4, 409]
t= 21 hr
Voyager Spec #1[BP = 1101.9, 9091]
t= 46 hr
% Intensity
Mass (m/z)

FIGURE 1

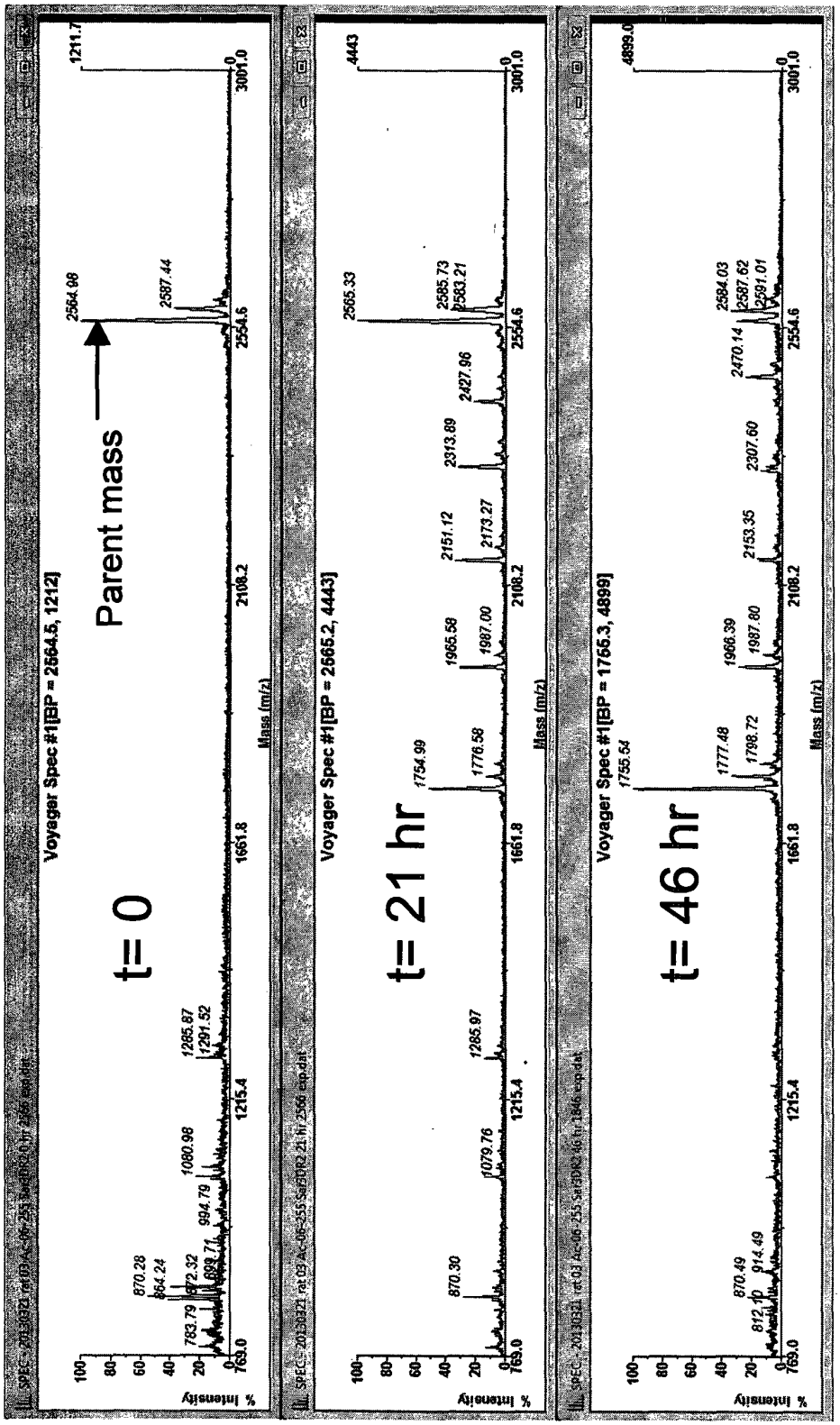

Ac-06-255-Sar3-(D-Arg)2
Voyager Spec #1[BP = 2564.5, 1212]
Parent mass
t= 0
Voyager Spec #1[BP = 2665.2, 4443]
t= 21 hr
Voyager Spec #1[BP = 1755.3, 4899]
t= 46 hr
% Intensity
Mass (m/z)

FIGURE 1 (ctd)

