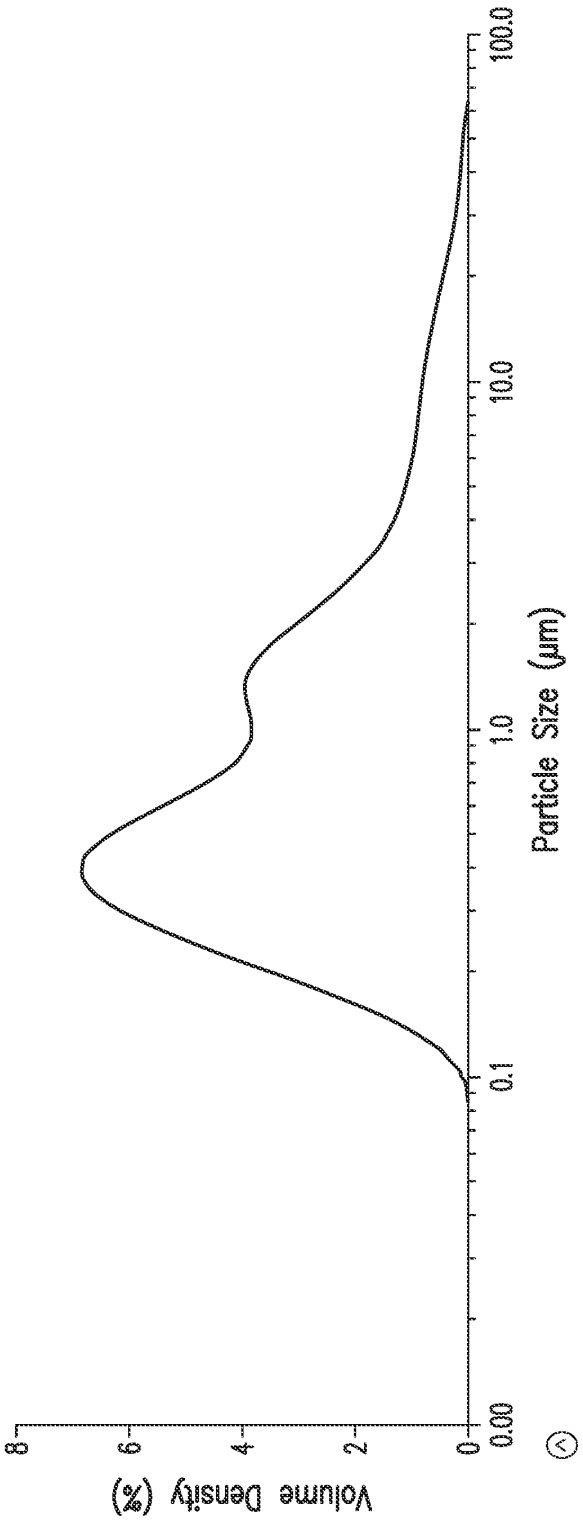

Volume Density (%)
0
2
4
6
8
0.00
0.1
1.0
10.0
100.0
Particle Size (µm)
(12) SCP ARQ 250 (2 min)

