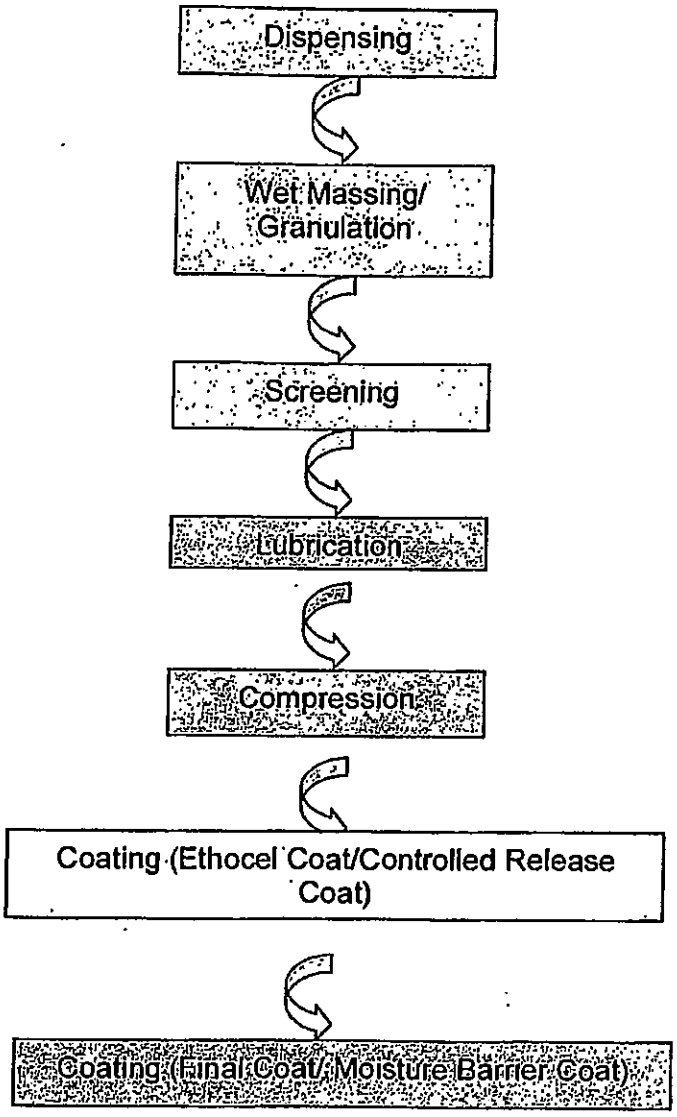

Dispensing
Wet Massing/ Granulation
Screening
Lubrication
Compression
Coating (Ethocel Coat/Controlled Release Coat)
Coating (Final Coat/ Moisture Barrier Coat)

Figure 1

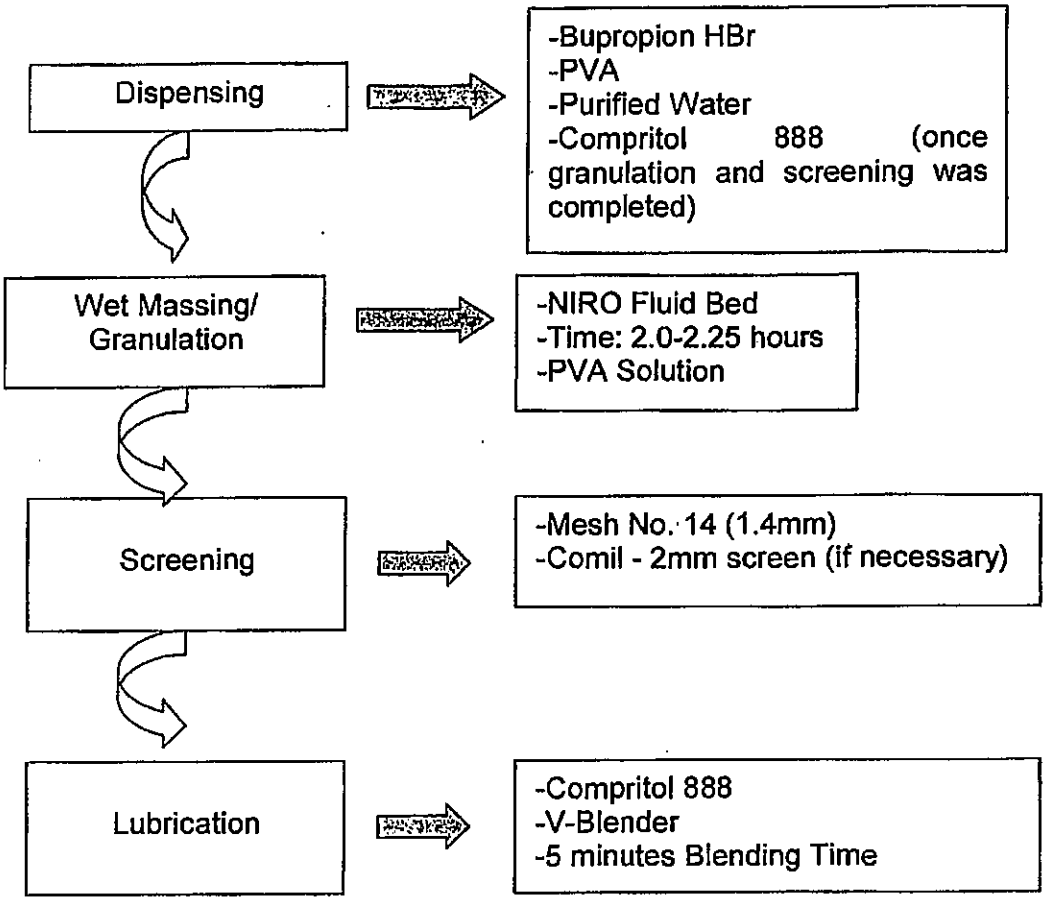

Dispensing
-Bupropion HBr
-PVA
-Purified Water
-Compritol 888 (once granulation and screening was completed)
Wet Massing/ Granulation
-NIRO Fluid Bed
-Time: 2.0-2.25 hours
-PVA Solution
Screening
-Mesh No. 14 (1.4mm)
-Comil - 2mm screen (if necessary)
Lubrication
-Compritol 888
-V-Blender
-5 minutes Blending Time

Figure 2

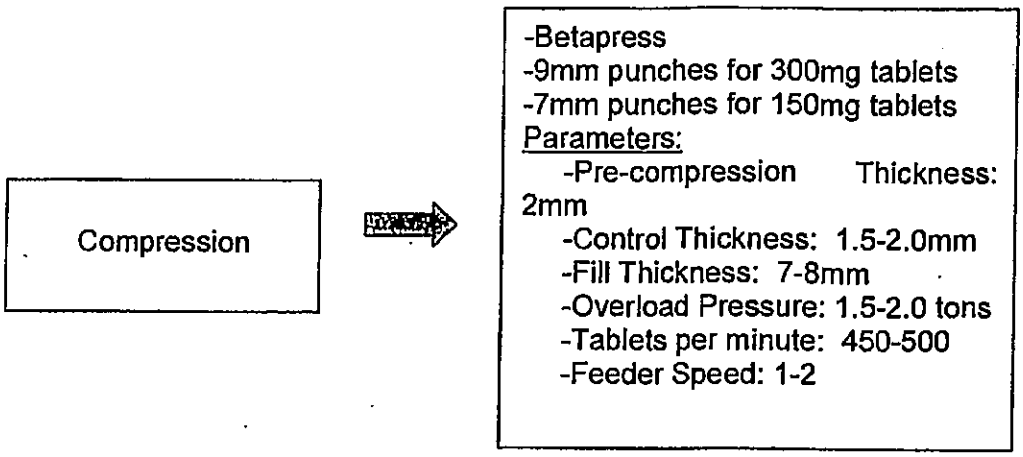


Figure 3

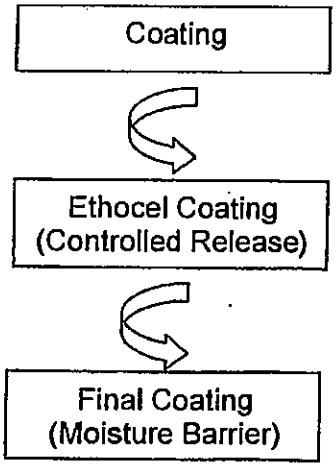


Figure 4

Figure 5

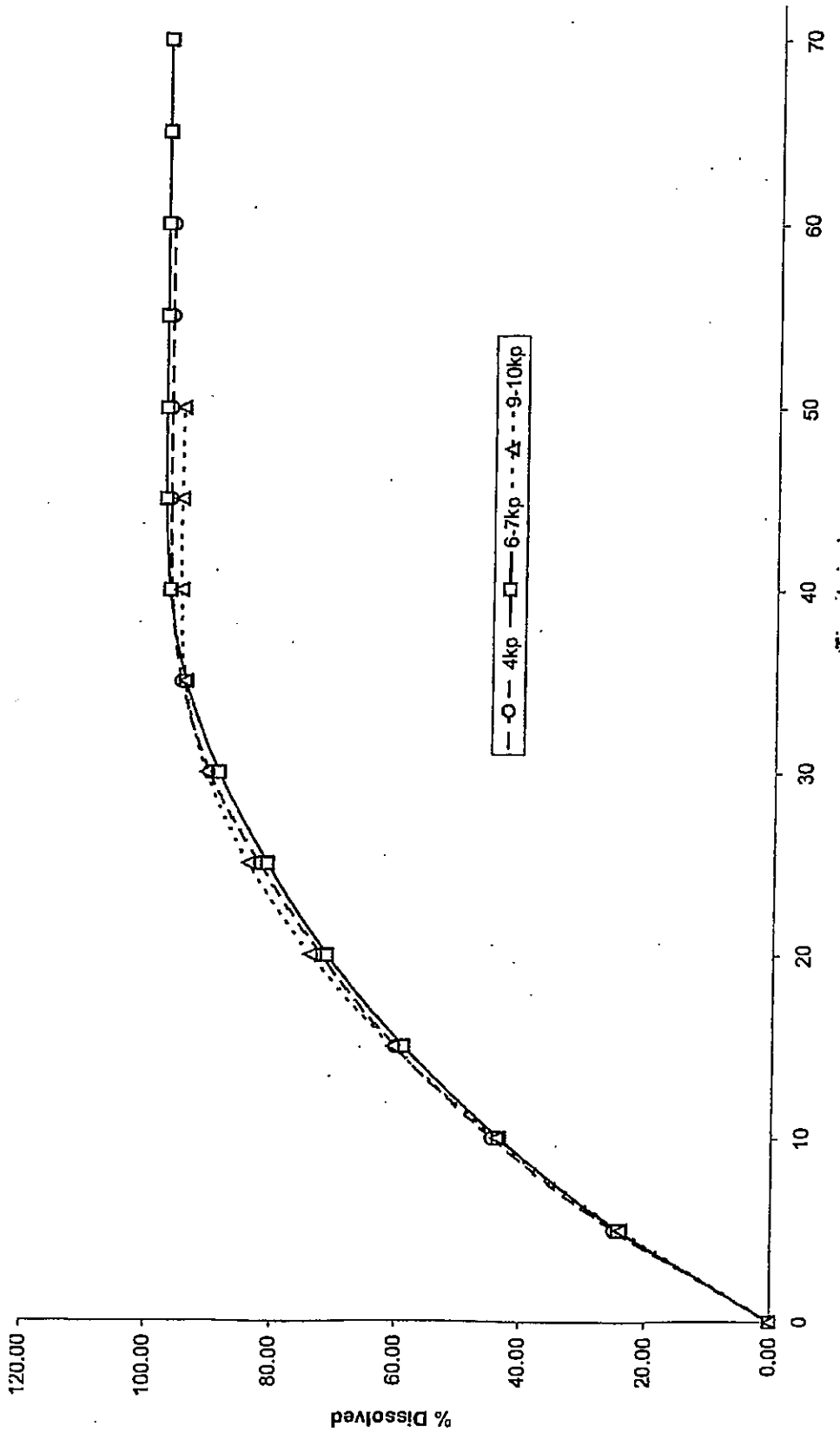

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
10
20
30
40
50
60
70
Time (mins)
4kp
6-7kp
9-10kp

Figure 6

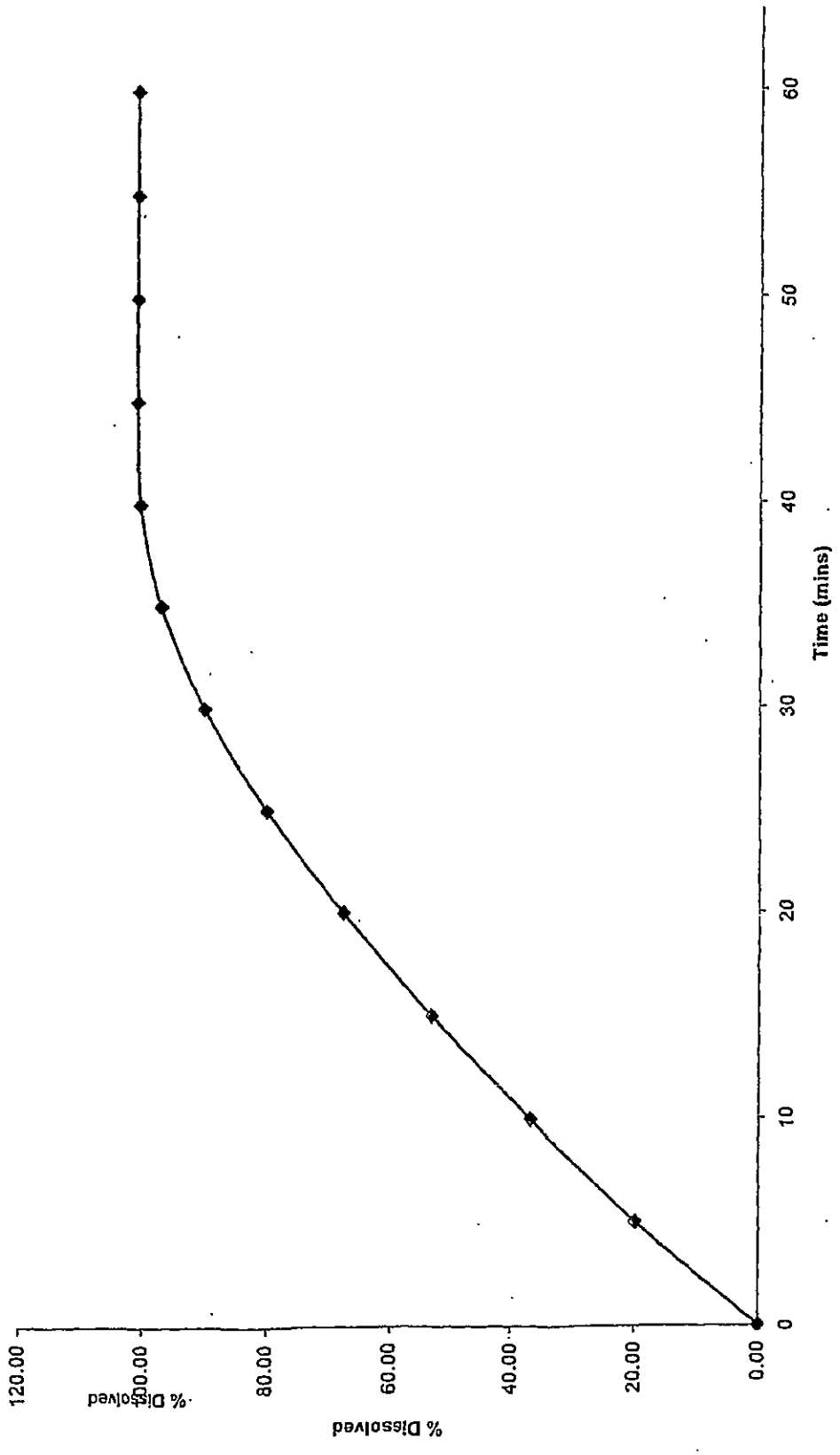

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
10
20
30
40
50
60
Time (mins)

Figure 7

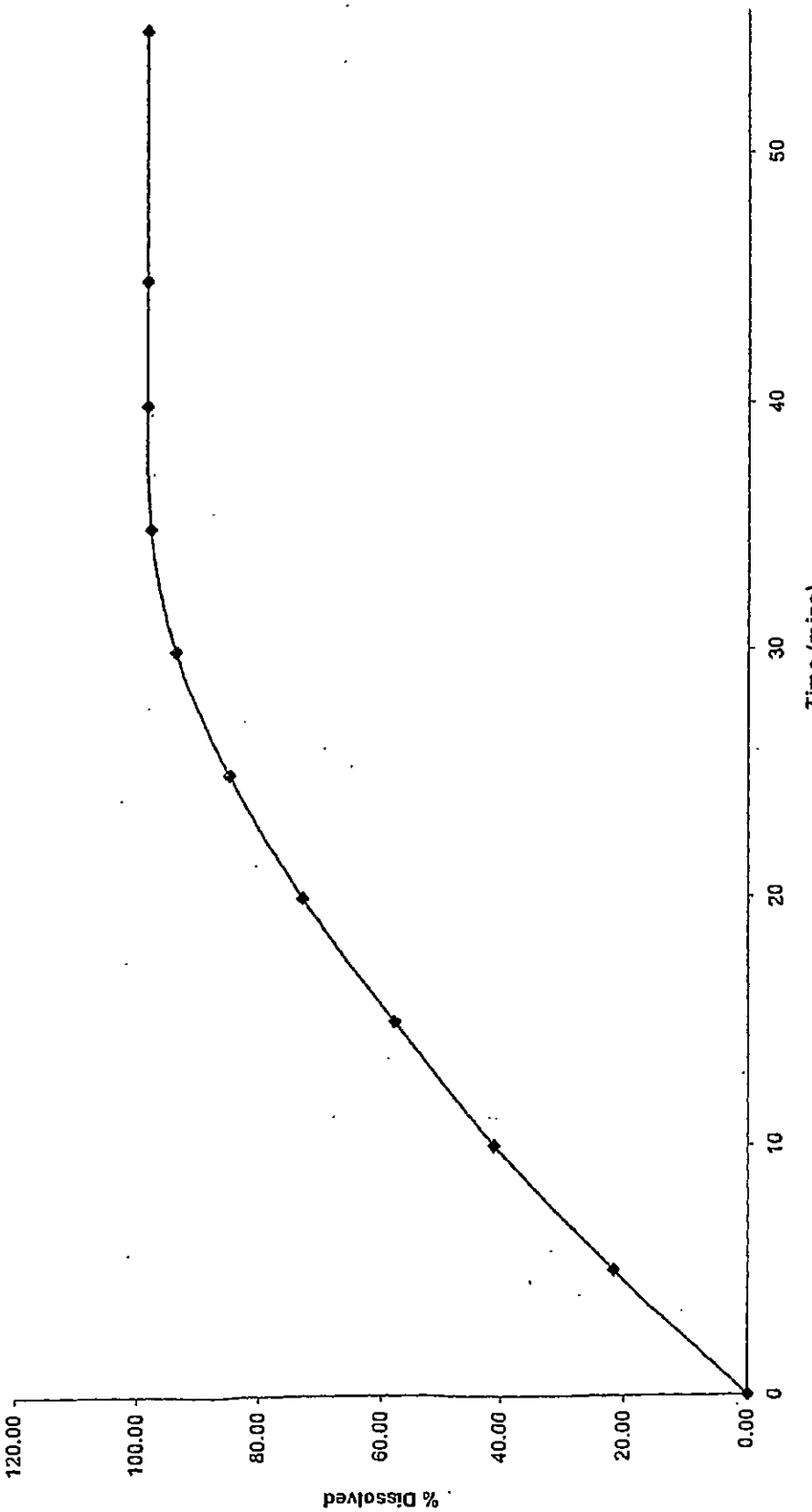

120.00
100.00
80.00
60.00
40.00
20.00
0.00
% Dissolved
0
10
20
30
40
50
Time (mins)

Figure 8

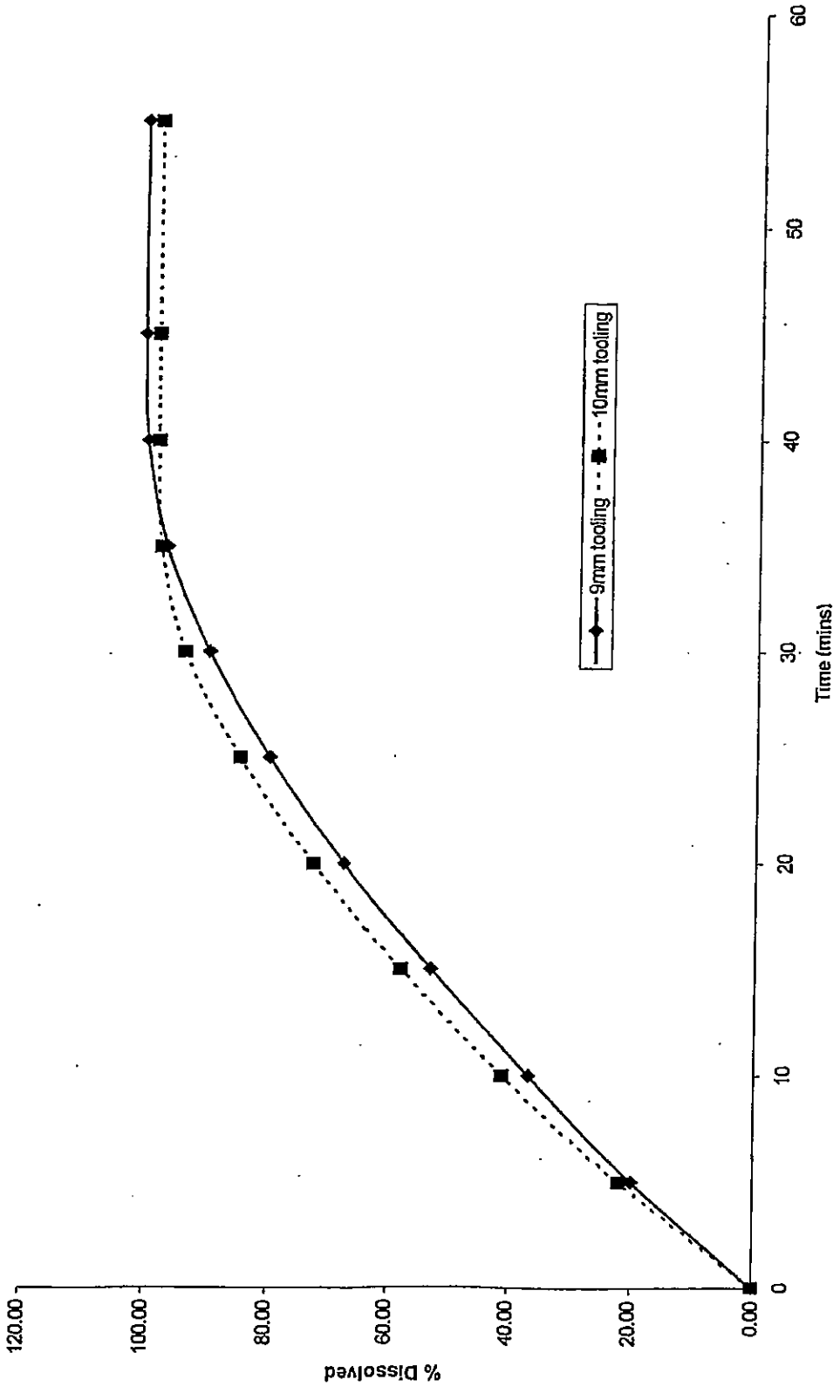

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
10
20
30
40
50
60
Time (mins)
9mm tooling
10mm tooling

