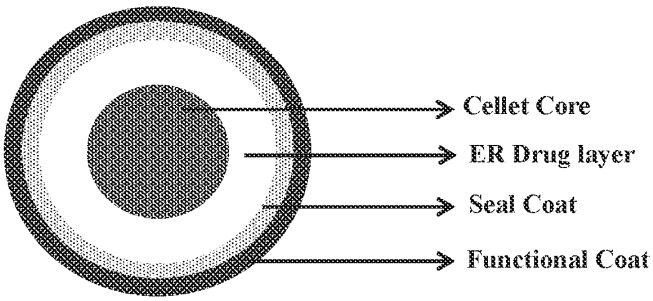


FIGURE 1A

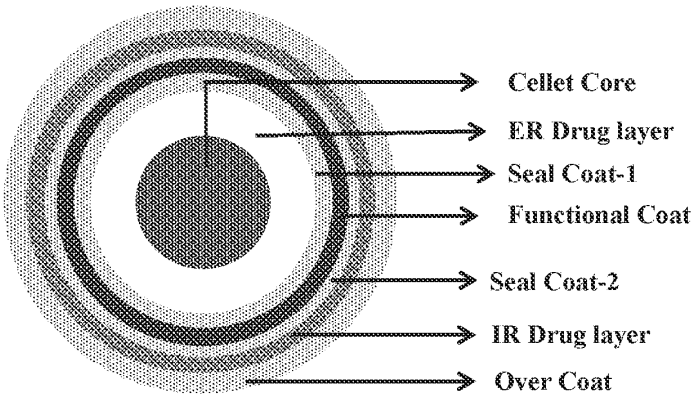


FIGURE 1B

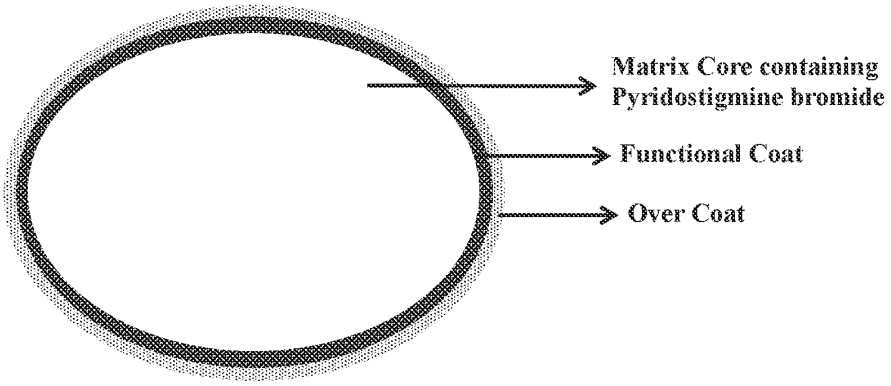


FIGURE 2A

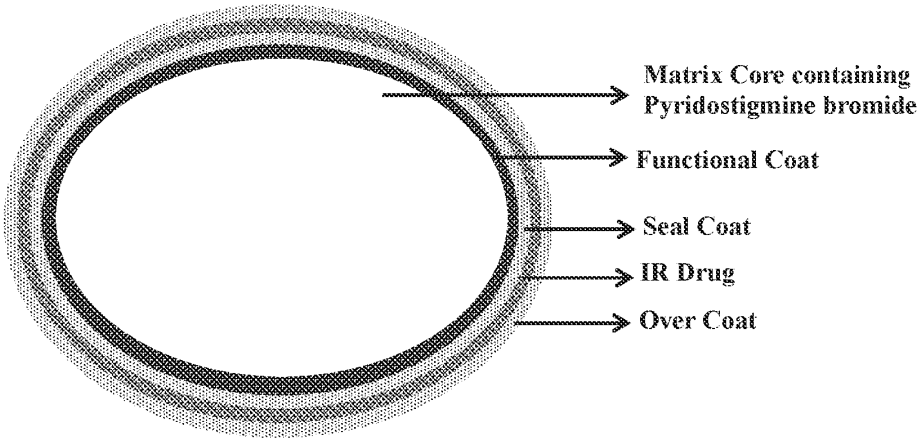


FIGURE 2B

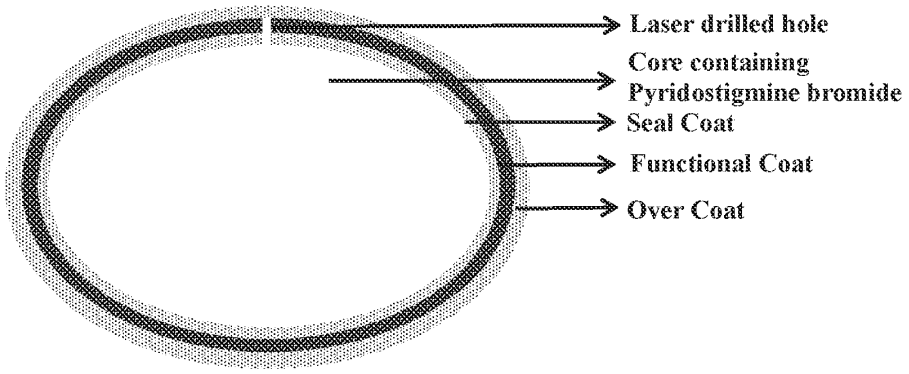


FIGURE 3A

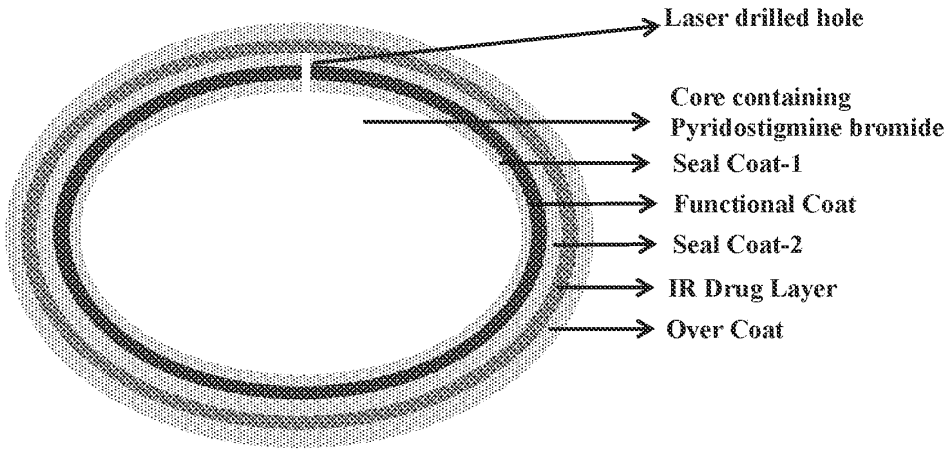


FIGURE 3B

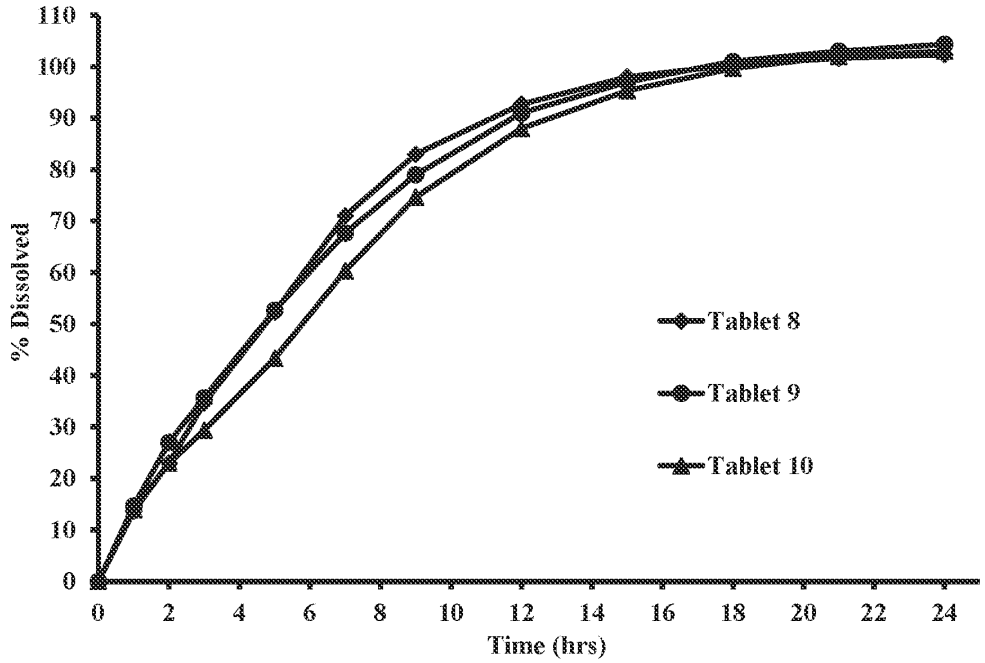

110
100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (hrs)
Tablet 8
Tablet 9
Tablet 10