FIG. 1

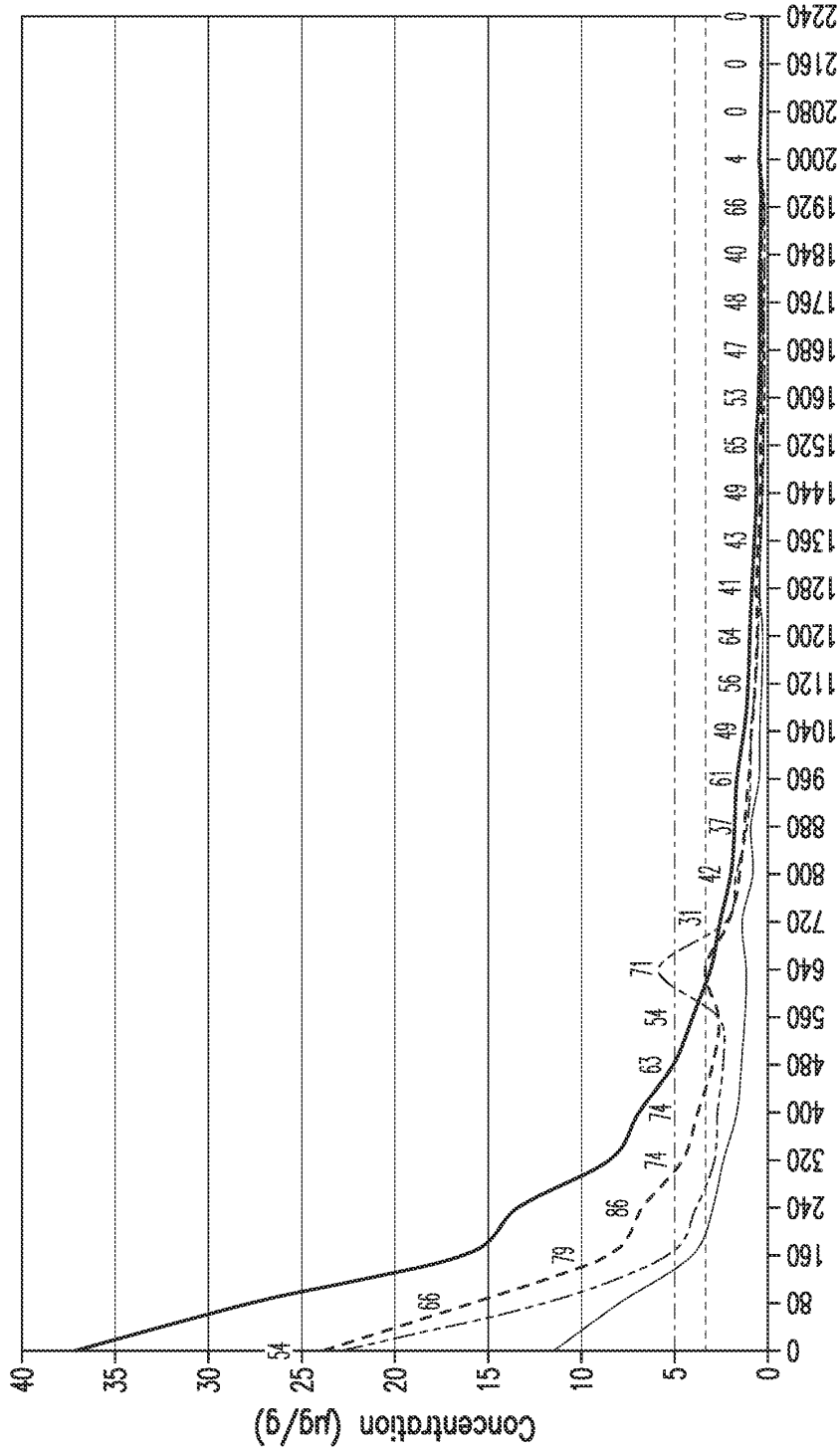

Concentration (µg/g)
40
35
30
25
20
15
10
5
0
Depth (µm)
0
80
160
240
320
400
480
560
640
720
800
880
960
1040
1120
1200
1280
1360
1440
1520
1600
1680
1760
1840
1920
2000
2080
2160
2240
0 0 0 4 66 40 48 47 53 65 49 43 41 64 56 49 61 37 42 31 71 54 63 74 74 86 79 66 54
LOQ (µg/g)
LOQ (µg/g)
Comp. Ex. 1–Sample 1
Comp. Ex. 1–Sample 2
Comp. Ex. 1–Sample 3
Comp. Ex. 1–Mean

FIG. 2

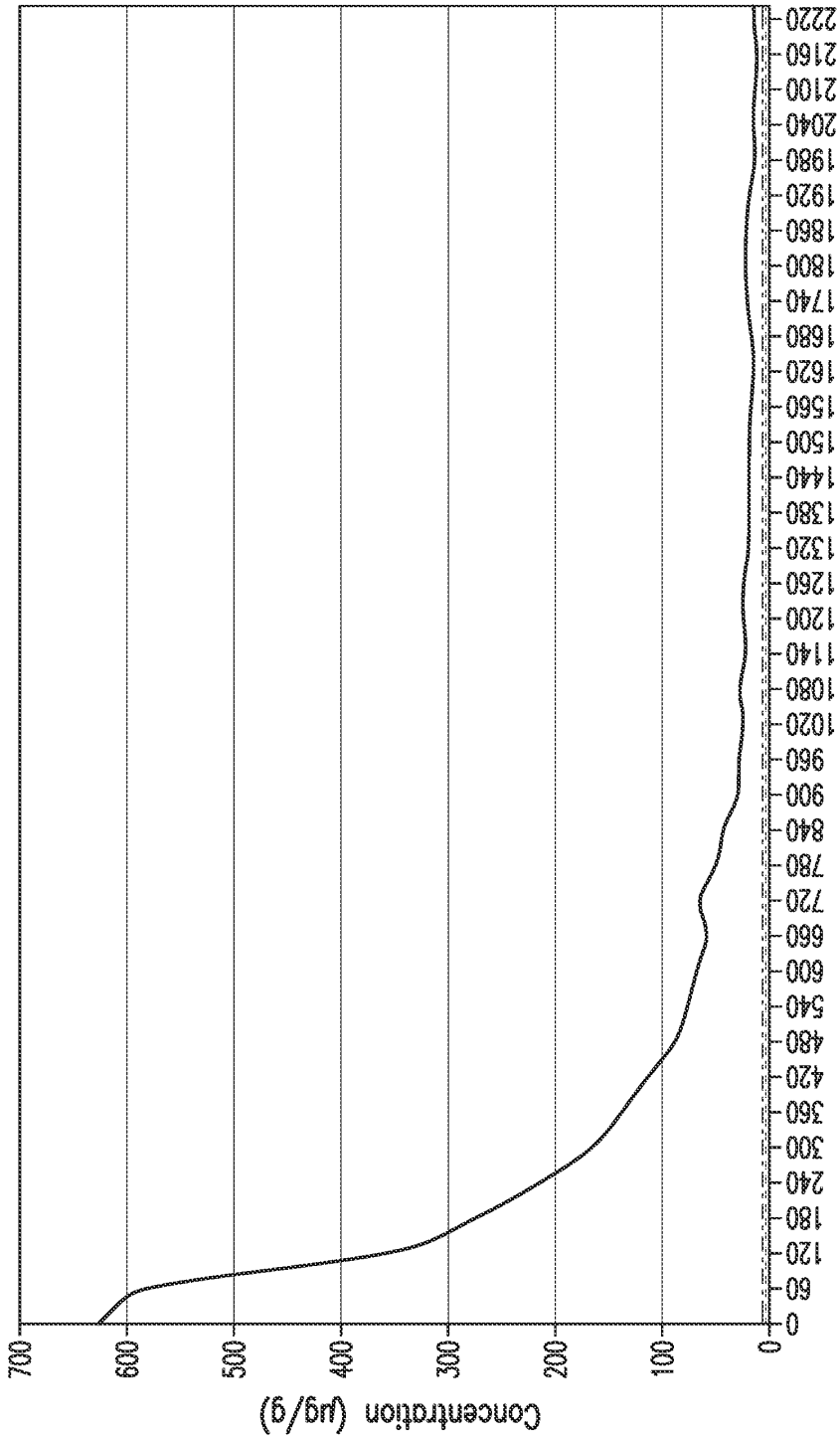

Concentration (µg/g)
0
100
200
300
400
500
600
700
Depth (µm)
0
60
120
180
240
300
360
420
480
540
600
660
720
780
840
900
960
1020
1080
1140
1200
1260
1320
1380
1440
1500
1560
1620
1680
1740
1800
1860
1920
1980
2040
2100
2160
2220
Ex. 1–Sample 1
LOD (µg/g)
LOQ (µg/g)

