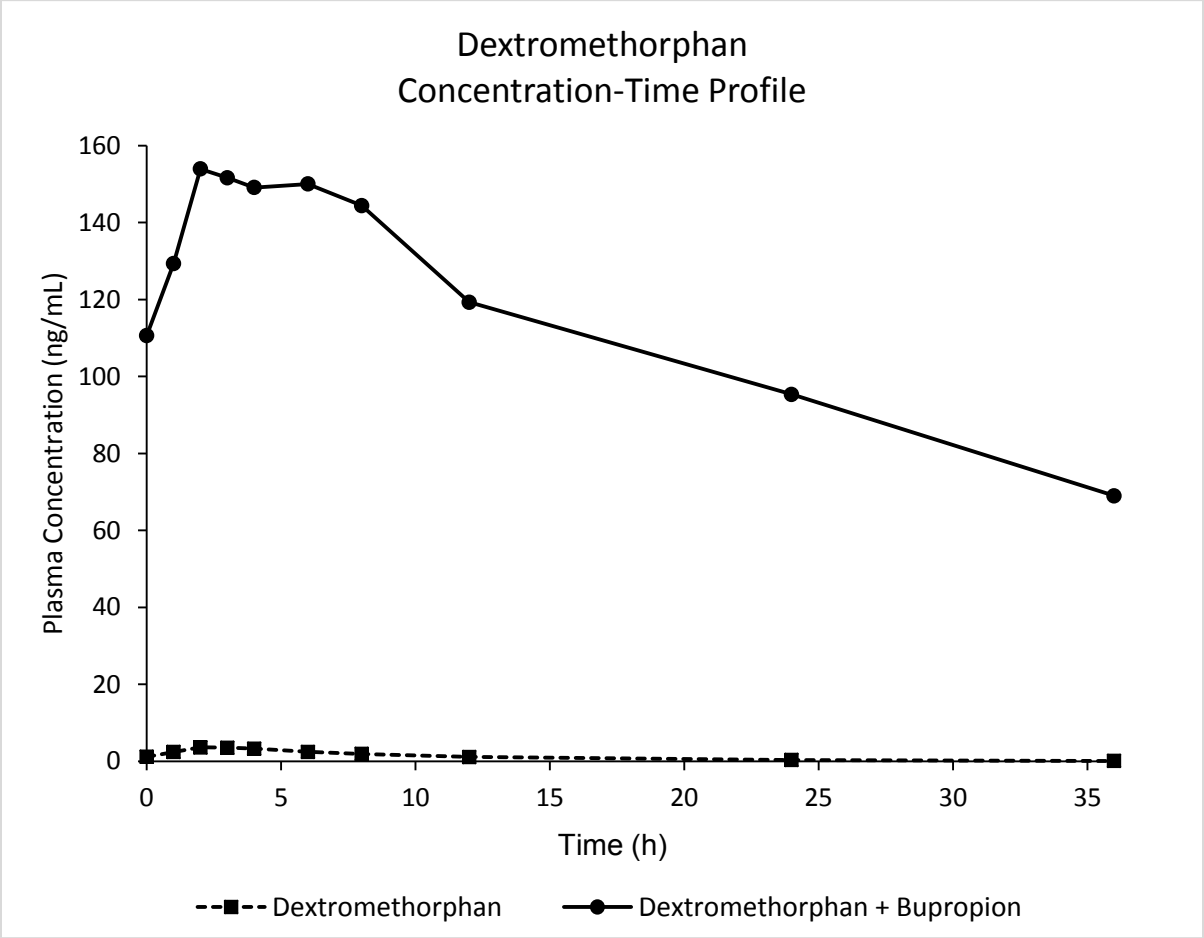

Dextromethorphan
Concentration-Time Profile
Plasma Concentration (ng/mL)
160
140
120
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Time (h)
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 1