FIGURE 4

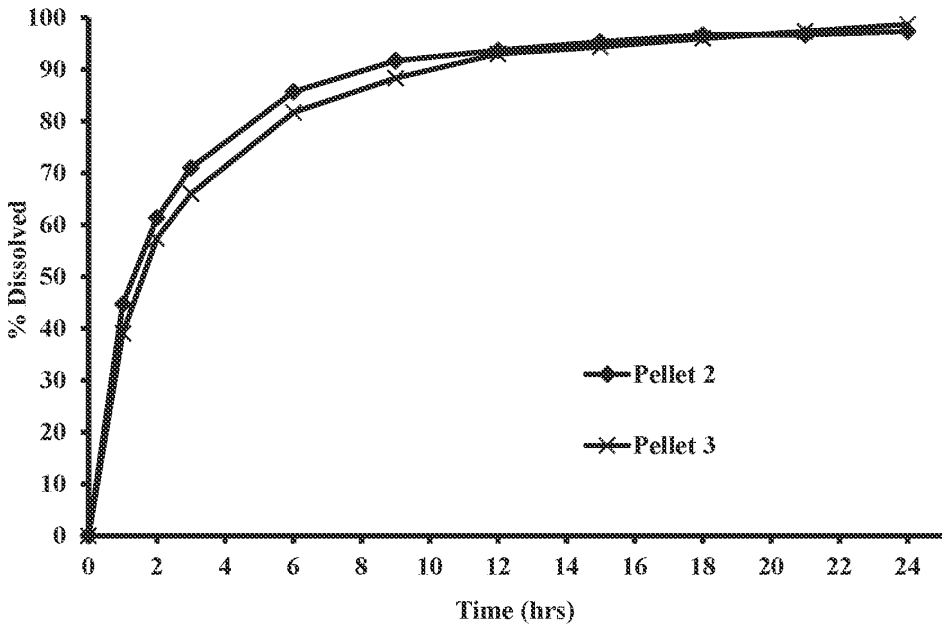

100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (hrs)
Pellet 2
Pellet 3

FIGURE 5

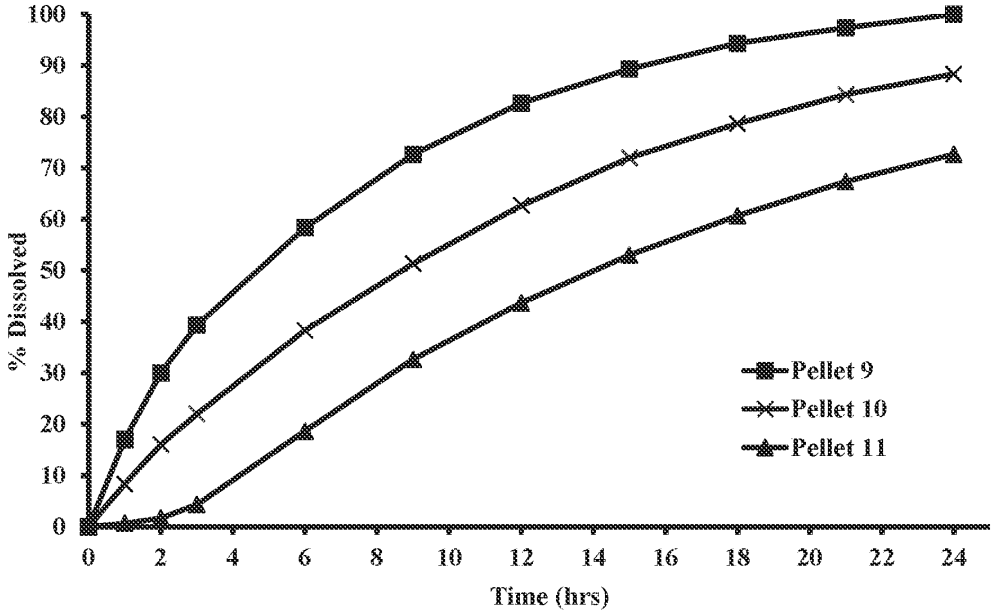

100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (hrs)
Pellet 9
Pellet 10
Pellet 11

FIGURE 6

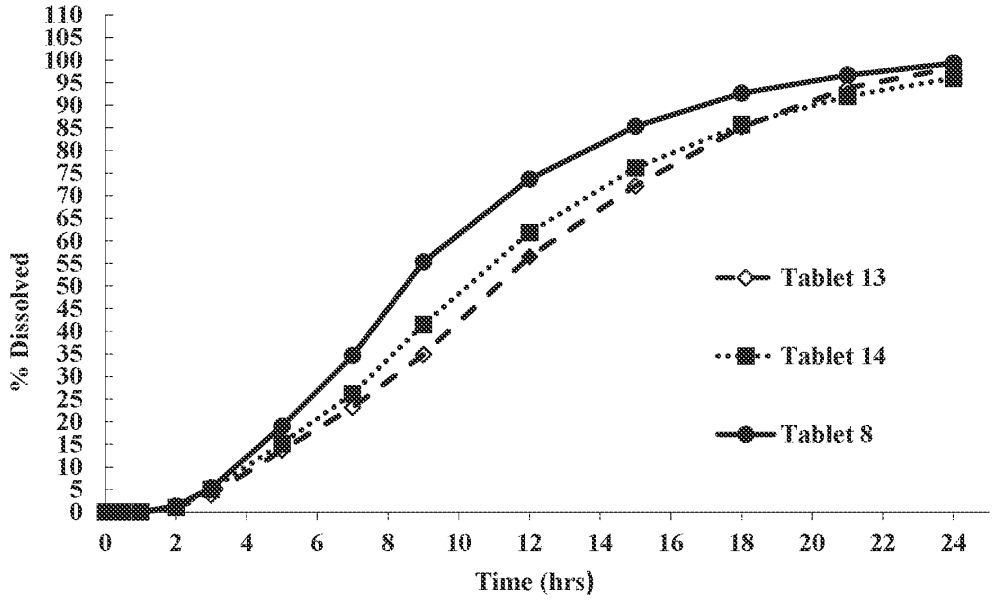

% Dissolved
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (hrs)
Tablet 13
Tablet 14
Tablet 8

FIGURE 7

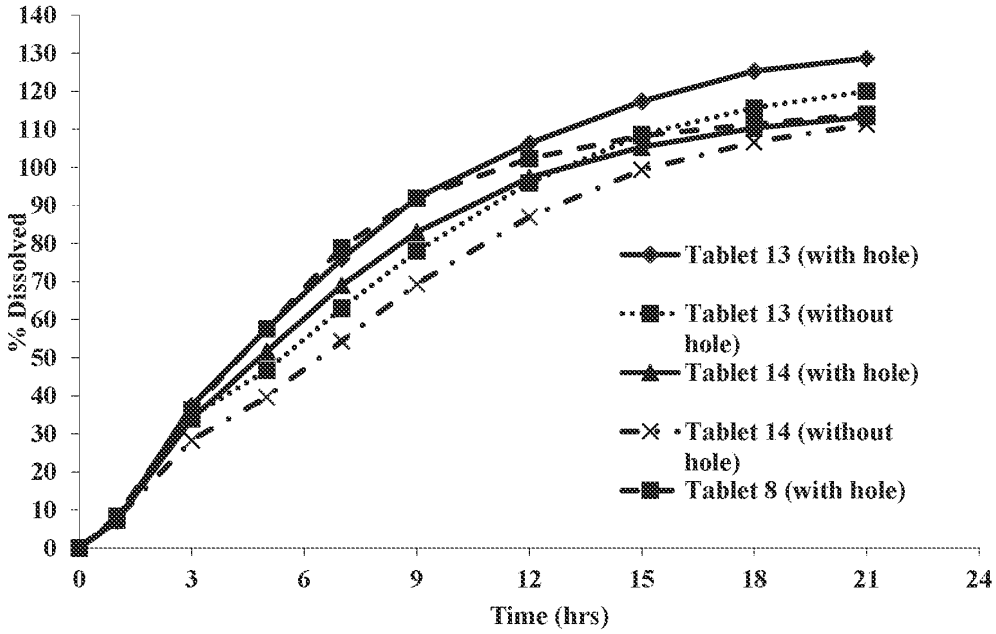

140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
3
6
9
12
15
18
21
24
Time (hrs)
Tablet 13 (with hole)
Tablet 13 (without hole)
Tablet 14 (with hole)
Tablet 14 (without hole)
Tablet 8 (with hole)

FIGURE 8

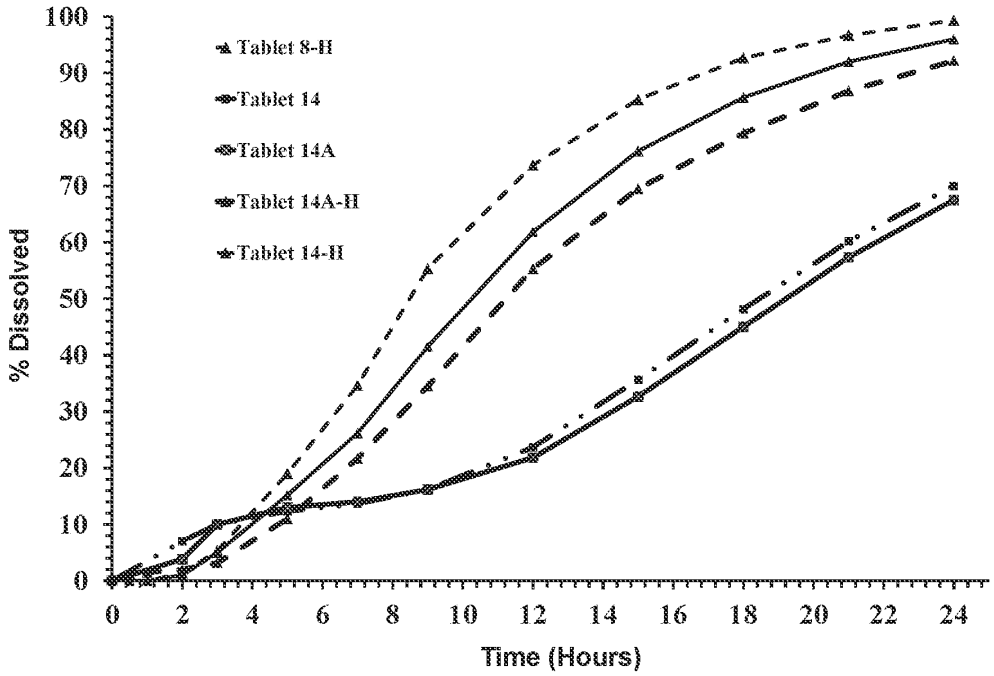

100
90
80
70
60
50
40
30
20
10
0
% Dissolved
Tablet 8-H
Tablet 14
Tablet 14A
Tablet 14A-H
Tablet 14-H
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (Hours)

