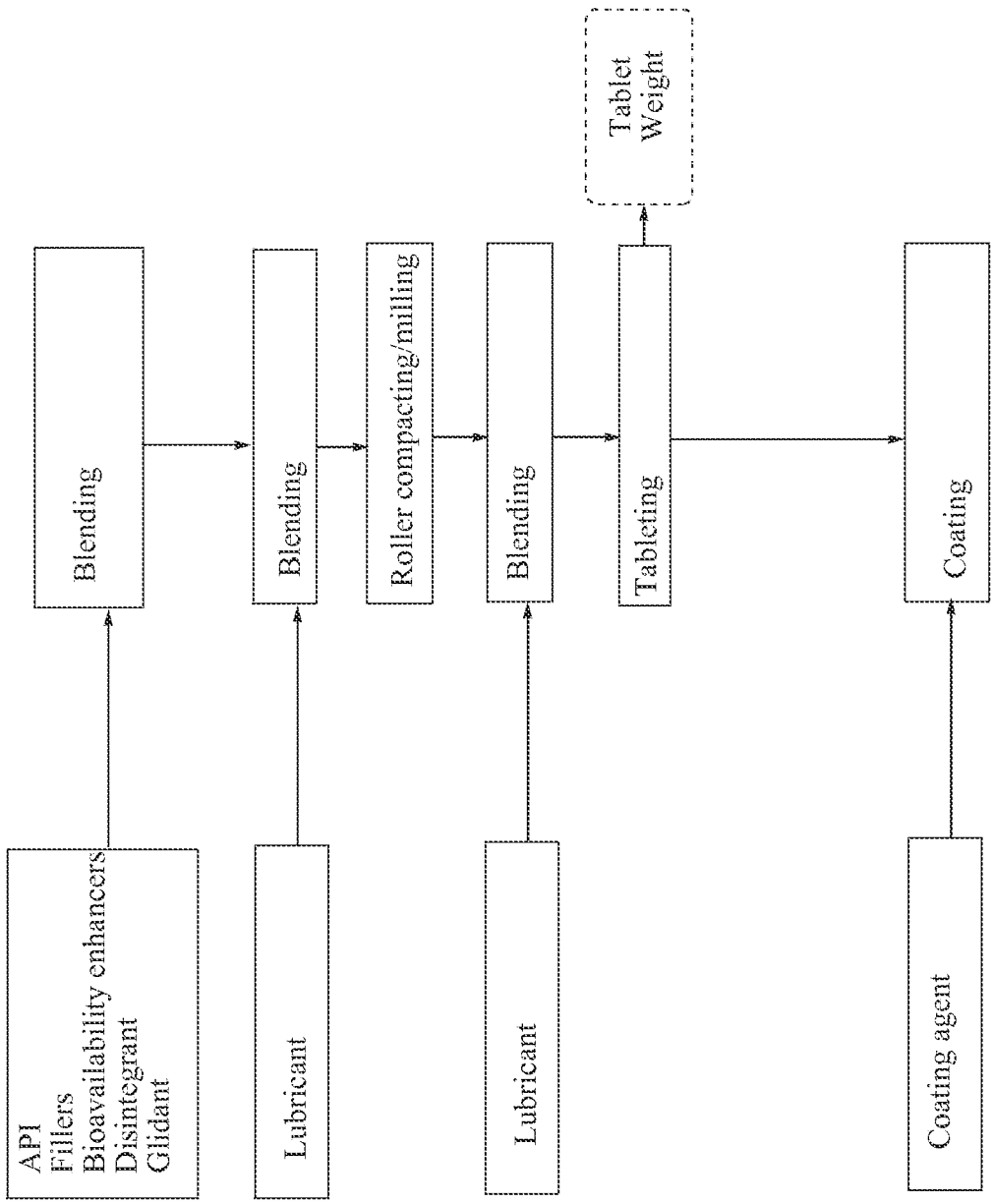
Figure 1


Material
Process
In-process control
API
Fillers
Bioavailability enhancers
Disintegrant
Glidant
Blending
Lubricant
Blending
Roller compacting/milling
Lubricant
Blending
Tablet Weight
Tableting
Coating agent
Coating

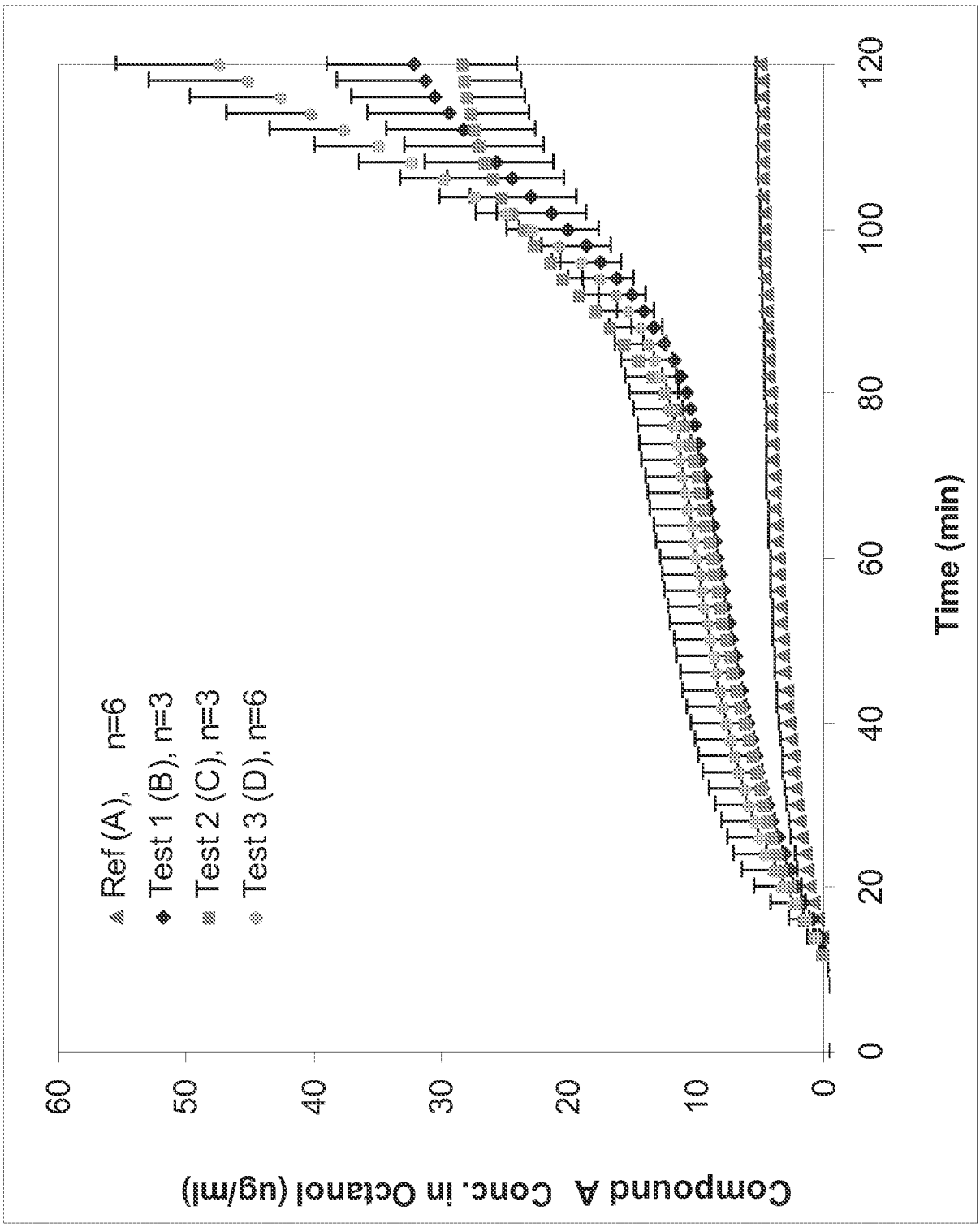

Compound A Conc. in Octanol (ug/ml)
0
10
20
30
40
50
60
0
20
40
60
80
100
120
Time (min)
Ref (A), n=6
Test 1 (B), n=3
Test 2 (C), n=3
Test 3 (D), n=6