FIG. 3

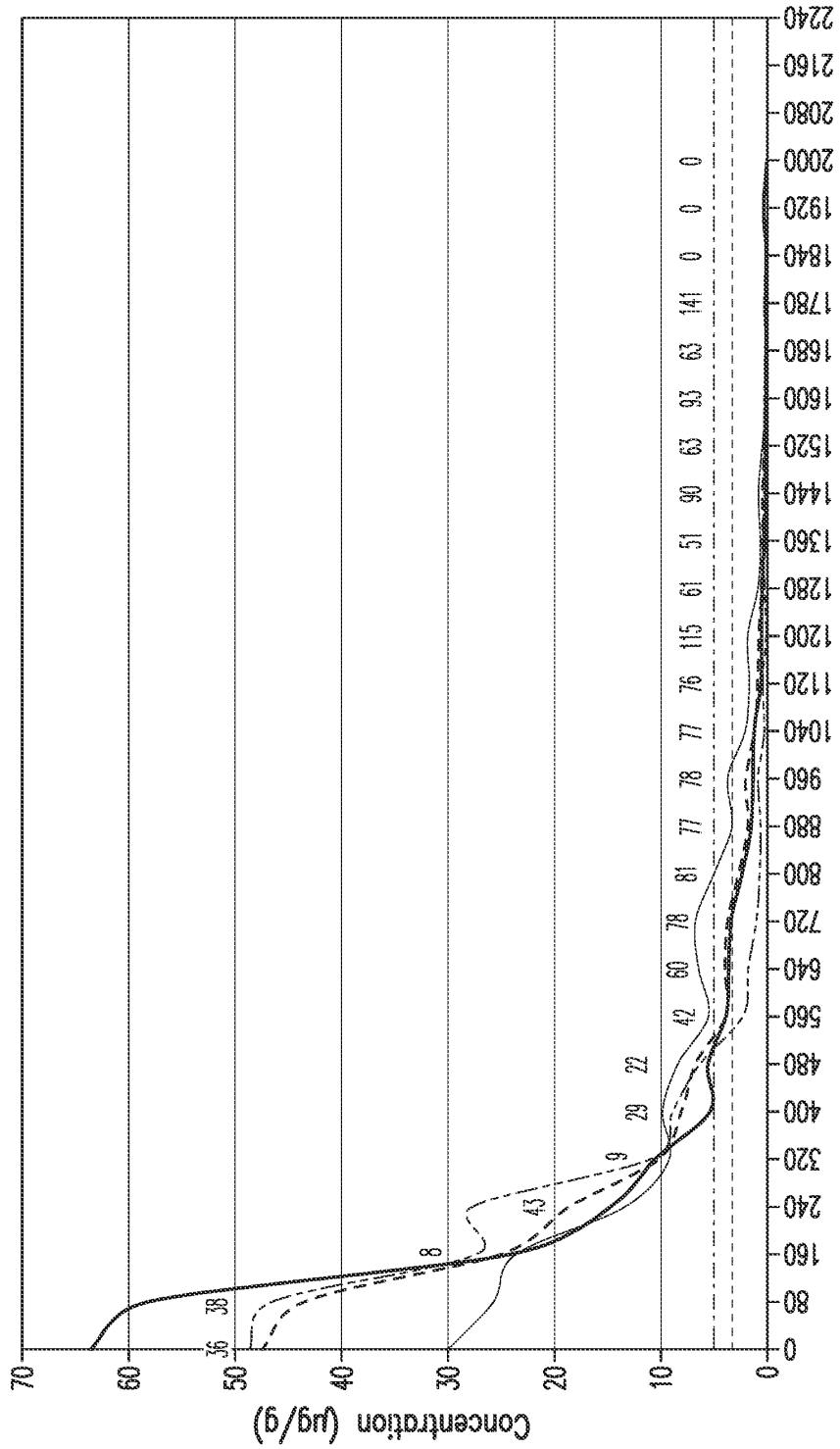

Concentration (µg/g)
0
10
20
30
40
50
60
70
Depth (µm)
0
80
160
240
320
400
480
560
640
720
800
880
960
1040
1120
1200
1280
1360
1440
1520
1600
1680
1780
1840
1920
2000
2080
2160
2240
36
38
8
43
9
29
22
42
60
78
81
77
78
77
76
115
61
51
90
63
93
63
141
0
0
0
LOQ (µg/g)
LOQ (µg/g)
Comp. Ex. 1–Sample 1
Comp. Ex. 1–Sample 2
Comp. Ex. 1–Sample 3
Comp. Ex. 1–Mean

