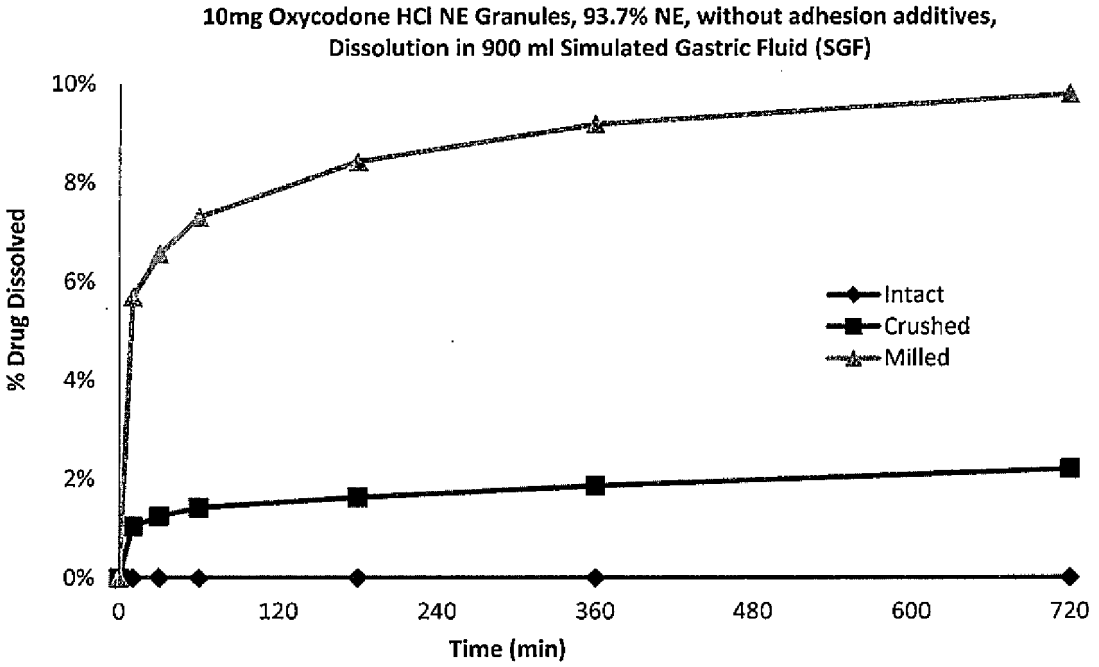


FIGURE 1A

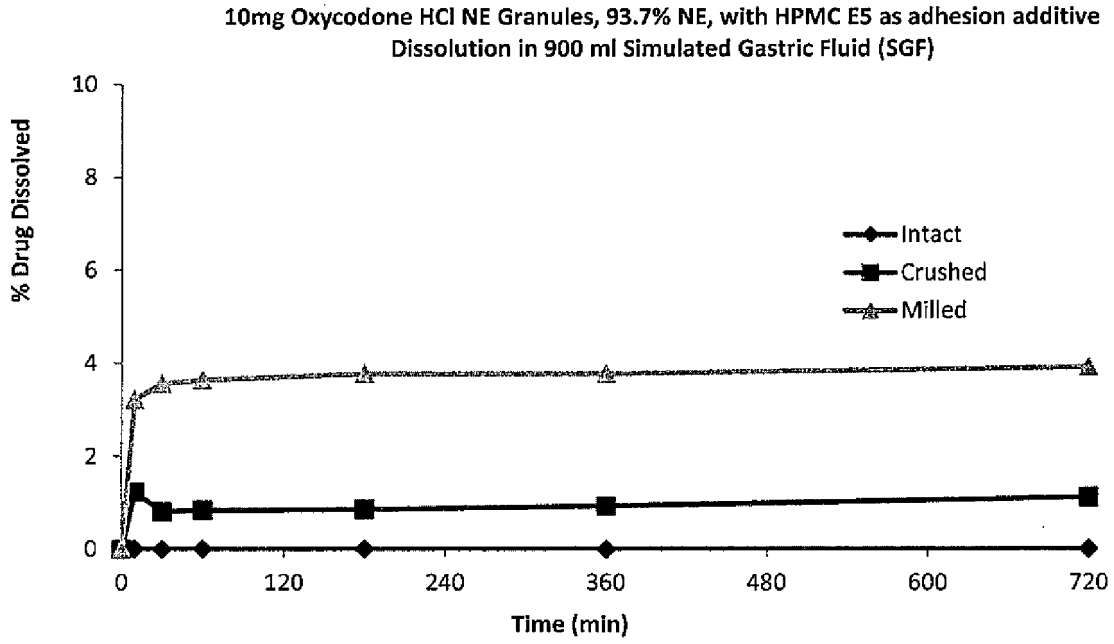


FIGURE 1B

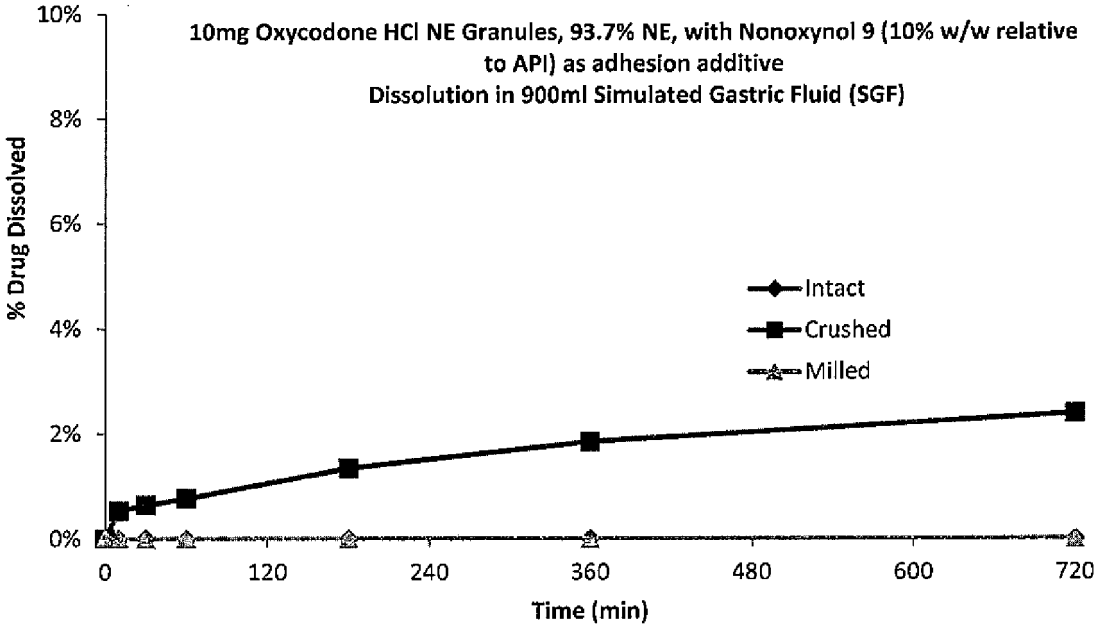


FIGURE 1C

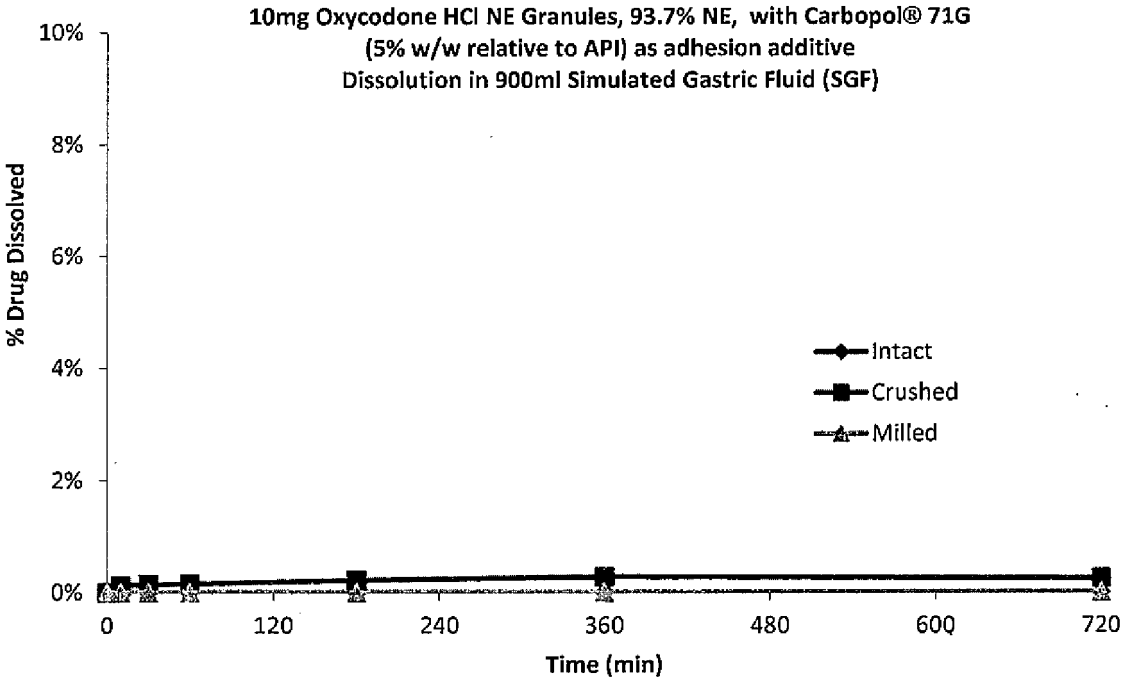


FIGURE 1D