Figure 2

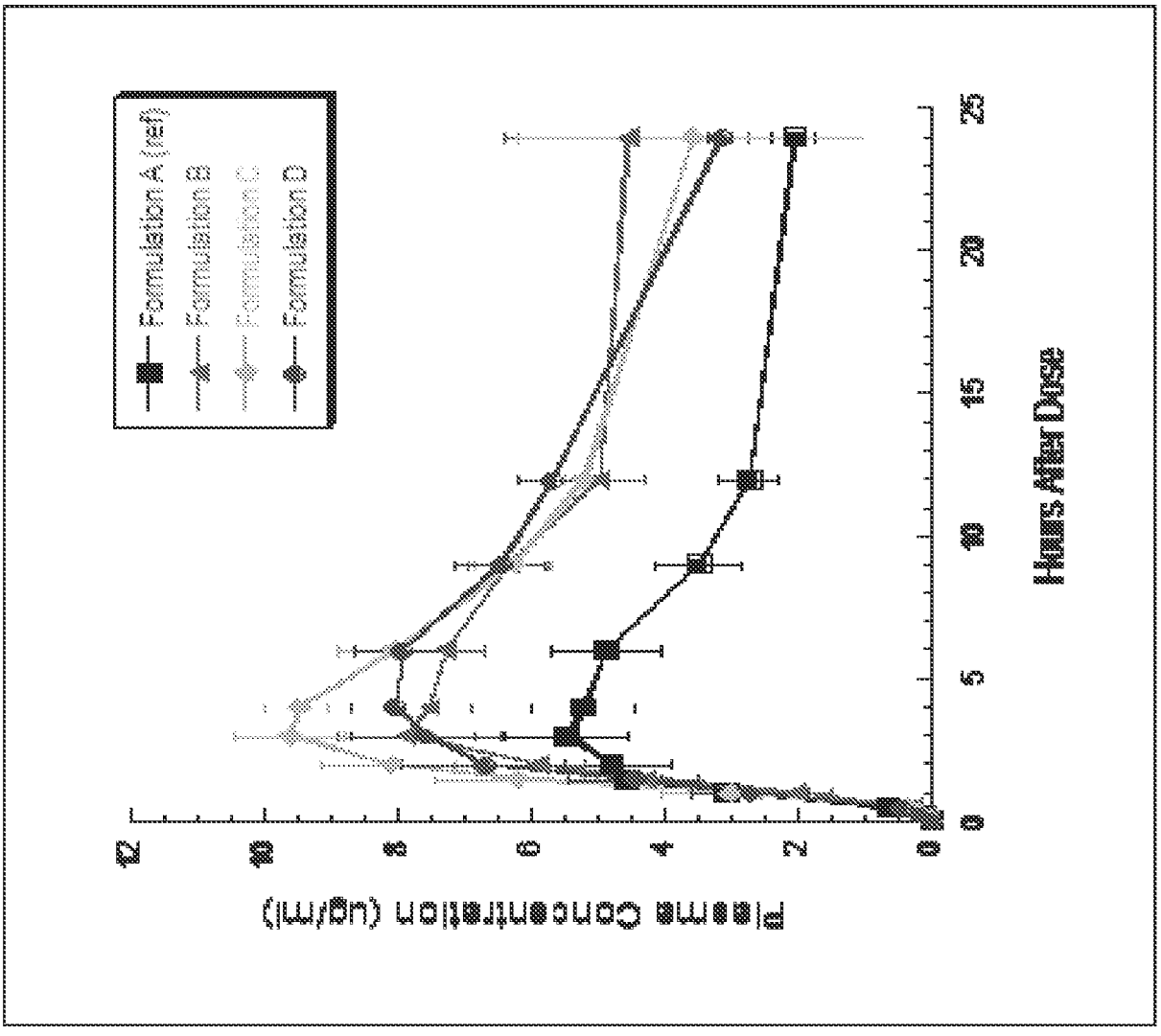

Formulation A (ref)
Formulation B
Formulation C
Formulation D
Plasma Concentration (ug/ml)
Hours After Dose
0
2
4
6
8
10
12
0
5
10
15
20
25

Figure 3

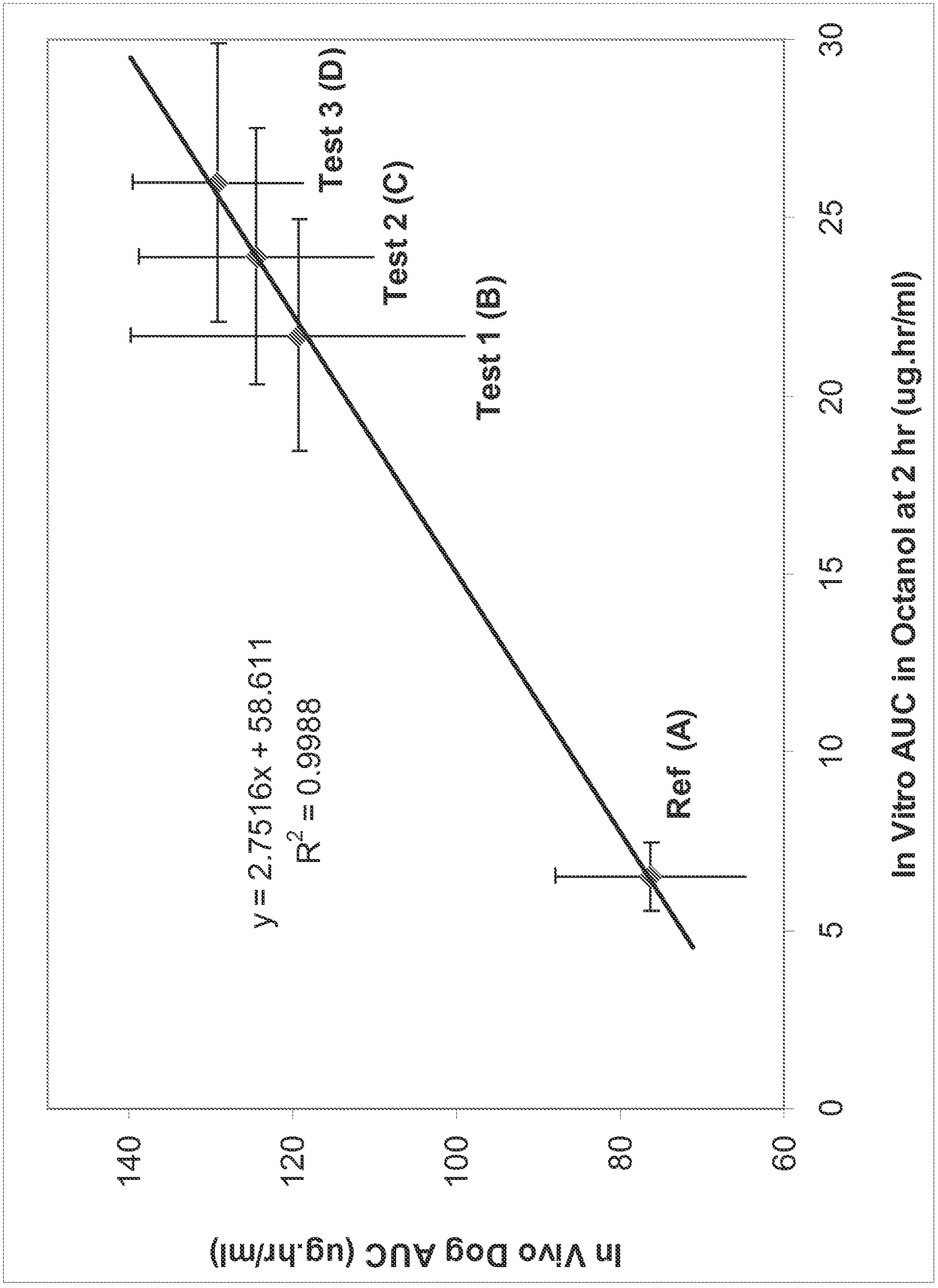

In Vivo Dog AUC (ug.hr/ml)
140
120
100
80
60
0
5
10
15
20
25
30
In Vitro AUC in Octanol at 2 hr (ug.hr/ml)
Test 3 (D)
Test 2 (C)
Test 1 (B)
Ref (A)
y = 2.7516x + 58.611
R2 = 0.9988