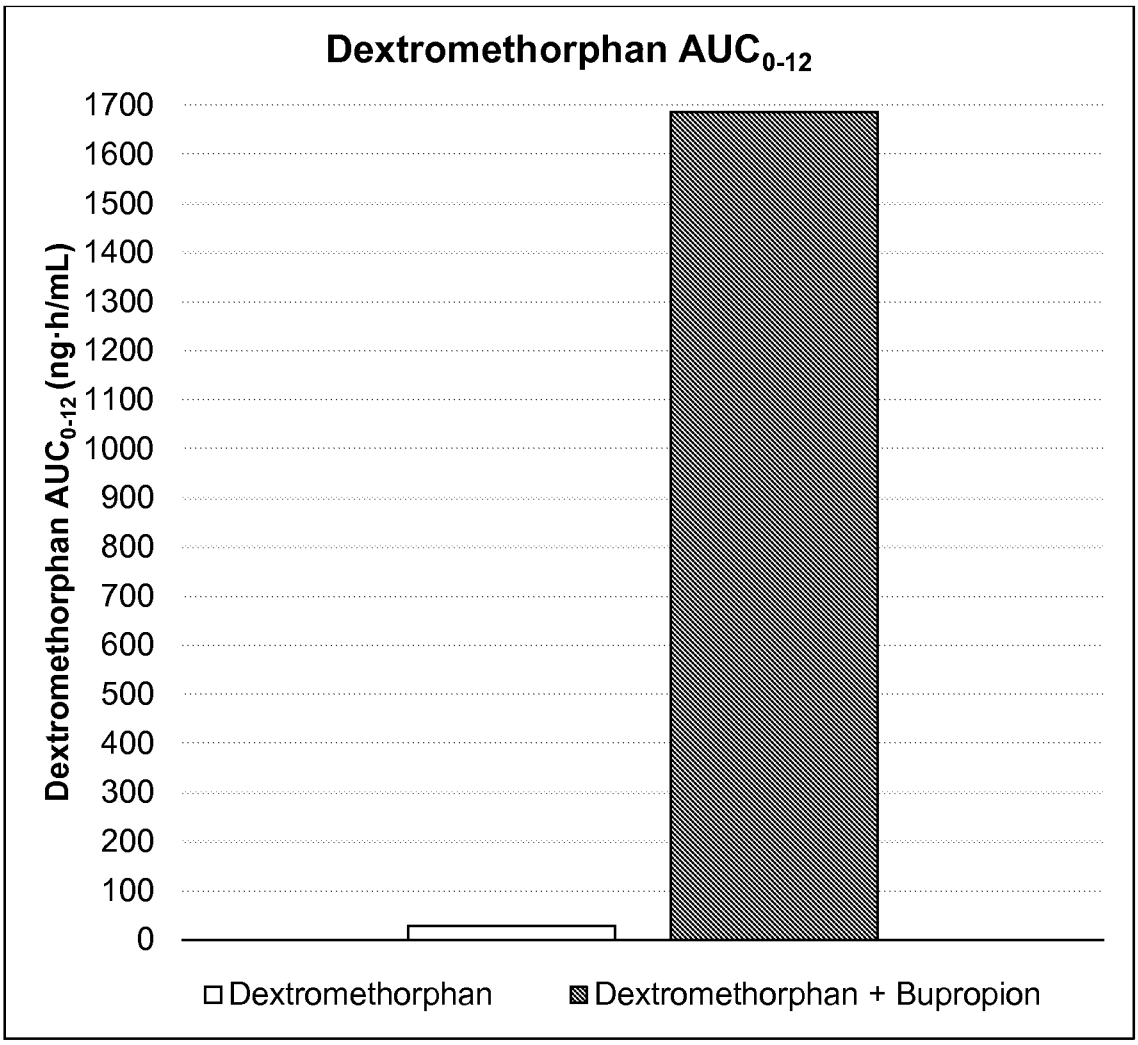

Dextromethorphan AUC0-12
Dextromethorphan AUC0-12 (ng·h/mL)
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 2

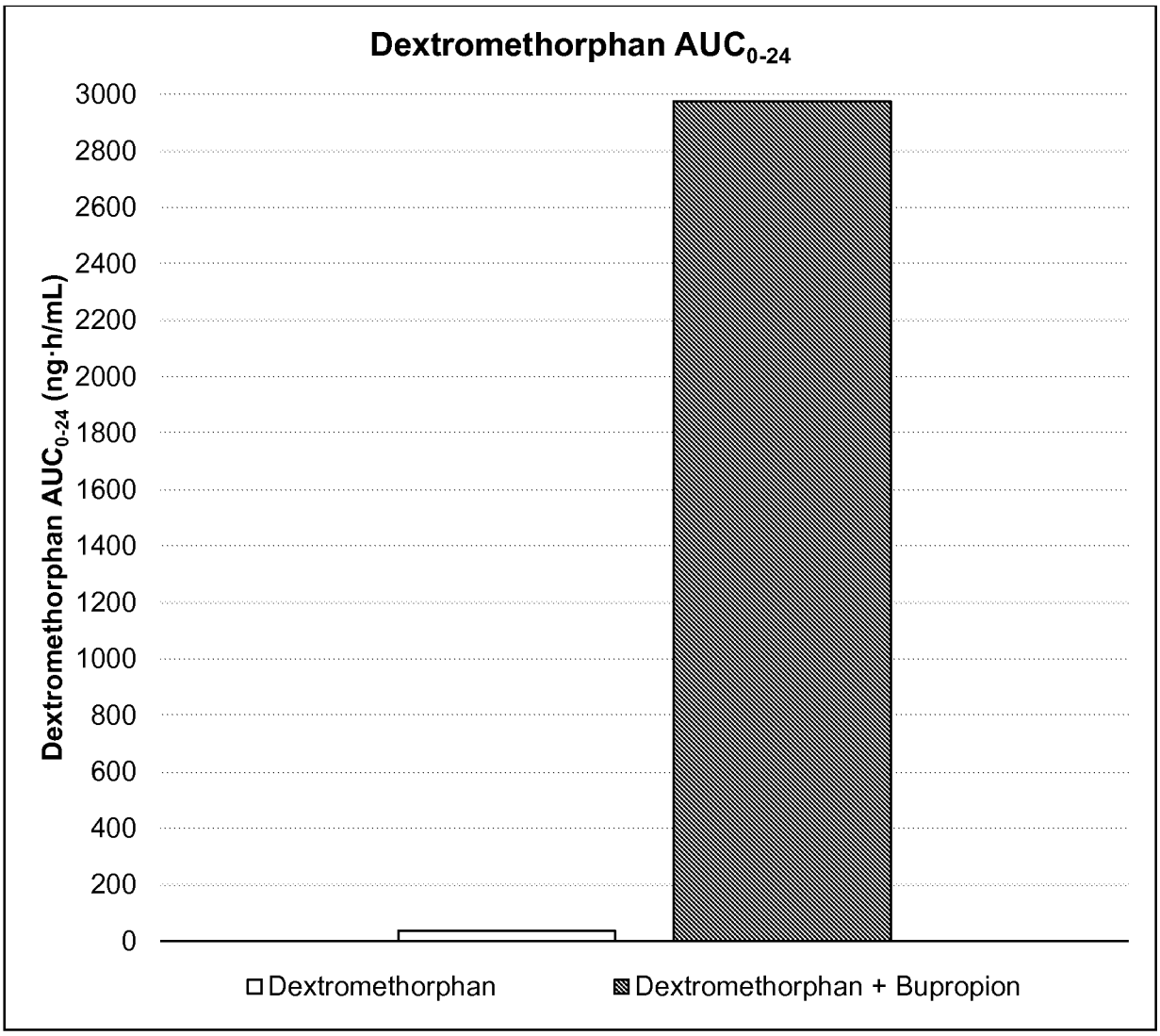

Dextromethorphan AUC0-24
Dextromethorphan AUC0-24 (ng·h/mL)
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 3