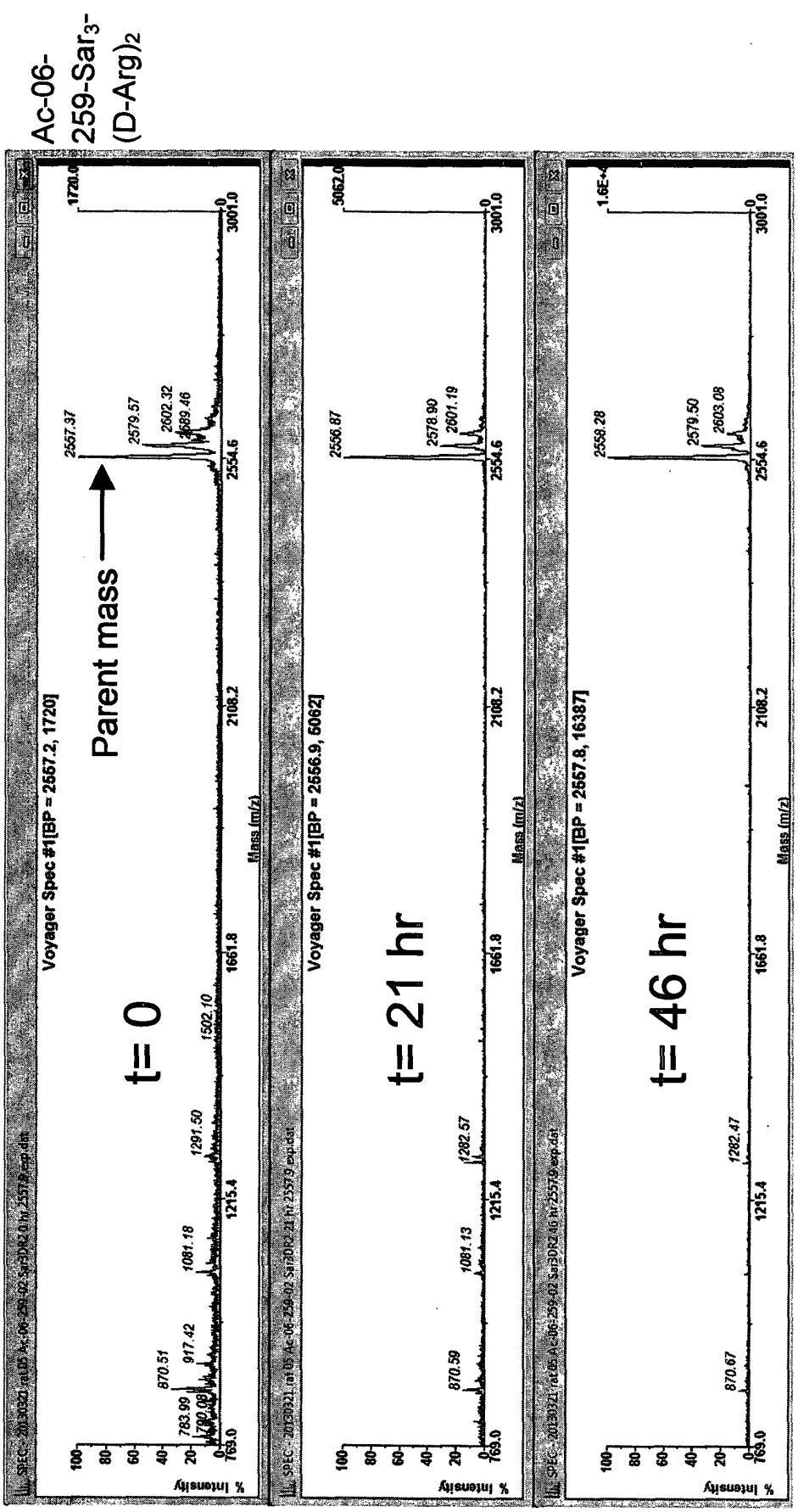

Ac-06-259-Sar3-(D-Arg)2
Parent mass
t= 0
t= 21 hr
t= 46 hr
Voyager Spec #1[BP = 2667.2, 1720]
Voyager Spec #1[BP = 2556.9, 6062]
Voyager Spec #1[BP = 2557.8, 16387]
% Intensity
Mass (m/z)
2567.37
2579.57
2602.32
2689.46
1502.10
1291.50
1081.18
917.42
870.51
783.99
1215.4
1661.8
2108.2
2554.6
3001.0
2556.87
2578.90
2601.19
1282.57
1081.13
870.59
2558.28
2579.50
2603.08
1282.47
870.67

FIGURE 1 (ctd)