Figure 4

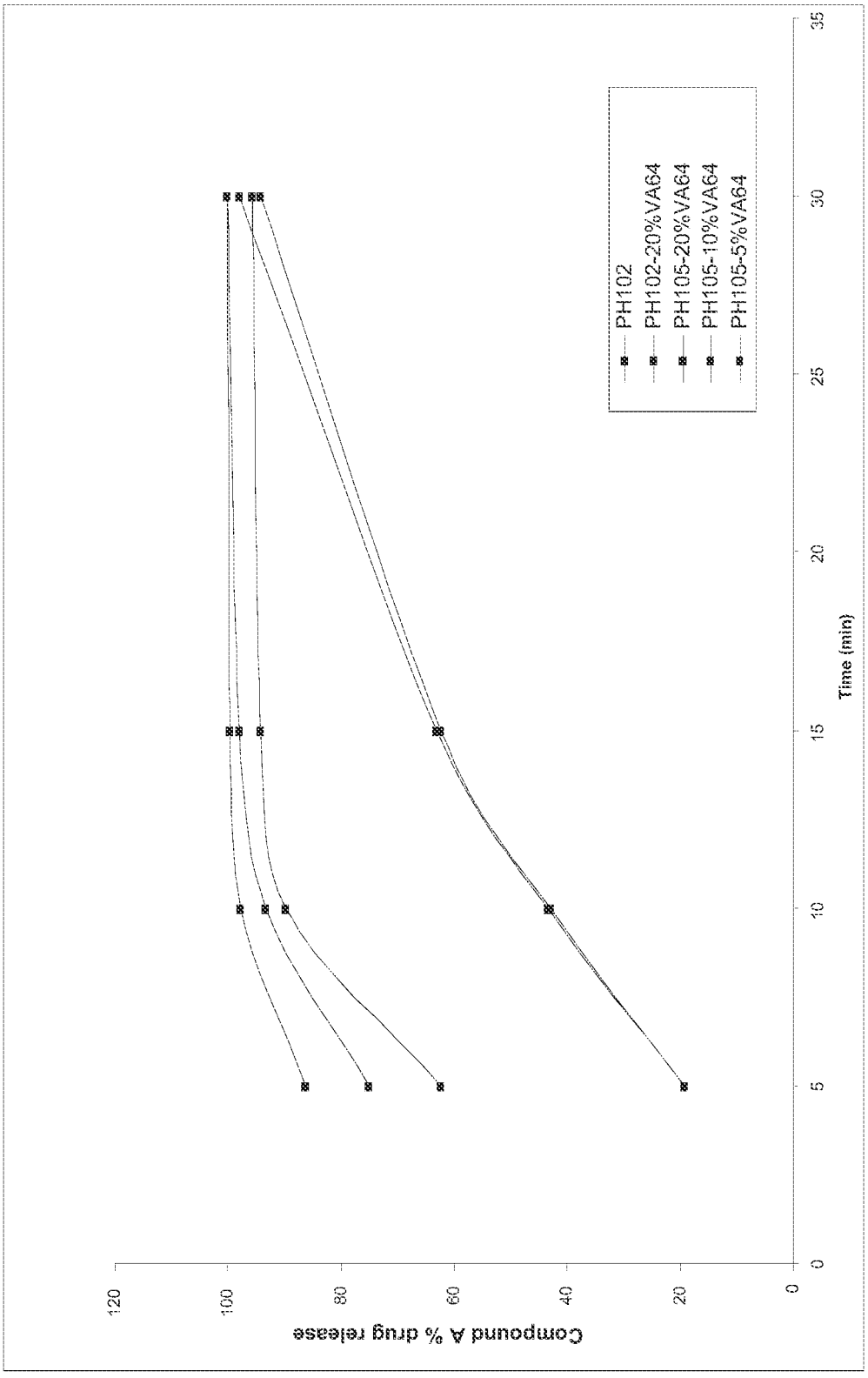

Compound A % drug release
Time (min)
0
20
40
60
80
100
120
0
5
10
15
20
25
30
35
PH102
PH102-20%VA64
PH105-20%VA64
PH105-10%VA64
PH105-5%VA64

Figure 5

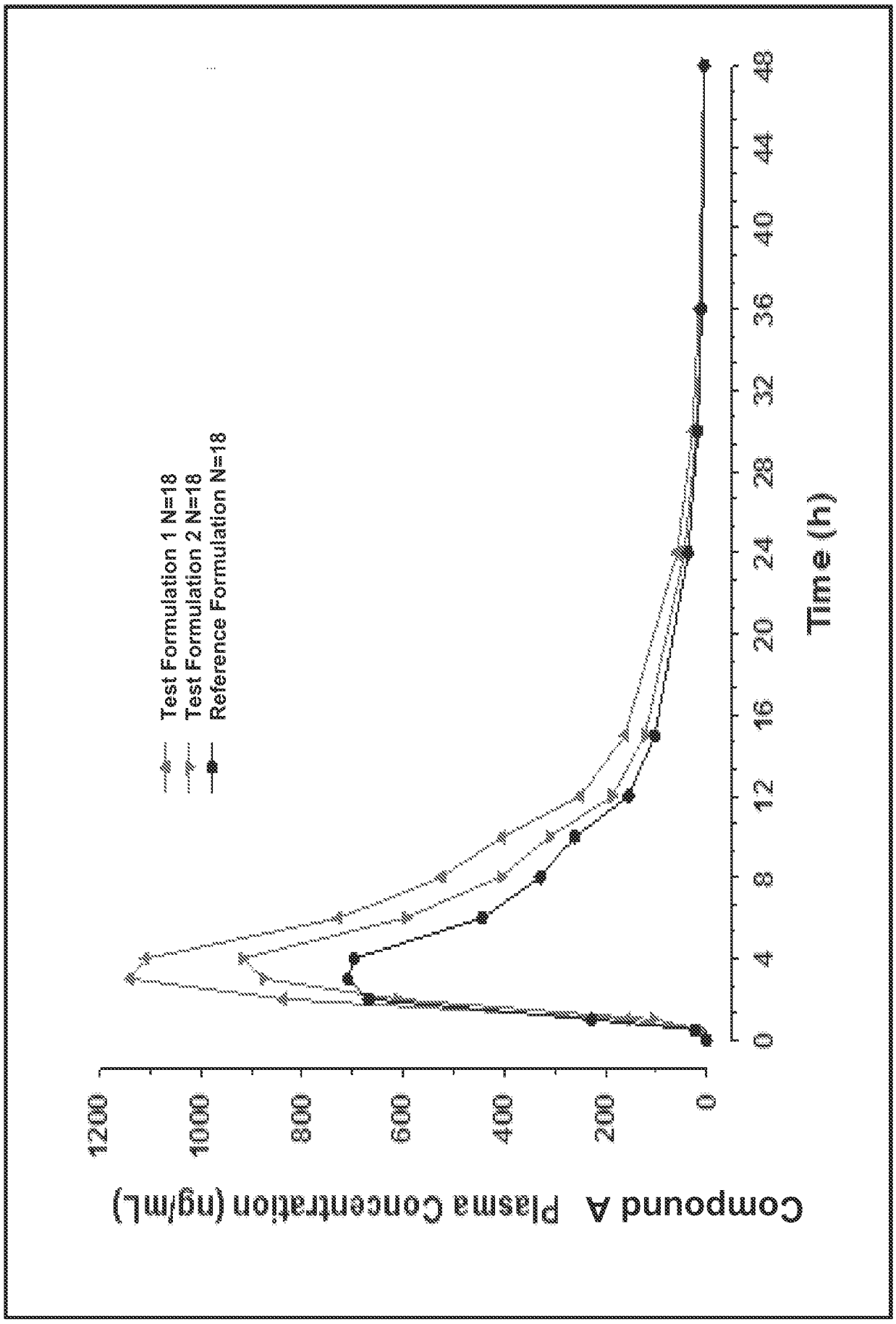

Compound A Plasma Concentration (ng/mL)
1200
1000
800
600
400
200
0
0
4
8
12
16
20
24
28
32
36
40
44
48
Time (h)
Test Formulation 1 N=18
Test Formulation 2 N=18
Reference Formulation N=18