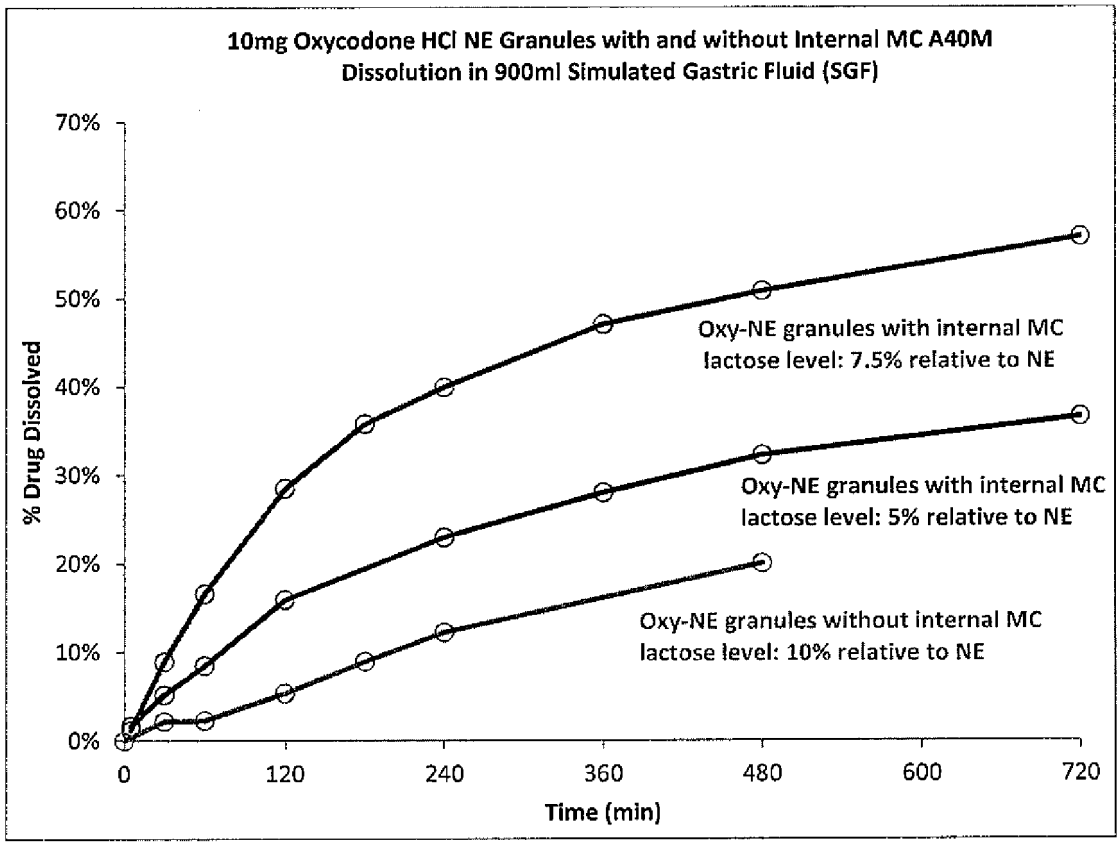

10mg Oxycodone HCl NE Granules with and without Internal MC A40M
Dissolution in 900ml Simulated Gastric Fluid (SGF)
% Drug Dissolved
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)
Oxy-NE granules with internal MC
lactose level: 7.5% relative to NE
Oxy-NE granules with internal MC
lactose level: 5% relative to NE
Oxy-NE granules without internal MC
lactose level: 10% relative to NE