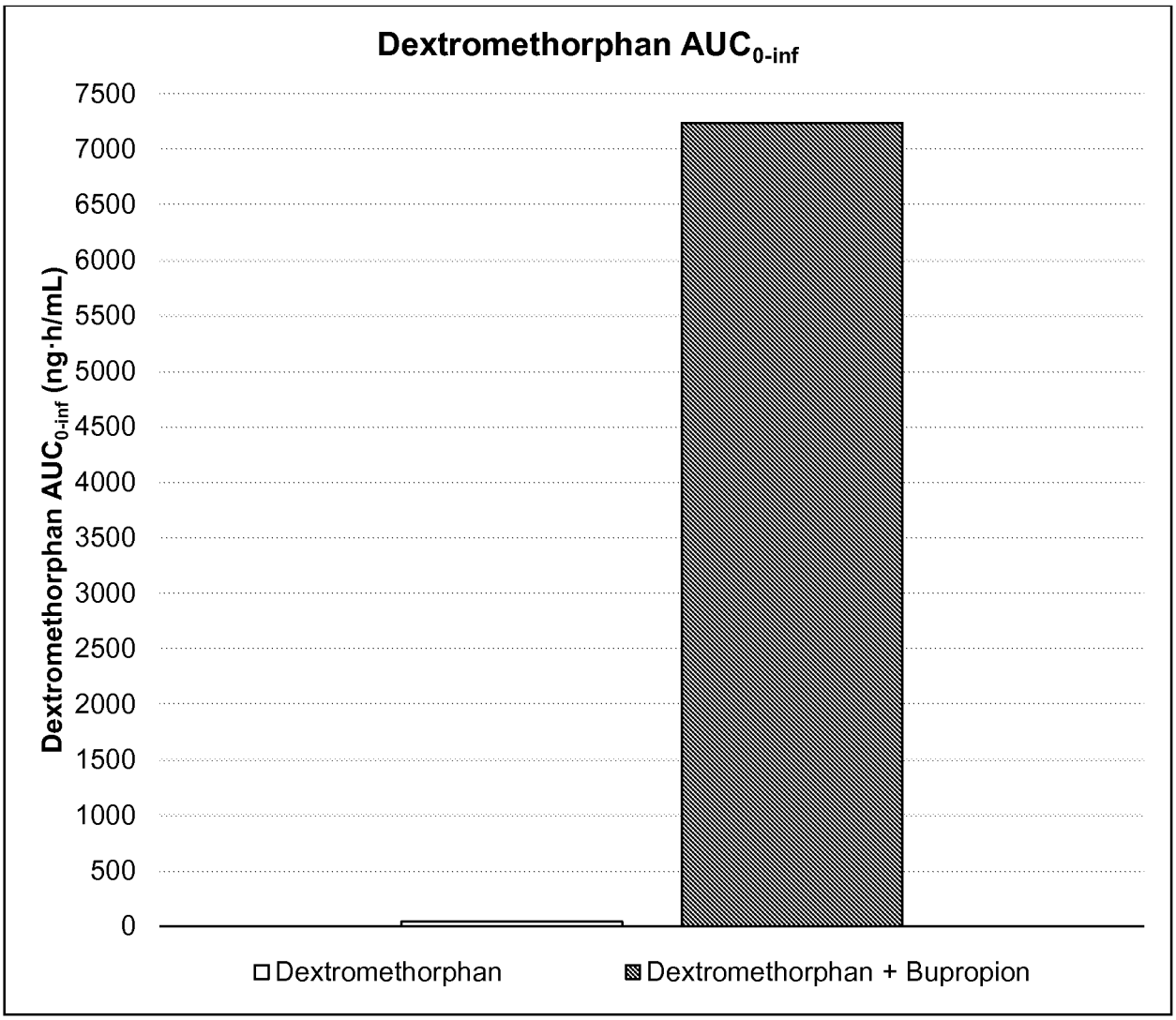

Dextromethorphan AUC0-inf
Dextromethorphan AUC0-inf (ng·h/mL)
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 4