Figure 6

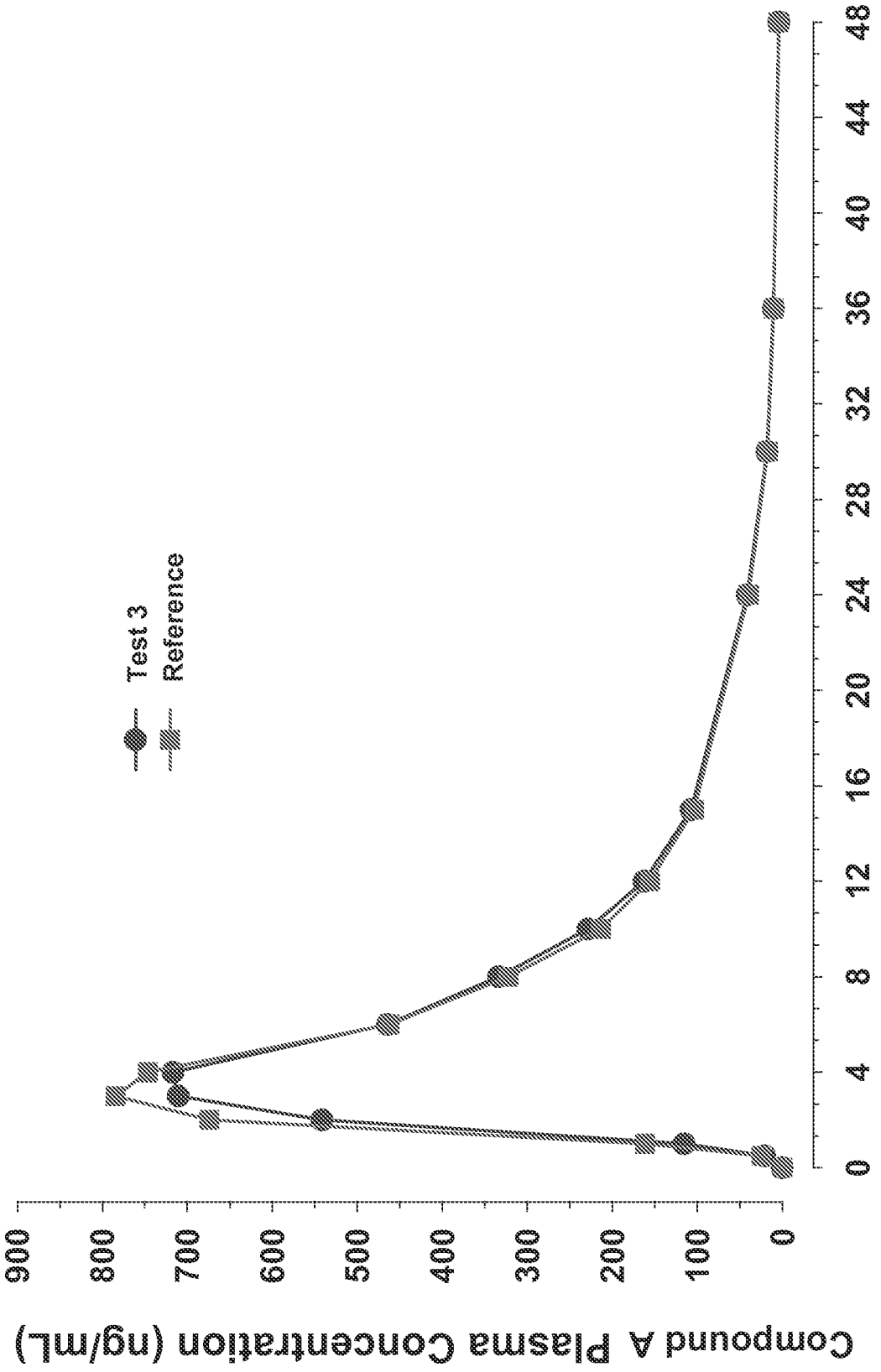

Compound A Plasma Concentration (ng/mL)
900
800
700
600
500
400
300
200
100
0
0
4
8
12
16
20
24
28
32
36
40
44
48
Test 3
Reference

Figure 7

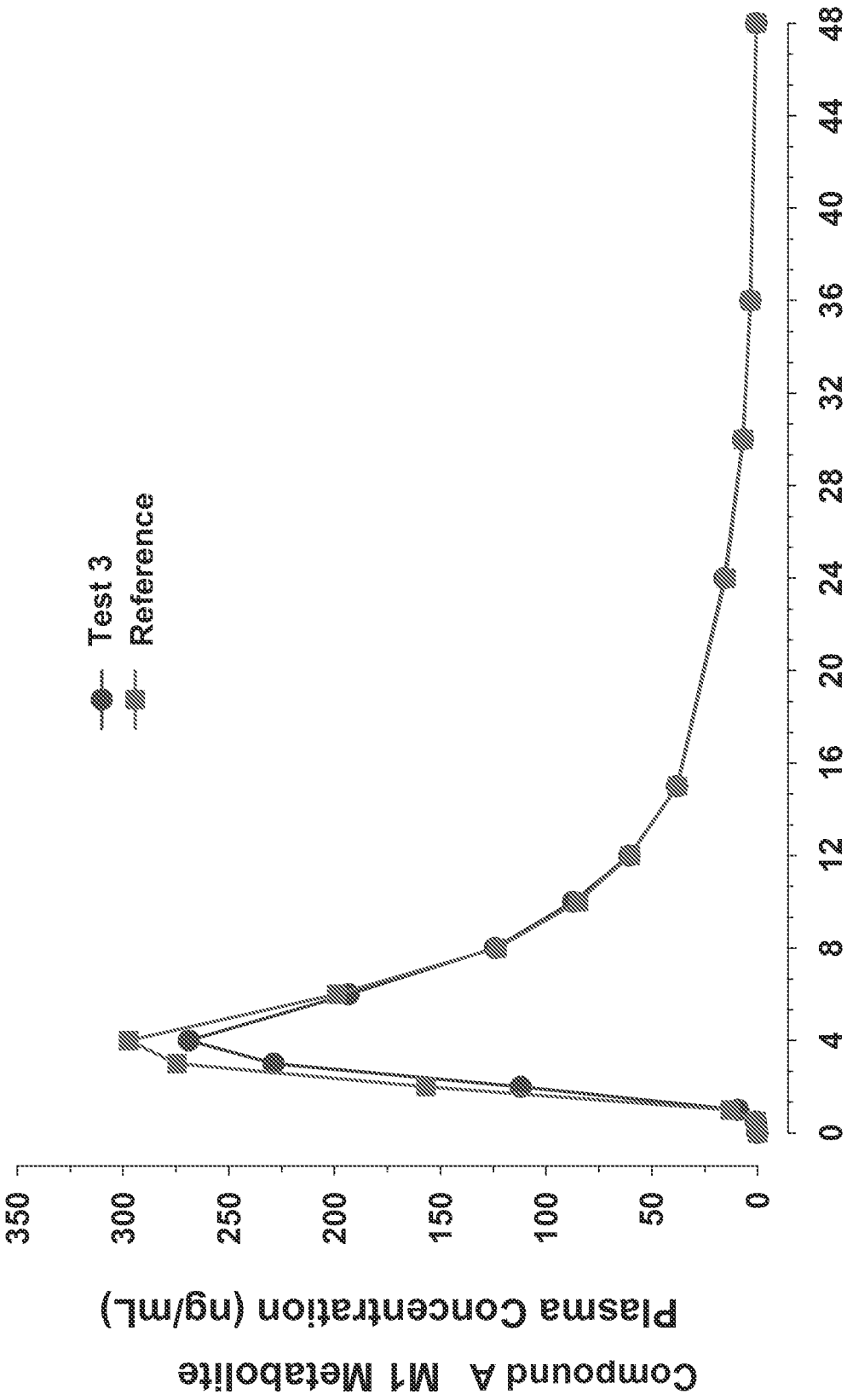

Compound A M1 Metabolite
Plasma Concentration (ng/mL)
350
300
250
200
150
100
50
0
0
4
8
12
16
20
24
28
32
36
40
44
48
Test 3
Reference

Figure 8

FIGURE 9

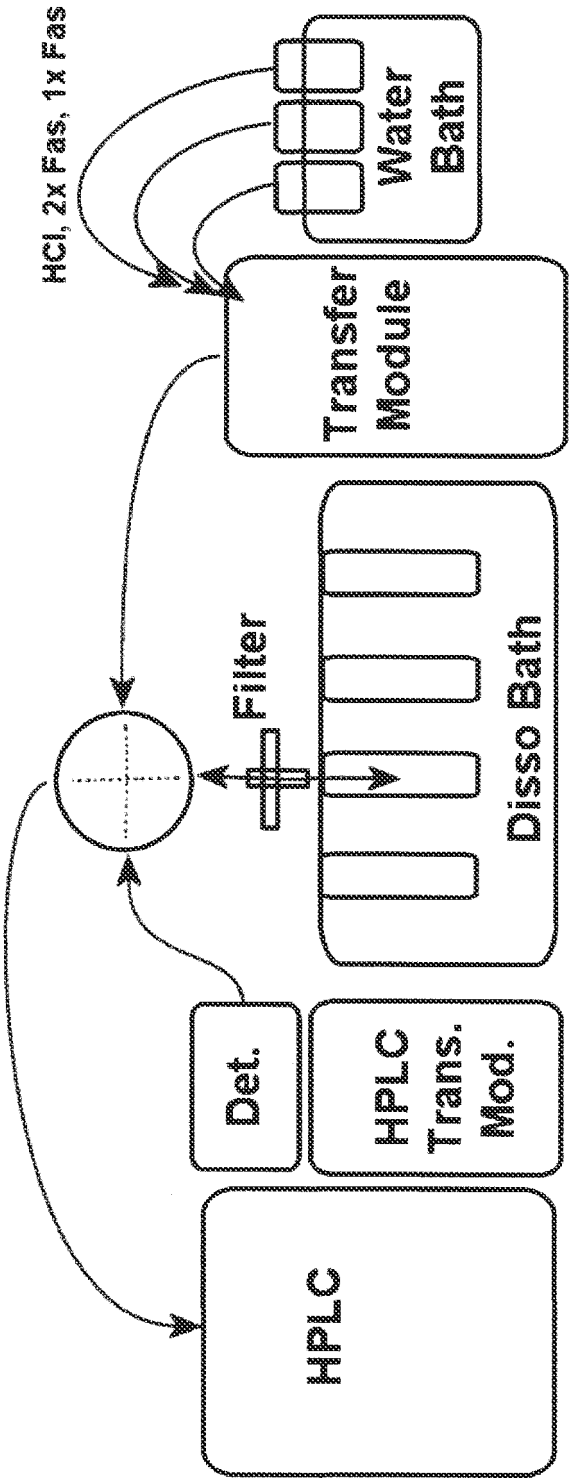
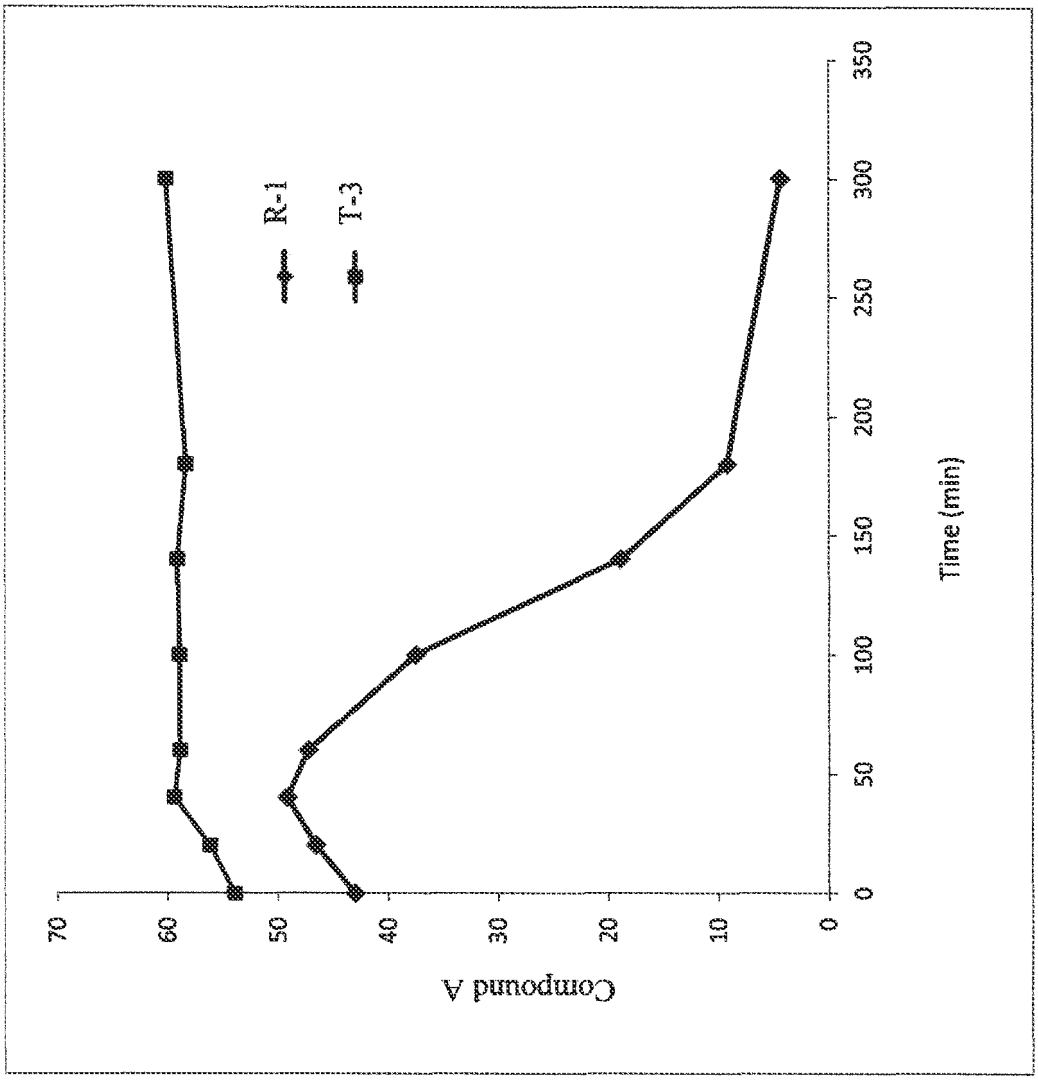