FIG. 4

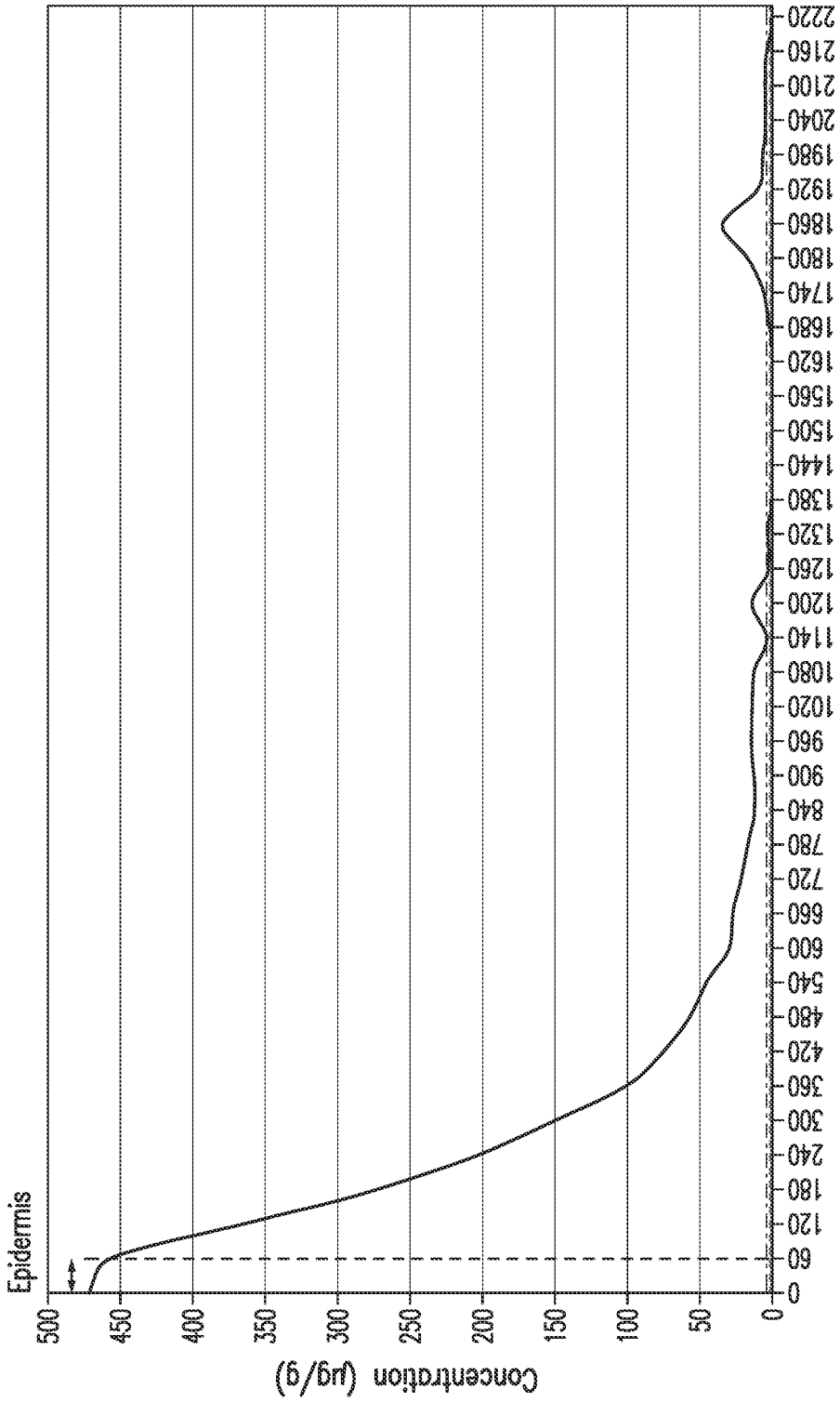

Epidermis
Concentration (µg/g)
500
450
400
350
300
250
200
150
100
50
0
Depth (µm)
0
60
120
180
240
300
360
420
480
540
600
660
720
780
840
900
960
1020
1080
1140
1200
1260
1320
1380
1440
1500
1560
1620
1680
1740
1800
1860
1920
1980
2040
2100
2160
2220
Ex. 1
LOD (µg/g)
LOQ (µg/g)

FIG. 5

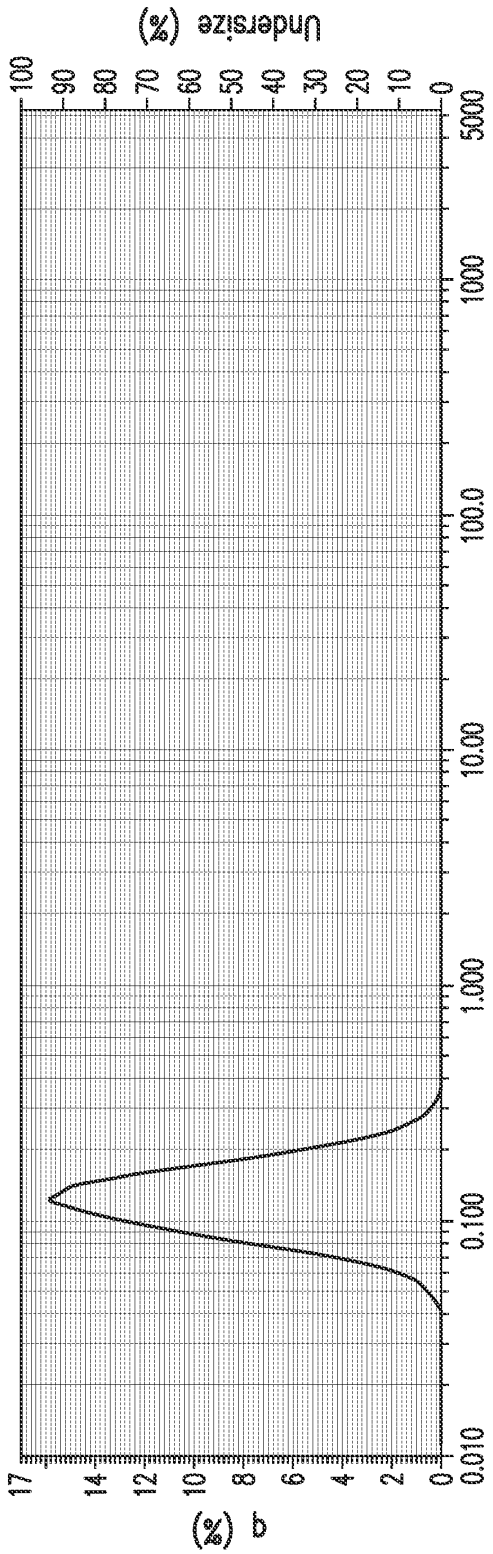

Undersize (%)
100
90
80
70
60
50
40
30
20
10
0
5000
1000
100.0
10.00
1.000
0.100
0.010
Diameter (µm)
q (%)
17
14
12
10
8
6
4
2
0