Figure 9

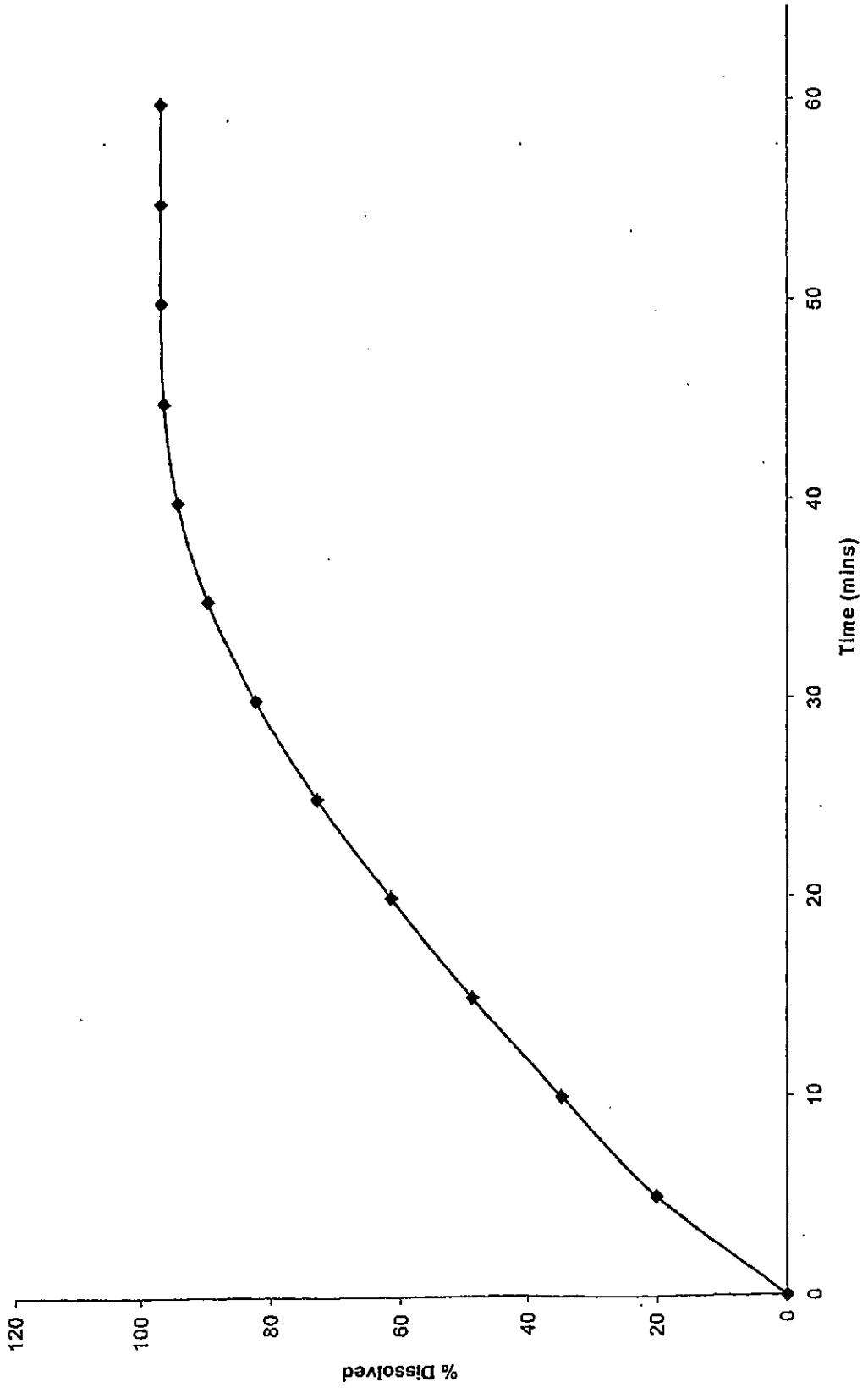


Figure 10

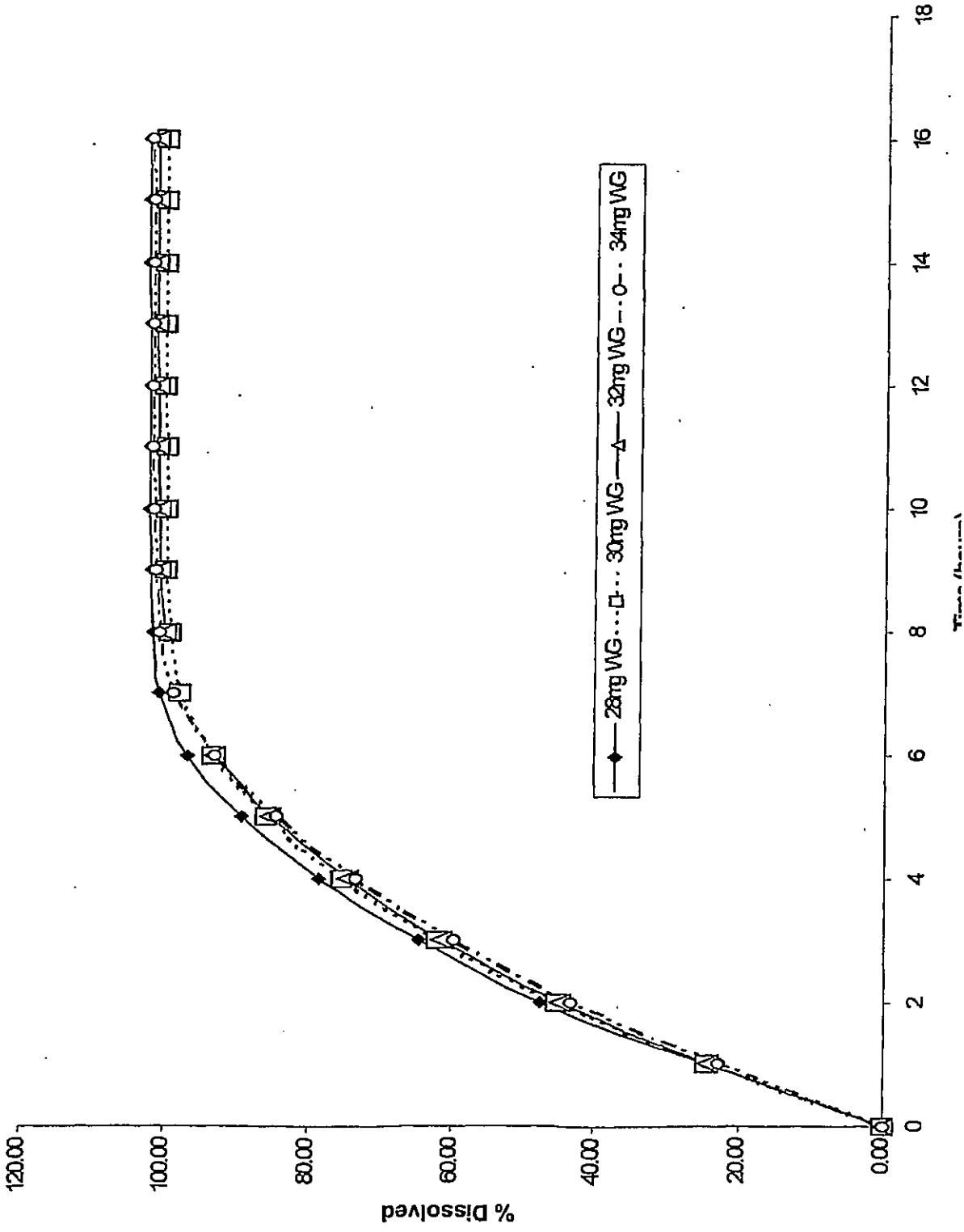

120.00
100.00
80.00
60.00
40.00
20.00
0.00
% Dissolved
0
2
4
6
8
10
12
14
16
18
28mg WG
30mg WG
32mg WG
34mg WG

Figure 11

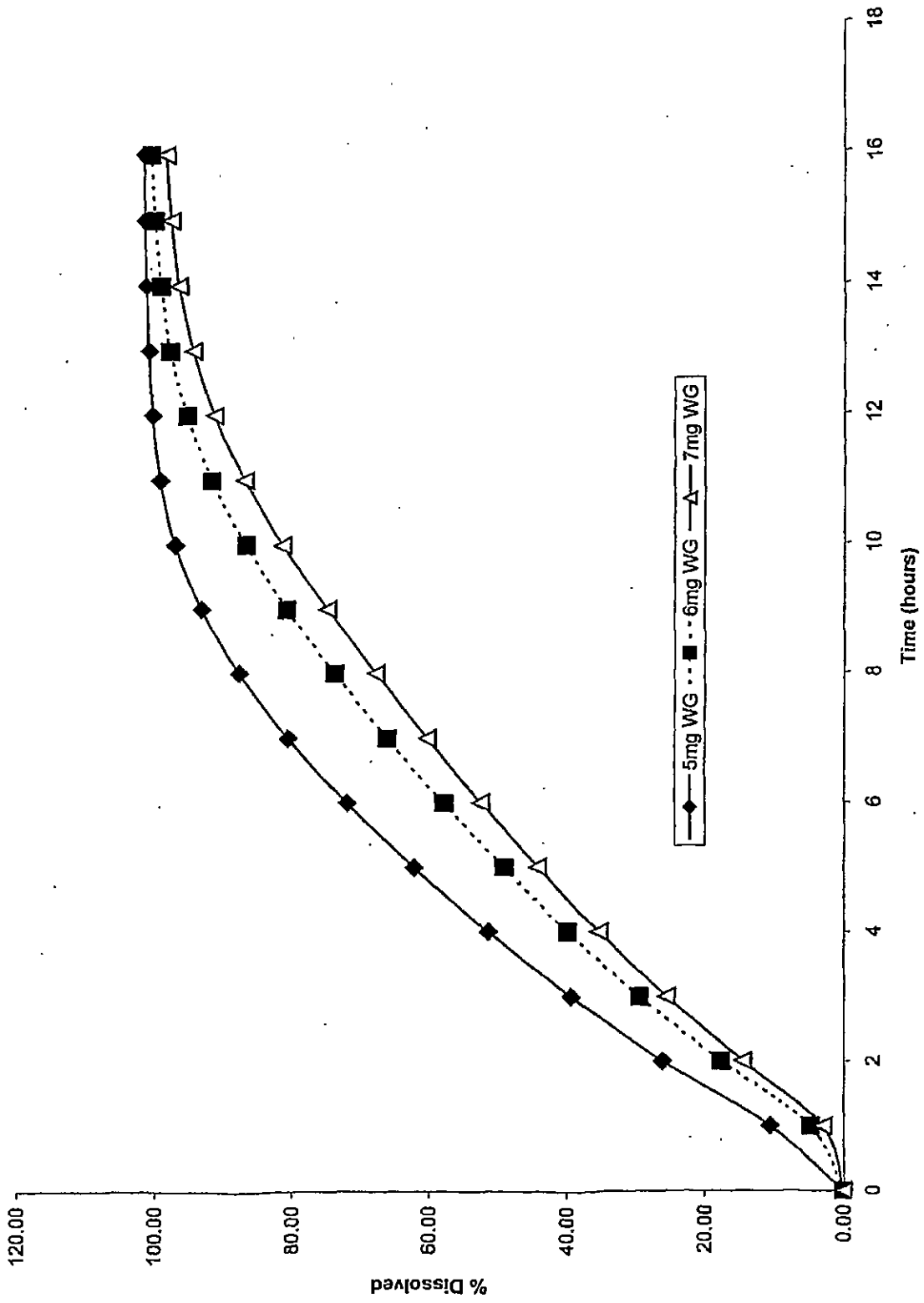

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
5mg WG
6mg WG
7mg WG

Figure 12

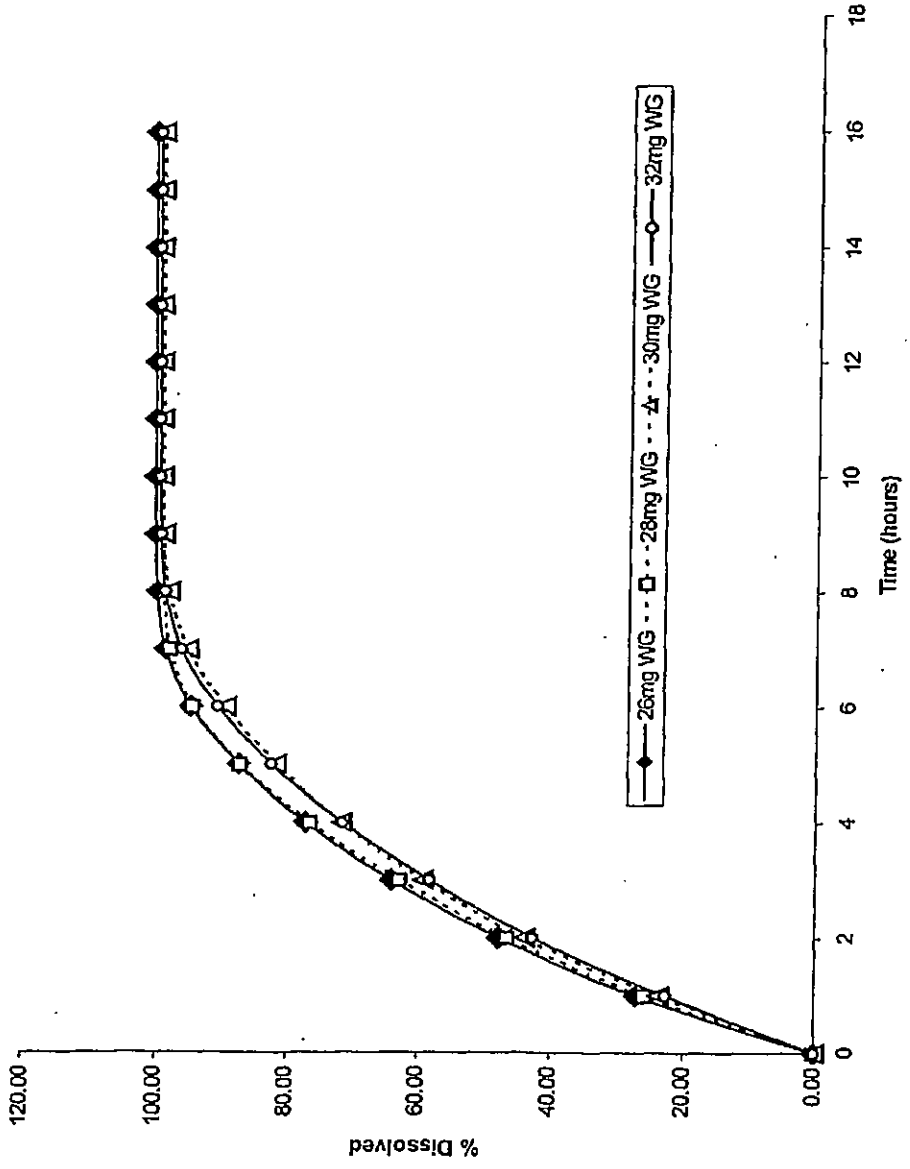

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
26mg WG
28mg WG
30mg WG
32mg WG

Figure 13

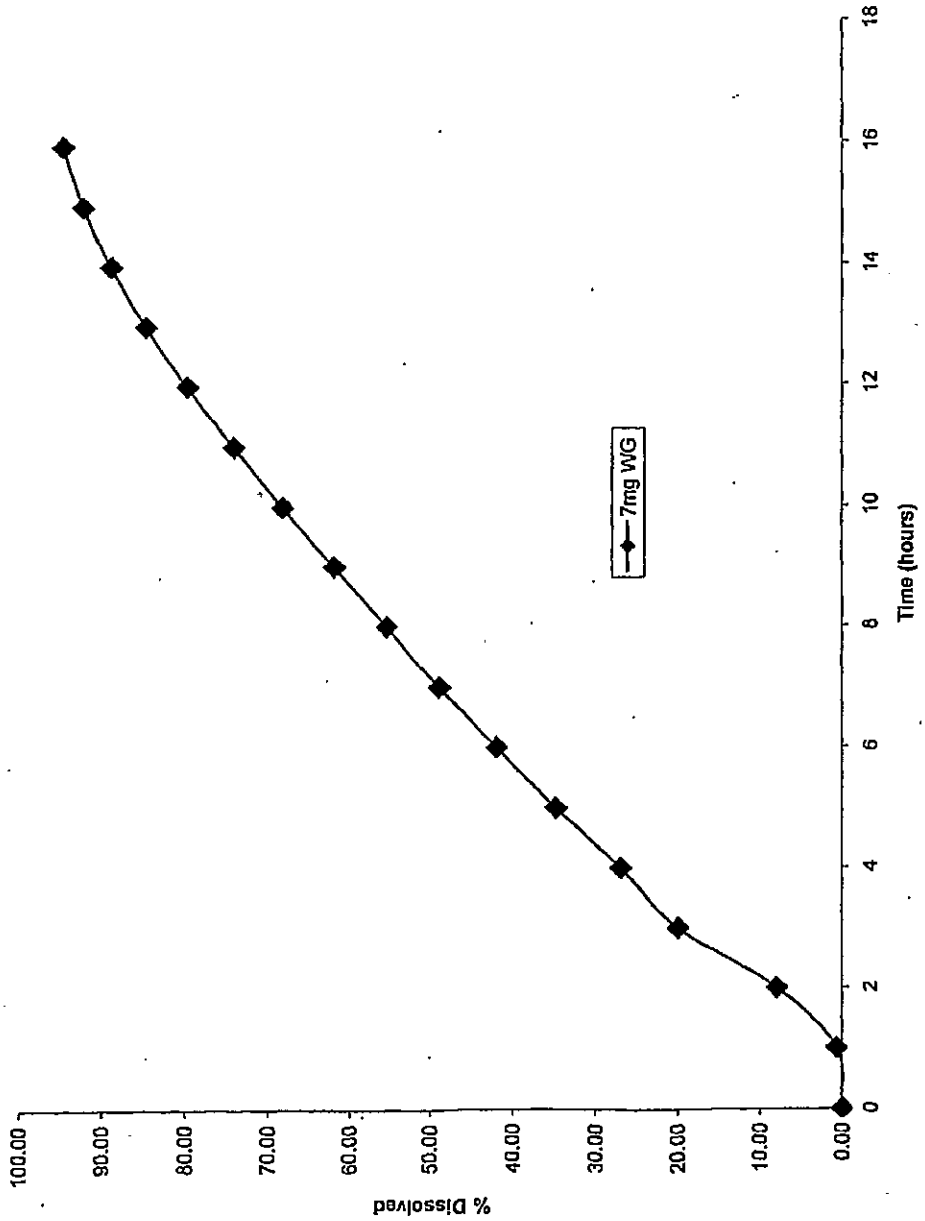

% Dissolved
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
7mg WG

Figure 14

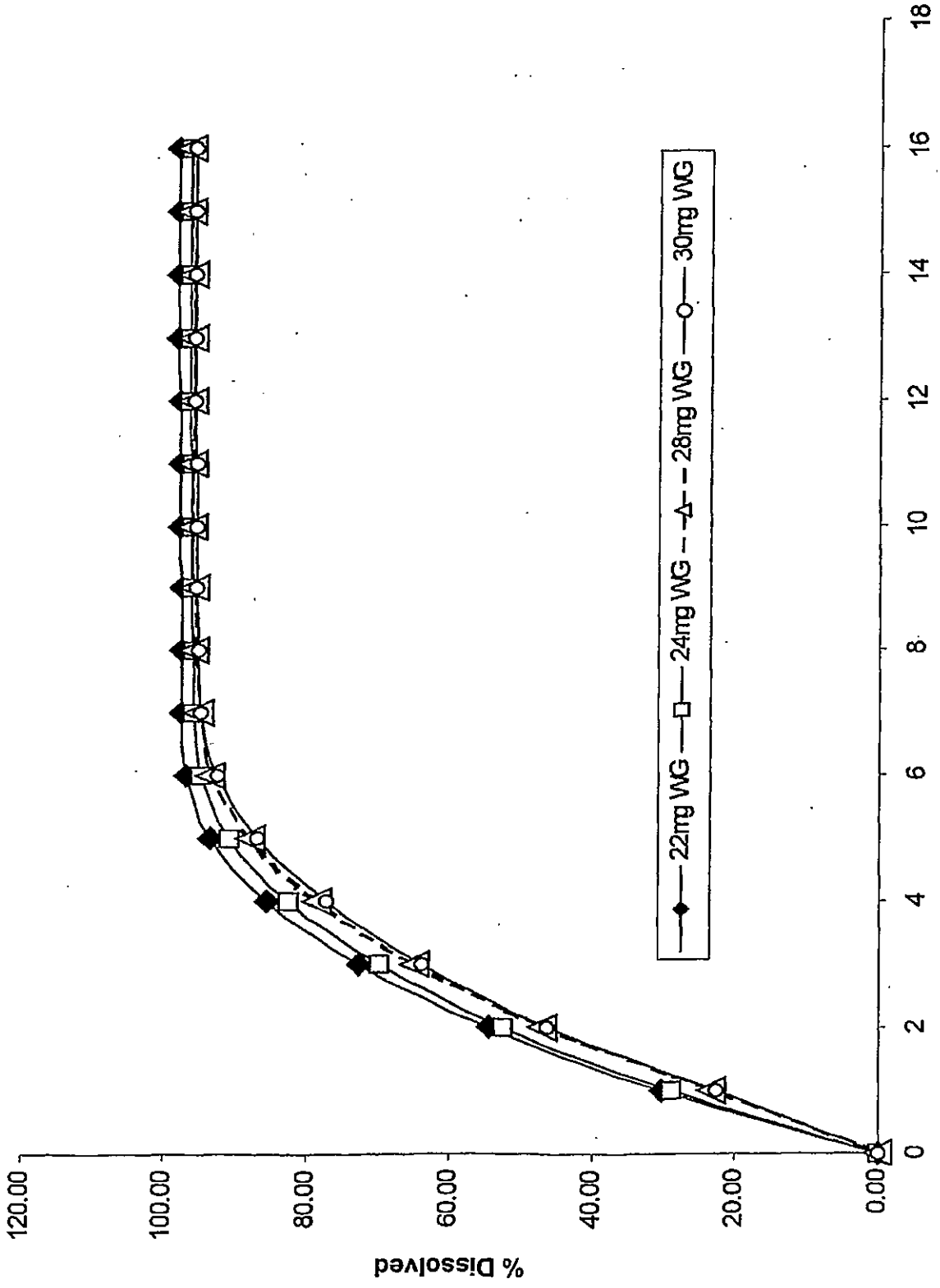

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
22mg WG
24mg WG
28mg WG
30mg WG