HCl, 2x Fas, 1x Fas
Water Bath
Transfer Module
Filter
Disso Bath
Det.
HPLC Trans. Mod.
HPLC

Figure 10


R-1
T-3
Compound A
Time (min)
0
10
20
30
40
50
60
70
0
50
100
150
200
250
300
350

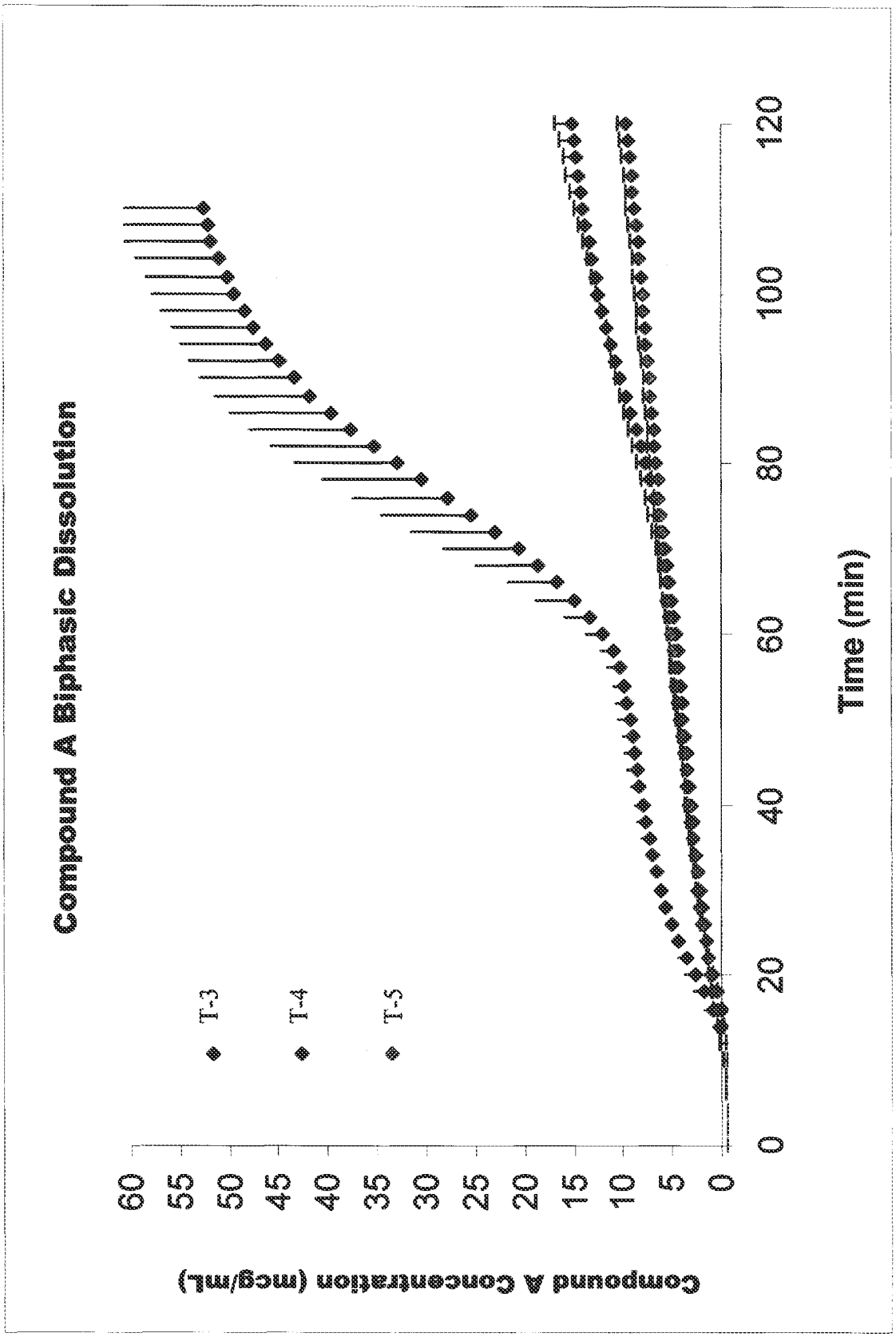

Compound A Biphasic Dissolution
T-3
T-4
T-5
Compound A Concentration (mcg/mL)
Time (min)
0
5
10
15
20
25
30
35
40
45
50
55
60
0
20
40
60
80
100
120