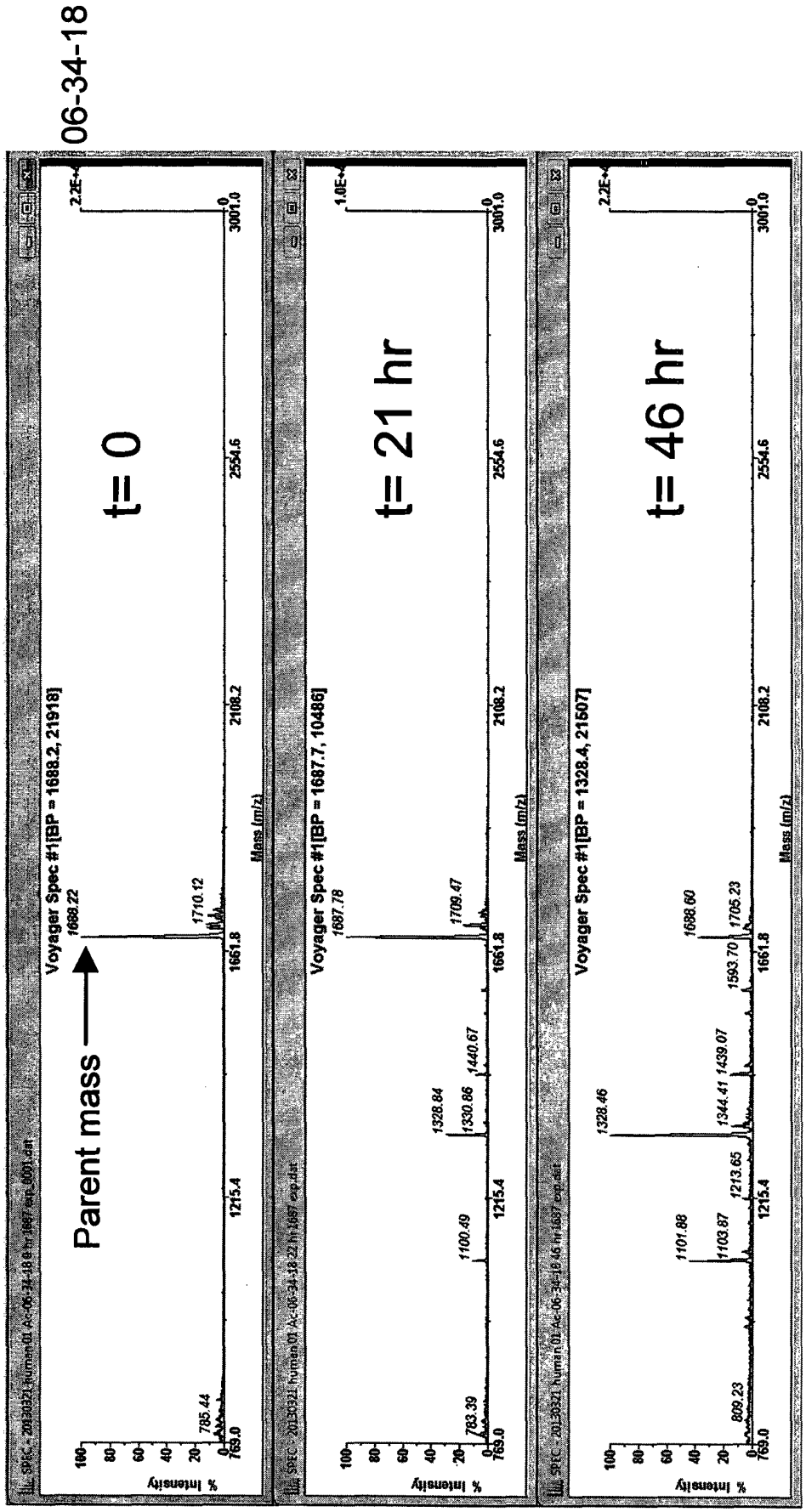

06-34-18
Parent mass
t= 0
t= 21 hr
t= 46 hr
Voyager Spec #1[BP = 1688.2, 21918]
Voyager Spec #1[BP = 1687.7, 10486]
Voyager Spec #1[BP = 1328.4, 21507]
% Intensity
Mass (m/z)
1688.22
1710.12
1687.78
1709.47
1328.46
1688.60
1705.23
1593.70
1439.07
1344.41
1440.67
1330.86
1328.84
1213.65
1103.87
1101.88
1100.49
809.23
785.44
783.39
1661.8
2554.6
2108.2
1215.4
769.0
3001.0