FIG. 6

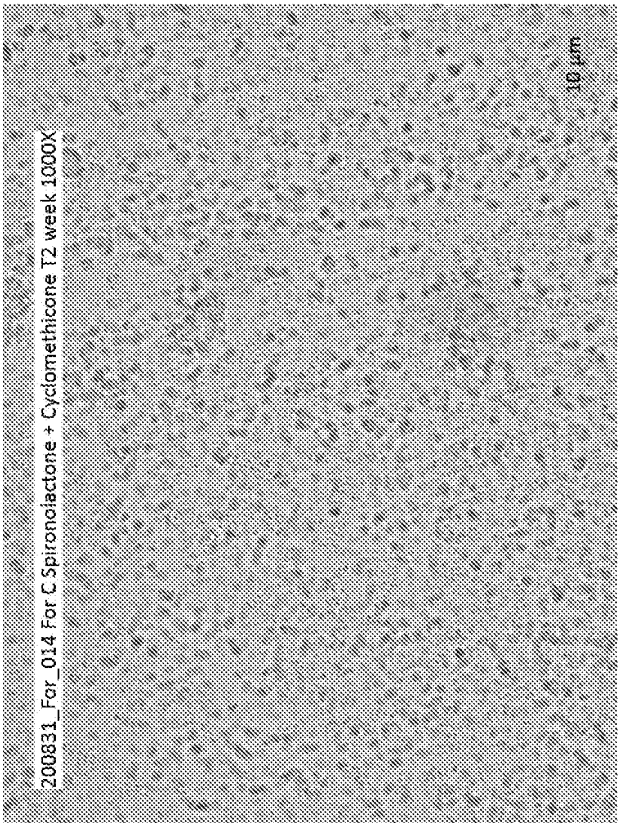

200831_For_014 For C Spironolactone + Cyclomethicone T2 week 1000X
10 µm

FIG. 7

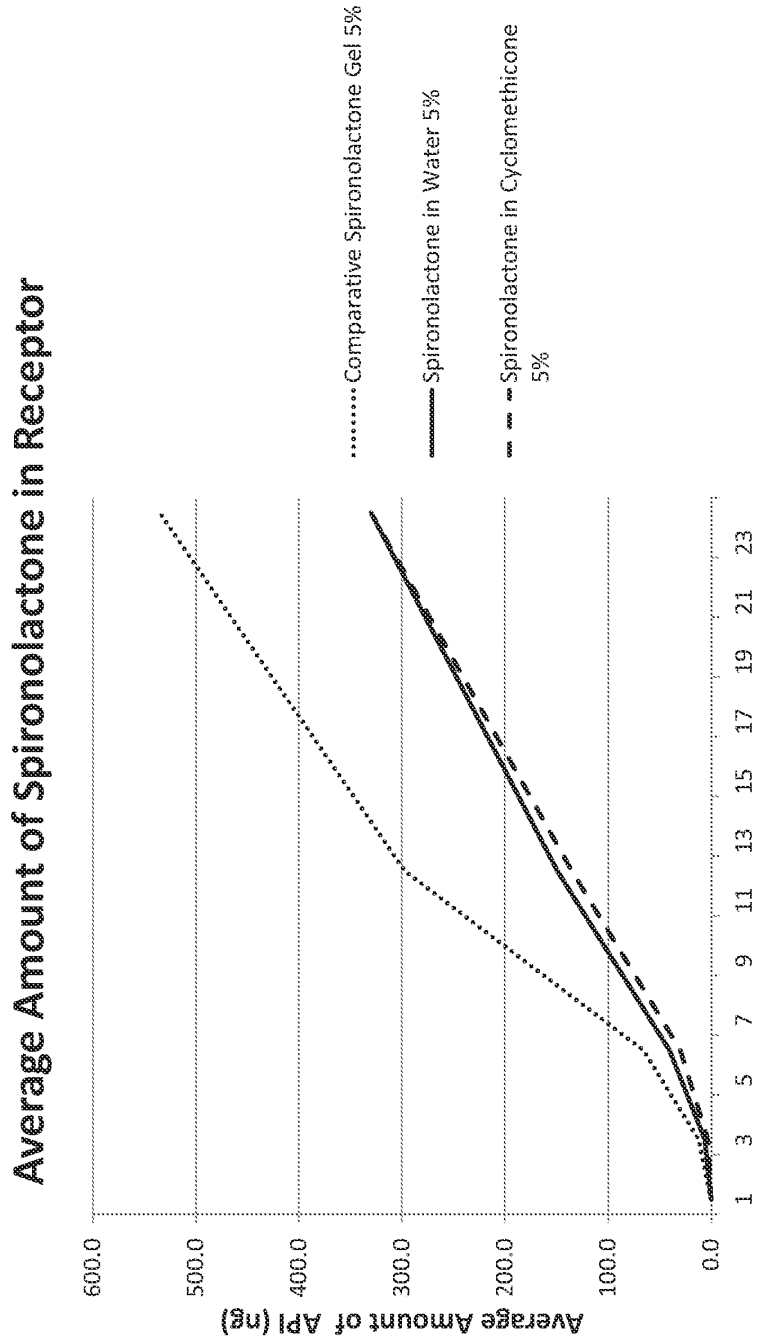

Average Amount of Spironolactone in Receptor
Comparative Spironolactone Gel 5%
Spironolactone in Water 5%
Spironolactone in Cyclomethicone 5%
Average Amount of API (ng)
600.0
500.0
400.0
300.0
200.0
100.0
0.0
1 3 5 7 9 11 13 15 17 19 21 23
Time Point (hr)

FIG. 8

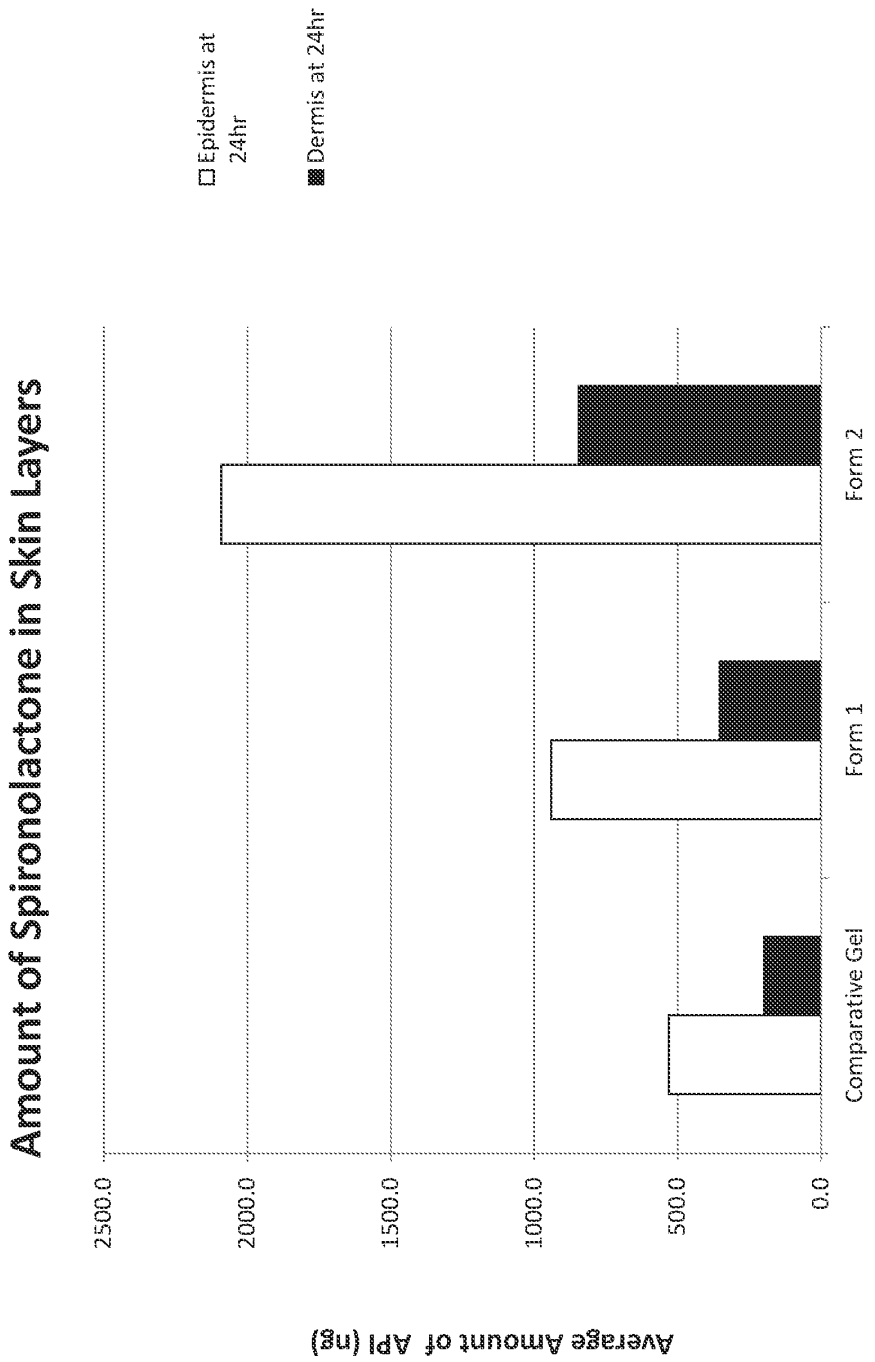

Amount of Spironolactone in Skin Layers
Epidermis at 24hr
Dermis at 24hr
2500.0
2000.0
1500.0
1000.0
500.0
0.0
Comparative Gel
Form 1
Form 2
Average Amount of API (ng)