FIGURE 11

FIGURE 12

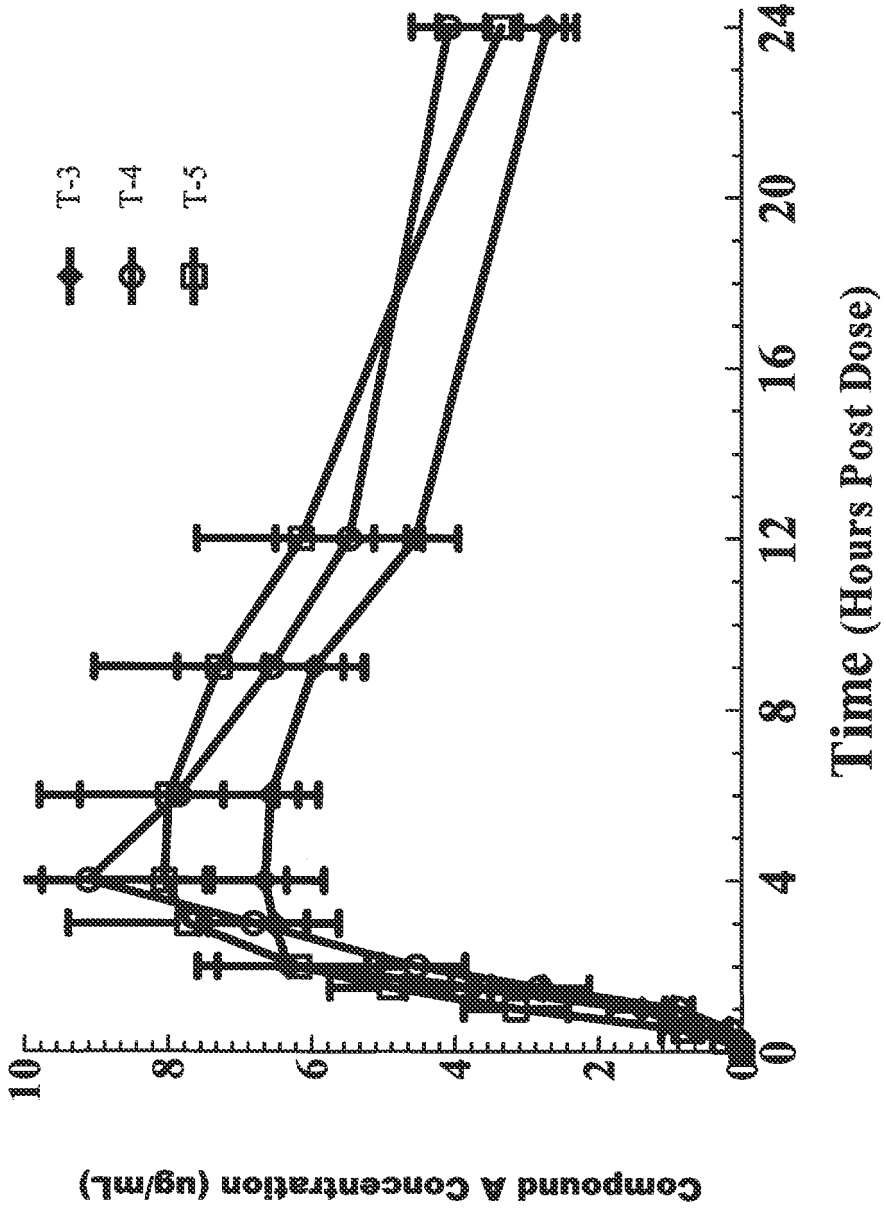

T-3
T-4
T-5
Compound A Concentration (ug/mL)
0
2
4
6
8
10
0
4
8
12
16
20
24
Time (Hours Post Dose)

FIGURE 13-A

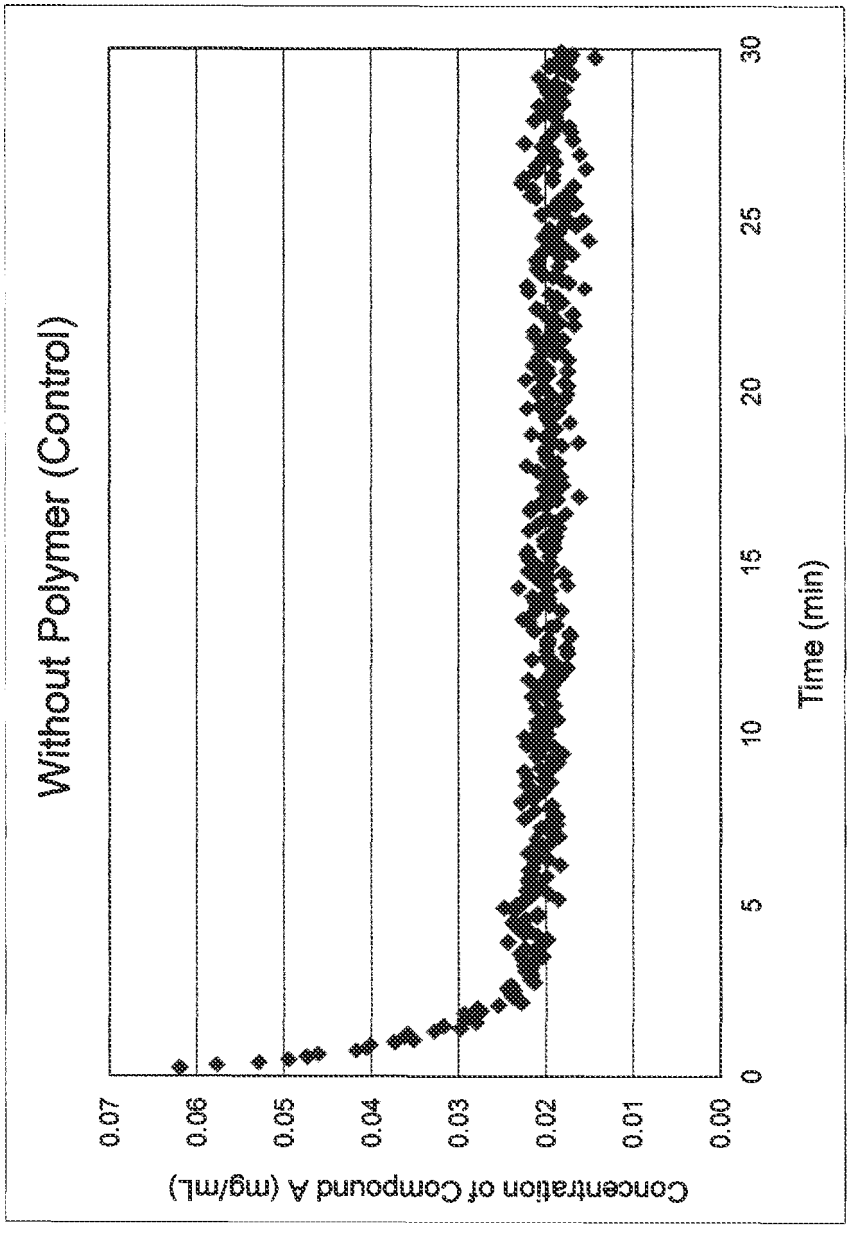

Without Polymer (Control)
Concentration of Compound A (mg/mL)
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
5
10
15
20
25
30
Time (min)

FIGURE 13-B

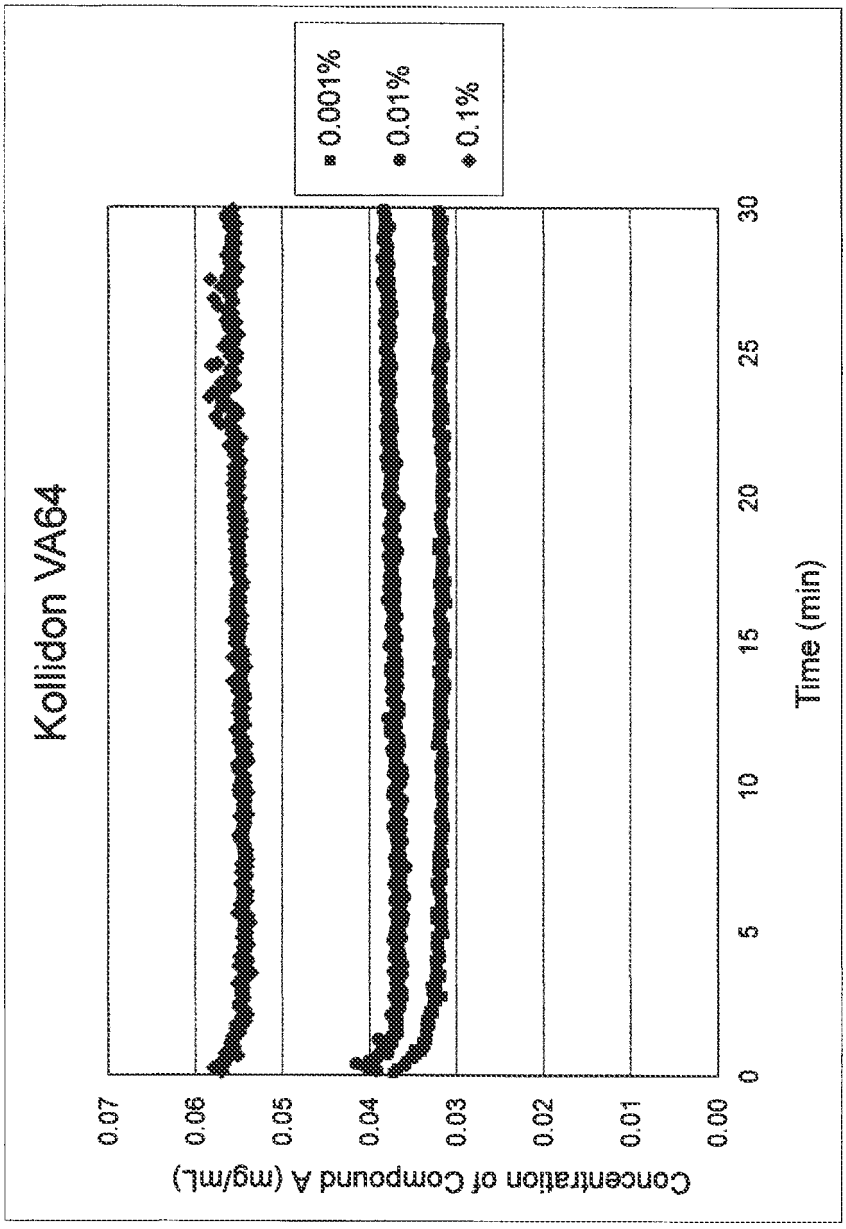

Kollidon VA64
0.001%
0.01%
0.1%
Concentration of Compound A (mg/mL)
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
5
10
15
20
25
30
Time (min)