FIGURE 2

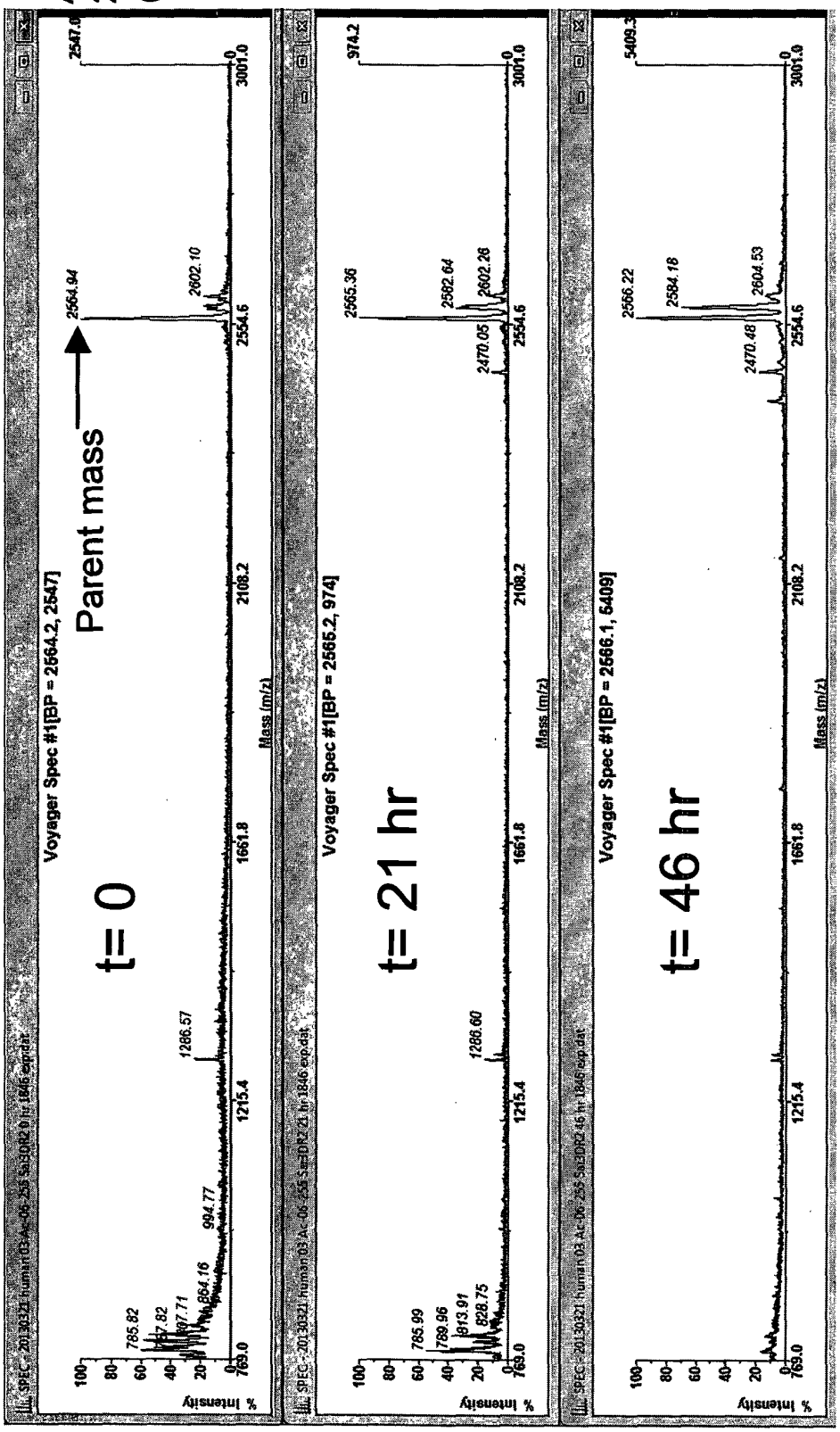

Ac-06-255-Sar3-(D-Arg)2
Parent mass
t= 0
t= 21 hr
t= 46 hr
Voyager Spec #1[BP = 2564.2, 2547]
Voyager Spec #1[BP = 2565.2, 974]
Voyager Spec #1[BP = 2566.1, 5409]
% Intensity
Mass (m/z)
2564.94
2602.10
1286.57
994.77
2565.36
2582.64
2602.26
2470.05
1286.60
2566.22
2584.18
2604.53
2470.48
2554.6
2108.2
1661.8
1215.4
769.0
3001.0

FIGURE 2 (ctd)