FIGURE 2

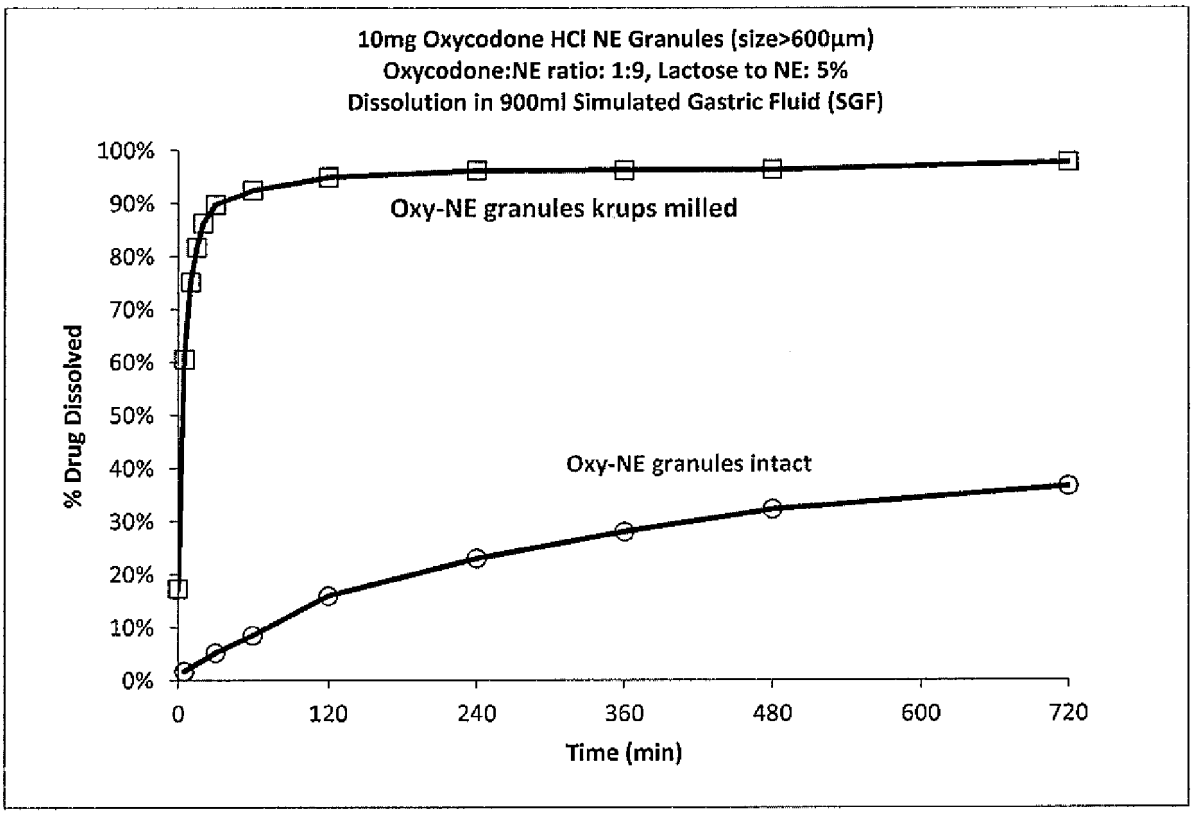


FIGURE 3A

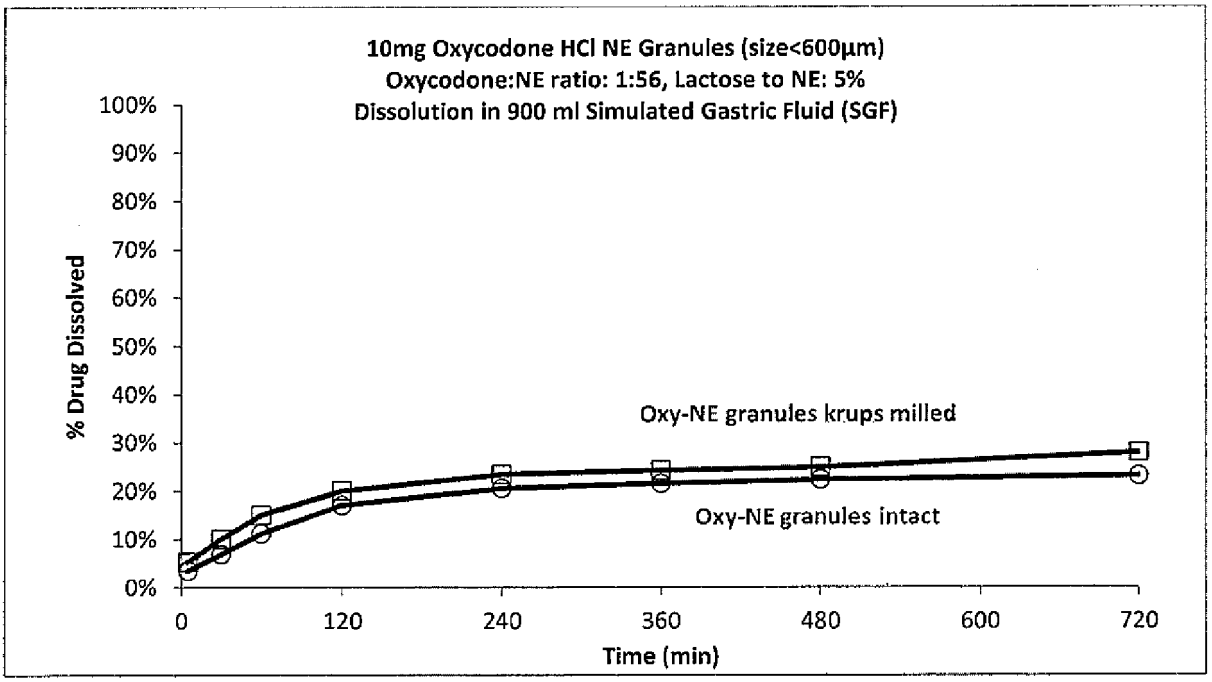


FIGURE 3B