FIGURE 13-C

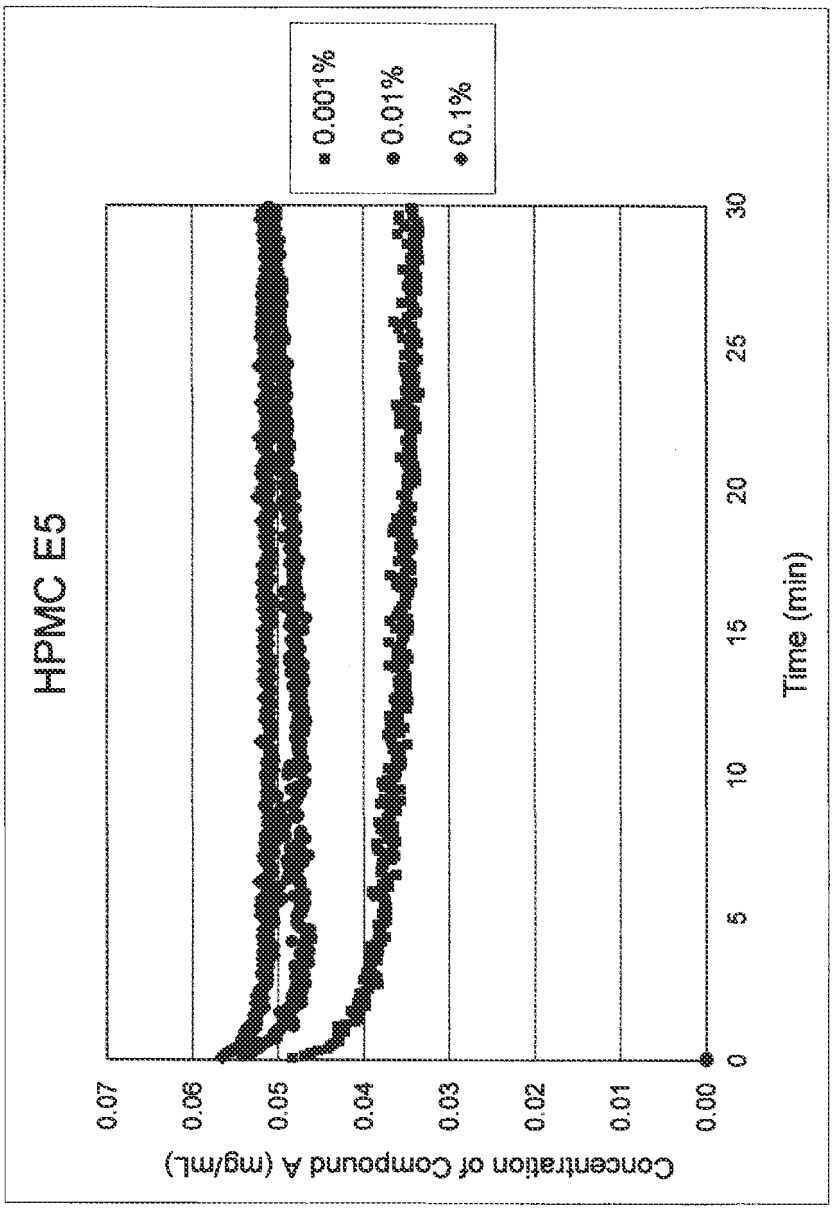

HPMC E5
0.001%
0.01%
0.1%
Concentration of Compound A (mg/mL)
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
5
10
15
20
25
30
Time (min)

FIGURE 13-D

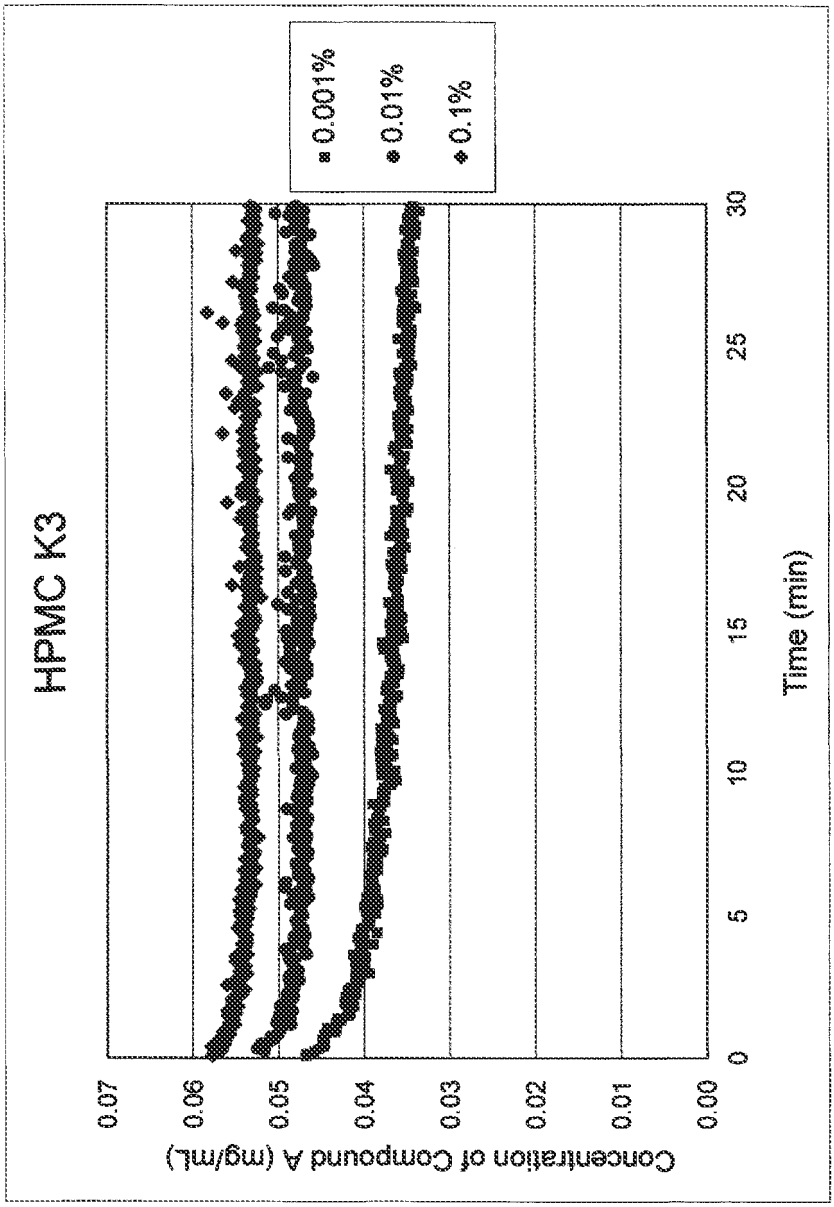

HPMC K3
0.001%
0.01%
0.1%
Concentration of Compound A (mg/mL)
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
5
10
15
20
25
30
Time (min)

FIGURE 13-E

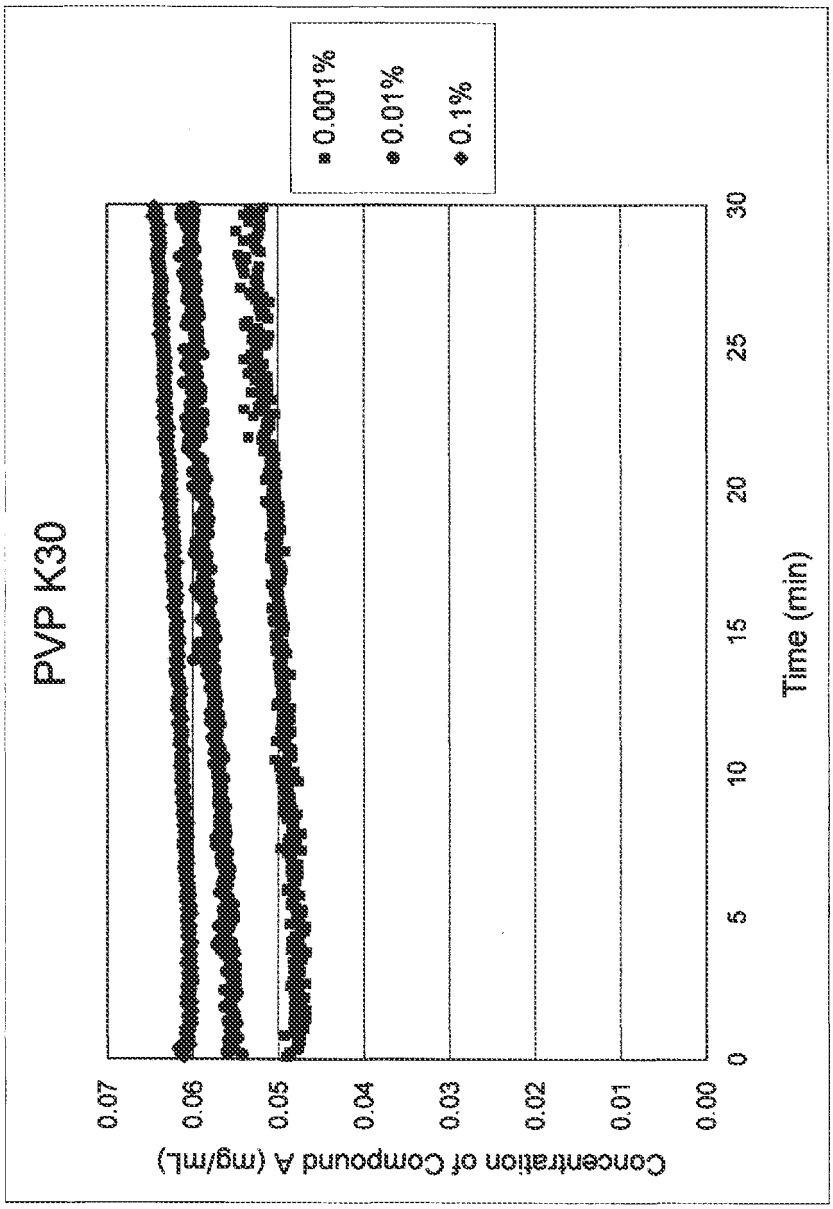

PVP K30
0.001%
0.01%
0.1%
Concentration of Compound A (mg/mL)
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
5
10
15
20
25
30
Time (min)