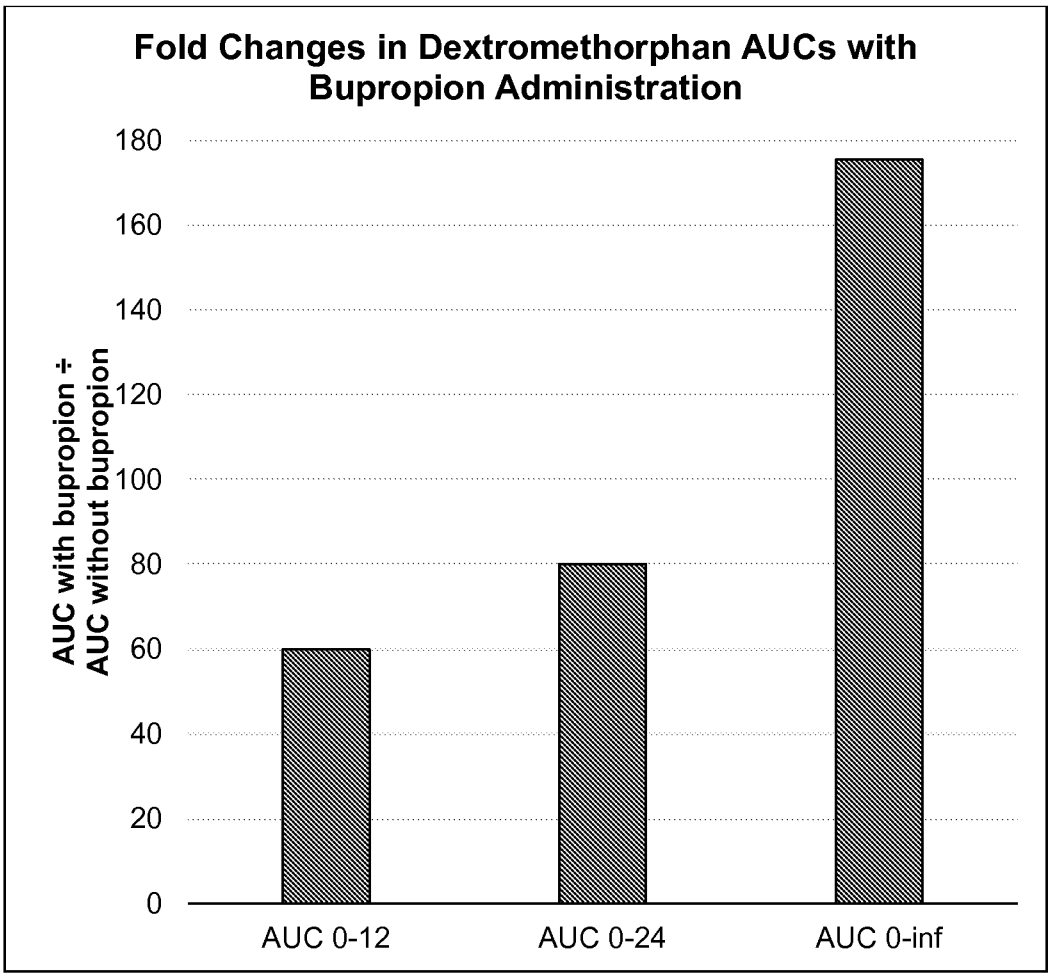

Fold Changes in Dextromethorphan AUCs with Bupropion Administration
AUC with bupropion ÷ AUC without bupropion
180
160
140
120
100
80
60
40
20
0
AUC 0-12
AUC 0-24
AUC 0-inf

FIG. 5

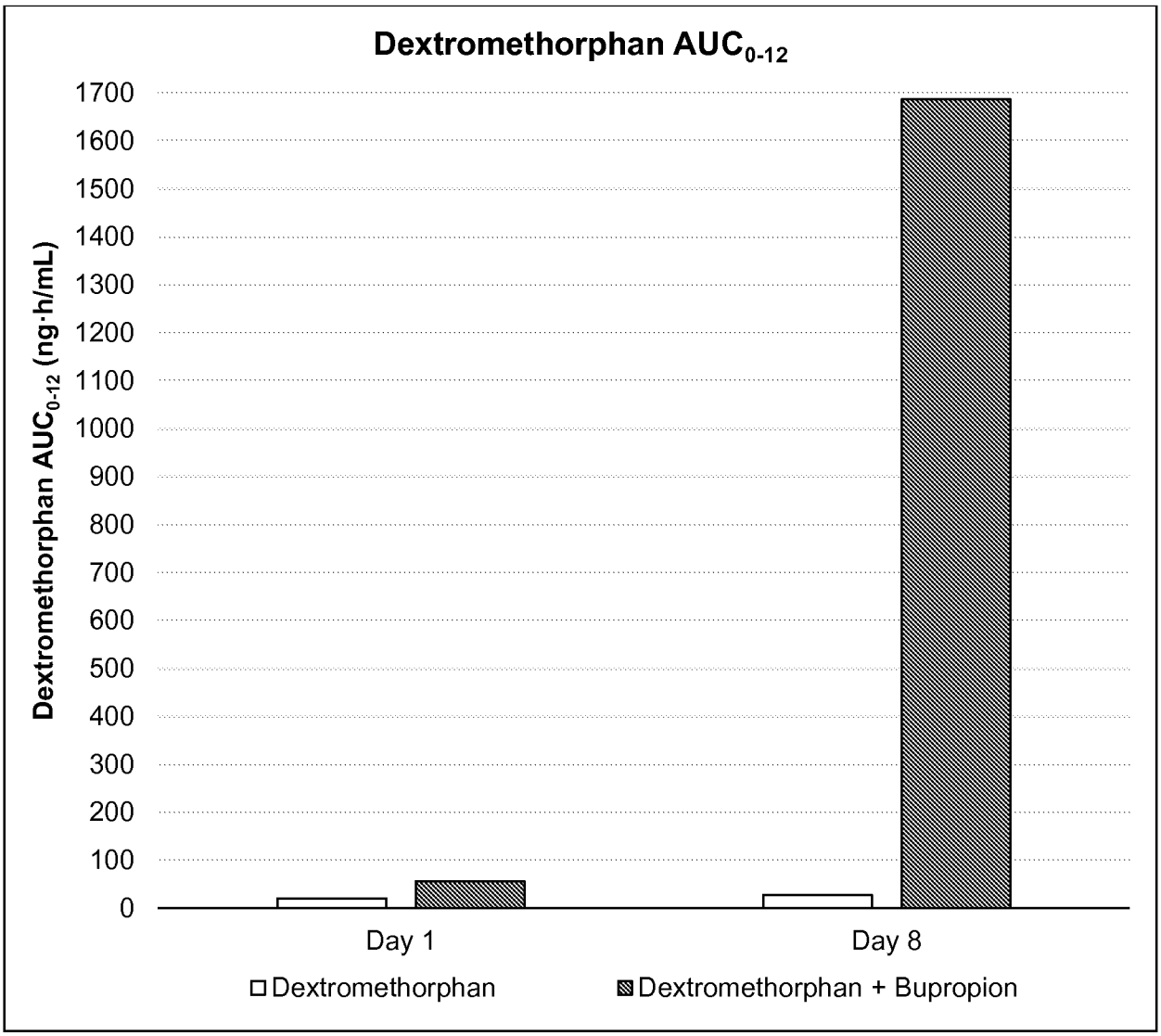

Dextromethorphan AUC0-12
Dextromethorphan AUC0-12 (ng·h/mL)
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Day 1
Day 8
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 6