FIG. 9

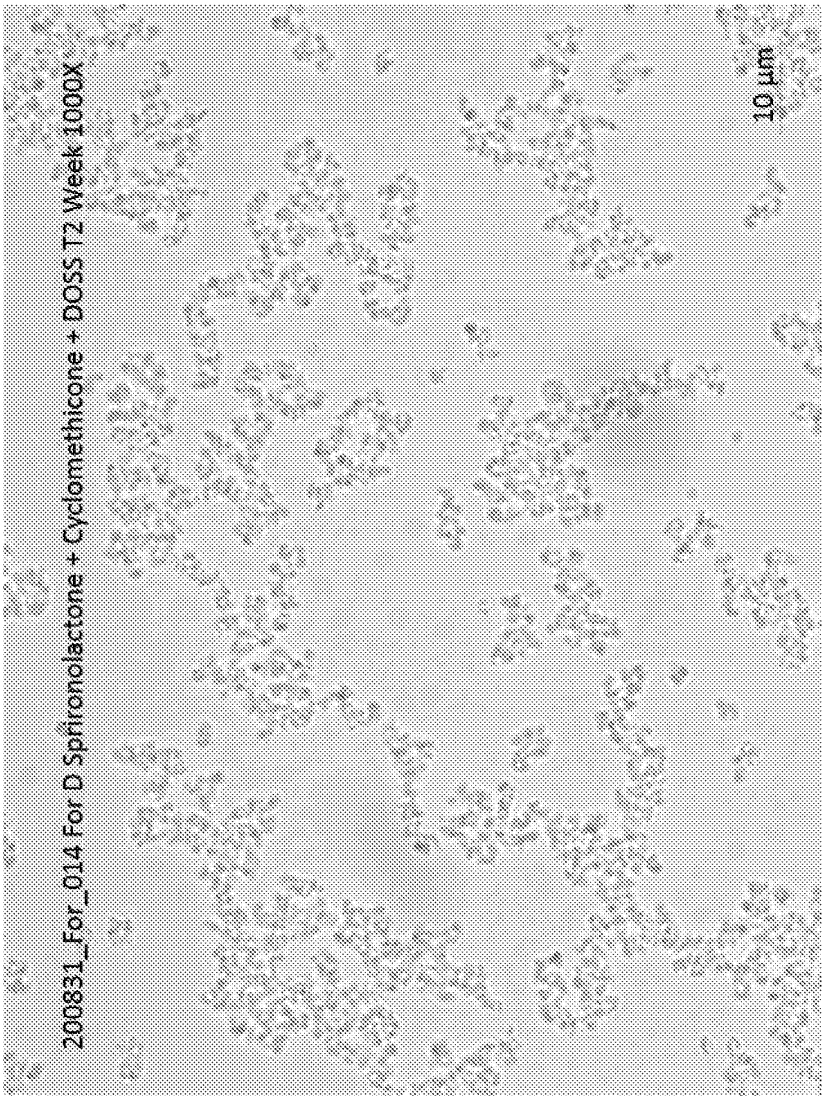

200831_For_014 For D Spironolactone + Cyclomethicone + DOSS T2 Week 1000X
10 µm

FIG. 10

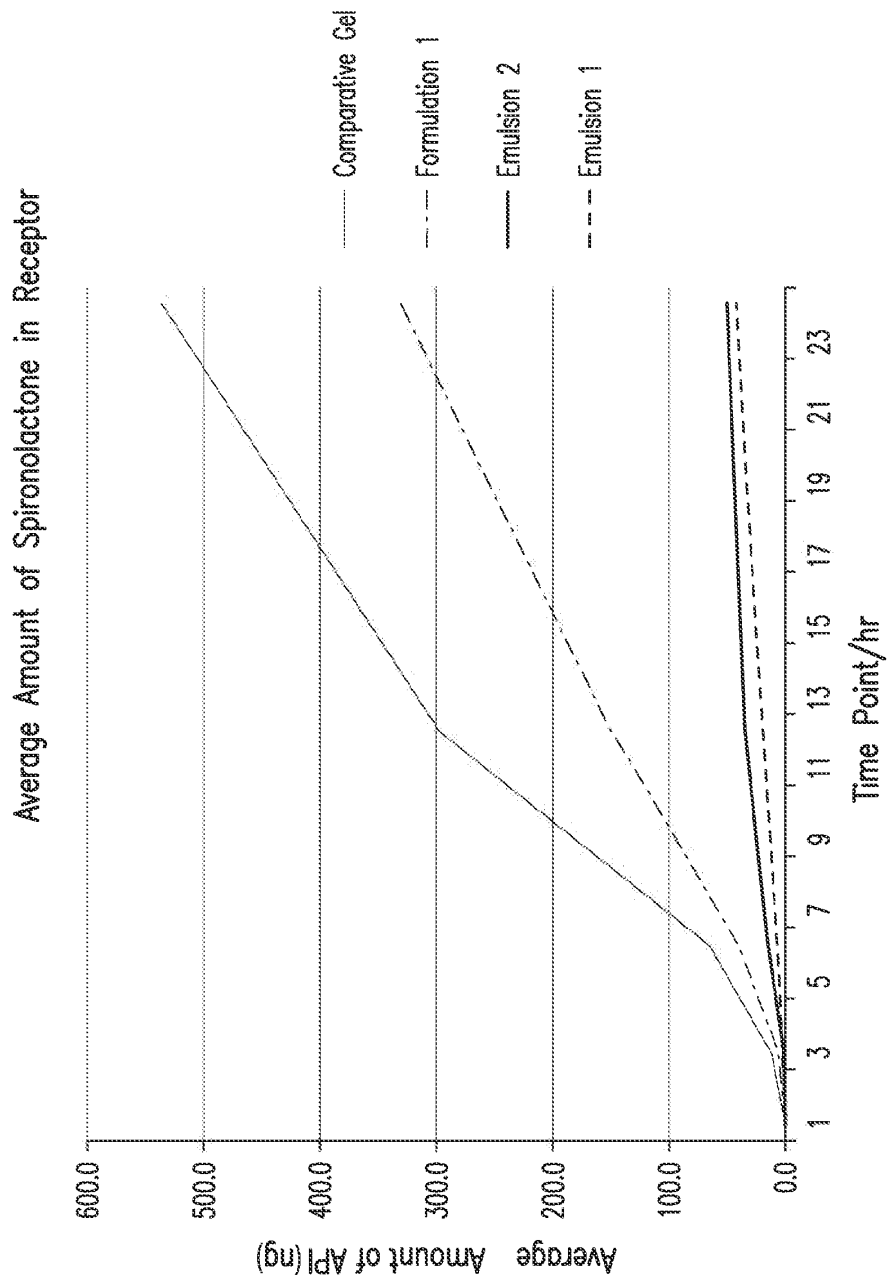

Average Amount of Spironolactone in Receptor
Comparative Gel
Formulation 1
Emulsion 2
Emulsion 1
Average Amount of API (ng)
600.0
500.0
400.0
300.0