Figure 15

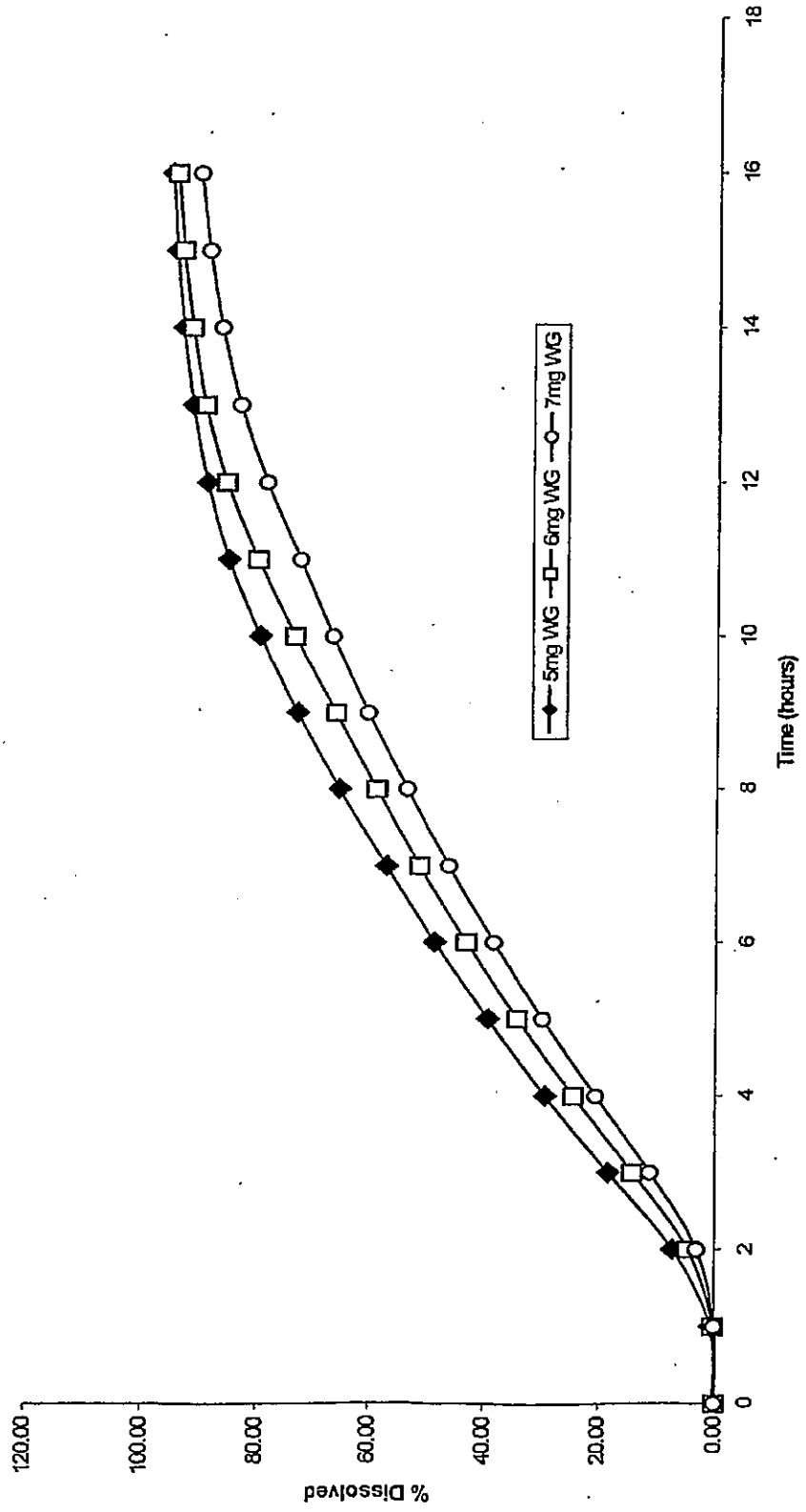

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
5mg WG
6mg WG
7mg WG

Figure 16

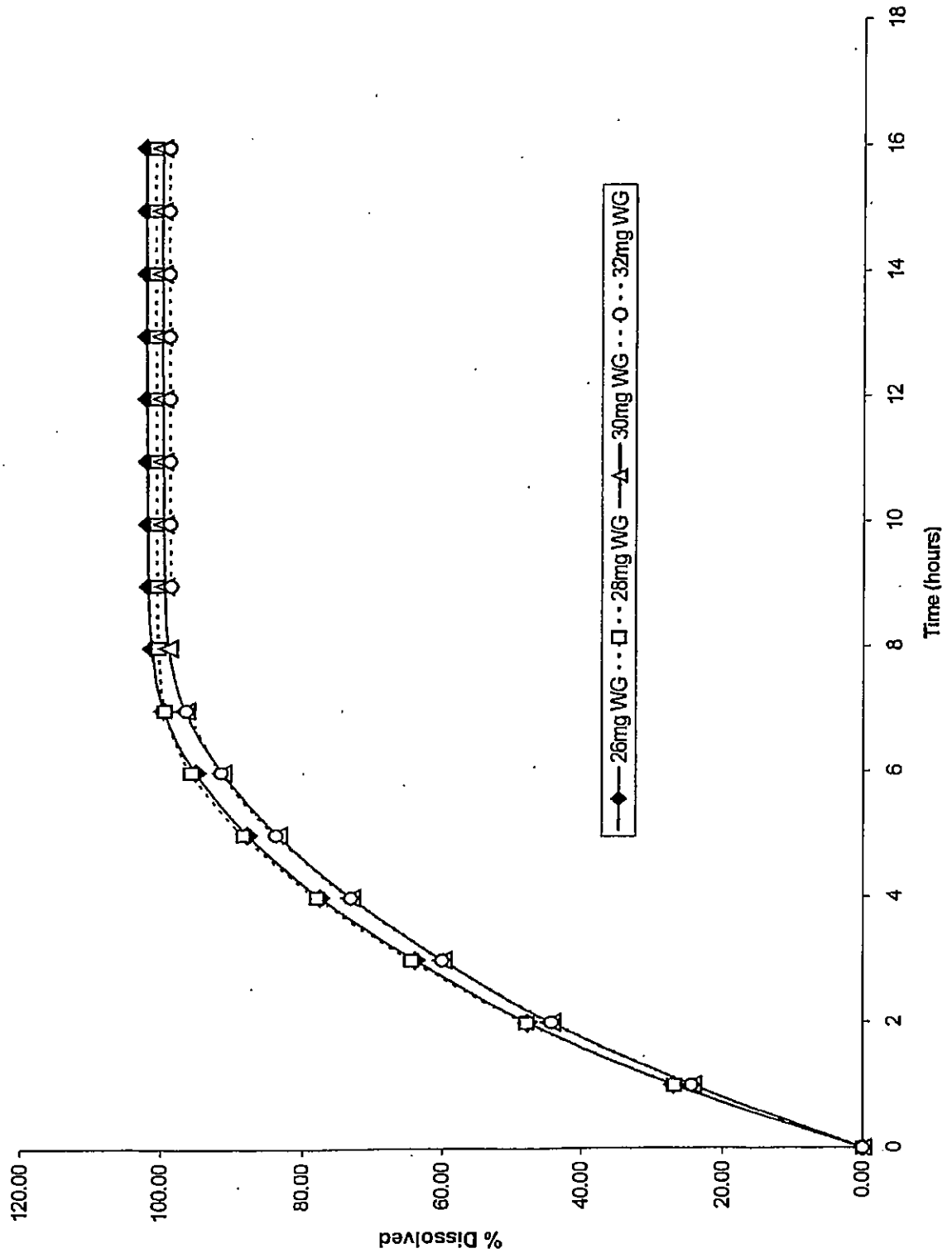

120.00
100.00
80.00
60.00
40.00
20.00
0.00
% Dissolved
0
2
4
6
8
10
12
14
16
18
Time (hours)
26mg WG
28mg WG
30mg WG
32mg WG

Figure 17

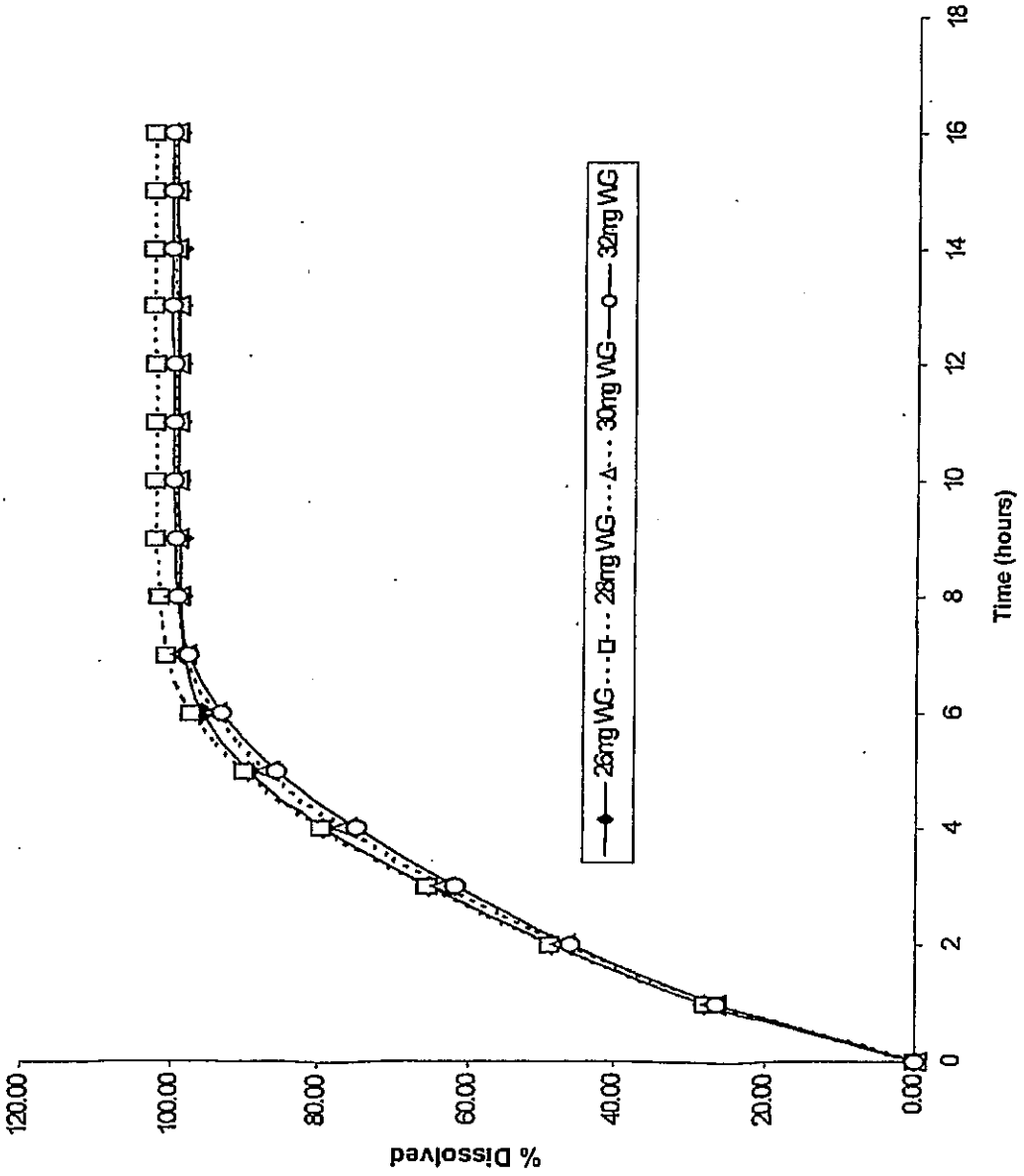

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
26mg WG
28mg WG
30mg WG
32mg WG

Figure 18

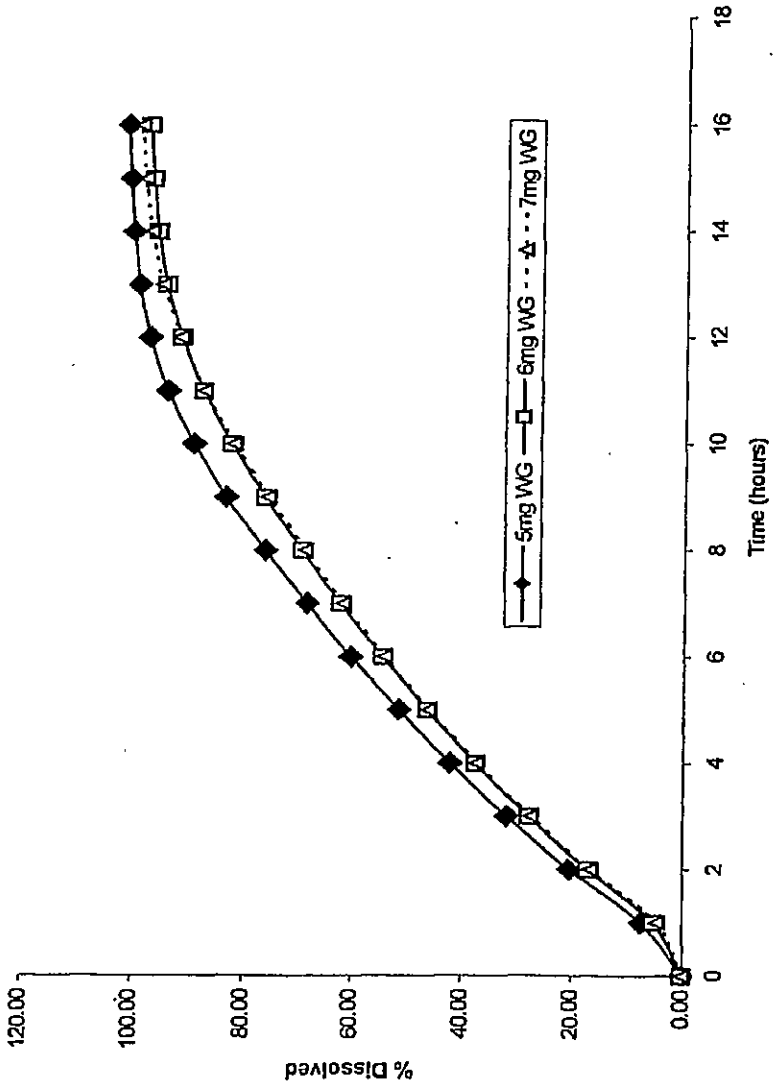

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
5mg WG
6mg WG
7mg WG

Figure 19

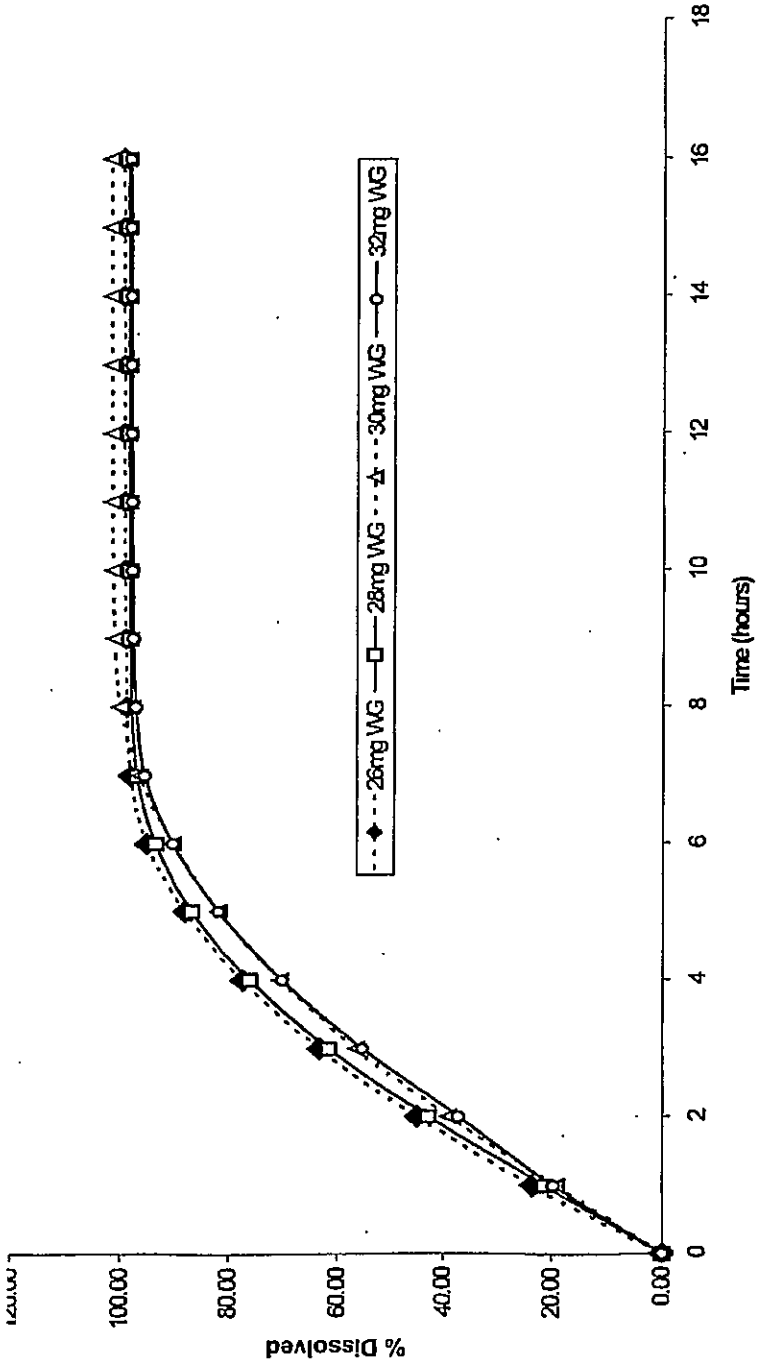

26mg WG
28mg WG
30mg WG
32mg WG
% Dissolved
Time (hours)
0.00
20.00
40.00
60.00
80.00
100.00
0
2
4
6
8
10
12
14
16
18