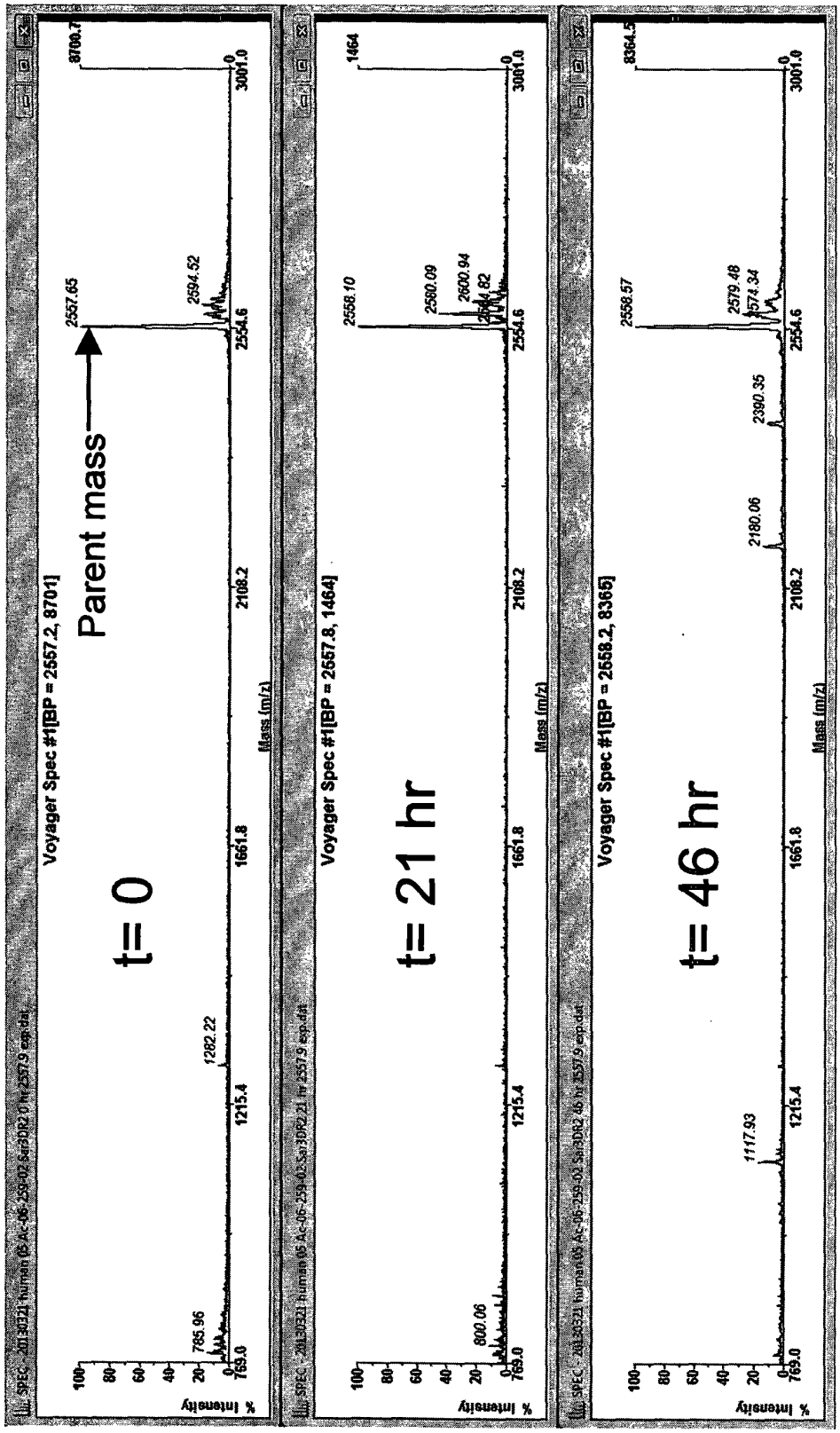

Ac-06-259-Sar3-(D-Arg)2
Parent mass
t= 0
t= 21 hr
t= 46 hr
Voyager Spec #1[BP = 2557.2, 8701]
Voyager Spec #1[BP = 2557.8, 1464]
Voyager Spec #1[BP = 2558.2, 8365]
% Intensity
Mass (m/z)
2557.65
2594.52
1282.22
765.96
2558.10
2580.09
2600.94
800.06
2558.57
2579.48
2574.34
2390.35
2180.06
1117.93
1661.8
2108.2
1215.4
2554.6
3001.0

FIGURE 2 (ctd)