200.0
100.0
0.0
1
3
5
7
9
11
13
15
17
19
21
23
Time Point/hr

FIG. 11

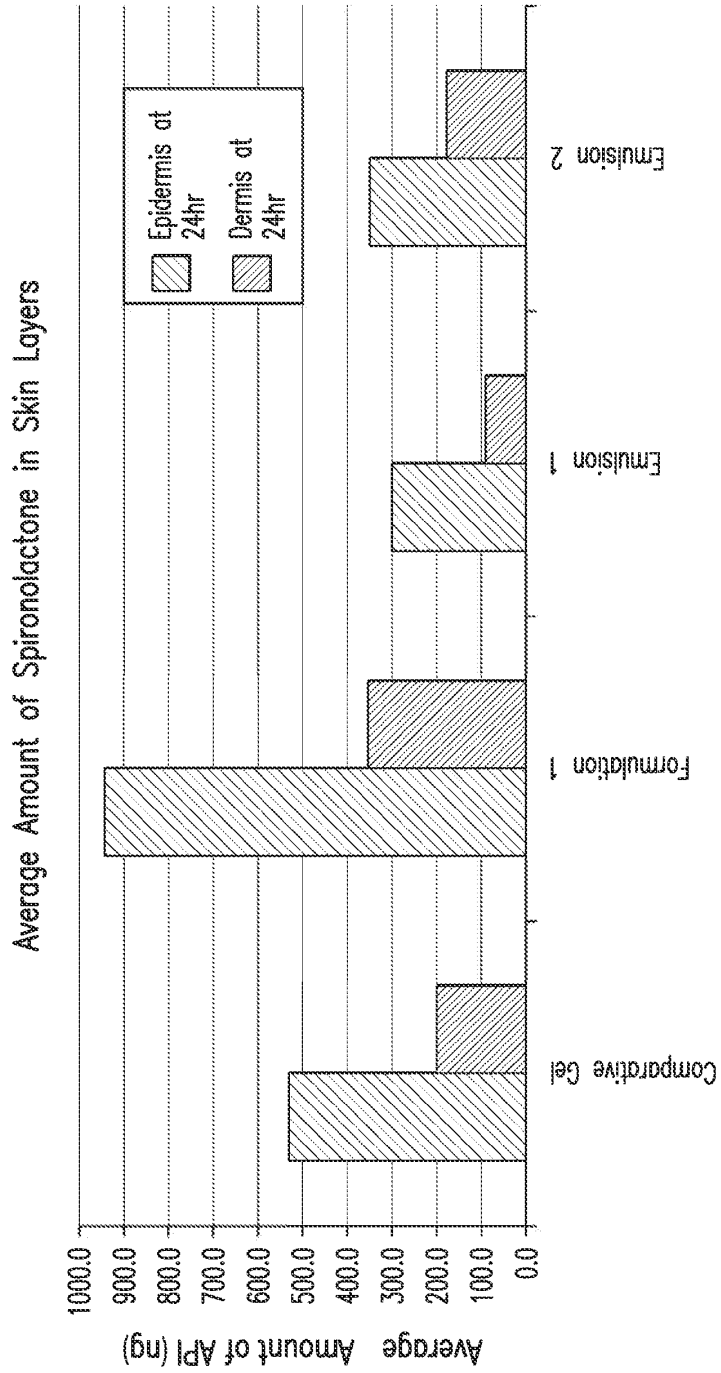

Average Amount of Spironolactone in Skin Layers
Epidermis at 24hr
Dermis at 24hr
Average Amount of API (ng)
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
Comparative Gel
Formulation 1
Emulsion 1
Emulsion 2