Figure 20

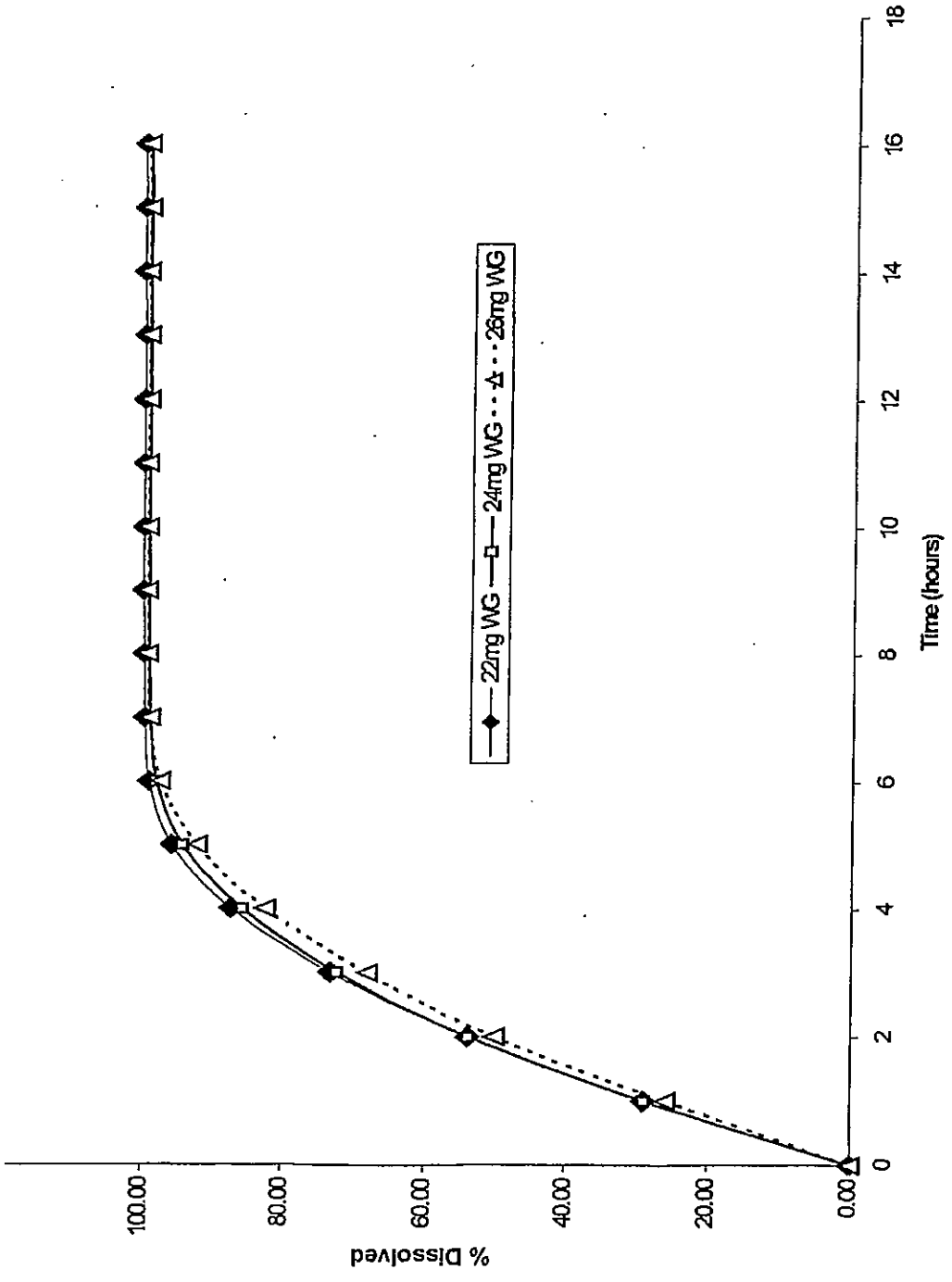

% Dissolved
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
22mg WG
24mg WG
26mg WG

Figure 21

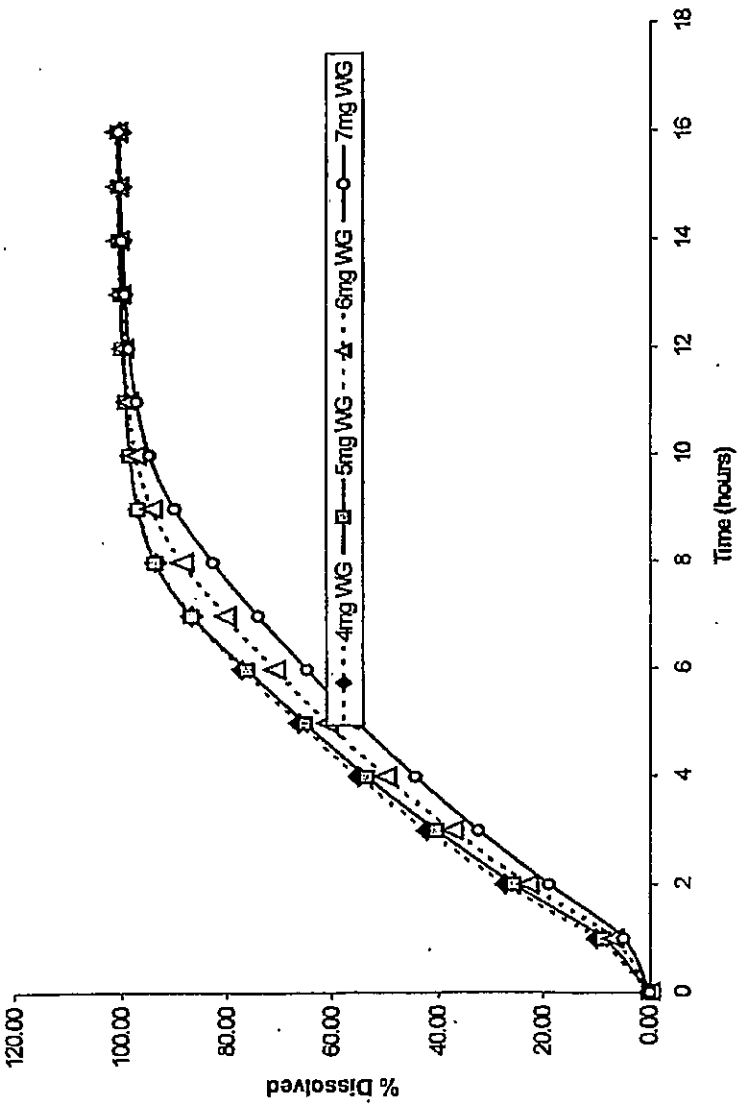

% Dissolved
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
2
4
6
8
10
12
14
16
18
Time (hours)
4mg WG
5mg WG
6mg WG
7mg WG

FIG. 22

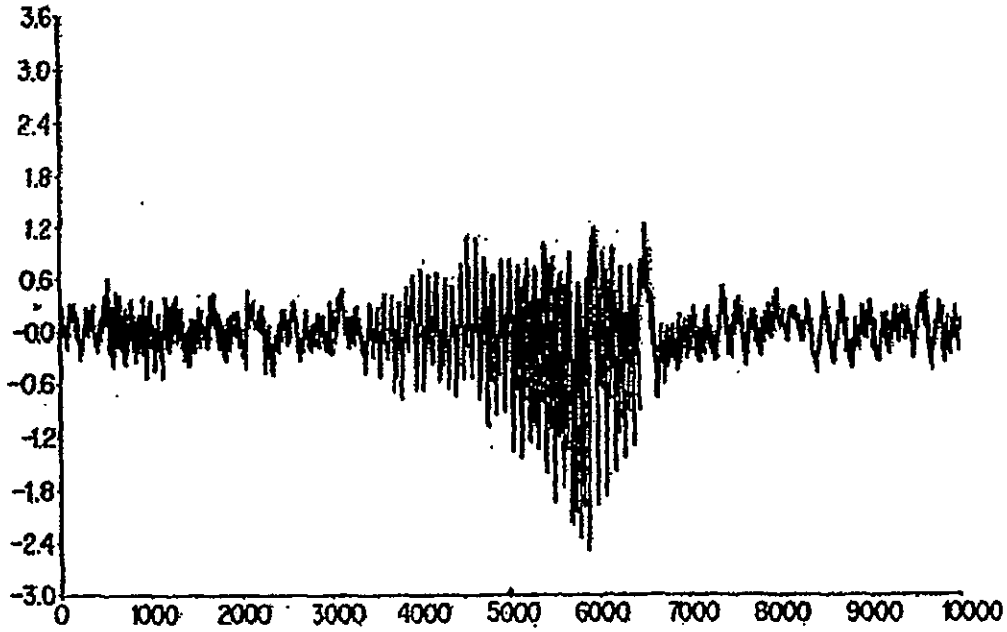

3.6
3.0
2.4
1.8
1.2
0.6
-0.0
-0.6
-1.2
-1.8
-2.4
-3.0
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000

FIG. 23

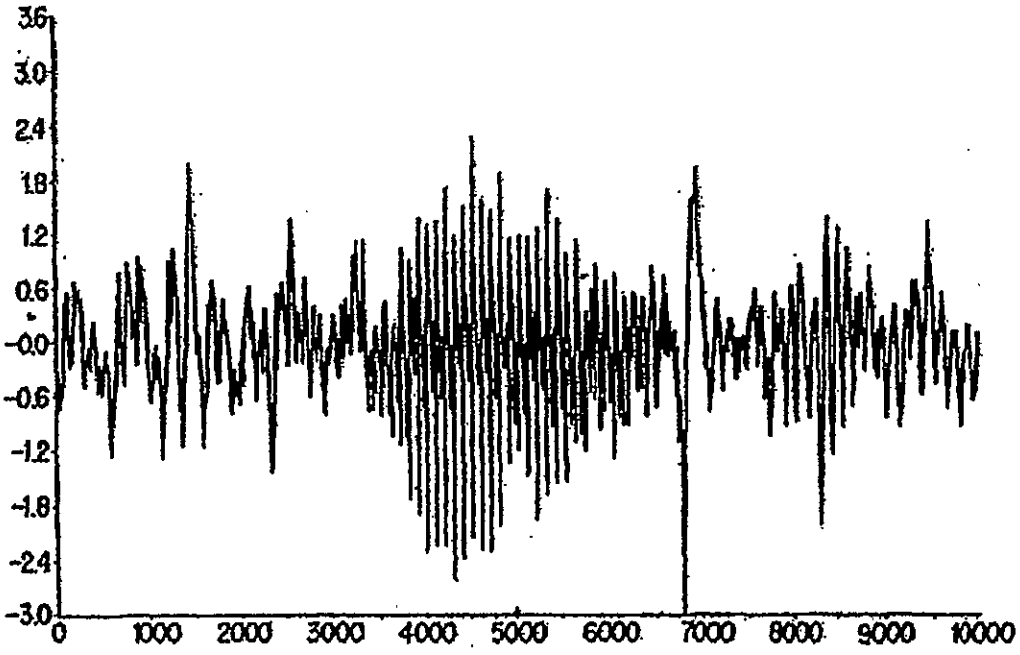

3.6
3.0
2.4
1.8
1.2
0.6
-0.0
-0.6
-1.2
-1.8
-2.4
-3.0
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000

FIG. 24A

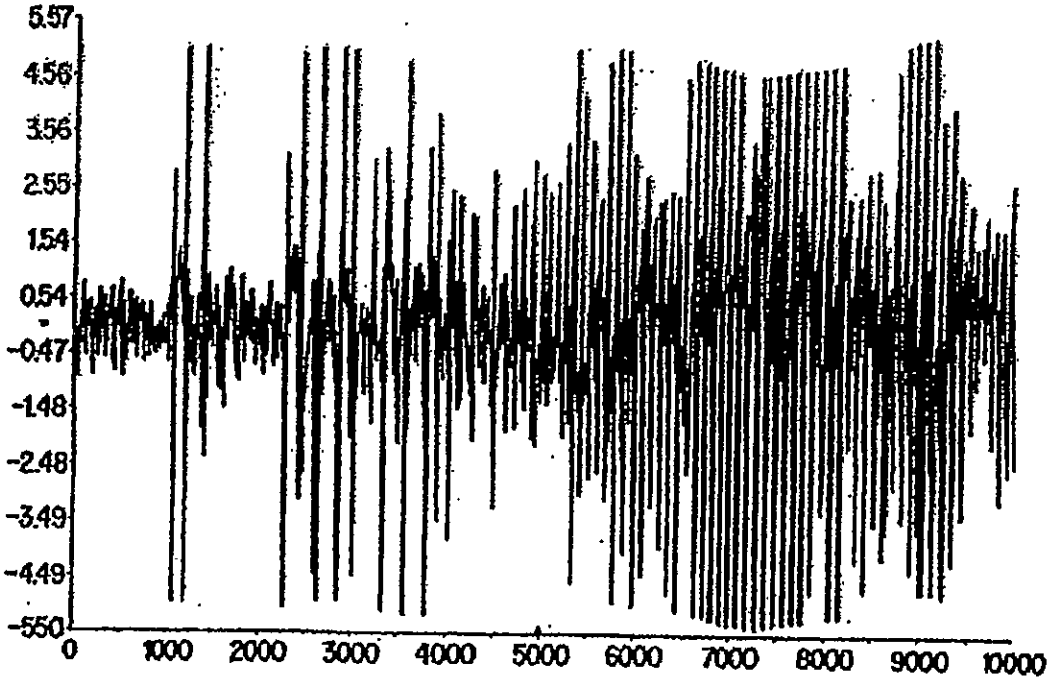

5.57
4.56
3.56
2.55
1.54
0.54
-0.47
-1.48
-2.48
-3.49
-4.49
-550
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000

FIG. 24B

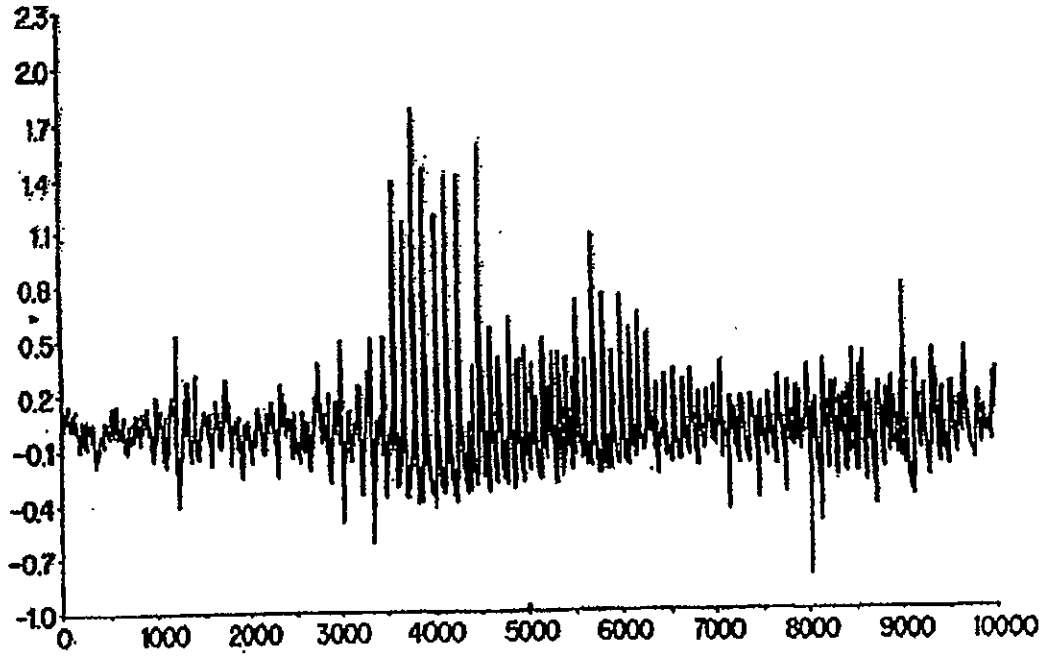

2.3
2.0
1.7
1.4
1.1
0.8
0.5
0.2
-0.1
-0.4
-0.7
-1.0
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000

FIG. 25A

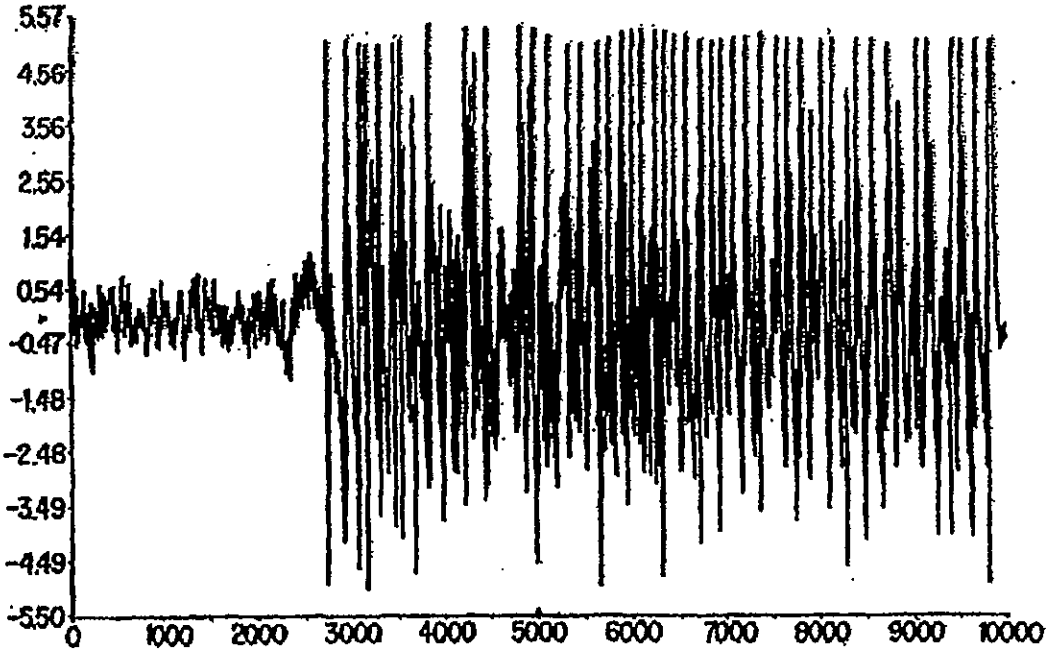

5.57
4.56
3.56
2.55
1.54
0.54
-0.47
-1.48
-2.48
-3.49
-4.49
-5.50
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000

FIG. 25B

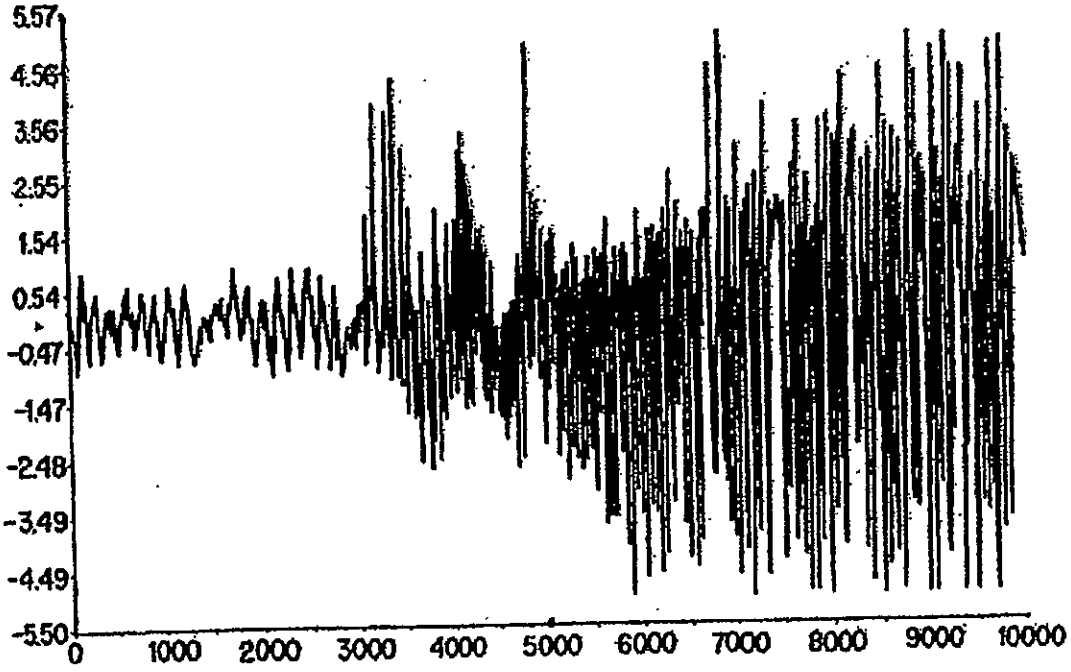
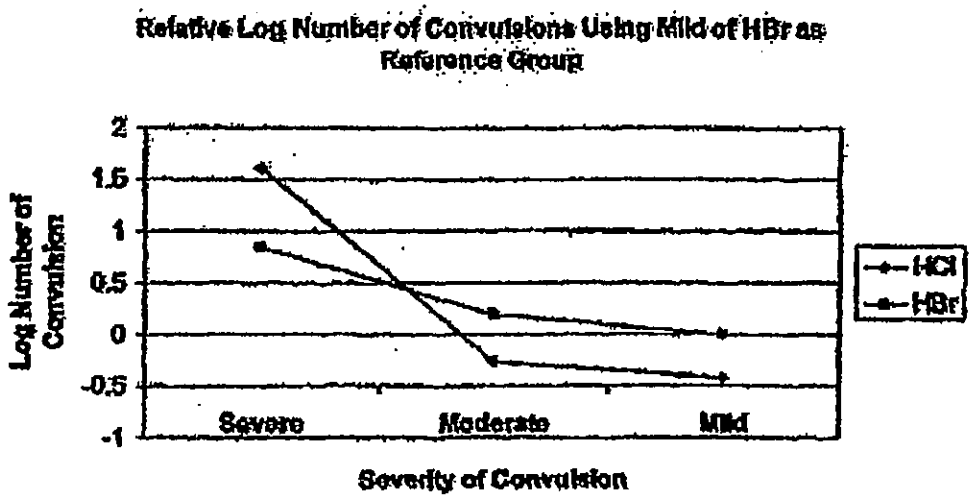

5.57
4.56
3.56
2.55
1.54
0.54
-0.47
-1.47
-2.48
-3.49
-4.49
-5.50
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000

FIG. 26


Relative Log Number of Convulsions Using Mild of HBr as Reference Group
Log Number of Convulsion
2
1.5
1
0.5
0
-0.5
-1
Severe
Moderate
Mild
Severity of Convulsion
HCl
HBr