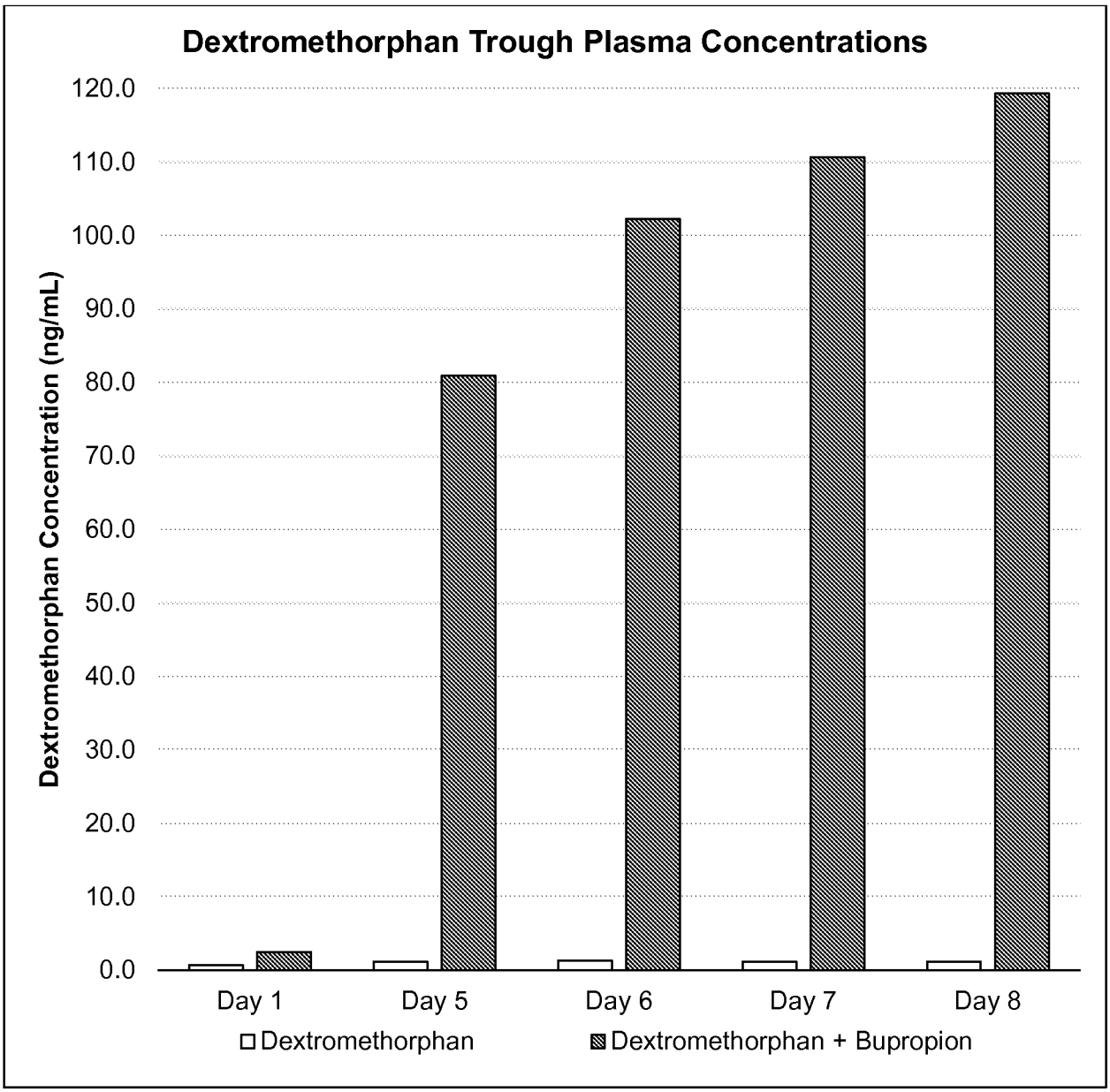

Dextromethorphan Trough Plasma Concentrations
Dextromethorphan Concentration (ng/mL)
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Day 1
Day 5
Day 6
Day 7
Day 8
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 7