FIGURE 9

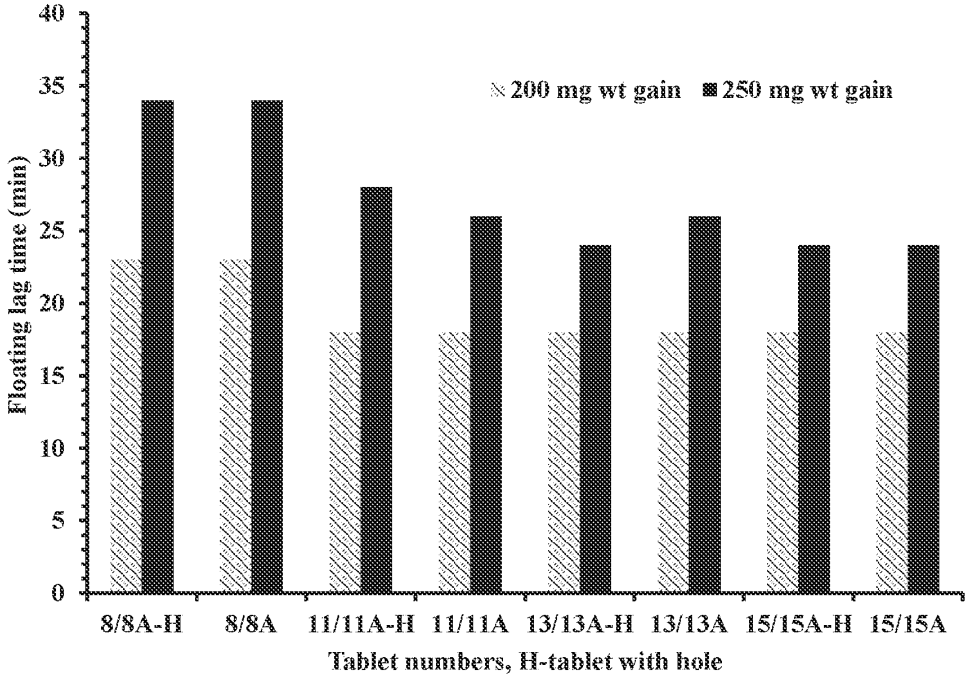

40
35
30
25
20
15
10
5
0
Floating lag time (min)
200 mg wt gain
250 mg wt gain
8/8A-H
8/8A
11/11A-H
11/11A
13/13A-H
13/13A
15/15A-H
15/15A
Tablet numbers, H-tablet with hole

FIGURE 10

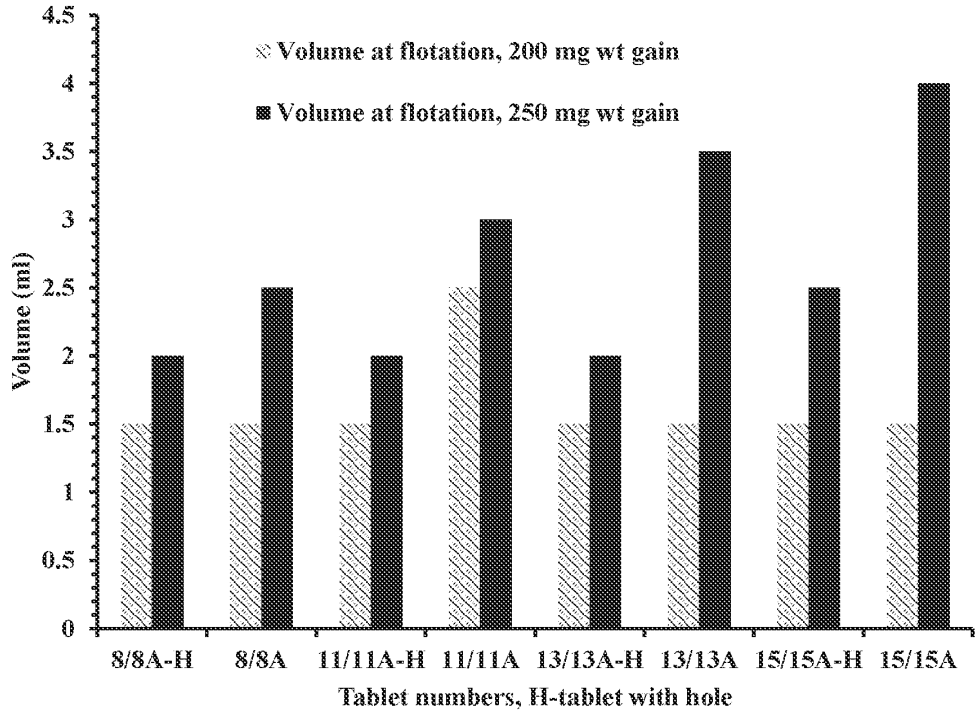

Volume at flotation, 200 mg wt gain
Volume at flotation, 250 mg wt gain
Volume (ml)
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
8/8A-H
8/8A
11/11A-H
11/11A
13/13A-H
13/13A
15/15A-H
15/15A
Tablet numbers, H-tablet with hole

FIGURE 11

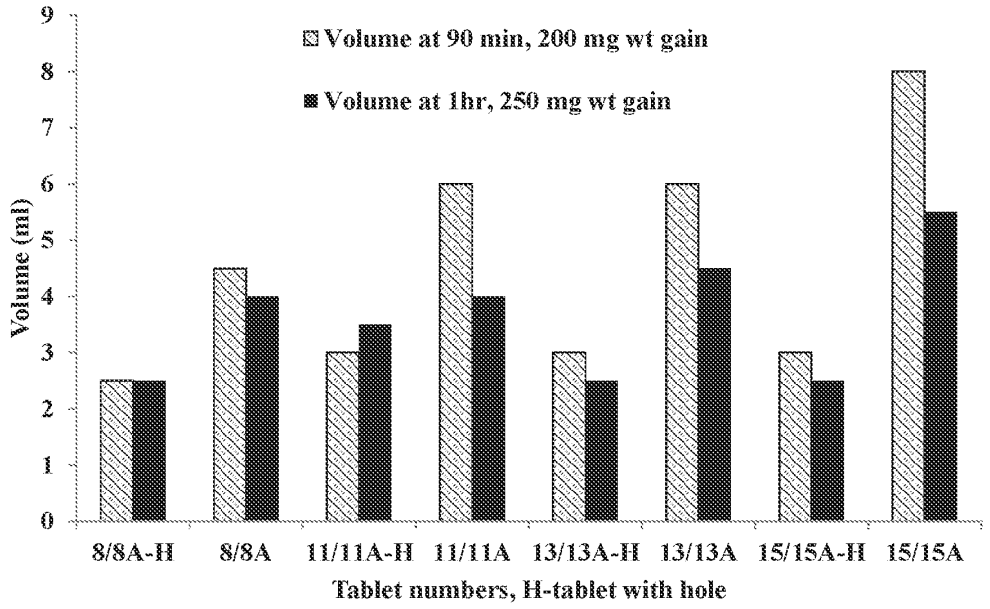

Volume at 90 min, 200 mg wt gain
Volume at 1hr, 250 mg wt gain
Volume (ml)
0
1
2
3
4
5
6
7
8
9
8/8A-H
8/8A
11/11A-H
11/11A
13/13A-H
13/13A
15/15A-H
15/15A
Tablet numbers, H-tablet with hole

FIGURE 12

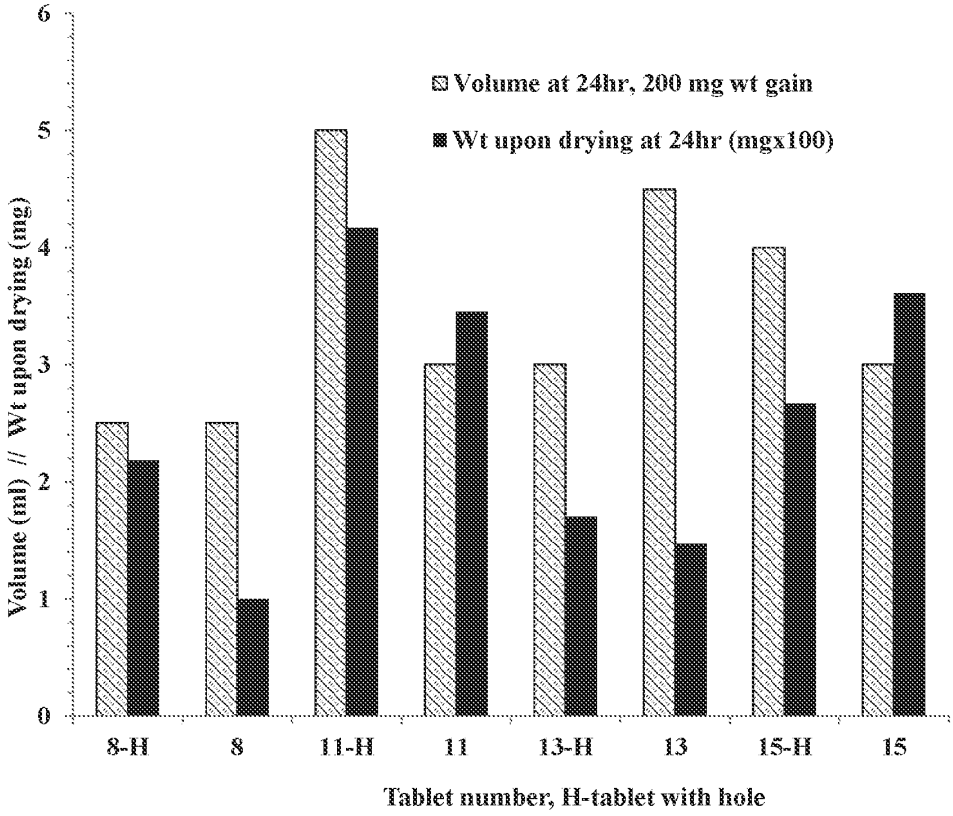

Volume at 24hr, 200 mg wt gain
Wt upon drying at 24hr (mgx100)
Volume (ml) // Wt upon drying (mg)
0
1
2
3
4
5
6
8-H
8
11-H
11
13-H
13
15-H
15
Tablet number, H-tablet with hole