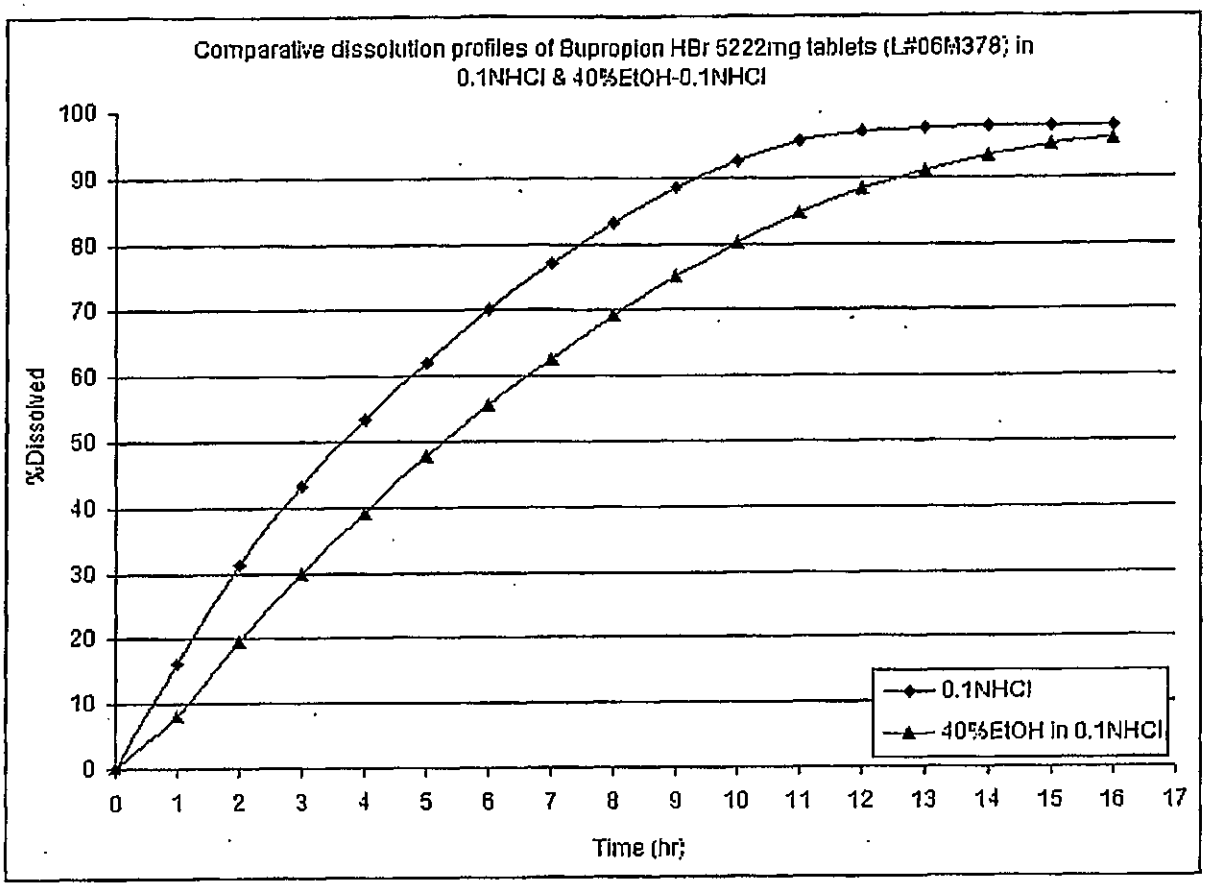

Comparative dissolution profiles of Bupropion HBr 5222mg tablets (L#06M378) in 0.1NHCl & 40%EtOH-0.1NHCl
%Dissolved
Time (hr)
0.1NHCl
40%EtOH in 0.1NHCl

Figure 27

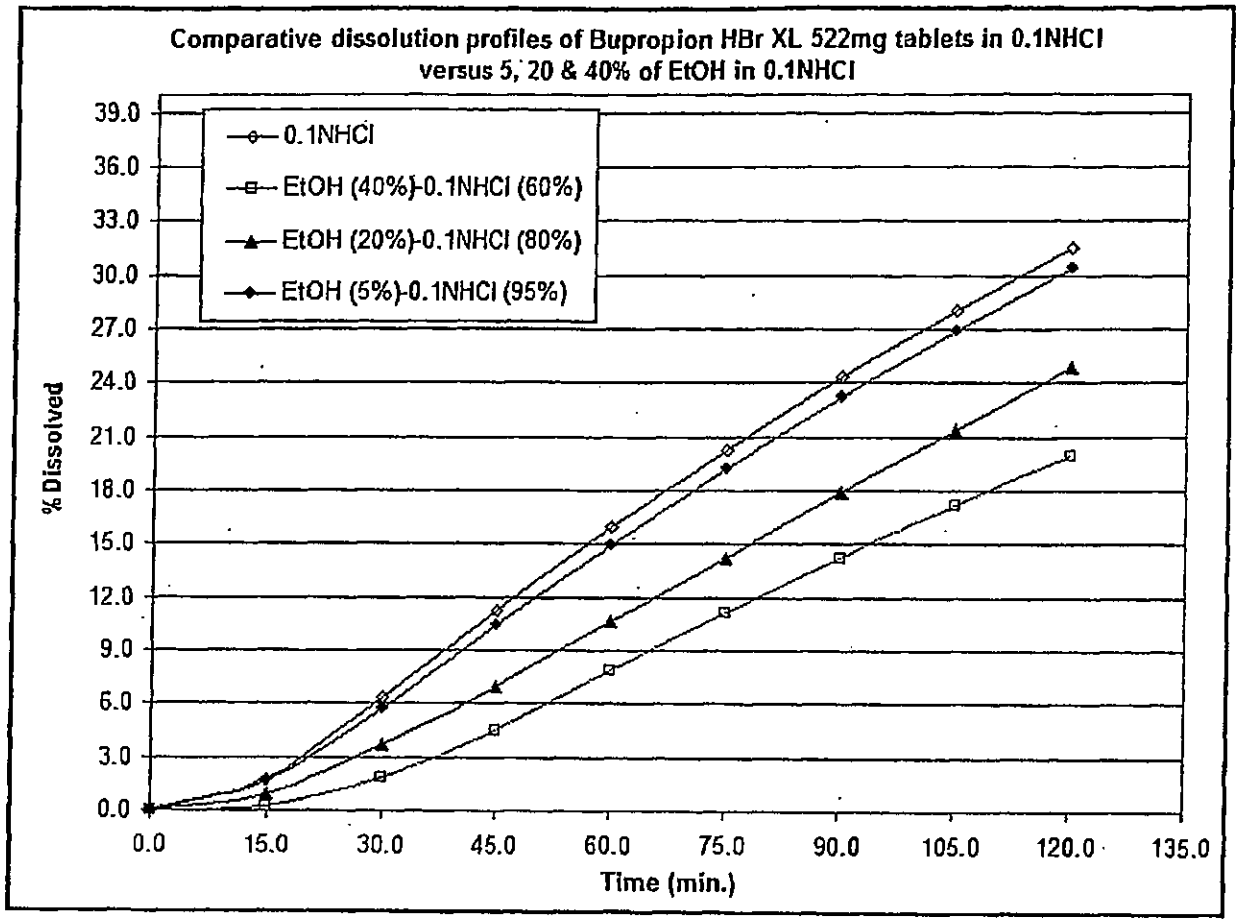

Comparative dissolution profiles of Bupropion HBr XL 522mg tablets in 0.1NHCl versus 5, 20 & 40% of EtOH in 0.1NHCl
0.1NHCl
EtOH (40%)-0.1NHCl (60%)
EtOH (20%)-0.1NHCl (80%)
EtOH (5%)-0.1NHCl (95%)
% Dissolved
39.0
36.0
33.0
30.0
27.0
24.0
21.0
18.0
15.0
12.0
9.0
6.0
3.0
0.0
0.0
15.0
30.0
45.0
60.0
75.0
90.0
105.0
120.0
135.0
Time (min.)

Figure 28

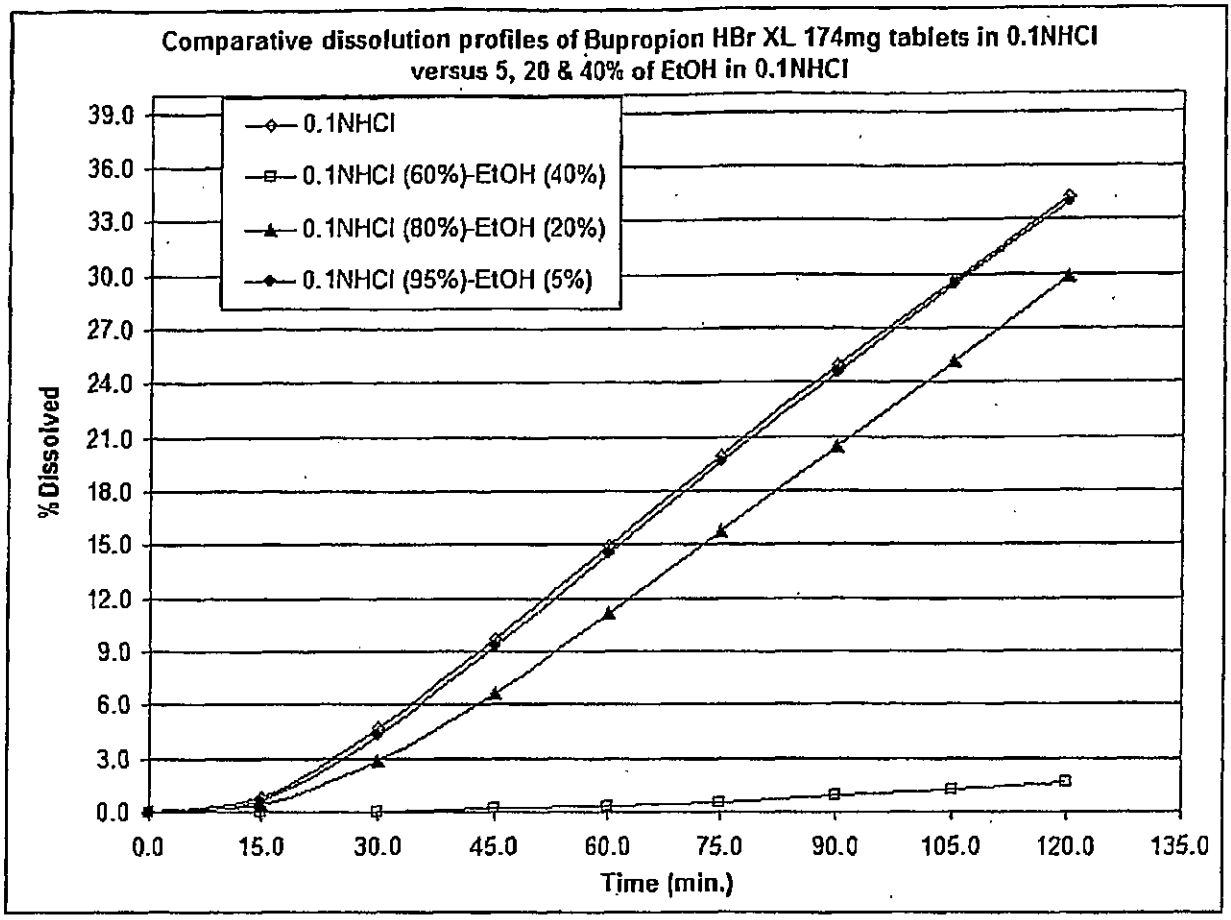

Comparative dissolution profiles of Bupropion HBr XL 174mg tablets in 0.1NHCl versus 5, 20 & 40% of EtOH in 0.1NHCl
0.1NHCl
0.1NHCl (60%)-EtOH (40%)
0.1NHCl (80%)-EtOH (20%)
0.1NHCl (95%)-EtOH (5%)
% Dissolved
39.0
36.0
33.0
30.0
27.0
24.0
21.0
18.0
15.0
12.0
9.0
6.0
3.0
0.0
0.0
15.0
30.0
45.0
60.0
75.0
90.0
105.0
120.0
135.0
Time (min.)

Figure 29

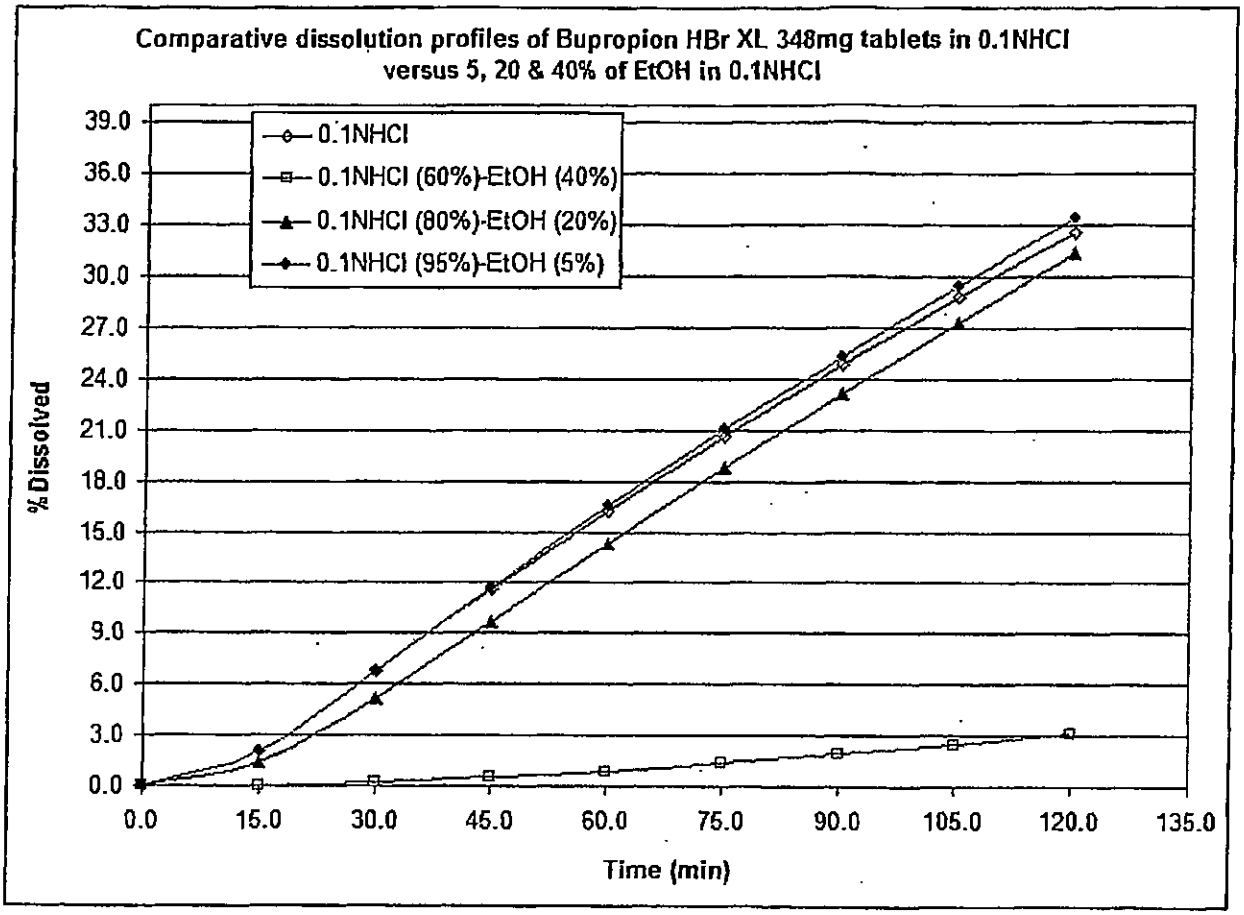

Comparative dissolution profiles of Bupropion HBr XL 348mg tablets in 0.1NHCl versus 5, 20 & 40% of EtOH in 0.1NHCl
0.1NHCl
0.1NHCl (60%)-EtOH (40%)
0.1NHCl (80%)-EtOH (20%)
0.1NHCl (95%)-EtOH (5%)
% Dissolved
39.0
36.0
33.0
30.0
27.0
24.0
21.0
18.0
15.0
12.0
9.0
6.0
3.0
0.0
0.0
15.0
30.0
45.0
60.0
75.0
90.0
105.0
120.0
135.0
Time (min)

Figure 30

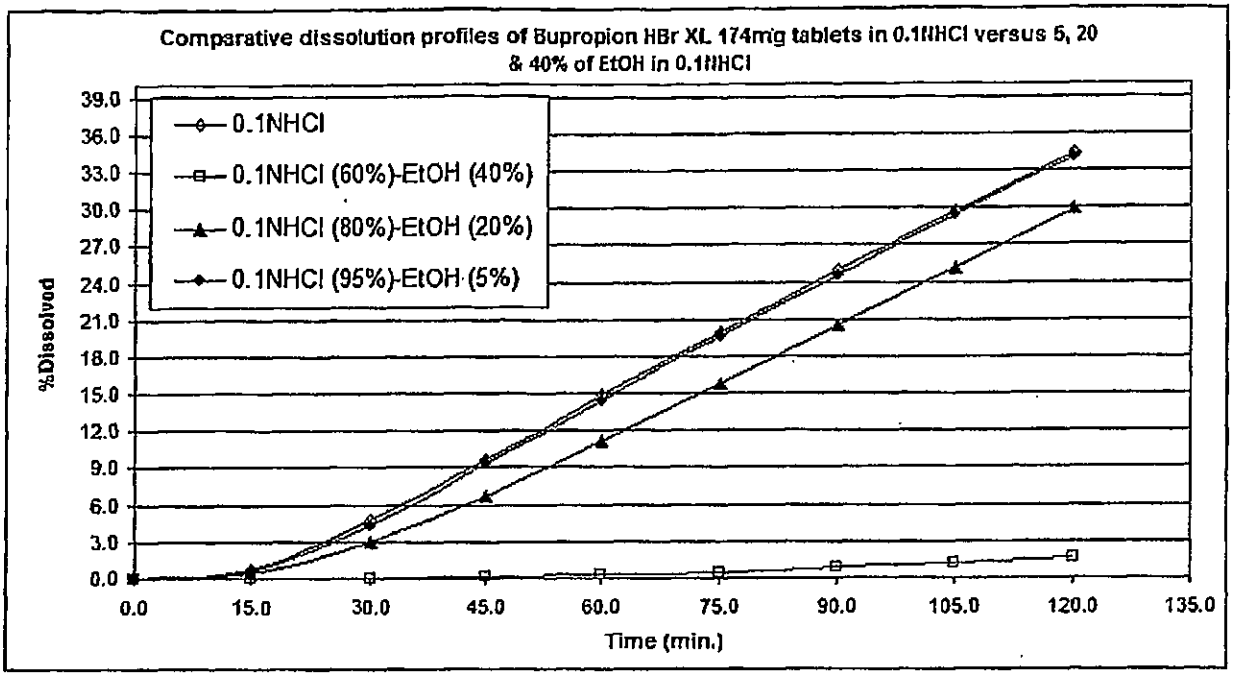

Comparative dissolution profiles of Bupropion HBr XL 174mg tablets in 0.1NHCl versus 5, 20 & 40% of EtOH in 0.1NHCl
0.1NHCl
0.1NHCl (60%)-EtOH (40%)
0.1NHCl (80%)-EtOH (20%)
0.1NHCl (95%)-EtOH (5%)
%Dissolved
Time (min.)
0.0
3.0
6.0
9.0
12.0
15.0
18.0
21.0
24.0
27.0
30.0
33.0
36.0
39.0
0.0
15.0
30.0
45.0
60.0
75.0
90.0
105.0
120.0
135.0

Figure 31

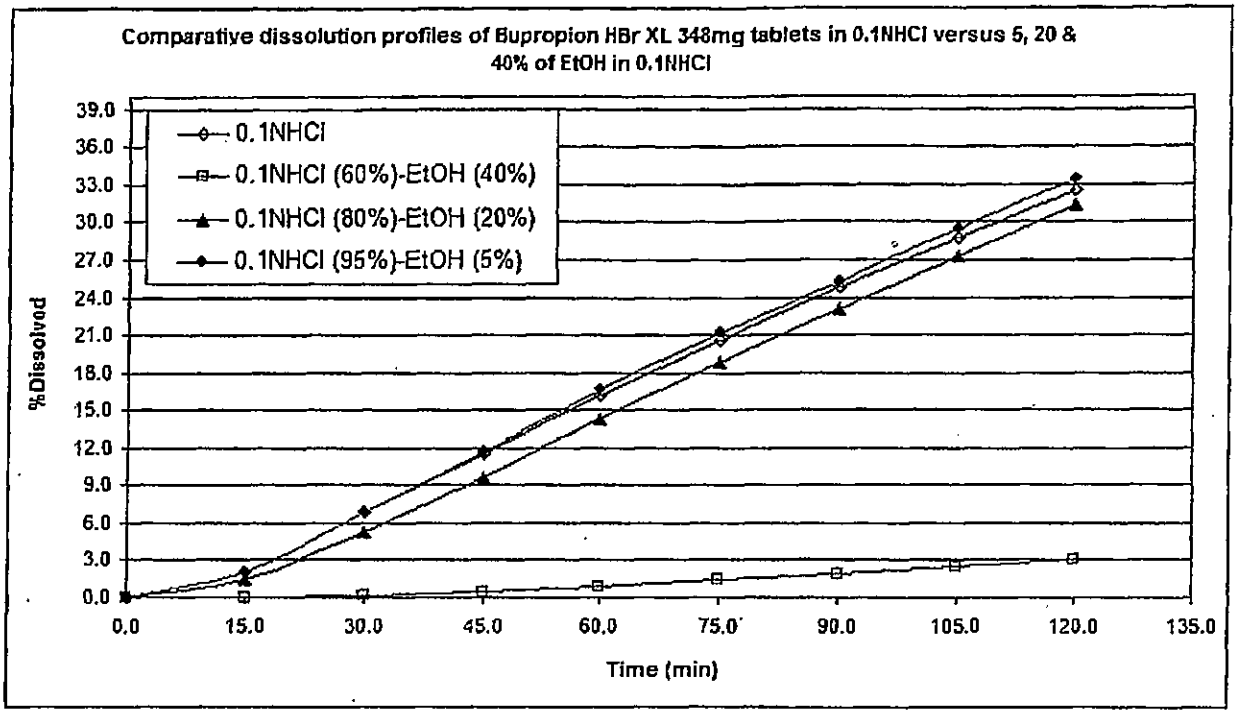

Comparative dissolution profiles of Bupropion HBr XL 348mg tablets in 0.1NHCl versus 5, 20 & 40% of EtOH in 0.1NHCl
0.1NHCl
0.1NHCl (60%)-EtOH (40%)
0.1NHCl (80%)-EtOH (20%)
0.1NHCl (95%)-EtOH (5%)
%Dissolved
39.0
36.0
33.0
30.0
27.0
24.0
21.0
18.0
15.0
12.0
9.0
6.0
3.0
0.0
0.0
15.0
30.0
45.0
60.0
75.0
90.0
105.0
120.0
135.0
Time (min)