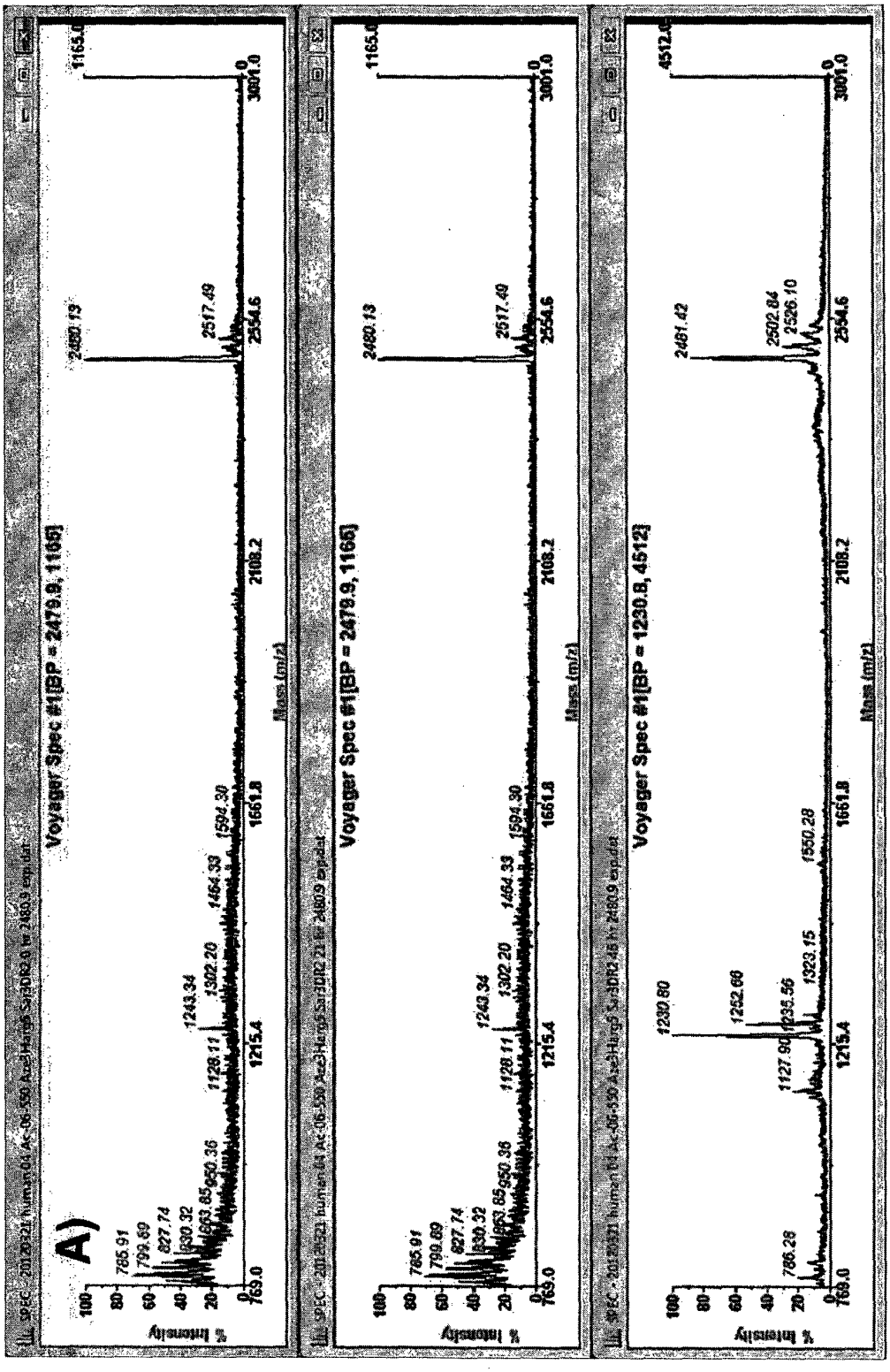

A)
Voyager Spec #1[BP = 2479.9, 1166]
% Intensity
Mass (m/z)
769.0
1215.4
1661.8
2108.2
2554.6
3001.0
785.91
799.89
827.74
830.32
863.85
950.36
1128.11
1243.34
1302.20
1464.33
1594.30
2480.13
2517.49
1165.6
Voyager Spec #1[BP = 2479.9, 1166]
Voyager Spec #1[BP = 1230.8, 4512]
1230.80
1252.66
1127.90
1236.56
1323.15
1550.28
2481.42
2502.84
2526.10
4512.6