FIGURE 13

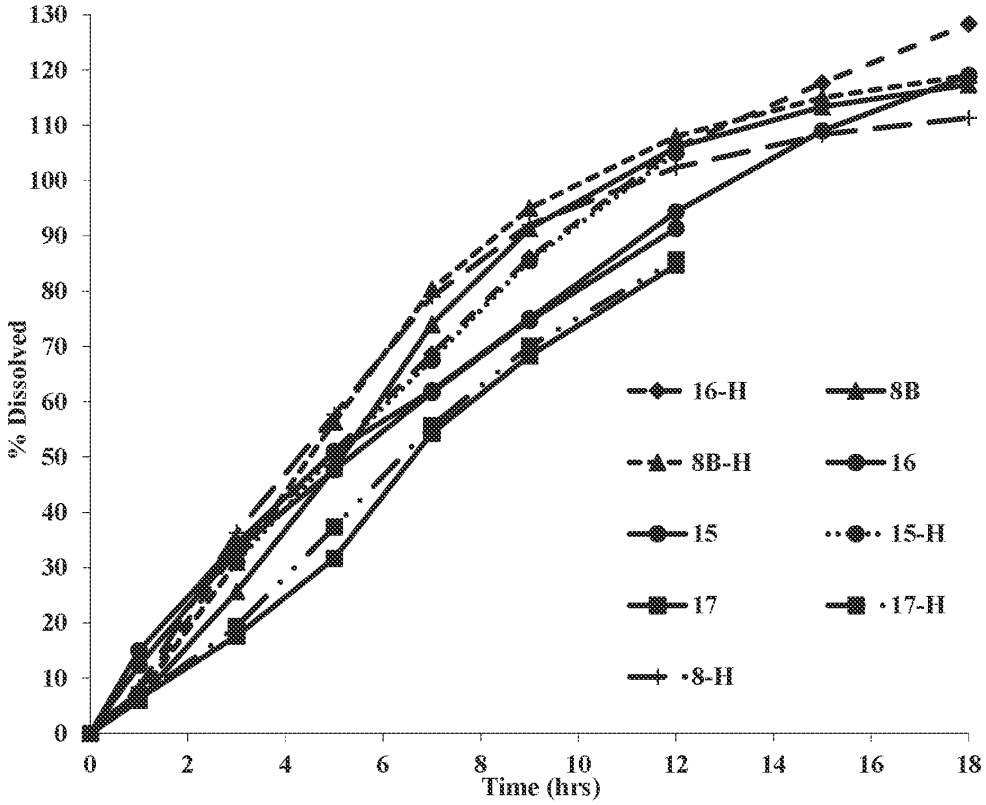


FIGURE 14

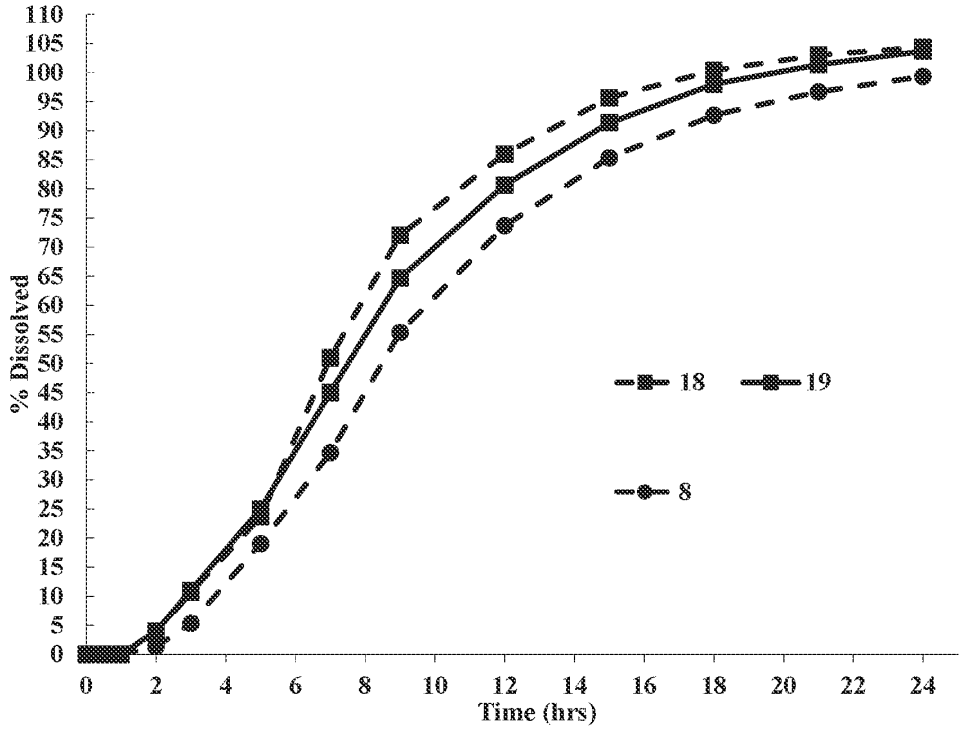


FIGURE 15

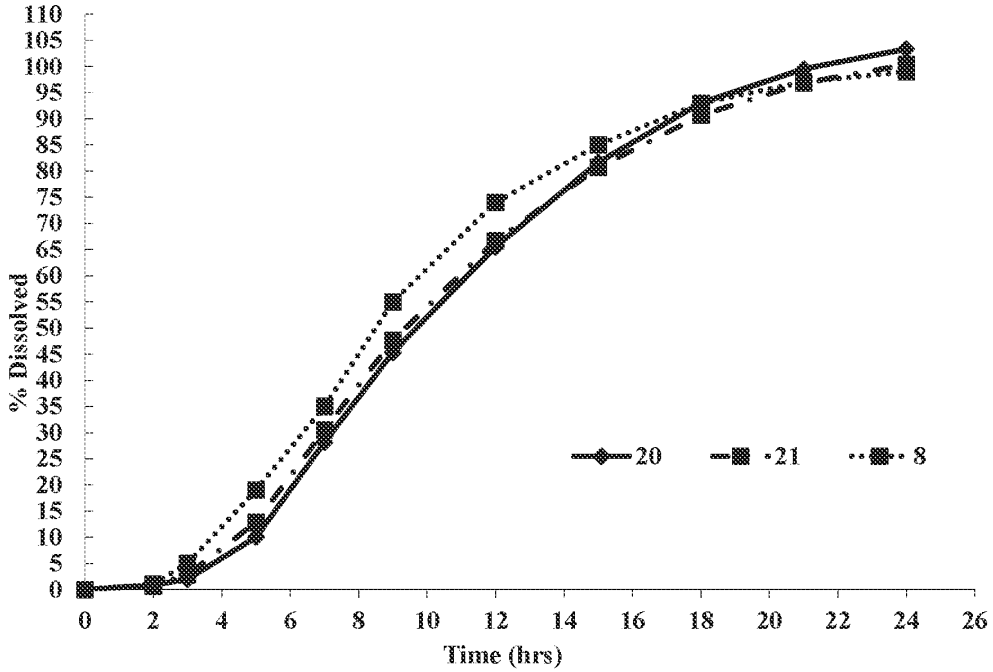


FIGURE 16

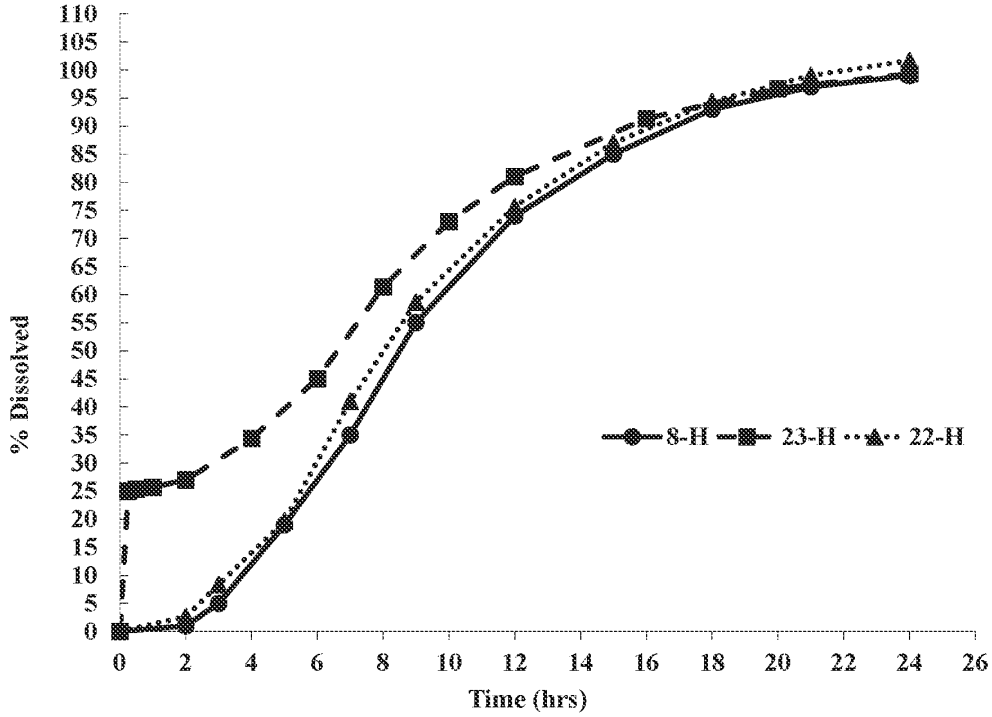

% Dissolved
Time (hrs)
8-H
23-H
22-H
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
0
2
4
6
8
10
12
14
16
18
20
22
24
26