Figure 32

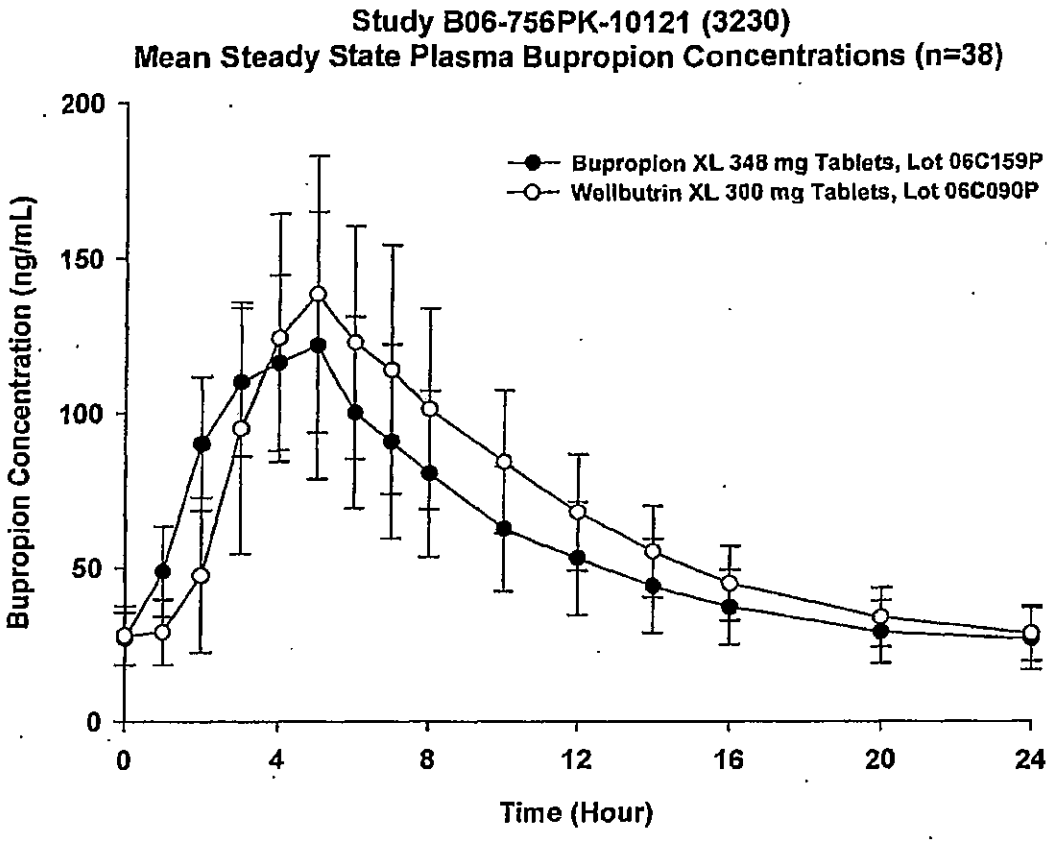


Figure 33: Mean Plasma Bupropion Concentration-Time Plot for Study B06-756PK-10121 (3230)

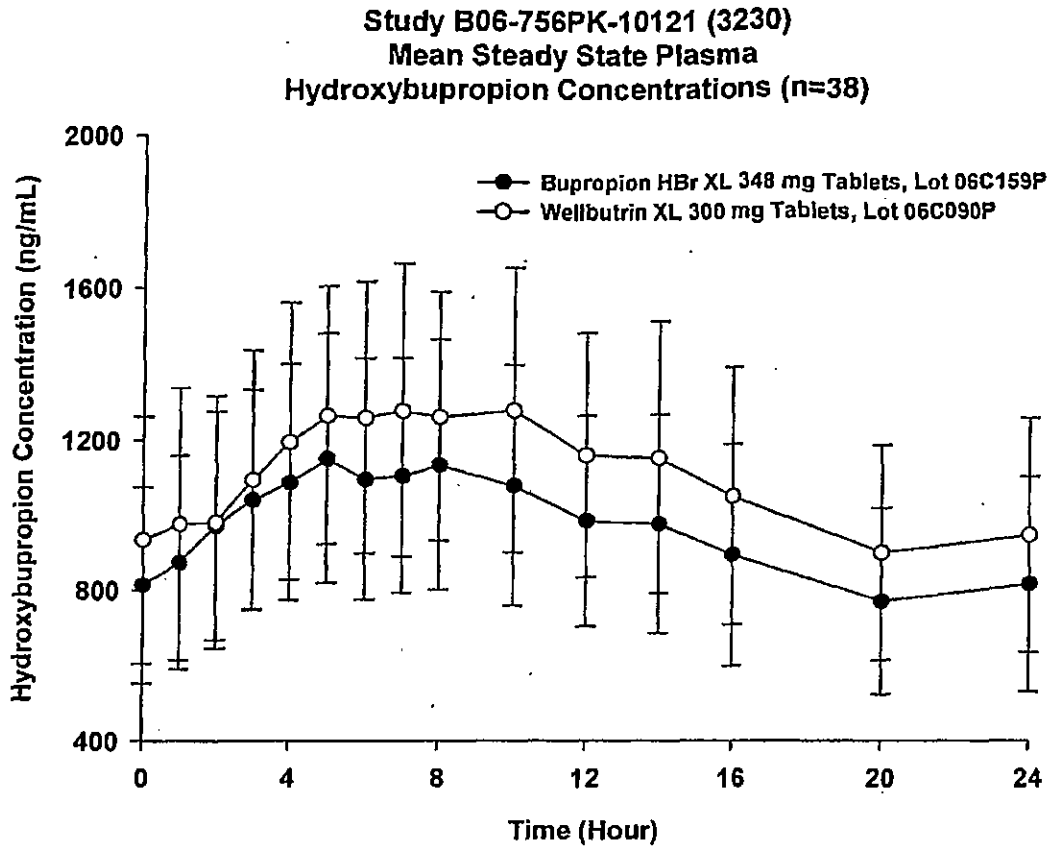


Figure 34: Mean Plasma Hydroxybupropion Concentration-Time Plot for Study B06-756PK-10121 (3230)

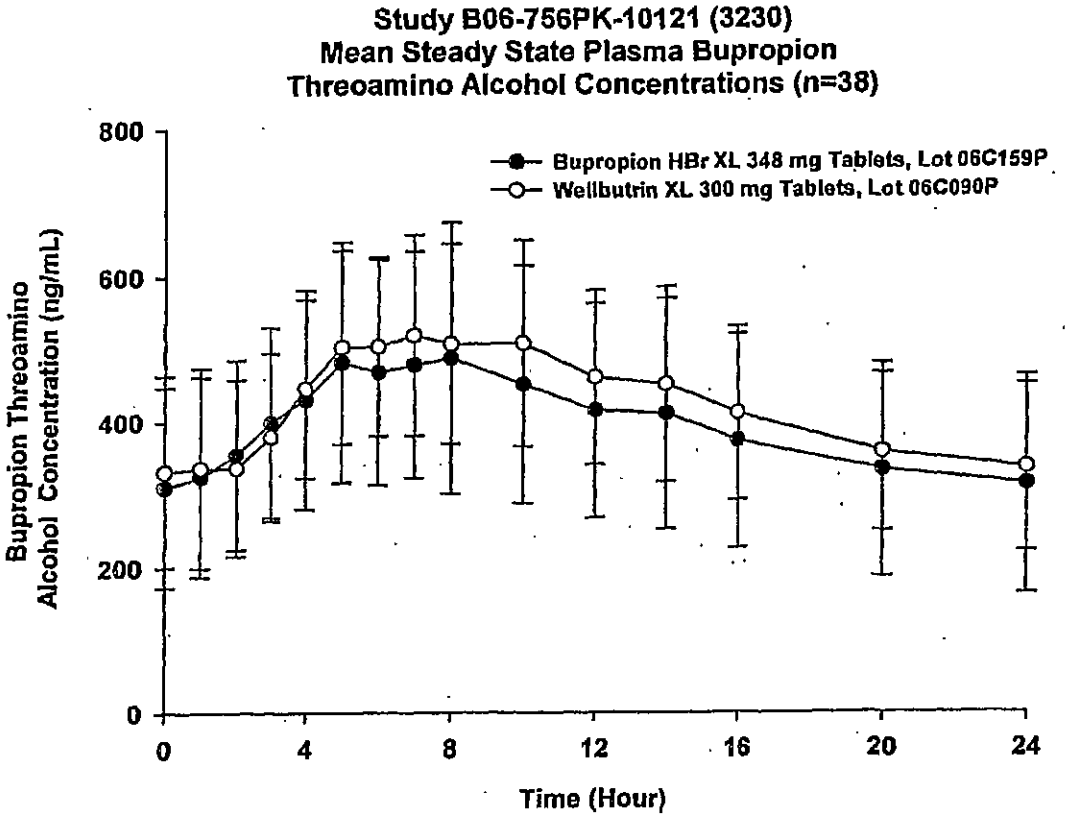


Figure 35: Mean Plasma Bupropion Threoamino Alcohol Concentration-Time Plot for Study B06-756PK-10121 (3230)

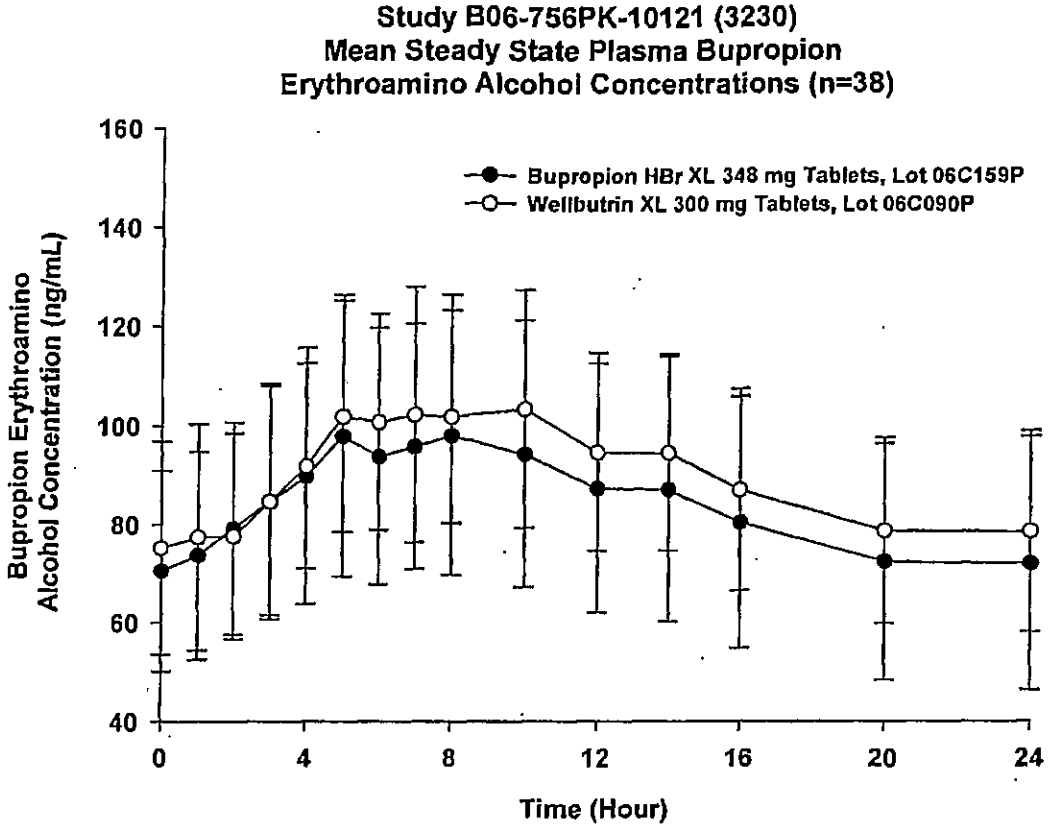


Figure 36: Mean Plasma Bupropion Erythroamino Alcohol Concentration-Time Plot for Study B06-756PK-10121 (3230)

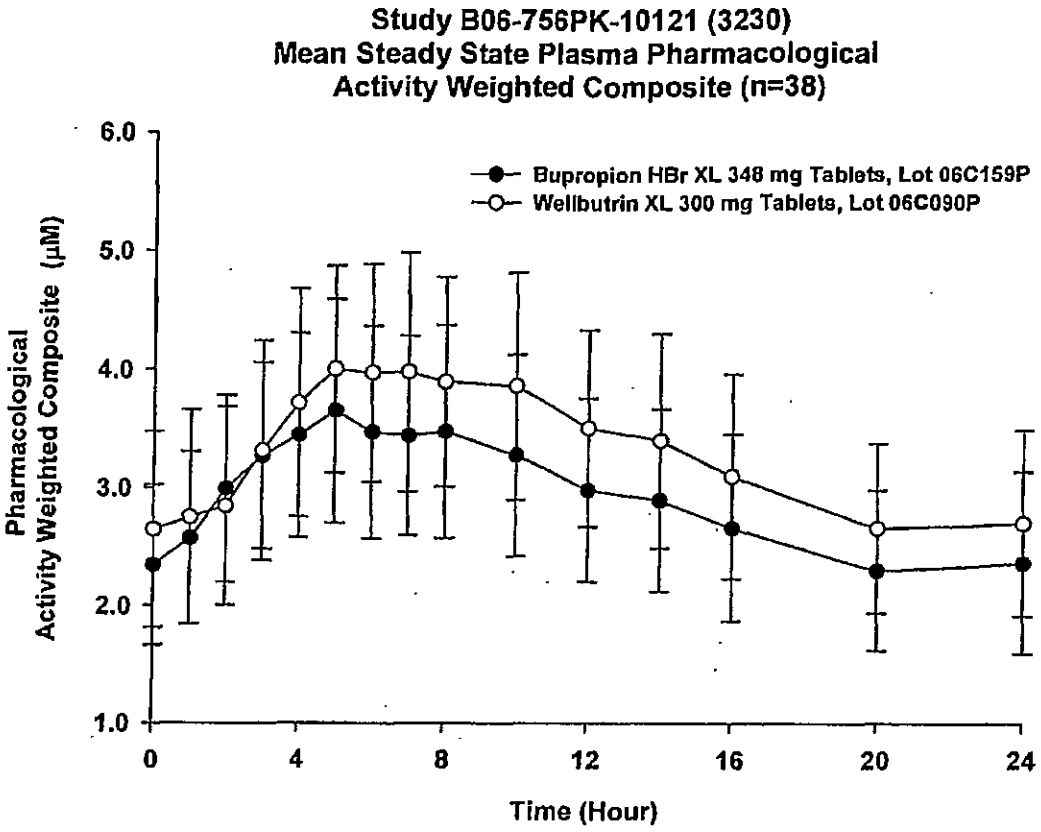


Figure 37: Mean Plasma Pharmacological Activity Weighted Composite (PAWC)-Time Plot for Study B06-756PK-10121 (3230)

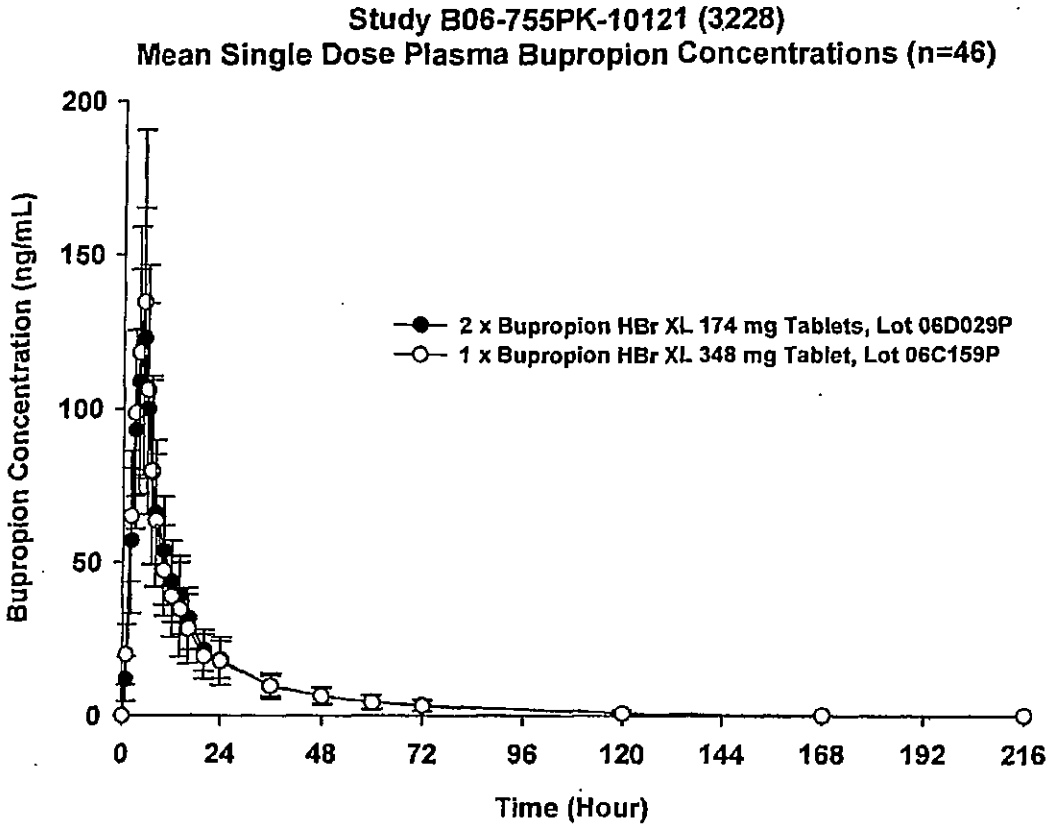


Figure 38. Mean Plasma Bupropion Concentration-Time Plot for Study B06-755PK-10121 (3228)

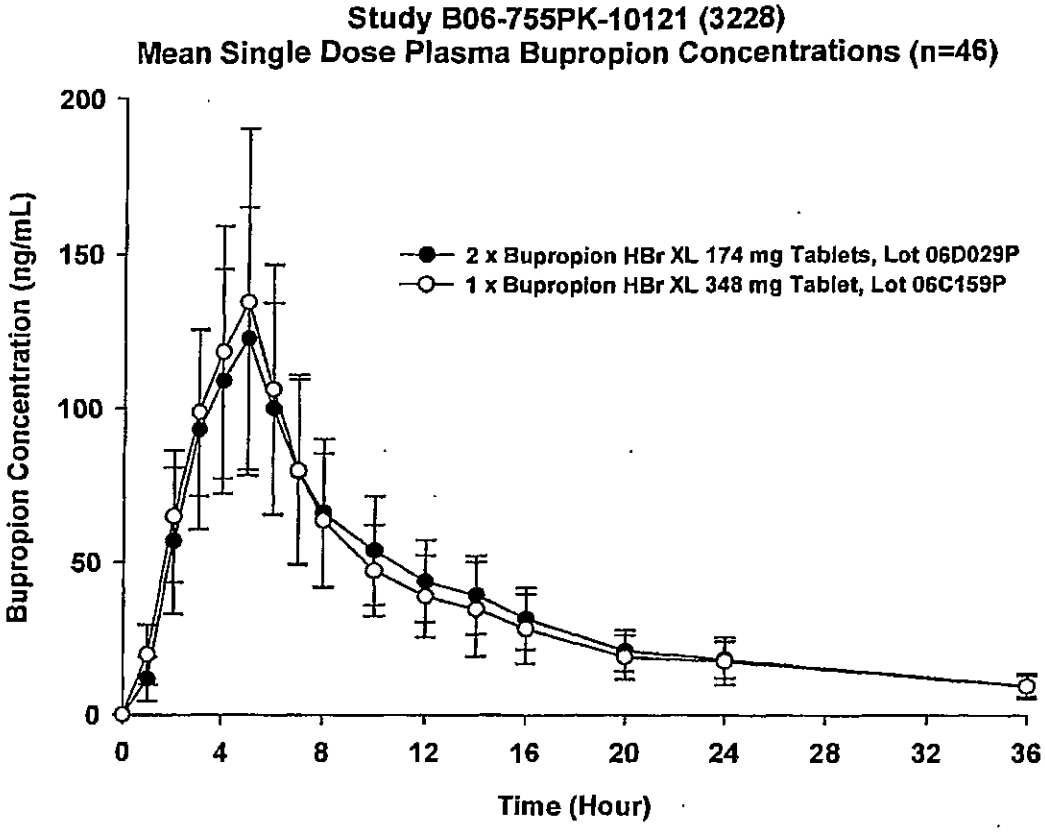


Figure 39: Mean Plasma Bupropion Concentration-Time Plot for Study B06-755PK-10121 (3228) – Magnified Showing Only Datapoints From 0 – 36 Hours