FIGURE 3

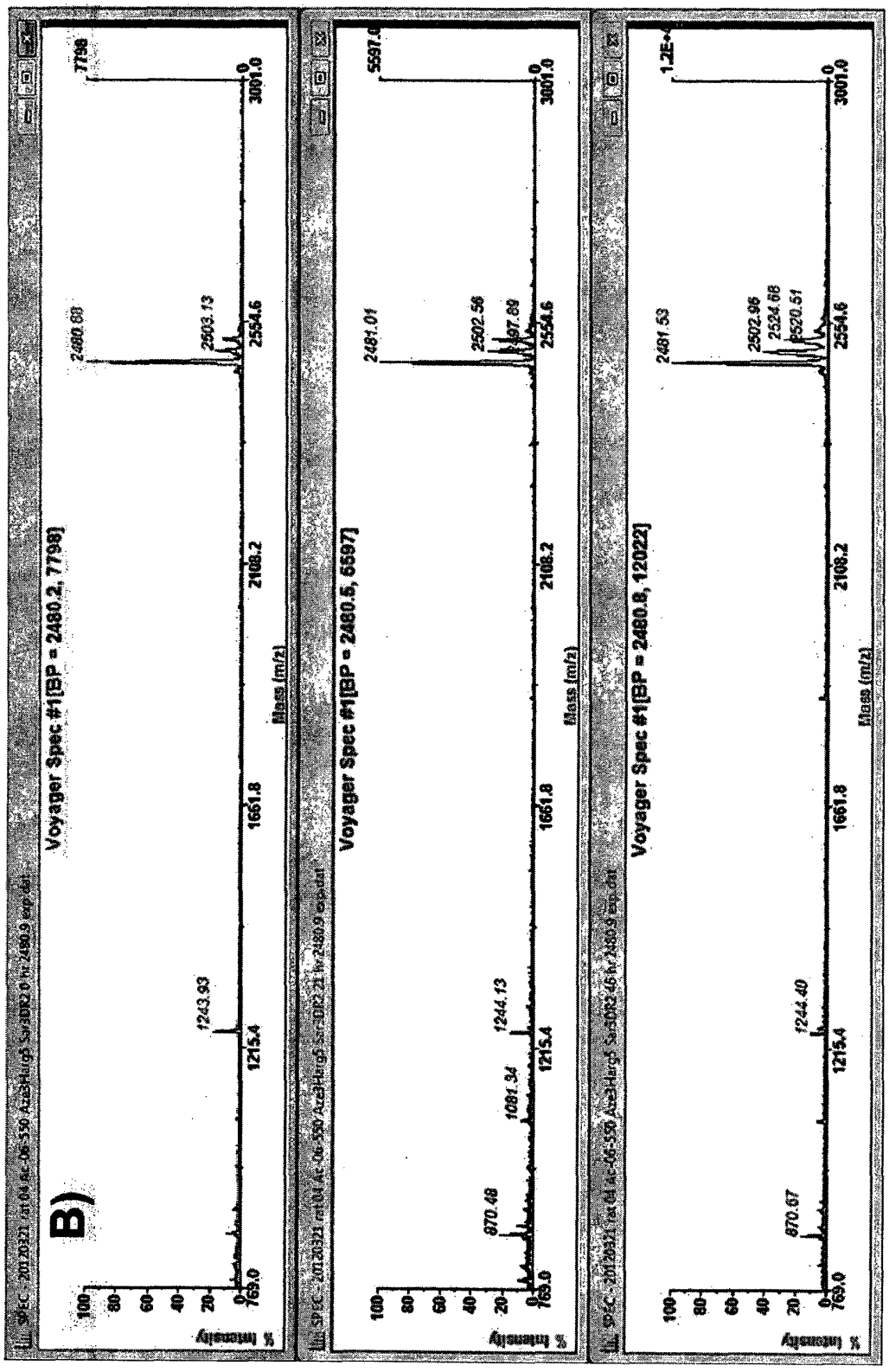

B)
Voyager Spec #1[BP = 2480.2, 7798]
Voyager Spec #1[BP = 2480.6, 6597]
Voyager Spec #1[BP = 2480.8, 12022]
% Intensity
Mass (m/z)
2480.68
2503.13
1243.93
1215.4
1661.8
2108.2
2554.6
870.48
1081.34
1244.13
2481.01
2502.56
2497.89
2481.53
2502.96
2534.68
2520.51
870.67
1244.40
769.0
3001.0
7798
6597
12022

FIGURE 3 (ctd)

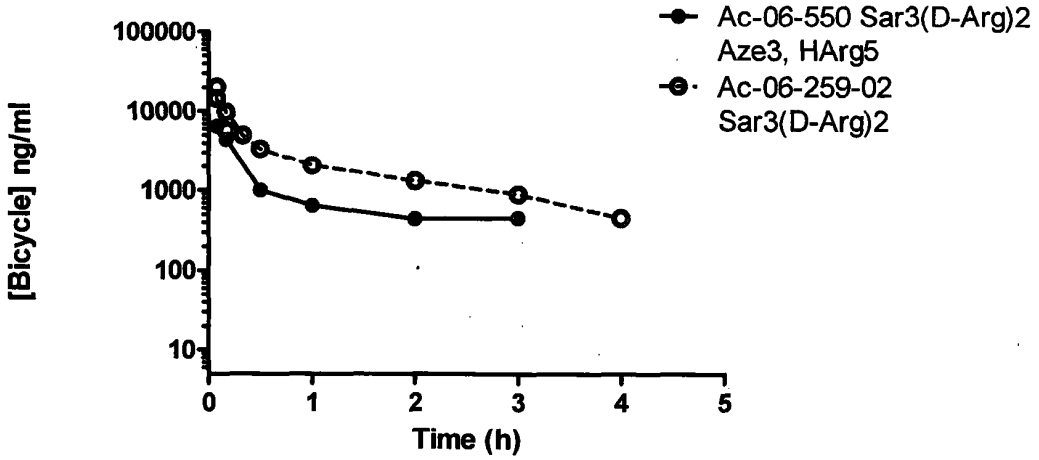

Ac-06-550 Sar3(D-Arg)2 Aze3, HArg5
Ac-06-259-02 Sar3(D-Arg)2
[Bicycle] ng/ml
100000
10000
1000
100
10
0
1
2
3
4
5
Time (h)