FIGURE 17

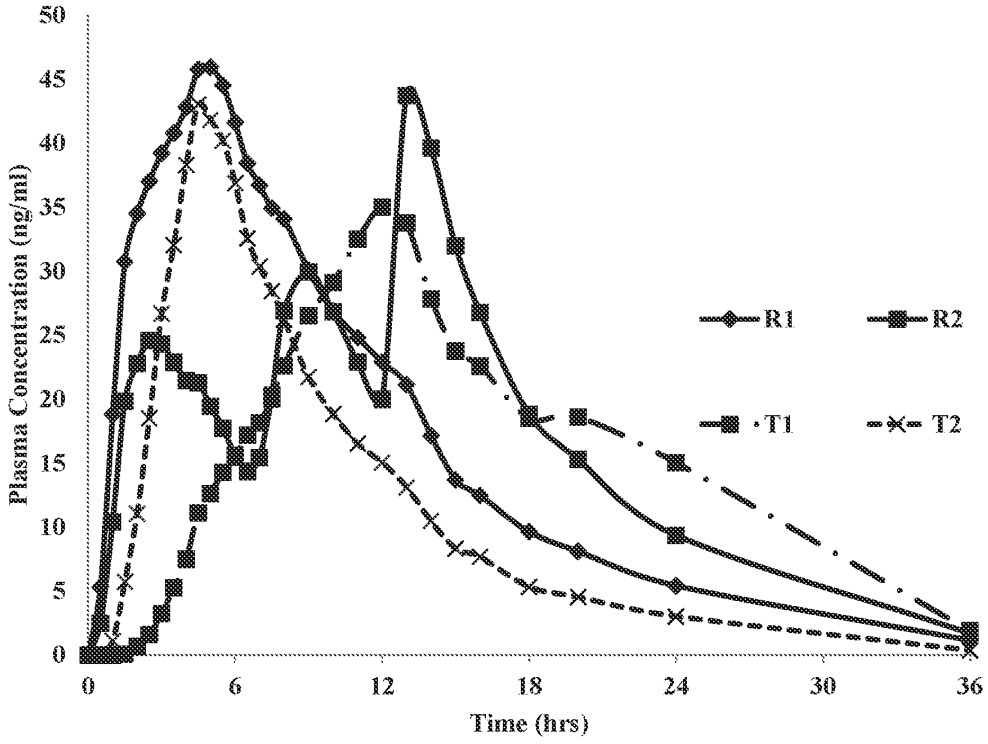
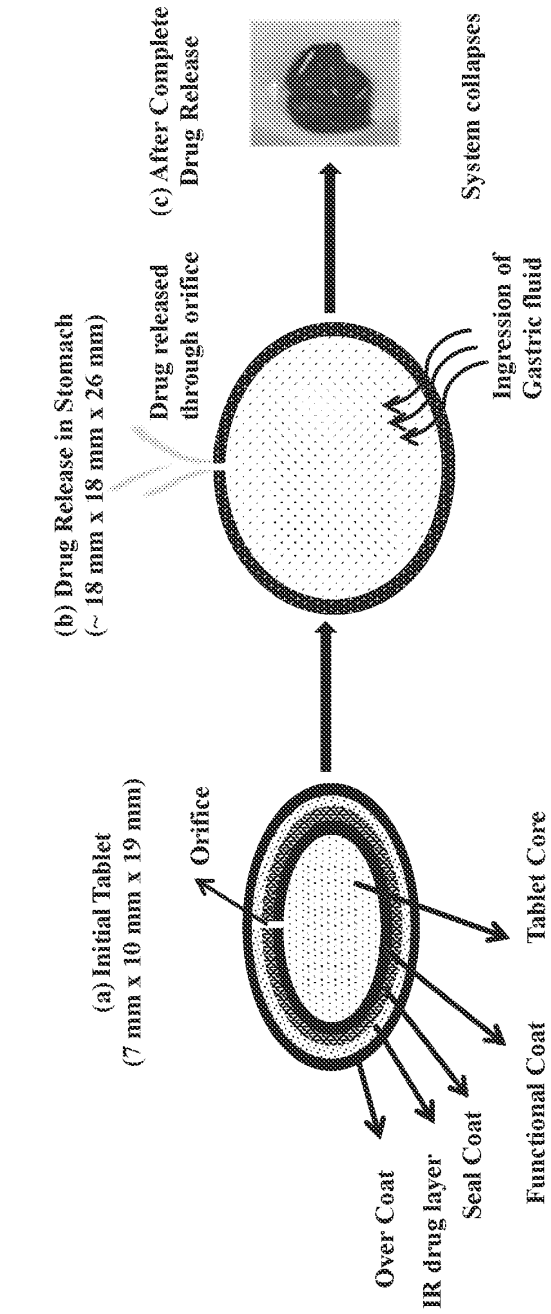

50
45
40
35
30
25
20
15
10
5
0
Plasma Concentration (ng/ml)
0
6
12
18
24
30
36
Time (hrs)
R1
R2
T1
T2

FIGURE 18

FIGURE 19


(a) Initial Tablet
(7 mm x 10 mm x 19 mm)
Orifice
Over Coat
IR drug layer
Seal Coat
Functional Coat
Tablet Core
(b) Drug Release in Stomach
(~ 18 mm x 18 mm x 26 mm)
Drug released through orifice
Ingression of Gastric fluid
(c) After Complete Drug Release
System collapses
In-Vitro Attributes
Reasonably small to enable swallowability
Tablet floats in ~15 min
Tablet size doubles in ~15 min
Drug released for ~24 hrs

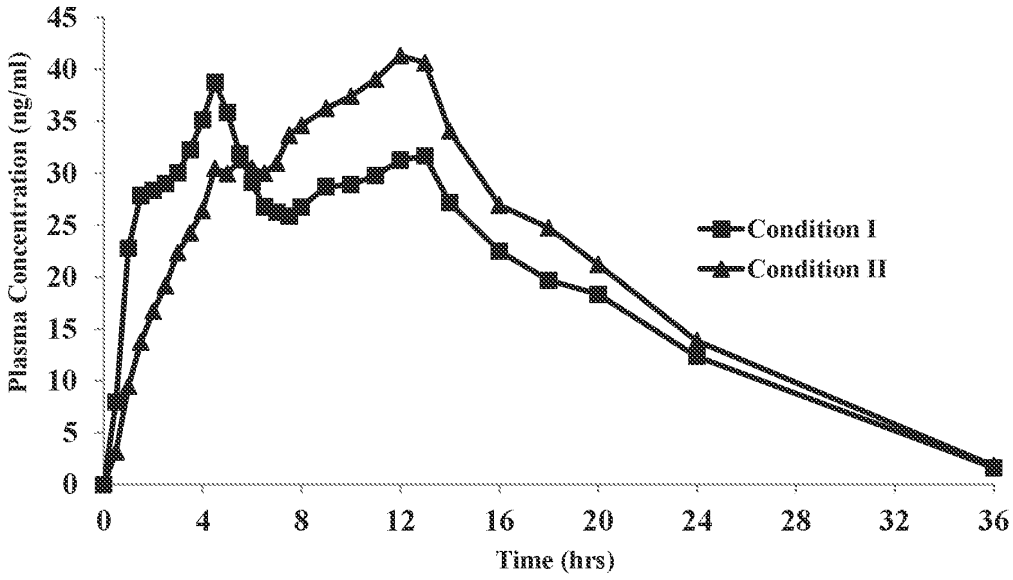

Plasma Concentration (ng/ml)
45
40
35
30
25
20
15
10
5
0
0
4
8
12
16
20
24
28
32
36
Time (hrs)
Condition I
Condition II

FIGURE 20

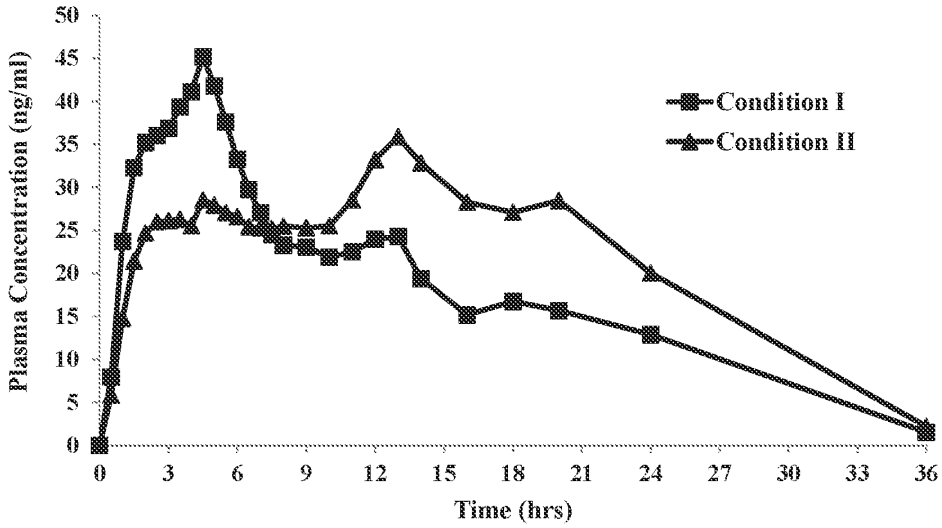

Plasma Concentration (ng/ml)
50
45
40
35
30
25
20
15
10
5
0
0
3
6
9
12
15
18
21
24
27
30
33
36
Time (hrs)
Condition I
Condition II