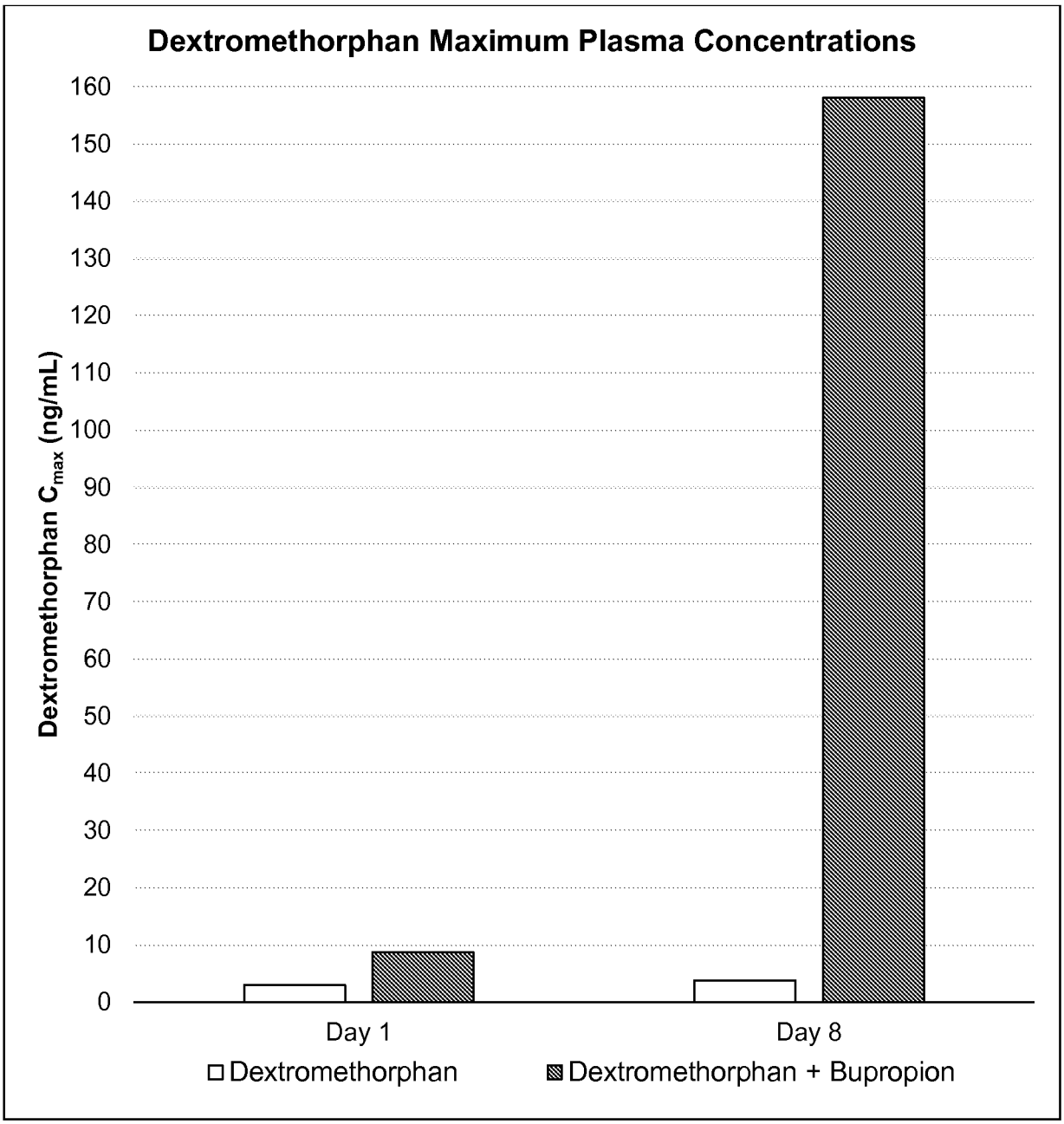

Dextromethorphan Maximum Plasma Concentrations
Dextromethorphan C_{max} (ng/mL)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Day 1
Day 8
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 8

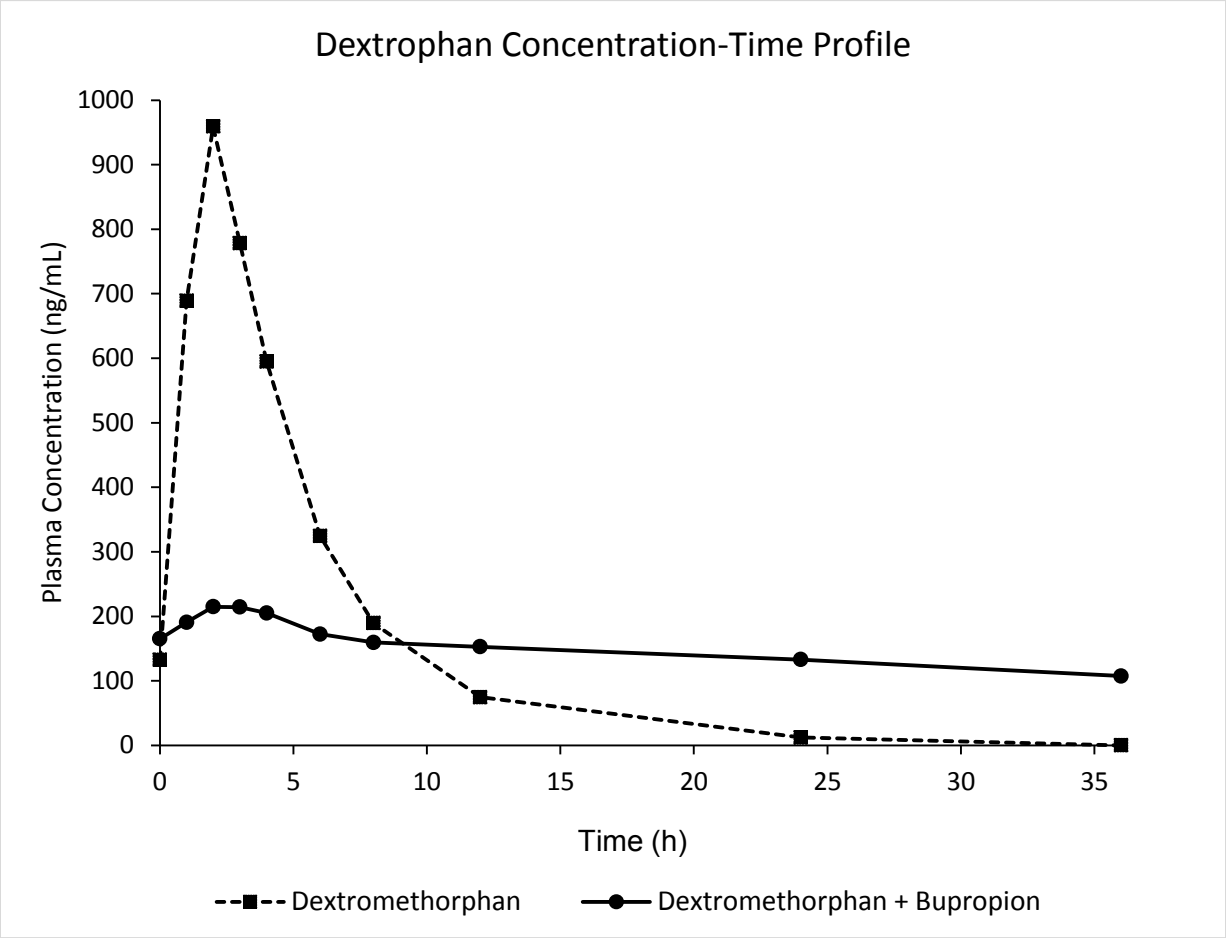

Dextrophan Concentration-Time Profile
Plasma Concentration (ng/mL)
1000
900
800
700
600
500
400
300
200
100
0
0
5
10
15
20
25
30
35
Time (h)
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 9