FIGURE 4

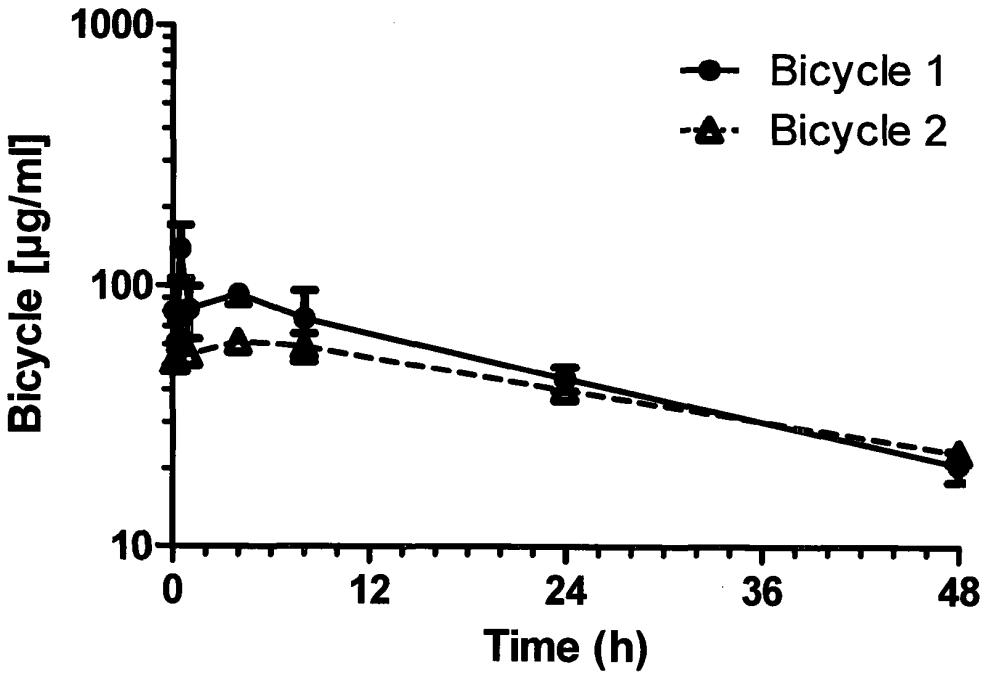

1000
100
10
Bicycle [µg/ml]
0
12
24
36
48
Time (h)
Bicycle 1
Bicycle 2

FIGURE 5

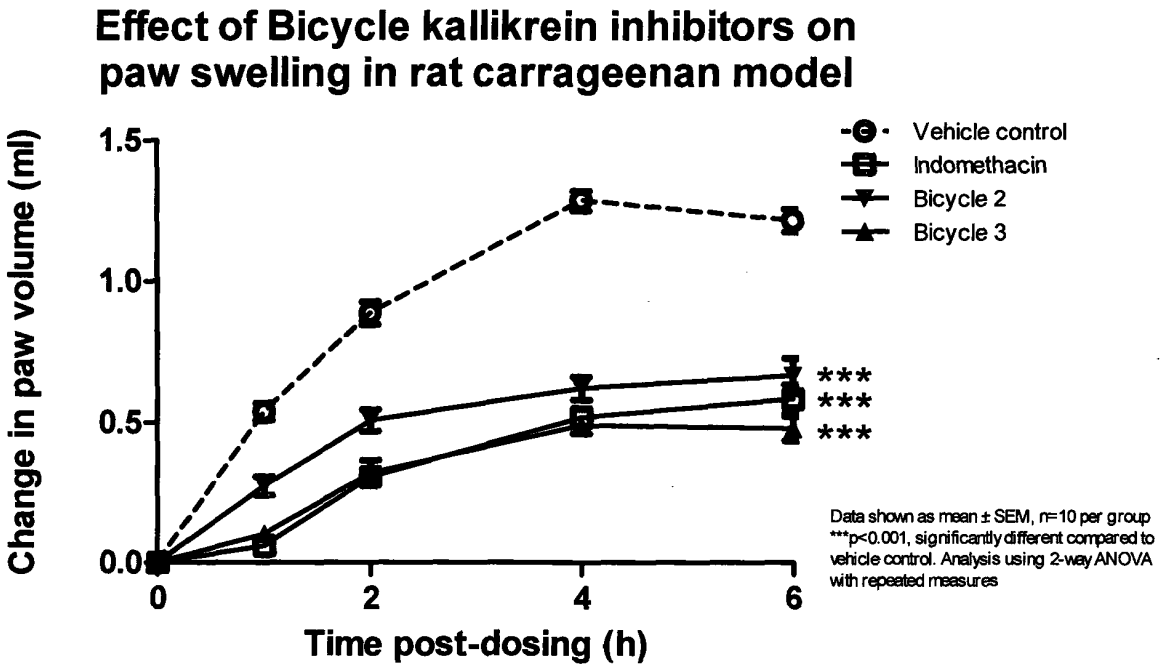

Effect of Bicycle kallikrein inhibitors on paw swelling in rat carrageenan model
Change in paw volume (ml)
1.5
1.0
0.5
0.0
0
2
4
6
Time post-dosing (h)
Vehicle control
Indomethacin
Bicycle 2
Bicycle 3
***
***
***
Data shown as mean ± SEM, n=10 per group
***p<0.001, significantly different compared to vehicle control. Analysis using 2-way ANOVA with repeated measures

FIGURE 6