FIGURE 21

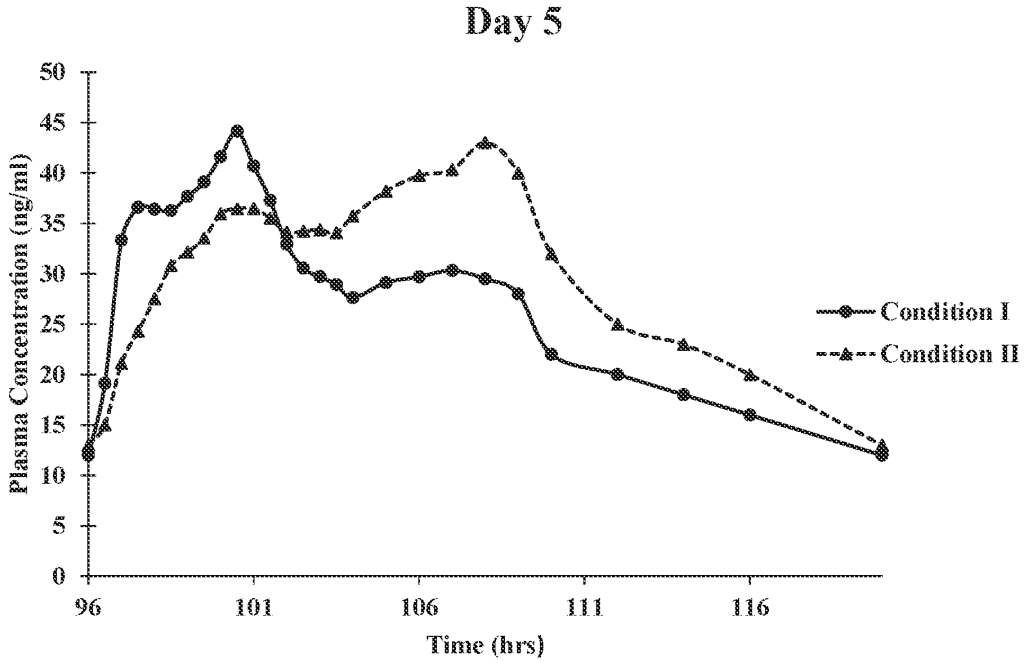

Day 5
Plasma Concentration (ng/ml)
50
45
40
35
30
25
20
15
10
5
0
96
101
106
111
116
Time (hrs)
Condition I
Condition II

FIGURE 22

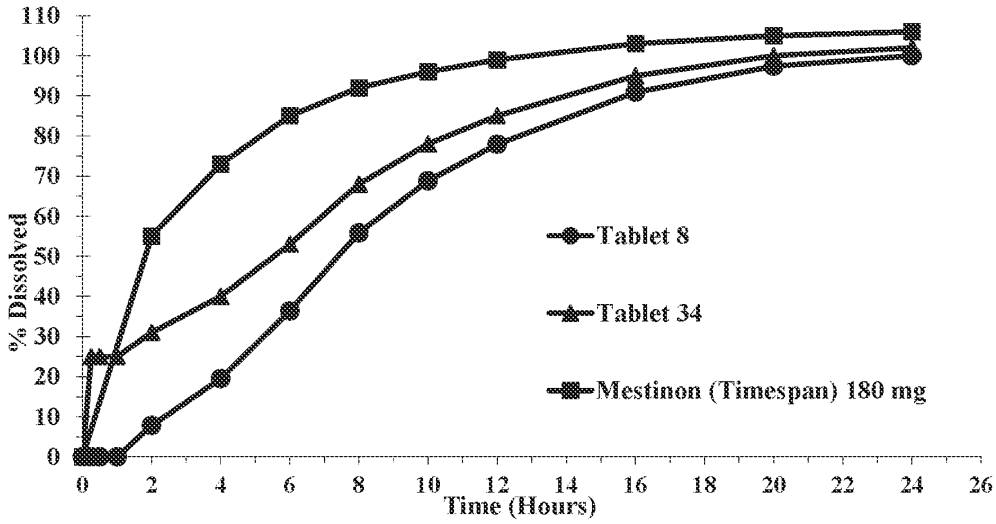

110
100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
4
6
8
10
12
14
16
18
20
22
24
26
Time (Hours)
Tablet 8
Tablet 34
Mestinon (Timespan) 180 mg

FIGURE 23

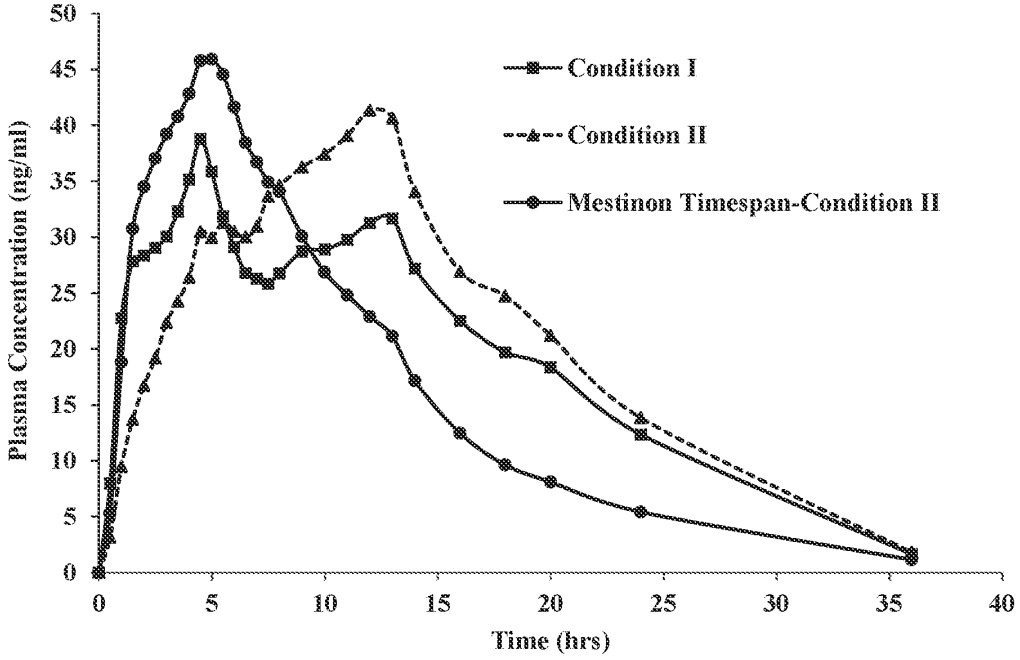

Plasma Concentration (ng/ml)
Time (hrs)
Condition I
Condition II
Mestinon Timespan-Condition II
0
5
10
15
20
25
30
35
40
45
50

FIGURE 24

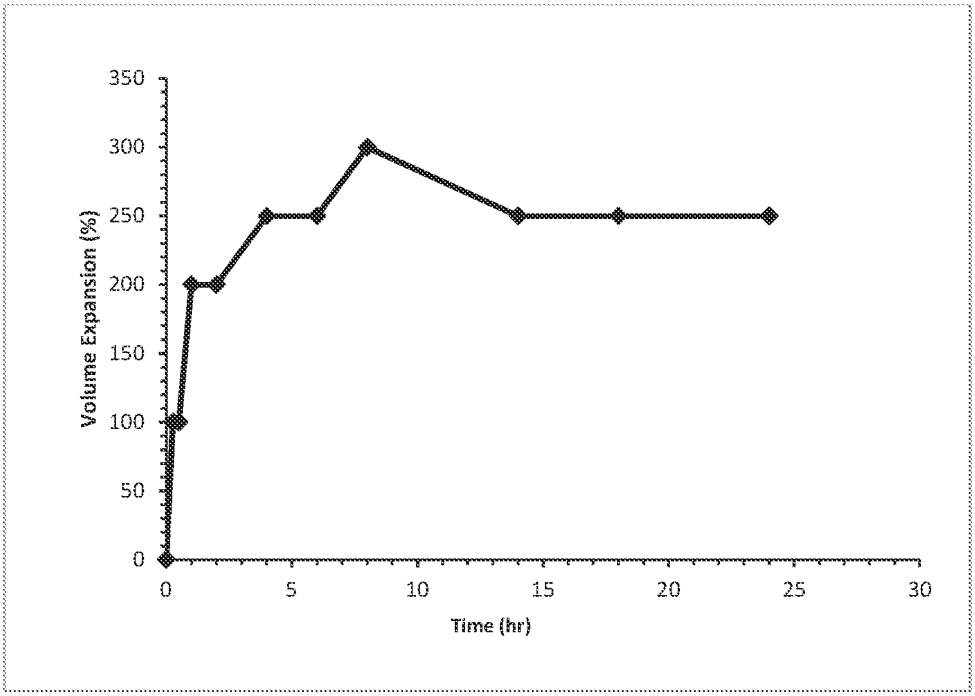

350
300
250
200
150
100
50
0
Volume Expansion (%)
0
5
10
15
20
25
30
Time (hr)

FIGURE 25A

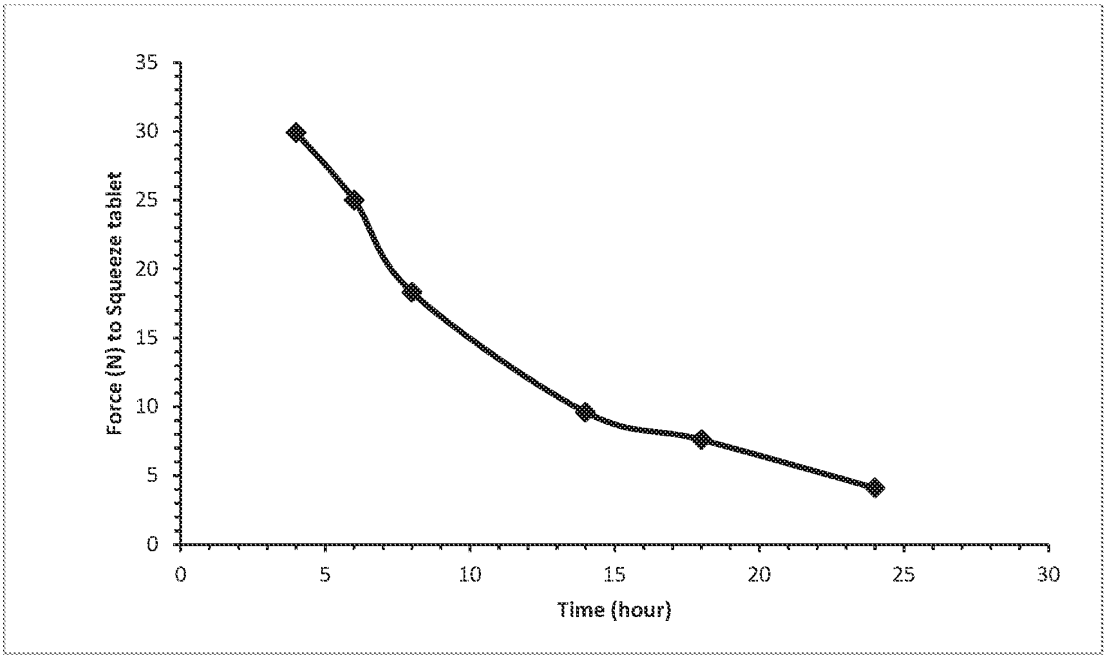

Force (N) to Squeeze tablet
35
30
25
20
15
10
5
0
0
5
10
15
20
25
30
Time (hour)