FIGURE 13-F

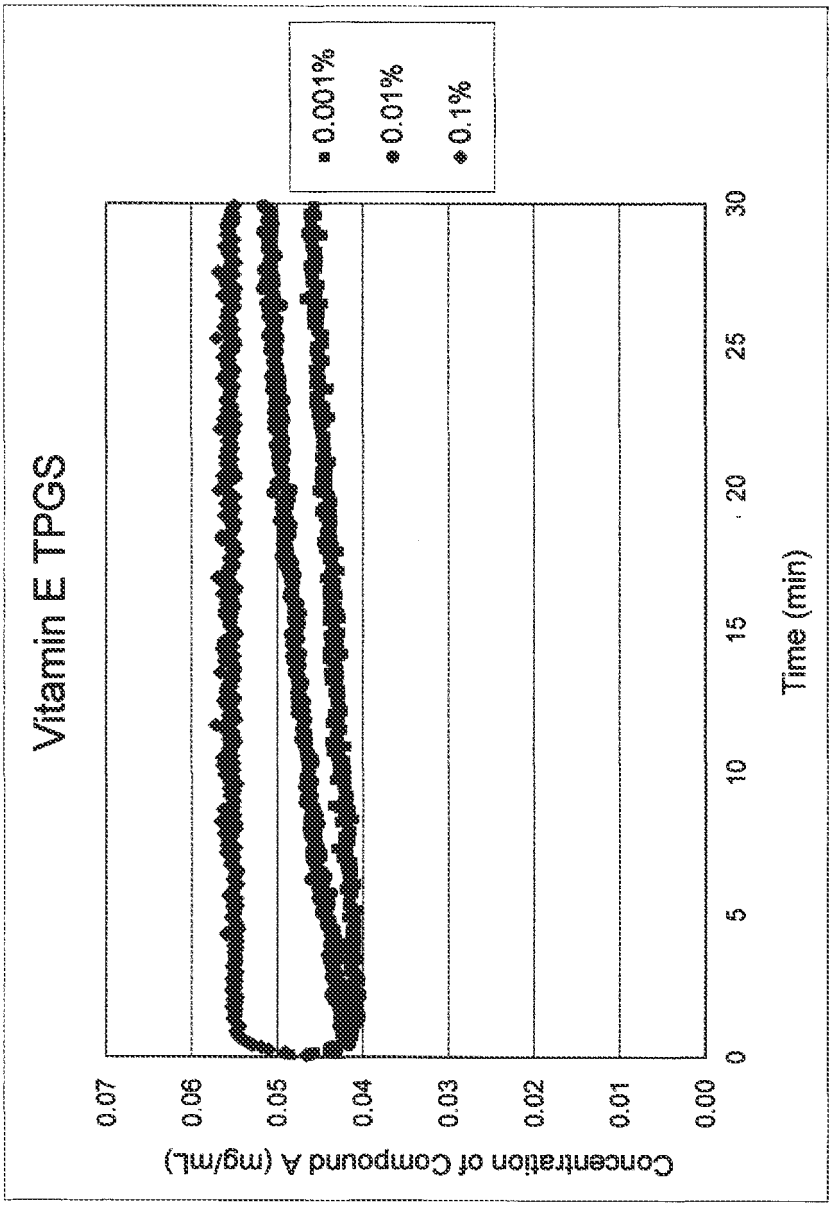
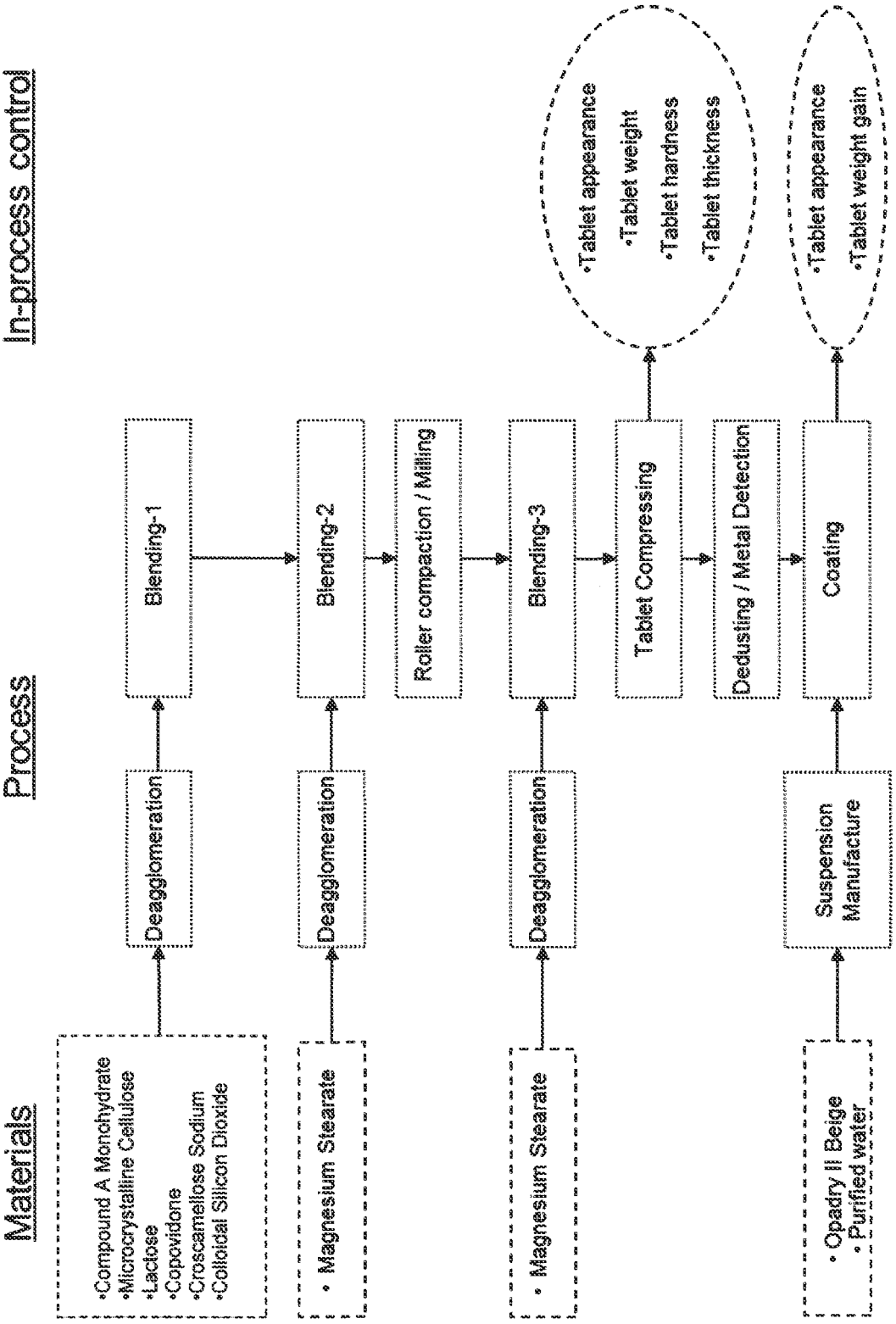

Vitamin E TPGS
0.001%
0.01%
0.1%
Concentration of Compound A (mg/mL)
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
0
5
10
15
20
25
30
Time (min)

FIGURE 14


Materials
Process
In-process control
•Compound A Monohydrate
•Microcrystalline Cellulose
•Lactose
•Copovidone
•Croscarmellose Sodium
•Colloidal Silicon Dioxide
• Magnesium Stearate
• Magnesium Stearate
• Opadry II Beige
• Purified water
Deagglomeration
Deagglomeration
Deagglomeration
Suspension Manufacture
Blending-1
Blending-2
Roller compaction / Milling
Blending-3
Tablet Compressing
Dedusting / Metal Detection
Coating
•Tablet appearance
•Tablet weight
•Tablet hardness
•Tablet thickness
•Tablet appearance
•Tablet weight gain