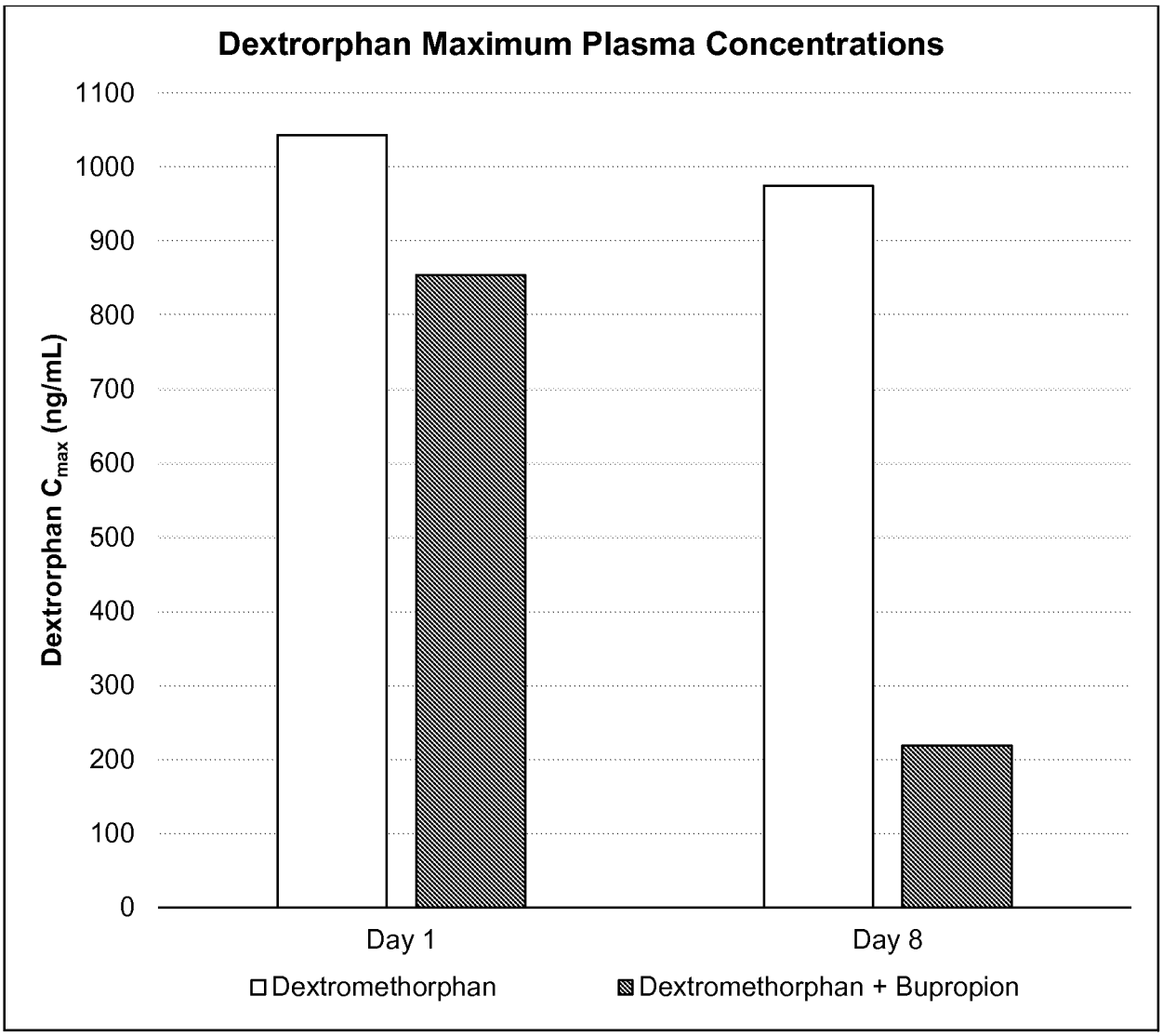

Dextrorphan Maximum Plasma Concentrations
1100
1000
900
800
700
600
500
400
300
200
100
0
Dextrorphan C_{max} (ng/mL)
Day 1
Day 8
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 10