FIGURE 25B

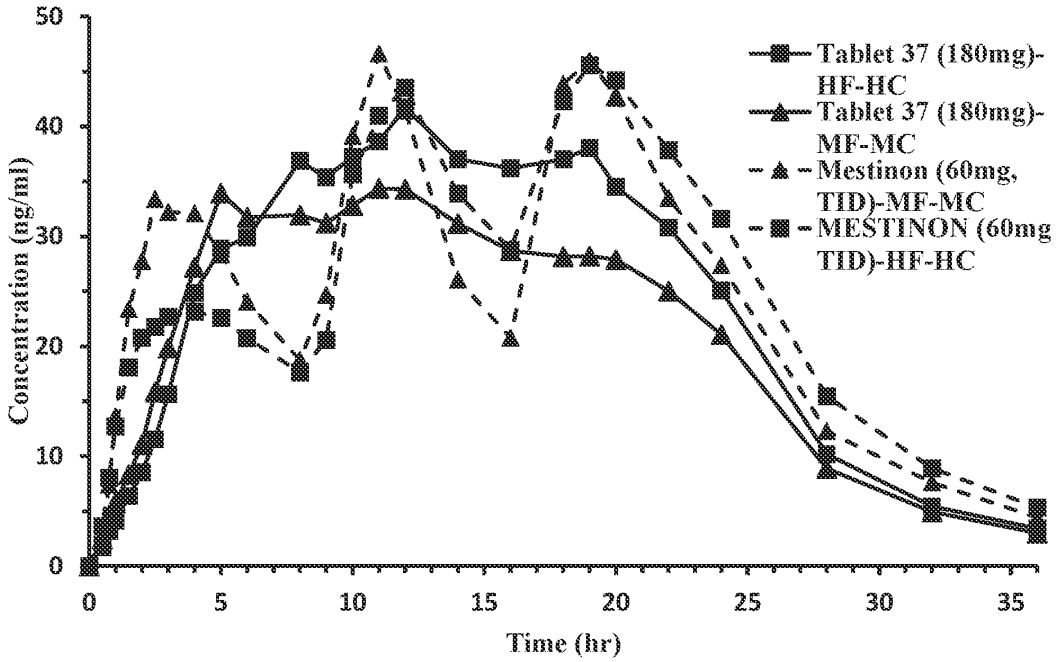

50
40
30
20
10
0
Concentration (ng/ml)
0
5
10
15
20
25
30
35
Time (hr)
Tablet 37 (180mg)-HF-HC
Tablet 37 (180mg)-MF-MC
Mestinon (60mg, TID)-MF-MC
MESTINON (60mg TID)-HF-HC

FIGURE 26

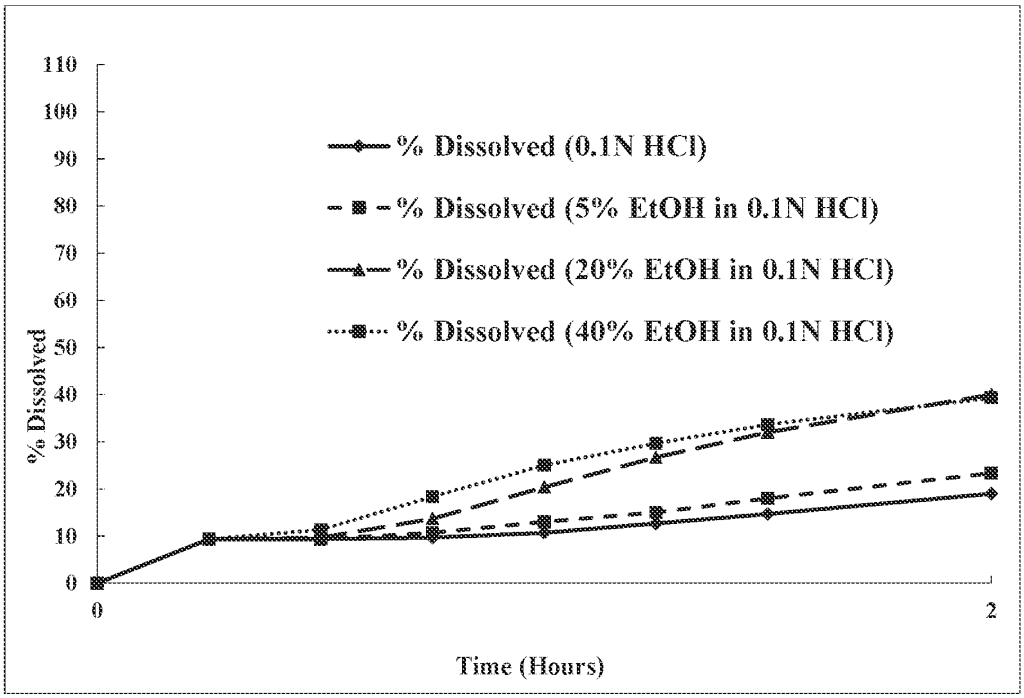

110
100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
Time (Hours)
% Dissolved (0.1N HCl)
% Dissolved (5% EtOH in 0.1N HCl)
% Dissolved (20% EtOH in 0.1N HCl)
% Dissolved (40% EtOH in 0.1N HCl)

FIGURE 27

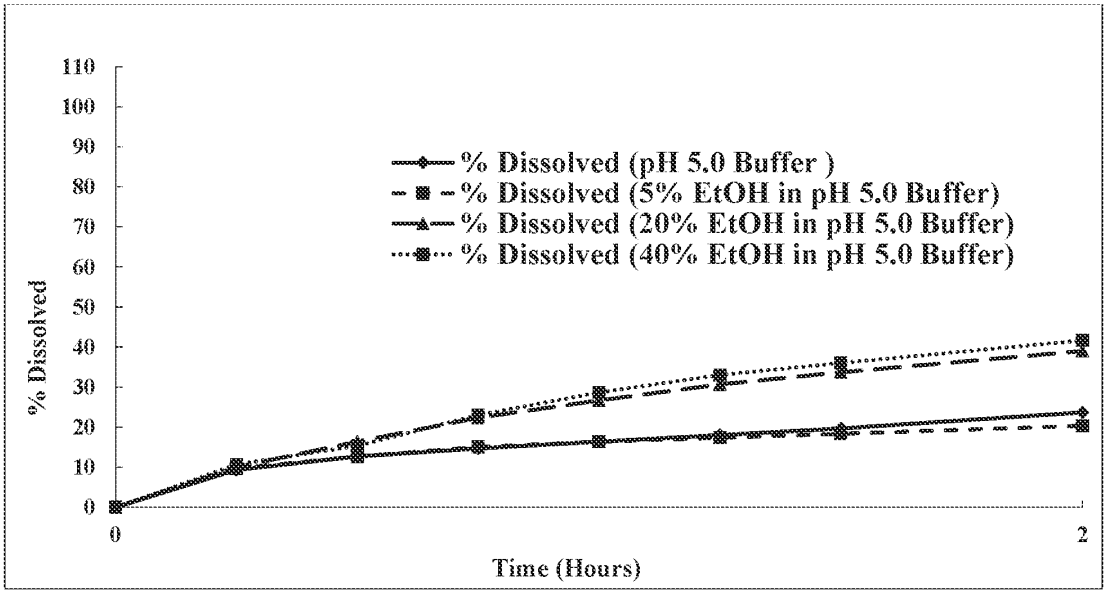

110
100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
Time (Hours)
% Dissolved (pH 5.0 Buffer)
% Dissolved (5% EtOH in pH 5.0 Buffer)
% Dissolved (20% EtOH in pH 5.0 Buffer)
% Dissolved (40% EtOH in pH 5.0 Buffer)

FIGURE 28

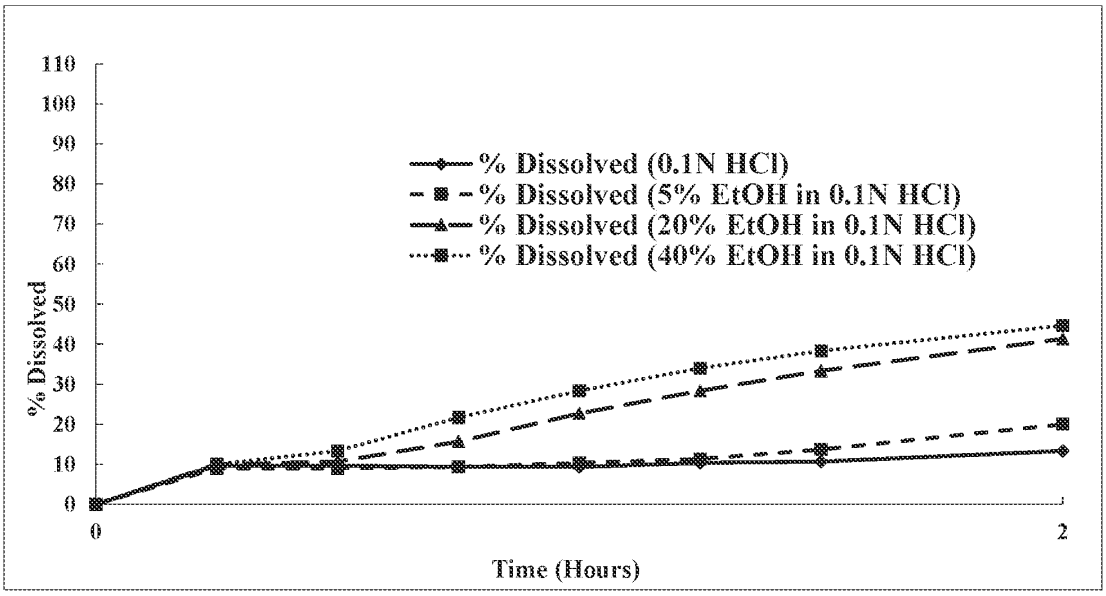

110
100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
Time (Hours)
% Dissolved (0.1N HCl)
% Dissolved (5% EtOH in 0.1N HCl)
% Dissolved (20% EtOH in 0.1N HCl)
% Dissolved (40% EtOH in 0.1N HCl)