FIG. 12

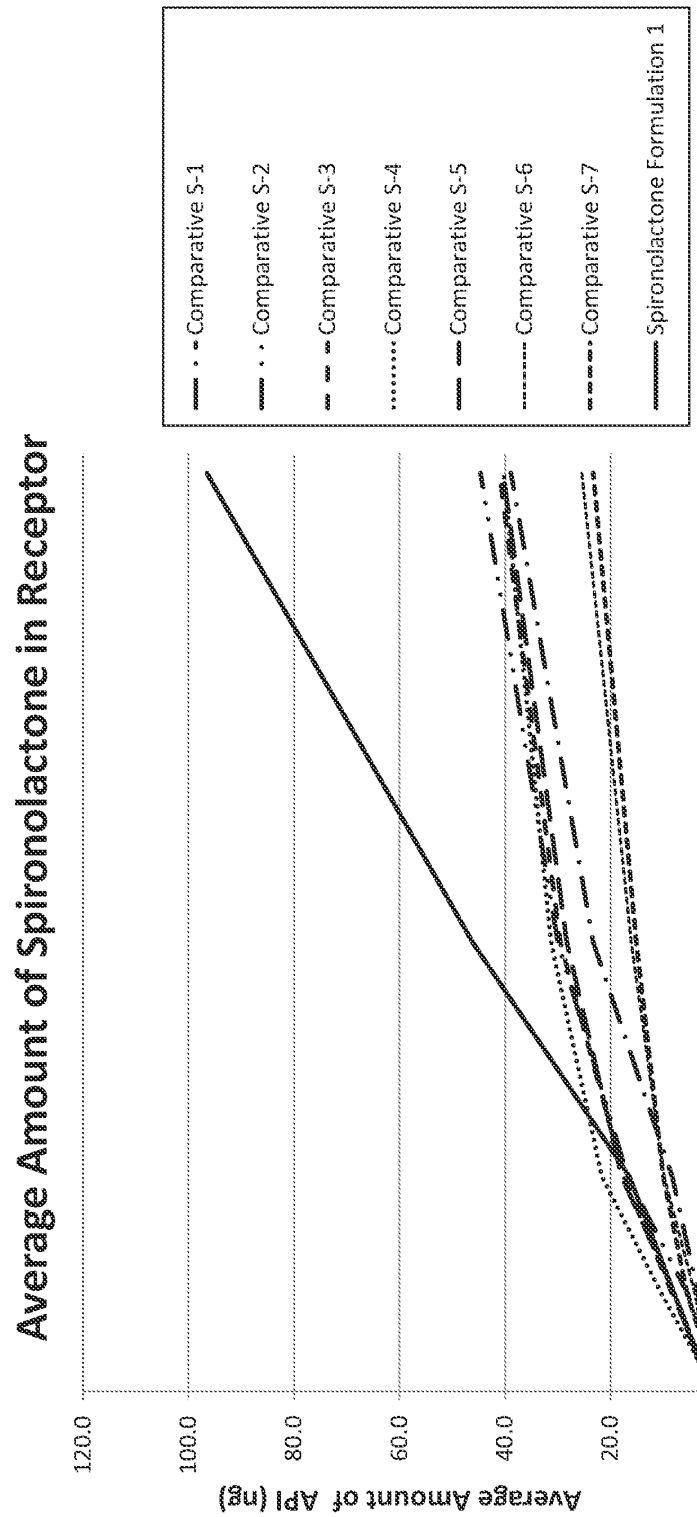

Average Amount of Spironolactone in Receptor
Average Amount of API (ng)
120.0
100.0
80.0
60.0
40.0
20.0
0.0
1
3
5
7
9
11
13
15
17
19
21
23
Time Point (hr)
Comparative S-1
Comparative S-2
Comparative S-3
Comparative S-4
Comparative S-5
Comparative S-6
Comparative S-7
Spironolactone Formulation 1

FIG. 13

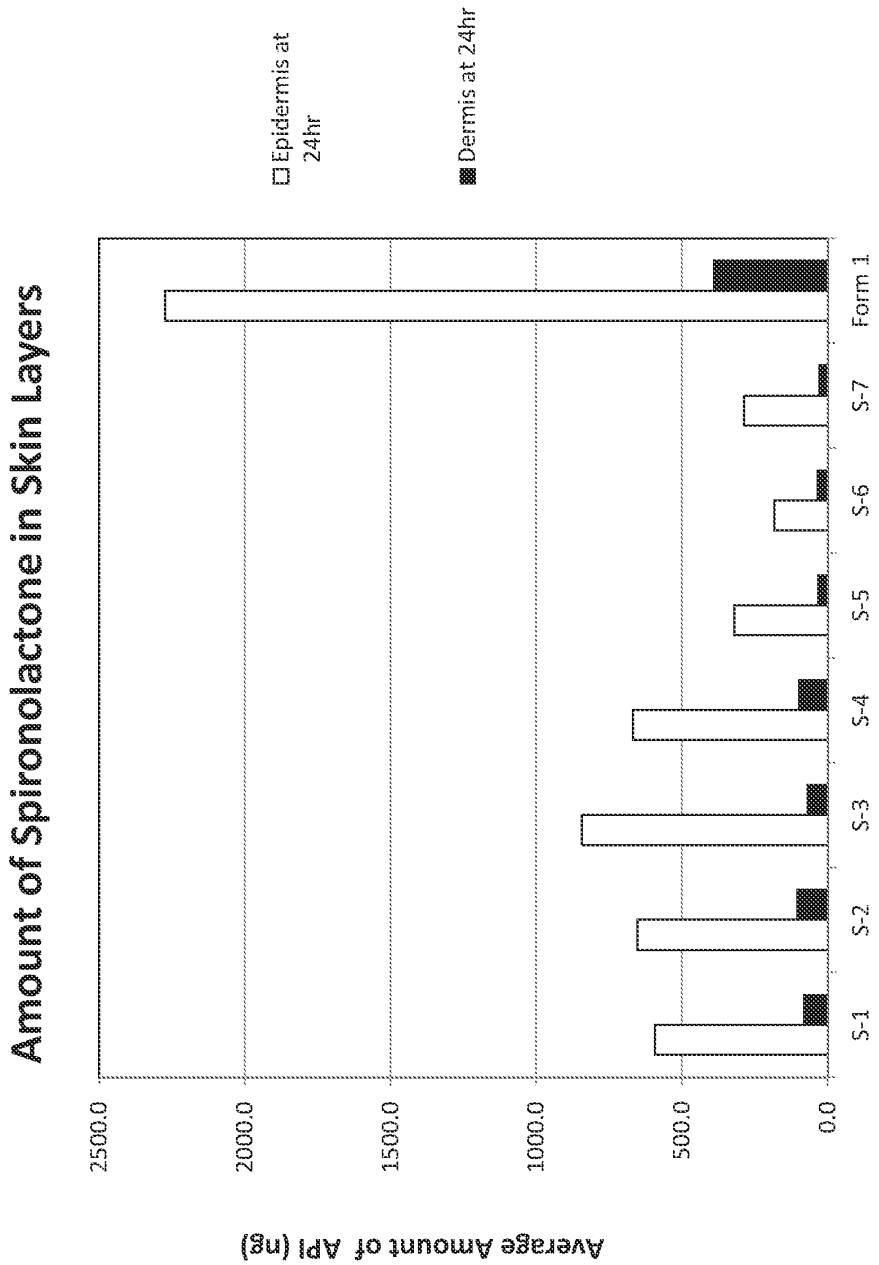

Amount of Spironolactone in Skin Layers
Epidermis at 24hr
Dermis at 24hr
Average Amount of API (ng)
2500.0
2000.0
1500.0
1000.0
500.0
0.0
S-1
S-2
S-3
S-4
S-5
S-6
S-7
Form 1

FIG. 14