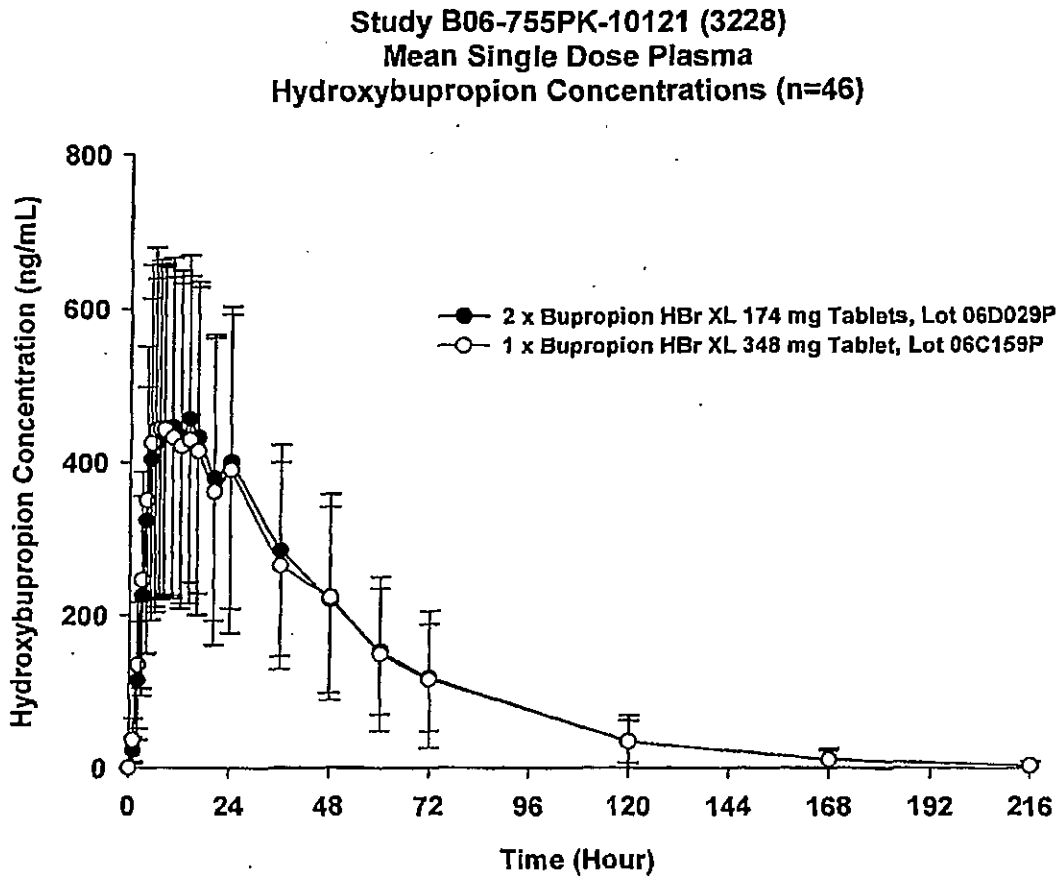


Figure 40: Mean Plasma Hydroxybupropion Concentration-Time Plot for Study B06-755PK-10121 (3228)

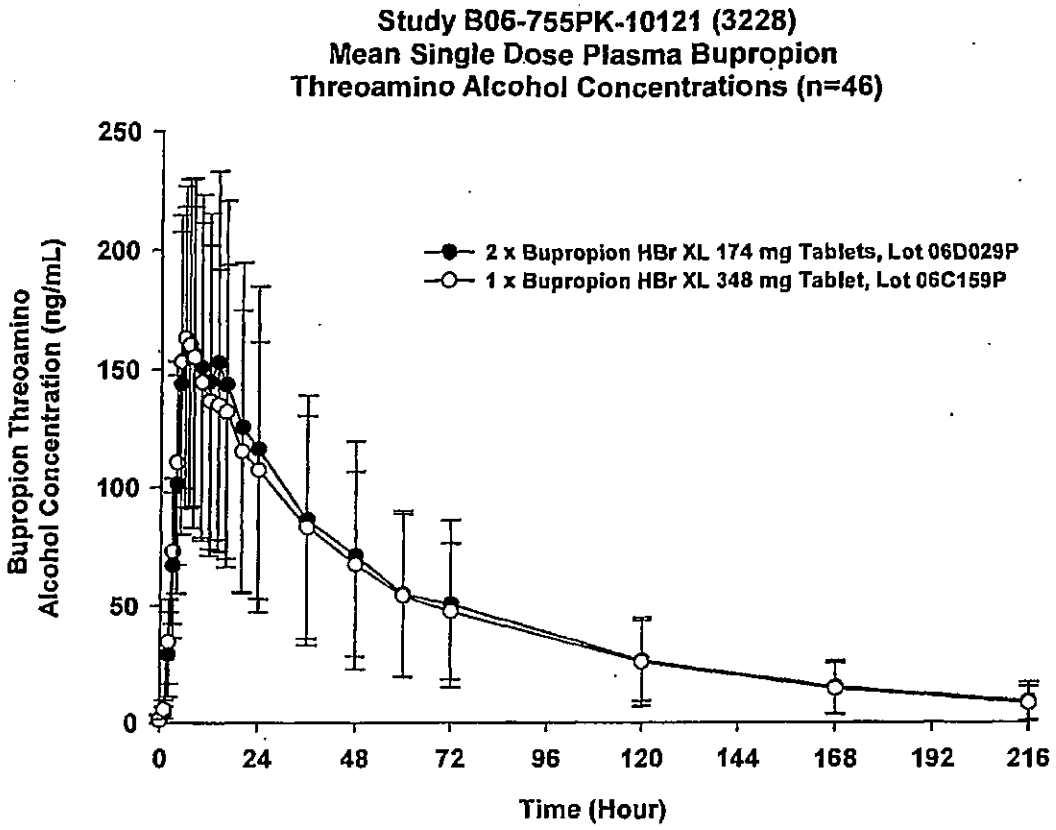


Figure 41: Mean Plasma Bupropion Threoamino Alcohol Concentration-Time Plot for Study B06-755PK-10121 (3228)

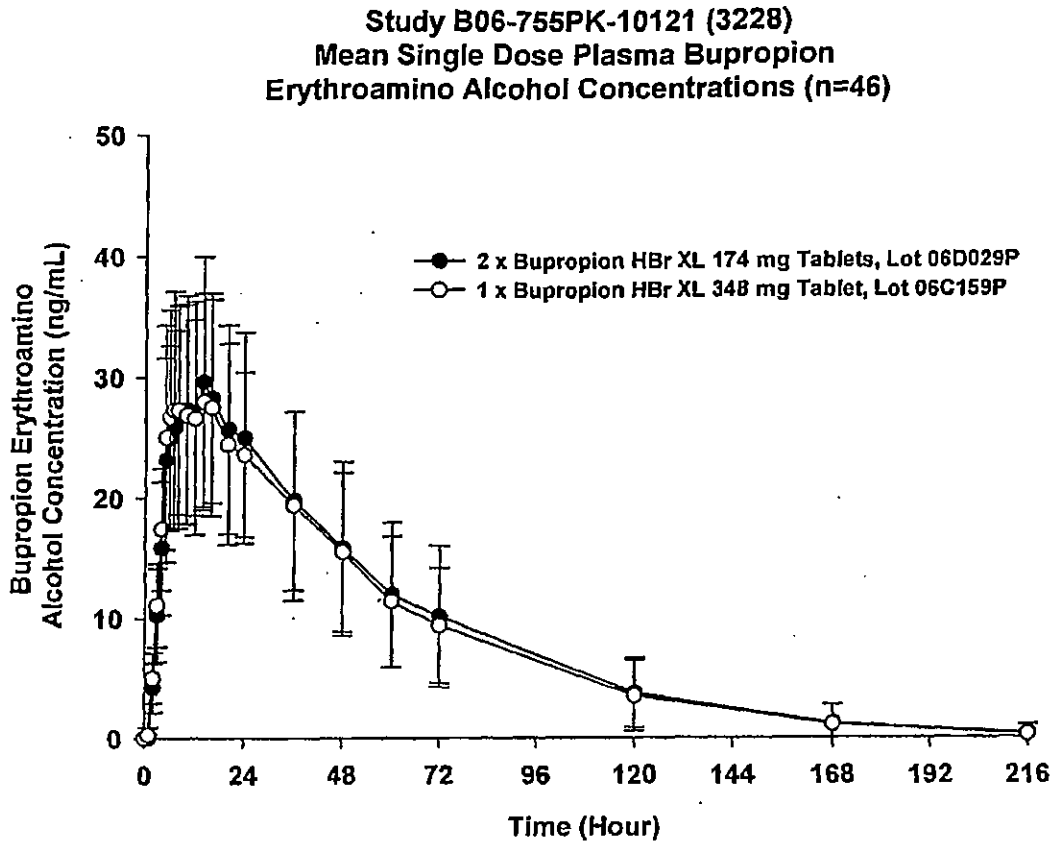


Figure 42: Mean Plasma Bupropion Erythroamino Alcohol Concentration-Time Plot for Study B06-755PK-10121 (3228)

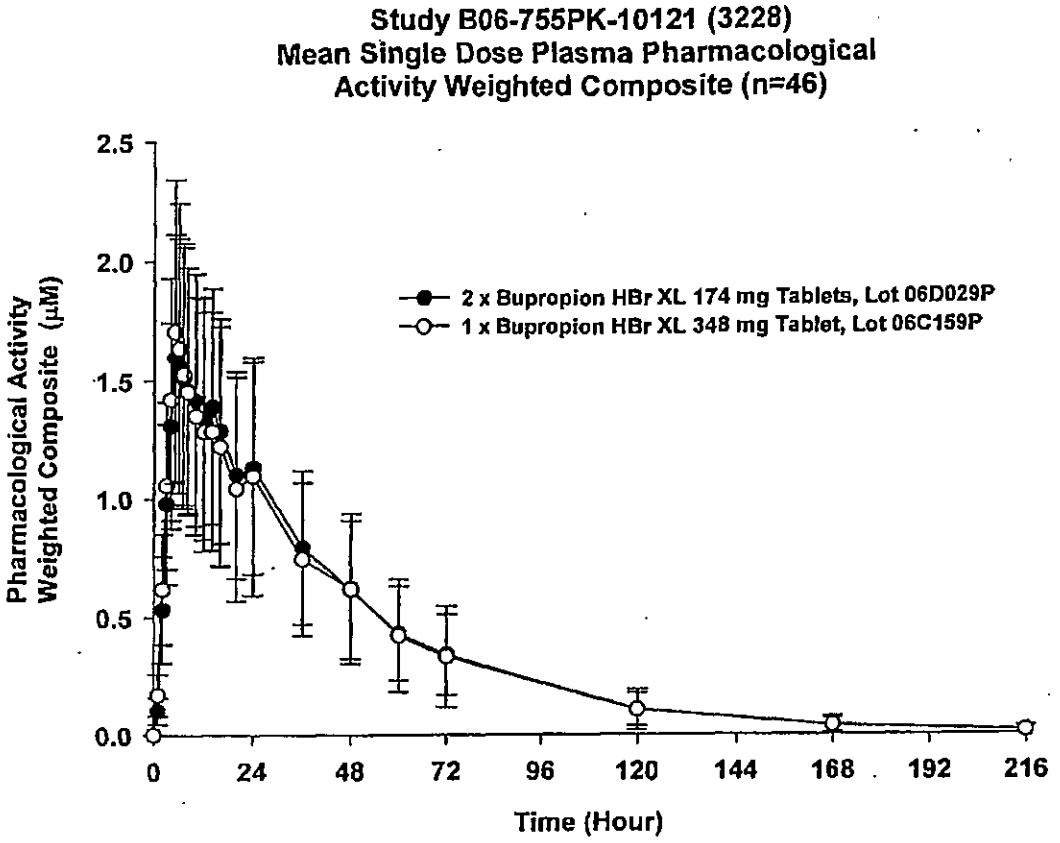


Figure 43: Mean Plasma Pharmacological Activity Weighted Composite (PAWC)-Time Plot for Study B06-755PK-10121 (3228)

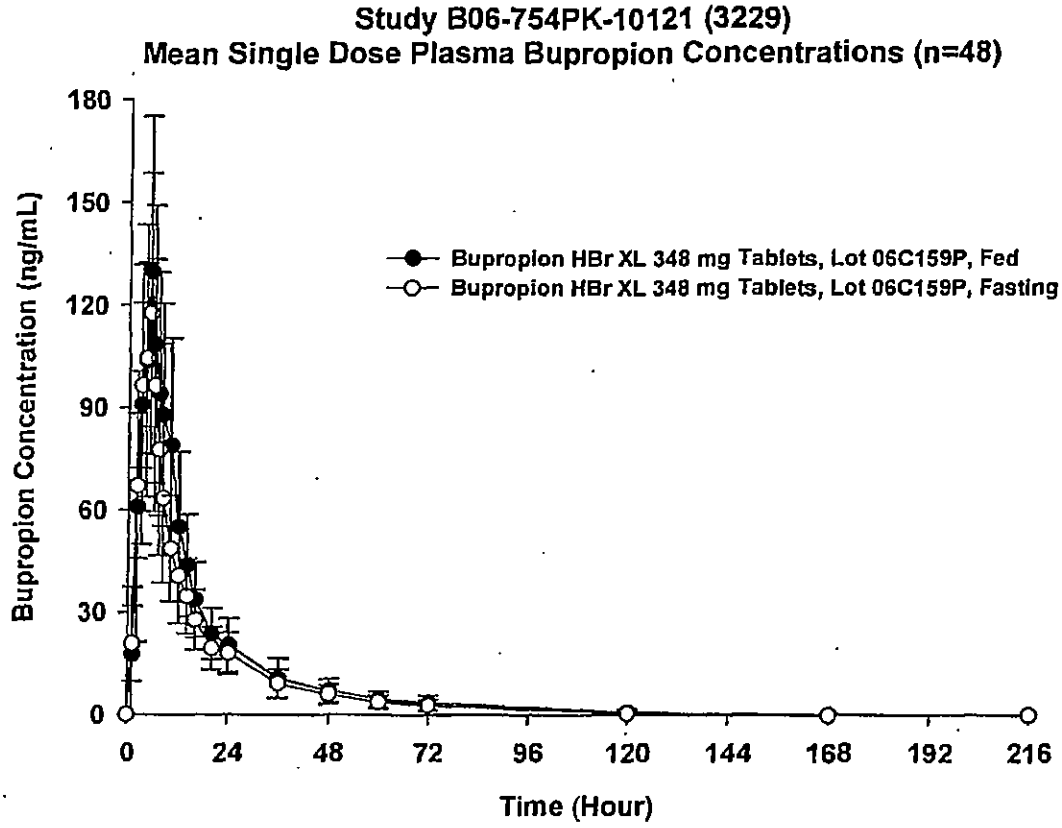


Figure 44: Mean Plasma Bupropion Concentration-Time Plot for Study B06-754PK-10121 (3229)

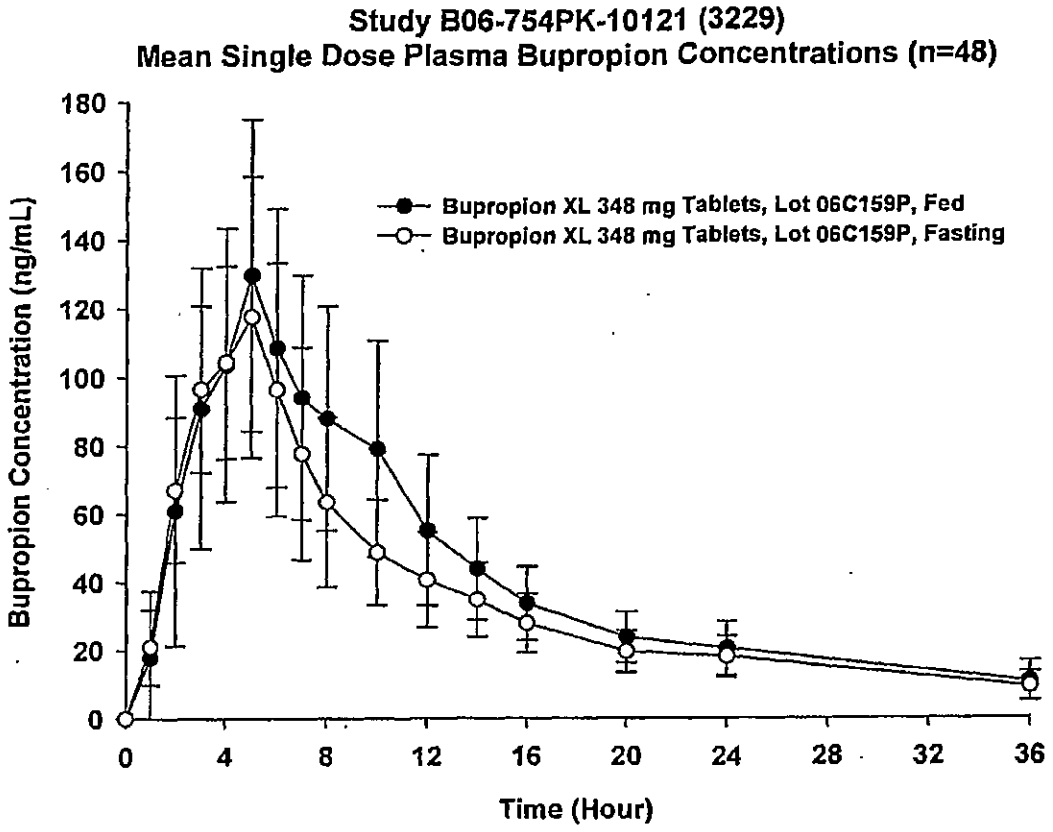


Figure 45: Mean Plasma Bupropion Concentration-Time Plot for Study B06-754PK-10121 (3229) – Magnified Showing Only Datapoints From 0 – 36 Hours

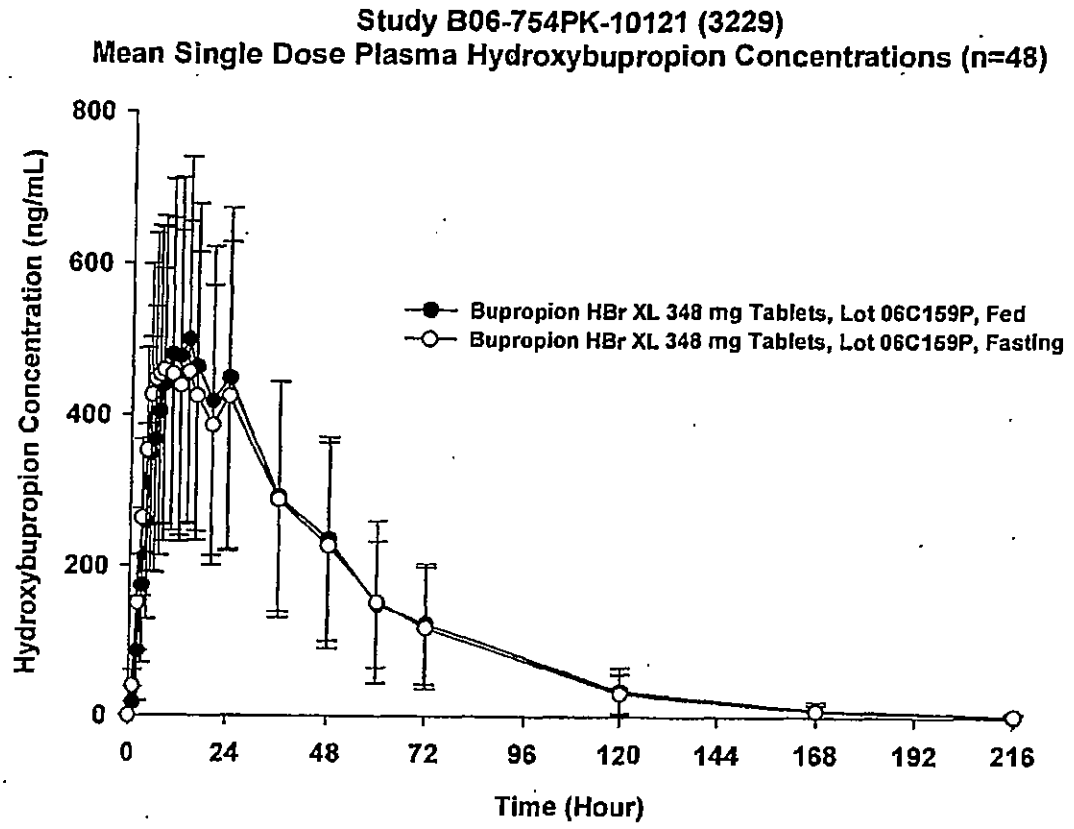


Figure 46: Mean Plasma Hydroxybupropion Concentration-Time Plot for Study B06-754PK-10121 (3229)

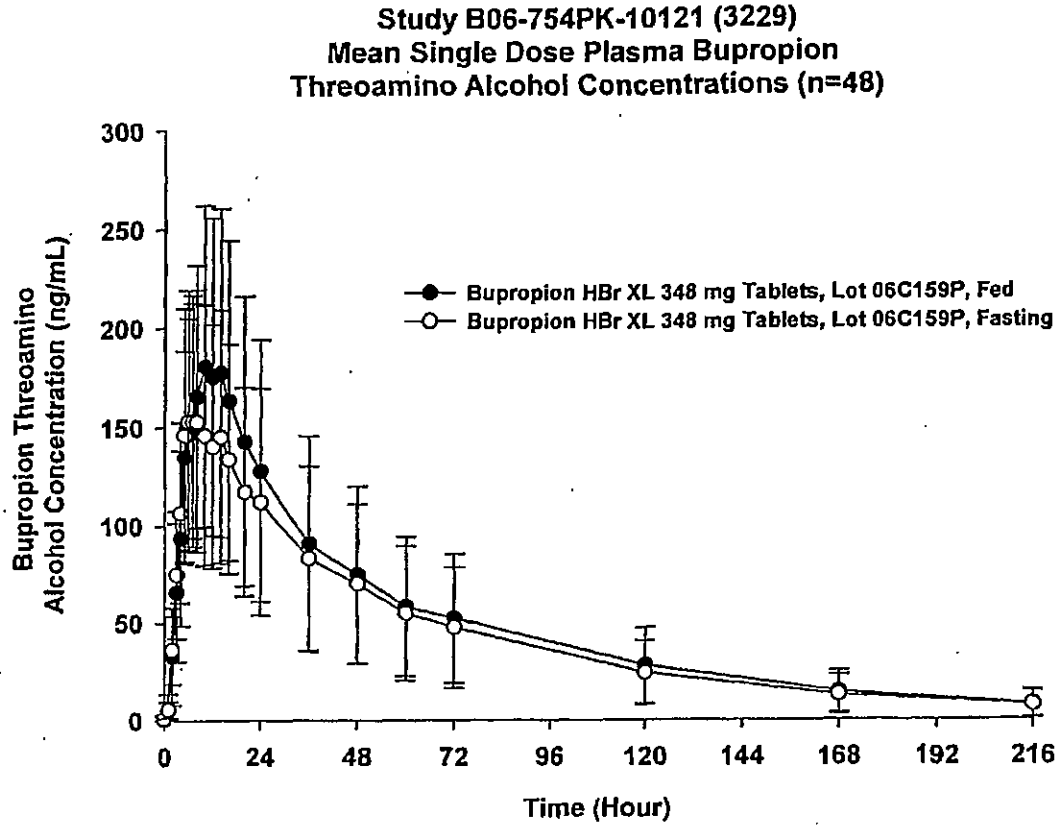


Figure 47: Mean Plasma Bupropion Threoamino Alcohol Concentration-Time Plot for Study B06-754PK-10121 (3229)