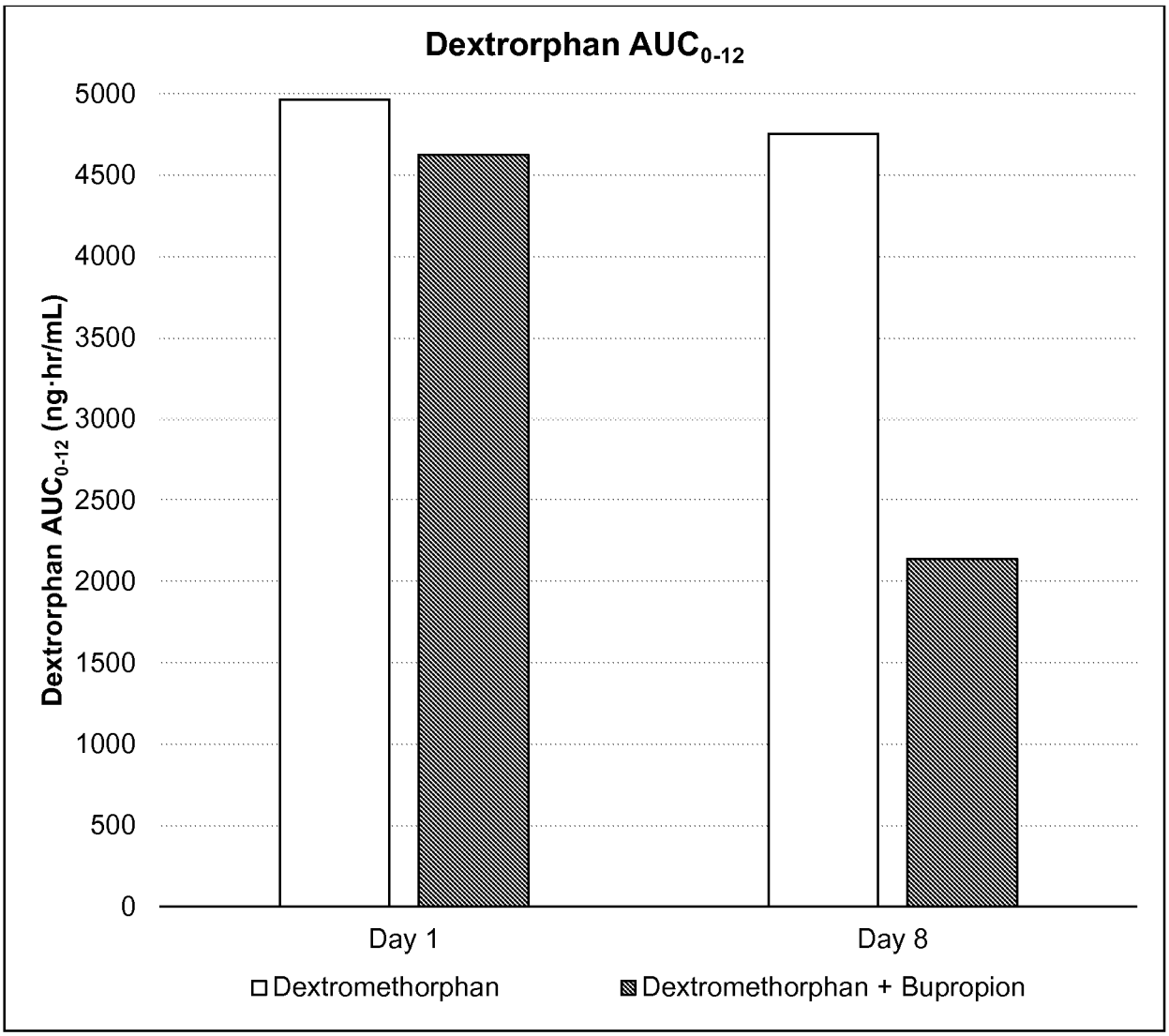

Dextrorphan AUC0-12
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Dextrorphan AUC0-12 (ng·hr/mL)
Day 1
Day 8
Dextromethorphan
Dextromethorphan + Bupropion

FIG. 11

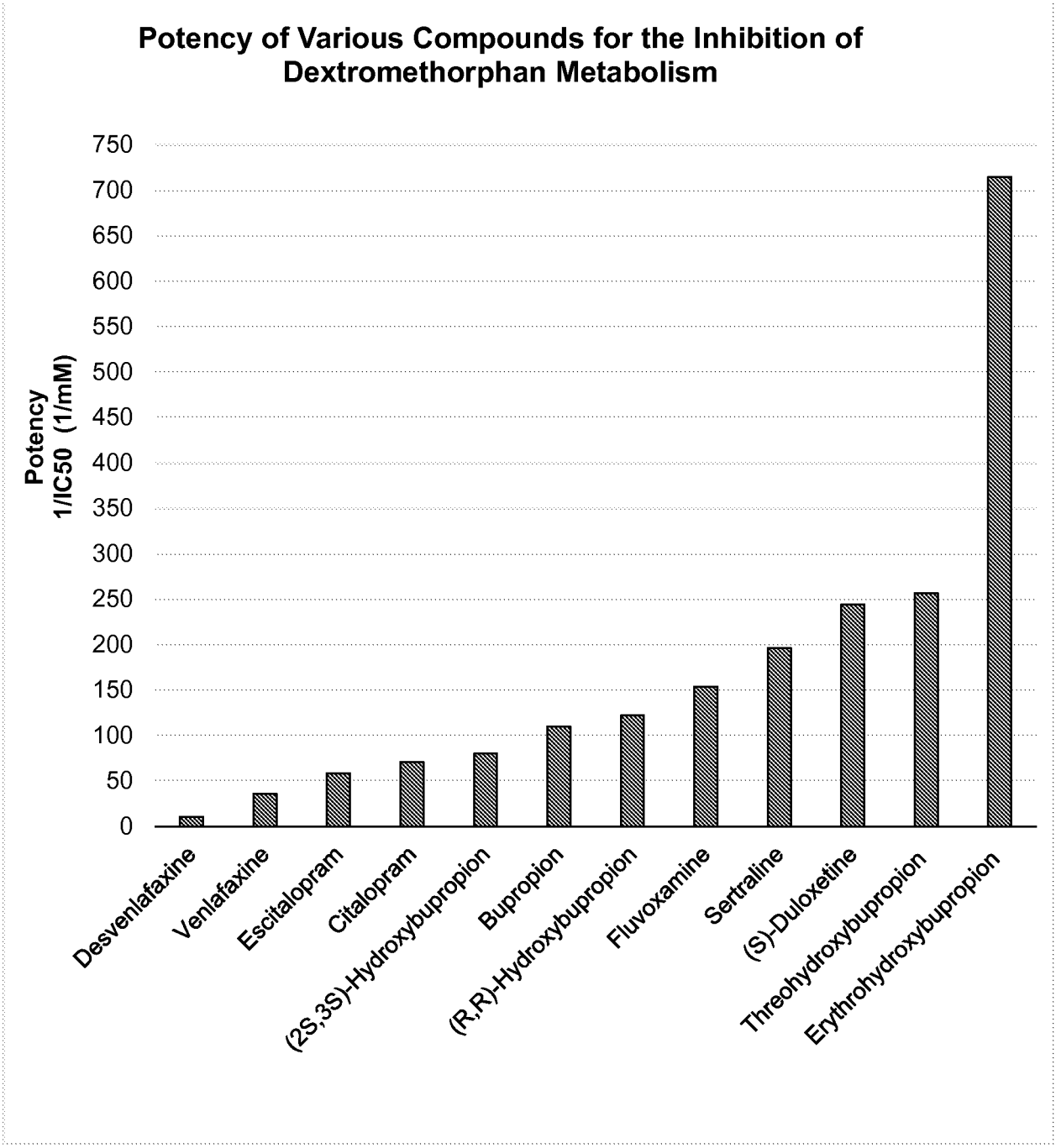

Potency of Various Compounds for the Inhibition of Dextromethorphan Metabolism
Potency 1/IC50 (1/mM)
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
Desvenlafaxine
Venlafaxine
Escitalopram
Citalopram
(2S,3S)-Hydroxybupropion
Bupropion
(R,R)-Hydroxybupropion
Fluvoxamine
Sertraline
(S)-Duloxetine
Threohydroxybupropion
Erythrohydroxybupropion

FIG. 12