FIGURE 29

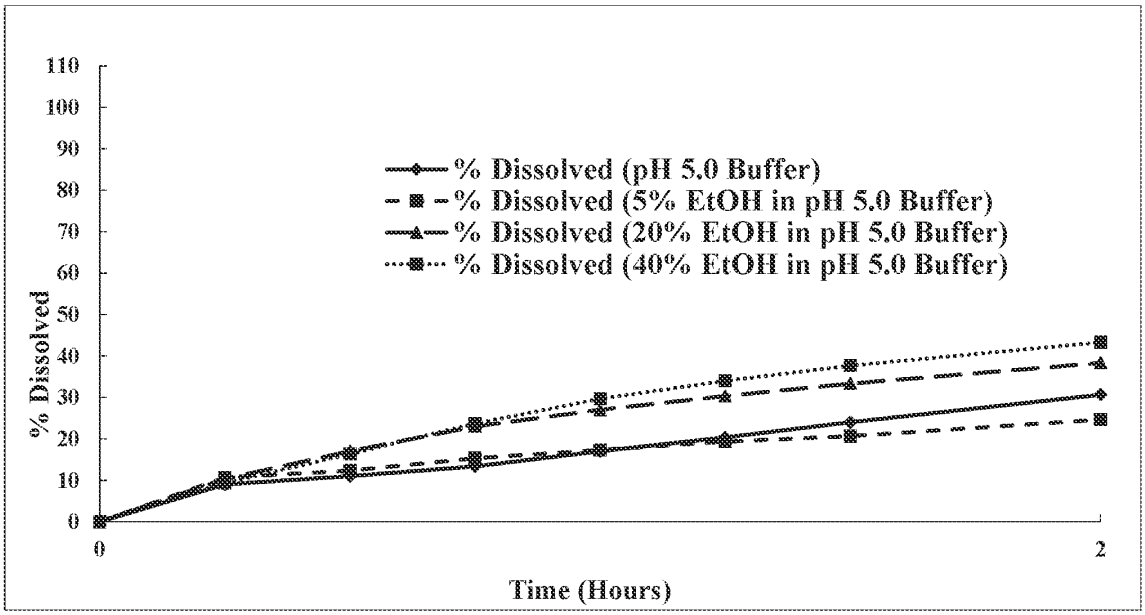

110
100
90
80
70
60
50
40
30
20
10
0
% Dissolved
0
2
Time (Hours)
% Dissolved (pH 5.0 Buffer)
% Dissolved (5% EtOH in pH 5.0 Buffer)
% Dissolved (20% EtOH in pH 5.0 Buffer)
% Dissolved (40% EtOH in pH 5.0 Buffer)

FIGURE 30

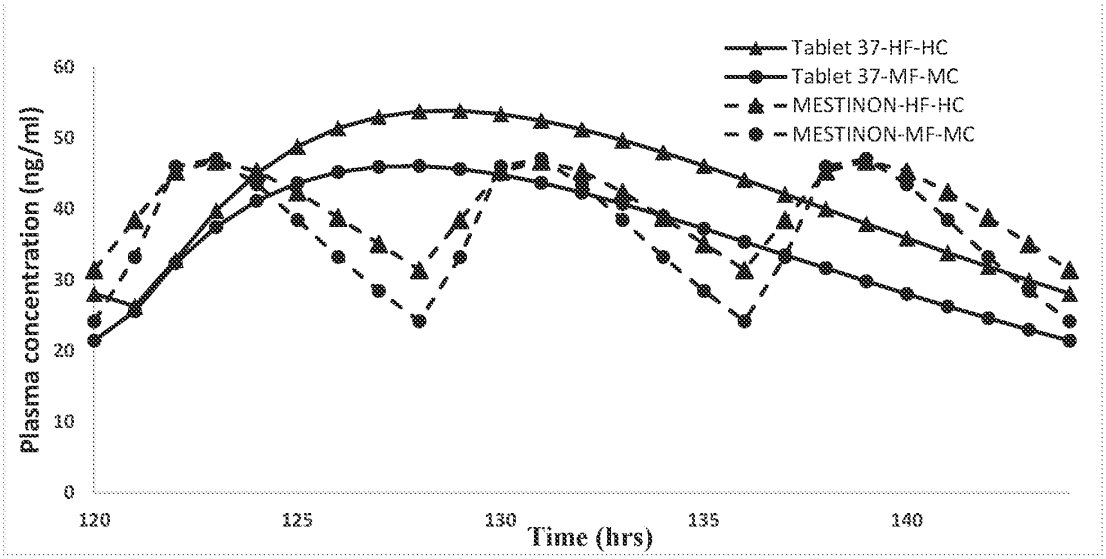

Tablet 37-HF-HC
Tablet 37-MF-MC
MESTINON-HF-HC
MESTINON-MF-MC
Plasma concentration (ng/ml)
60
50
40
30
20
10
0
120
125
130
135
140
Time (hrs)

FIGURE 31

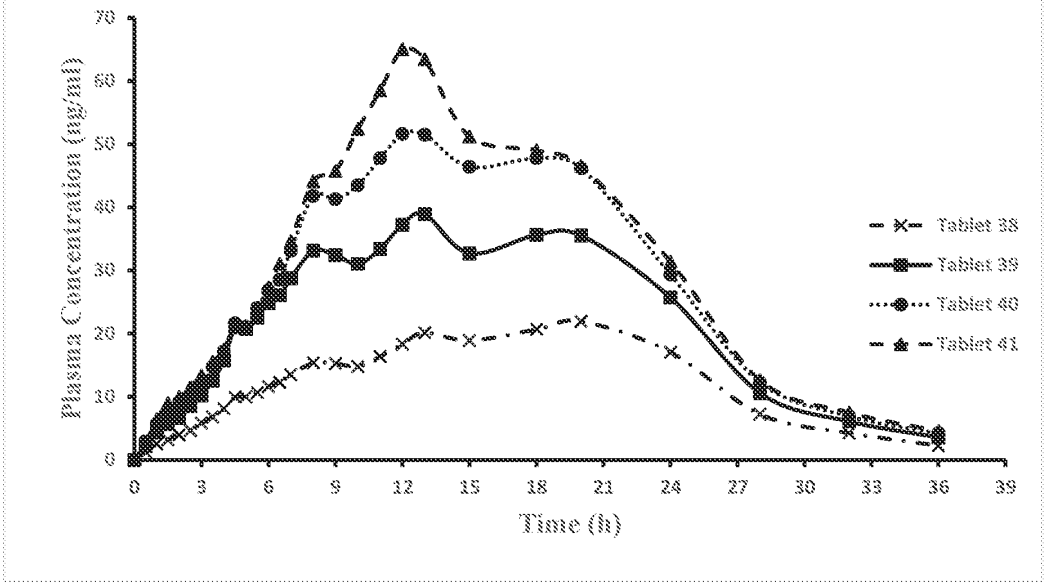

Plasma Concentration (ng/ml)
70
60
50
40
30
20
10
0
0
3
6
9
12
15
18
21
24
27
30
33
36
39
Time (h)
Tablet 38
Tablet 39
Tablet 40
Tablet 41

FIGURE 32

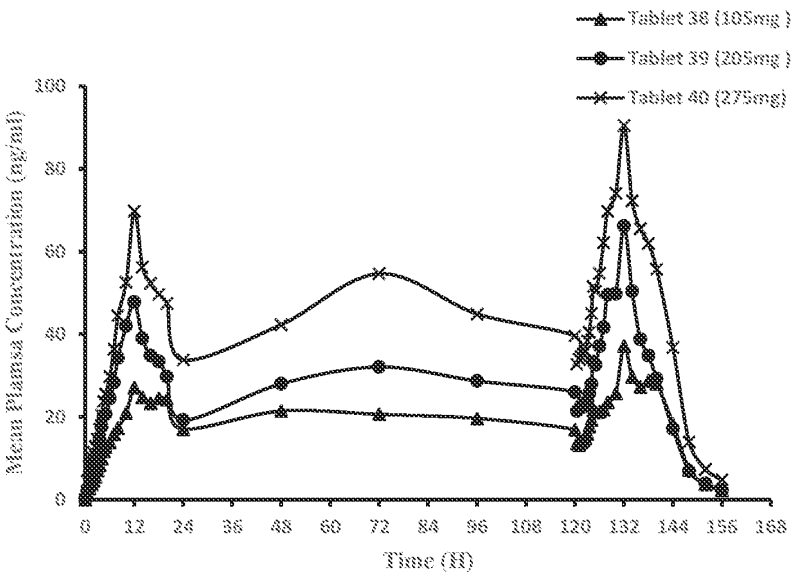

Tablet 38 (105mg)
Tablet 39 (205mg)
Tablet 40 (275mg)
Mean Plasma Concentration (ng/ml)
100
80
60
40
20
0
0
12
24
36
48
60
72
84
96
108
120
132
144
156
168
Time (H)

FIGURE 33