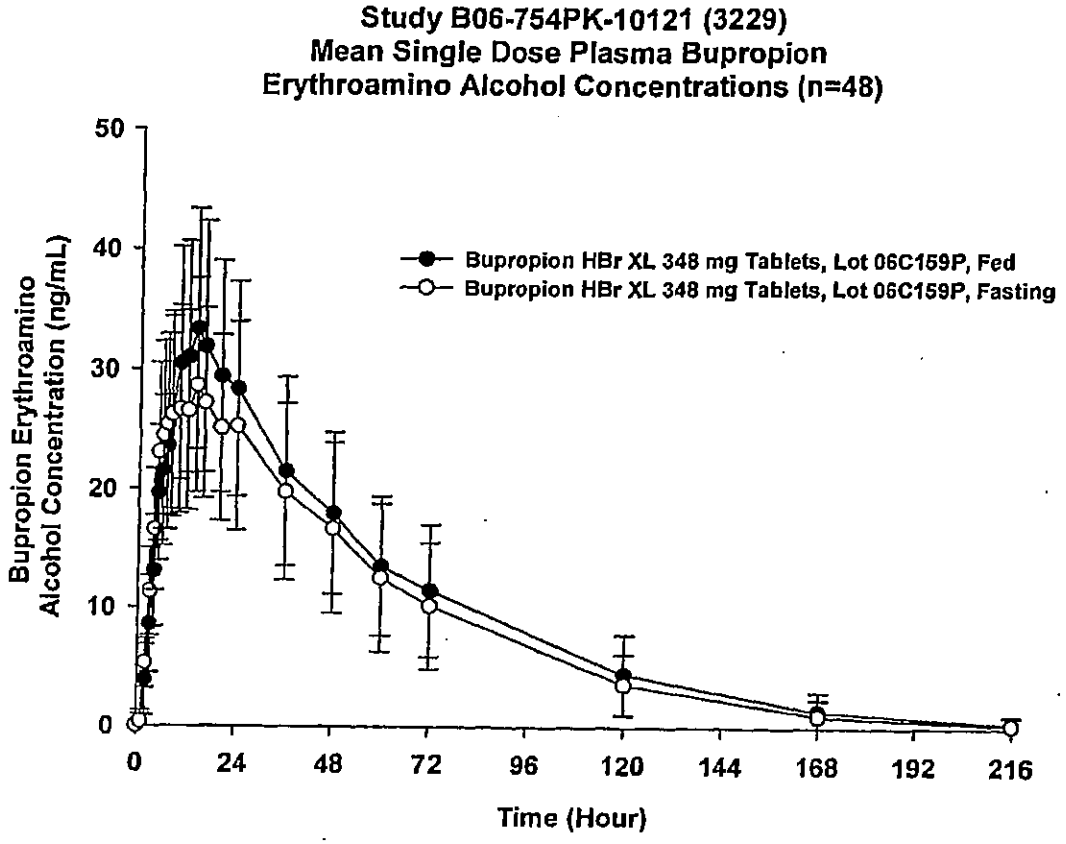


Figure 48: Mean Plasma Bupropion Erythroamino Alcohol Concentration-Time Plot for Study B06-754PK-10121 (3229)

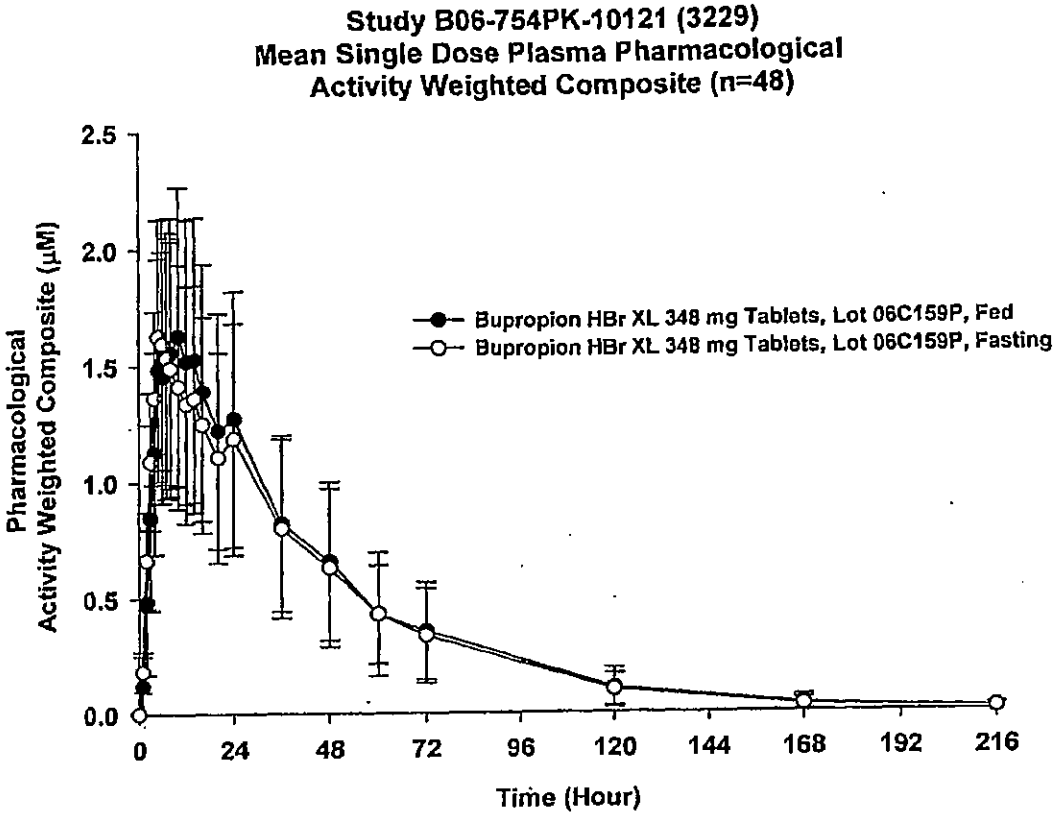


Figure 49: Mean Plasma Pharmacological Activity Weighted Composite (PAWC)-Time Plot for Study B06-754PK-10121 (3229)

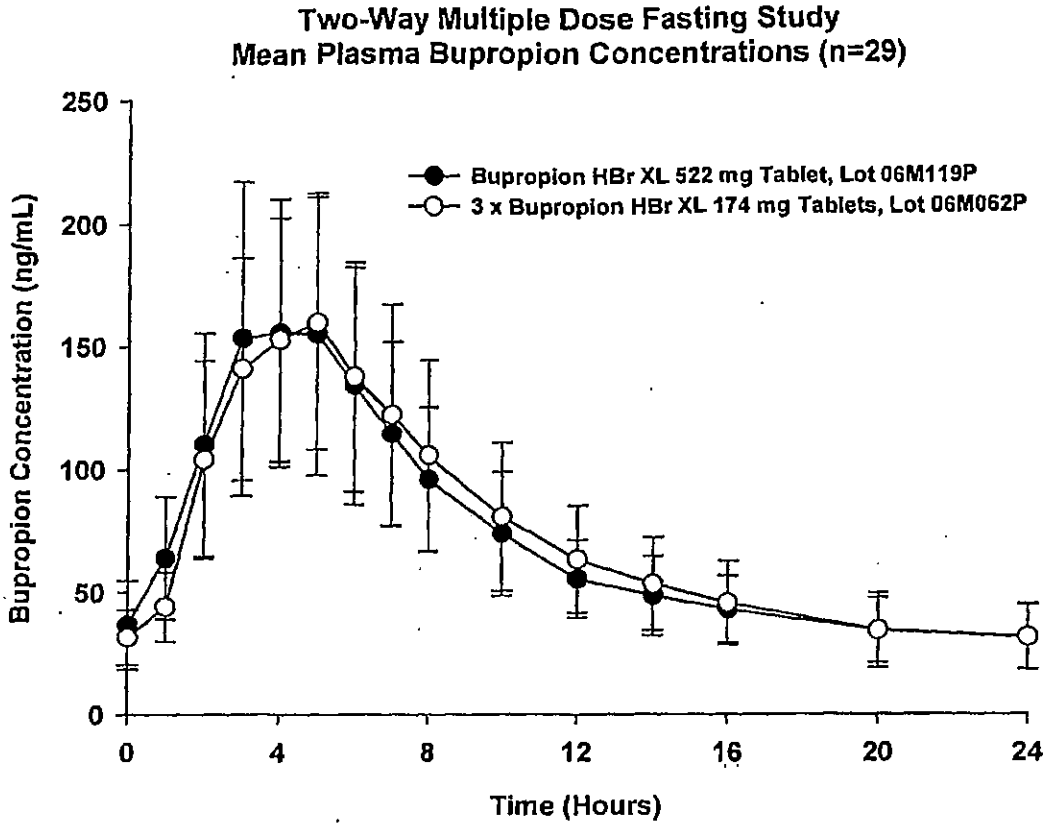


Figure 50: Mean Plasma Bupropion Concentration-Time Plot For Study B06-802PK-10121 (AA40055)

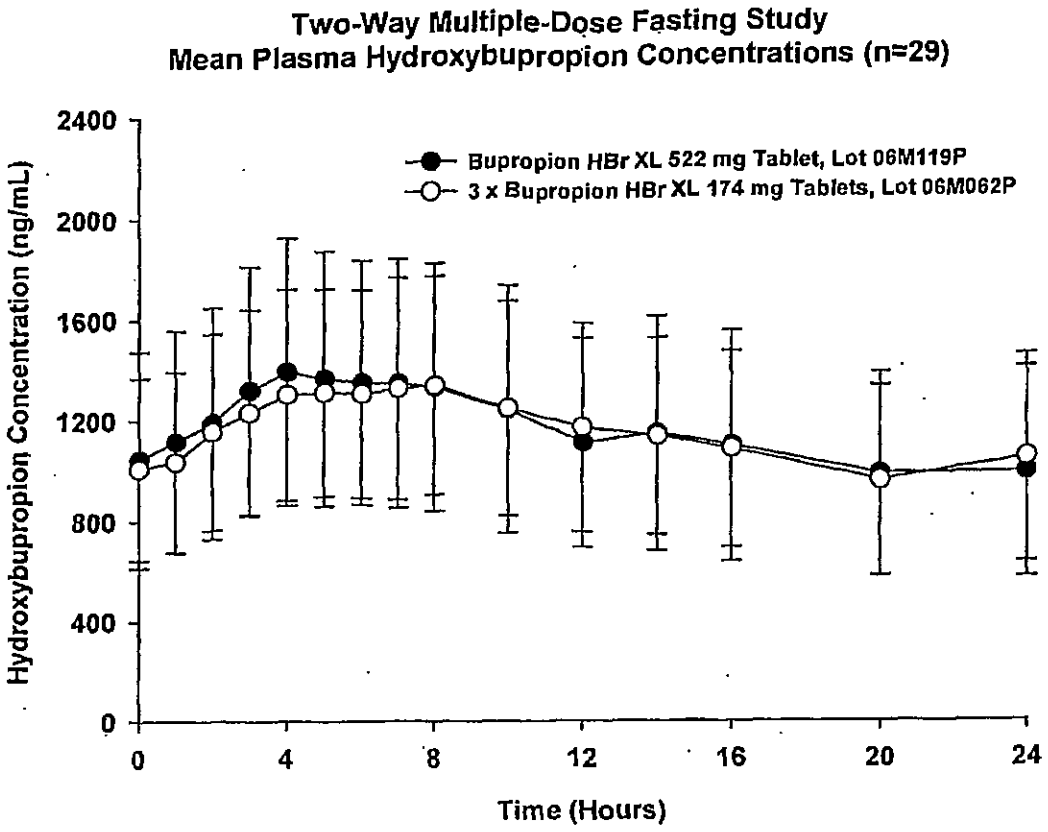


Figure 51: Mean Plasma Hydroxybupropion Concentration-Time Plot For Study B06-802PK-10121 (AA40055)

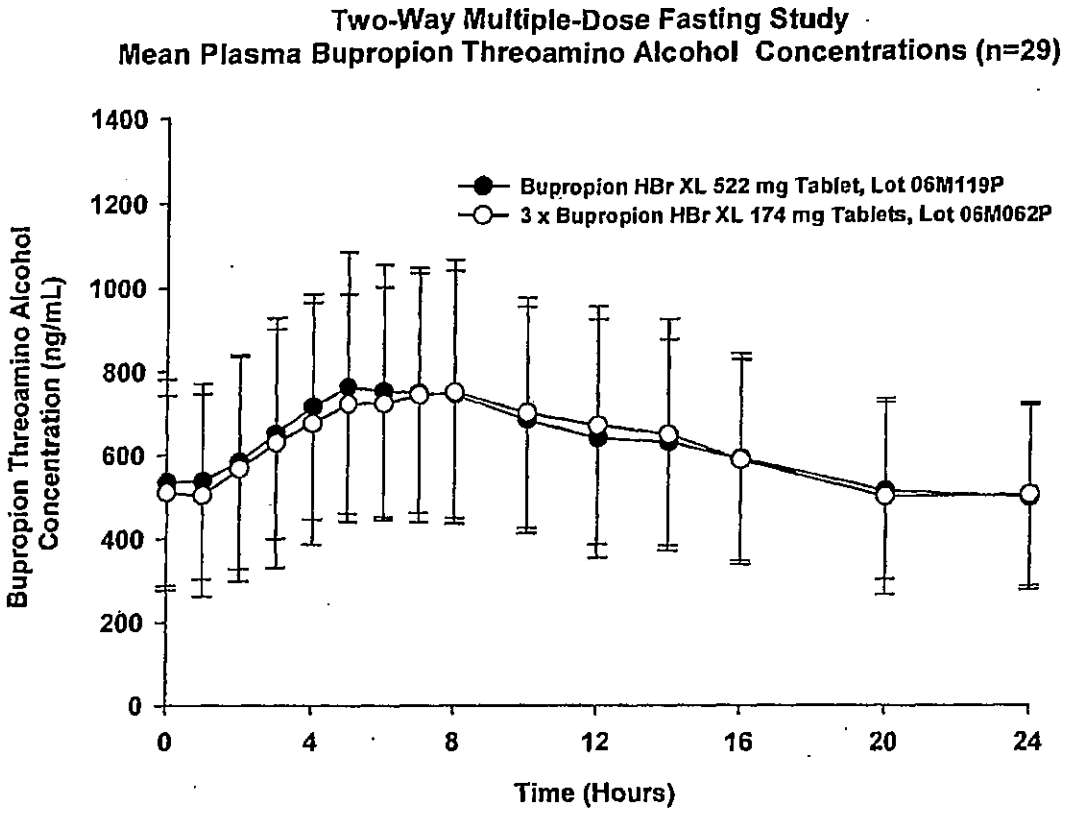


Figure 52: Mean Plasma Bupropion Threoamino Alcohol Concentration-Time Plot For Study B06-802PK-10121 (AA40055)

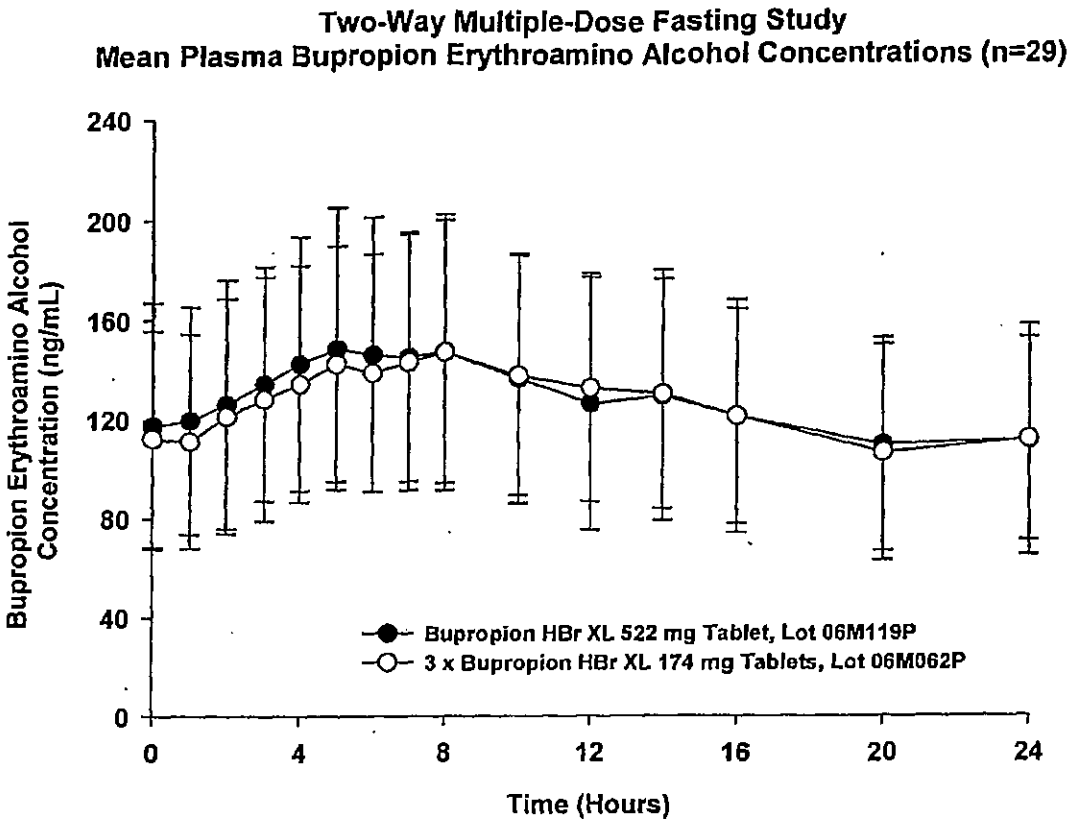


Figure 53: Mean Plasma Bupropion Erythroamino Alcohol Concentration-Time Plot

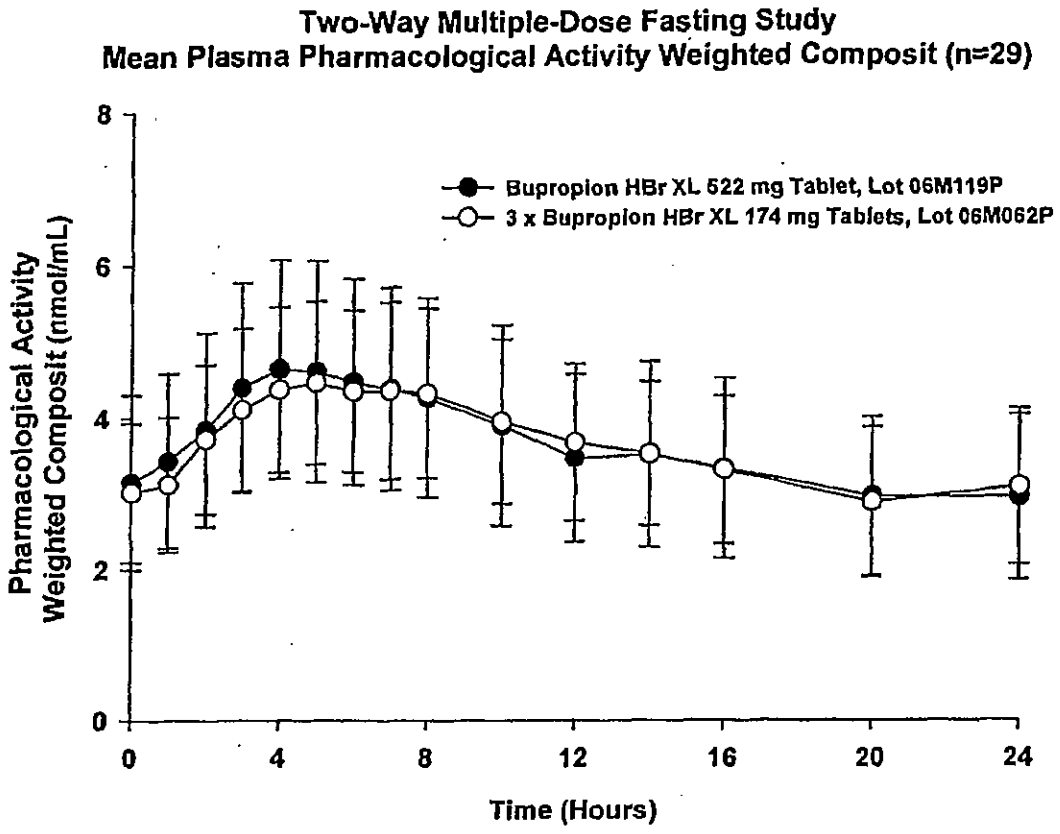


Figure 54: Mean Plasma Pharmacological Activity Weighted Composite (PAWC)-Time Plot