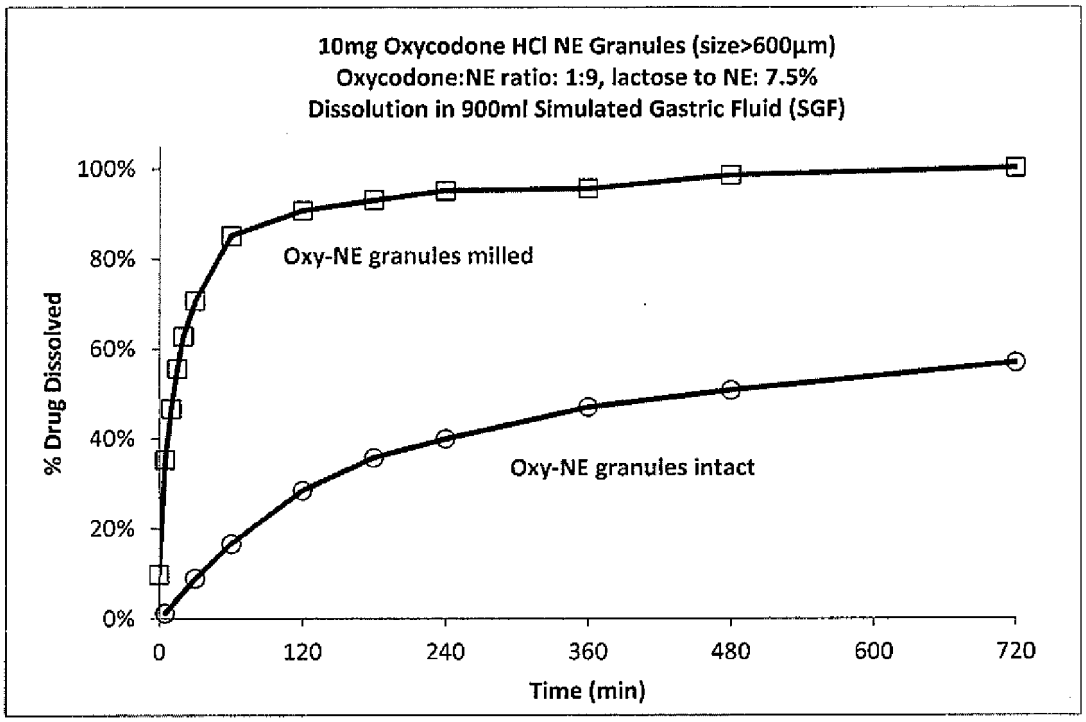


FIGURE 4A

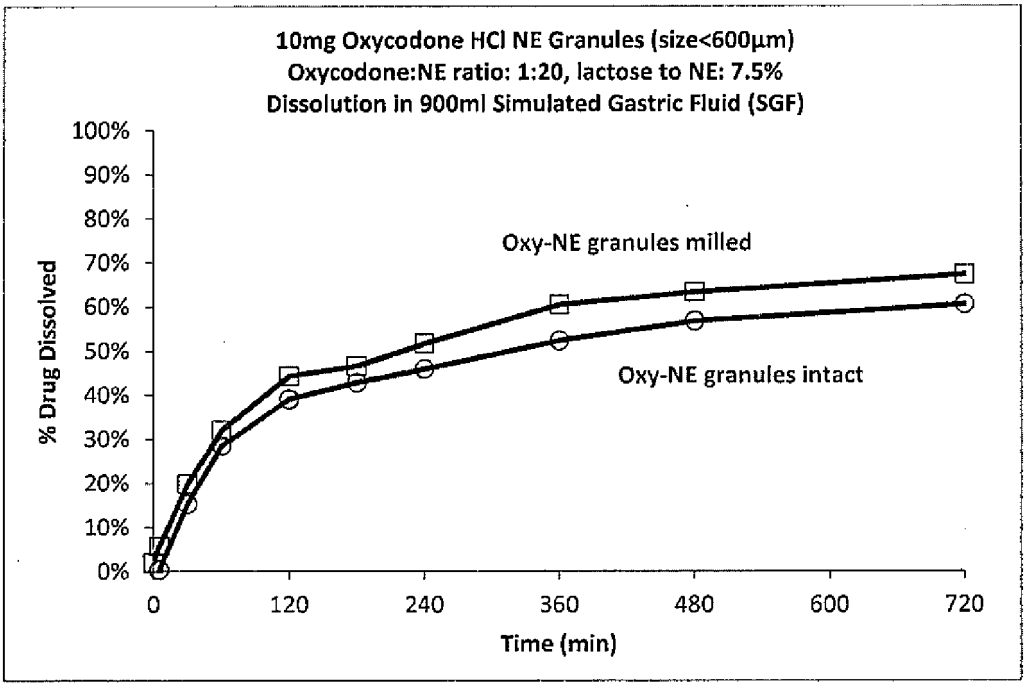


FIGURE 4B

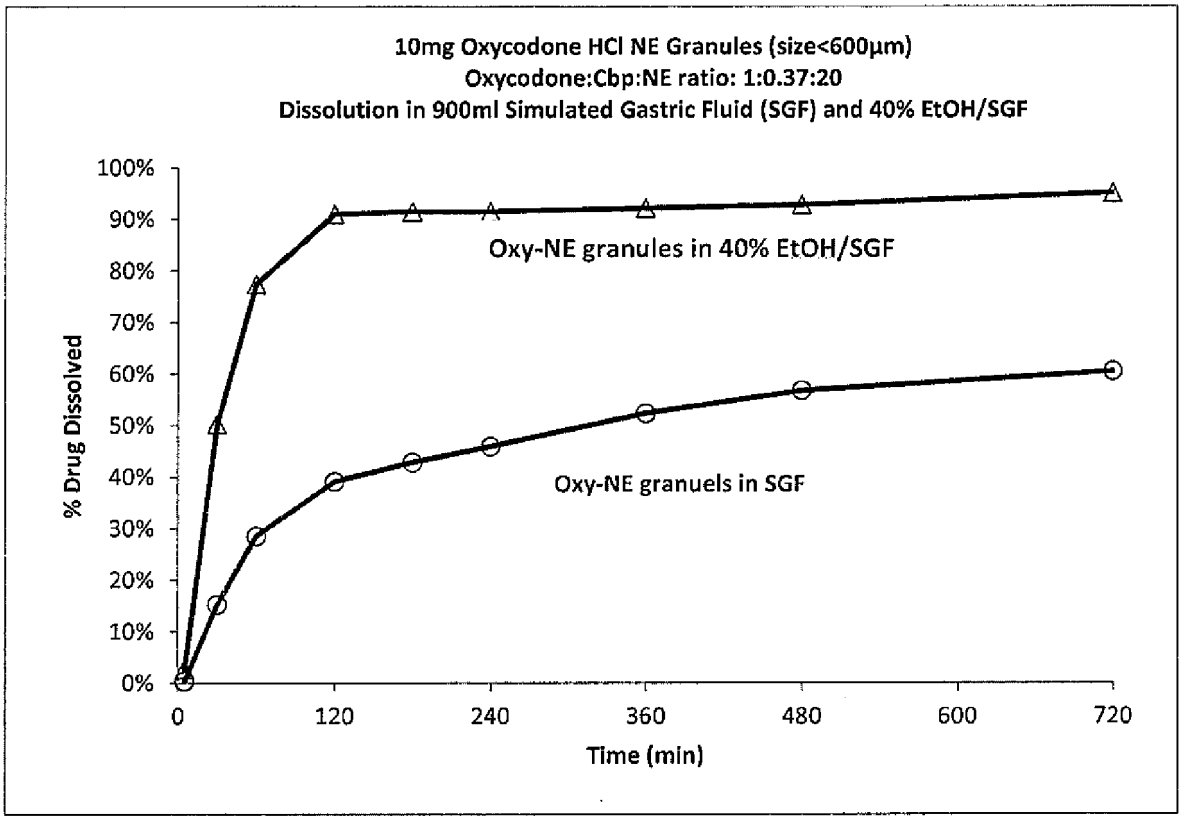

10mg Oxycodone HCl NE Granules (size<600µm)
Oxycodone:Cbp:NE ratio: 1:0.37:20
Dissolution in 900ml Simulated Gastric Fluid (SGF) and 40% EtOH/SGF
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)
Oxy-NE granules in 40% EtOH/SGF
Oxy-NE granuels in SGF

FIGURE 5

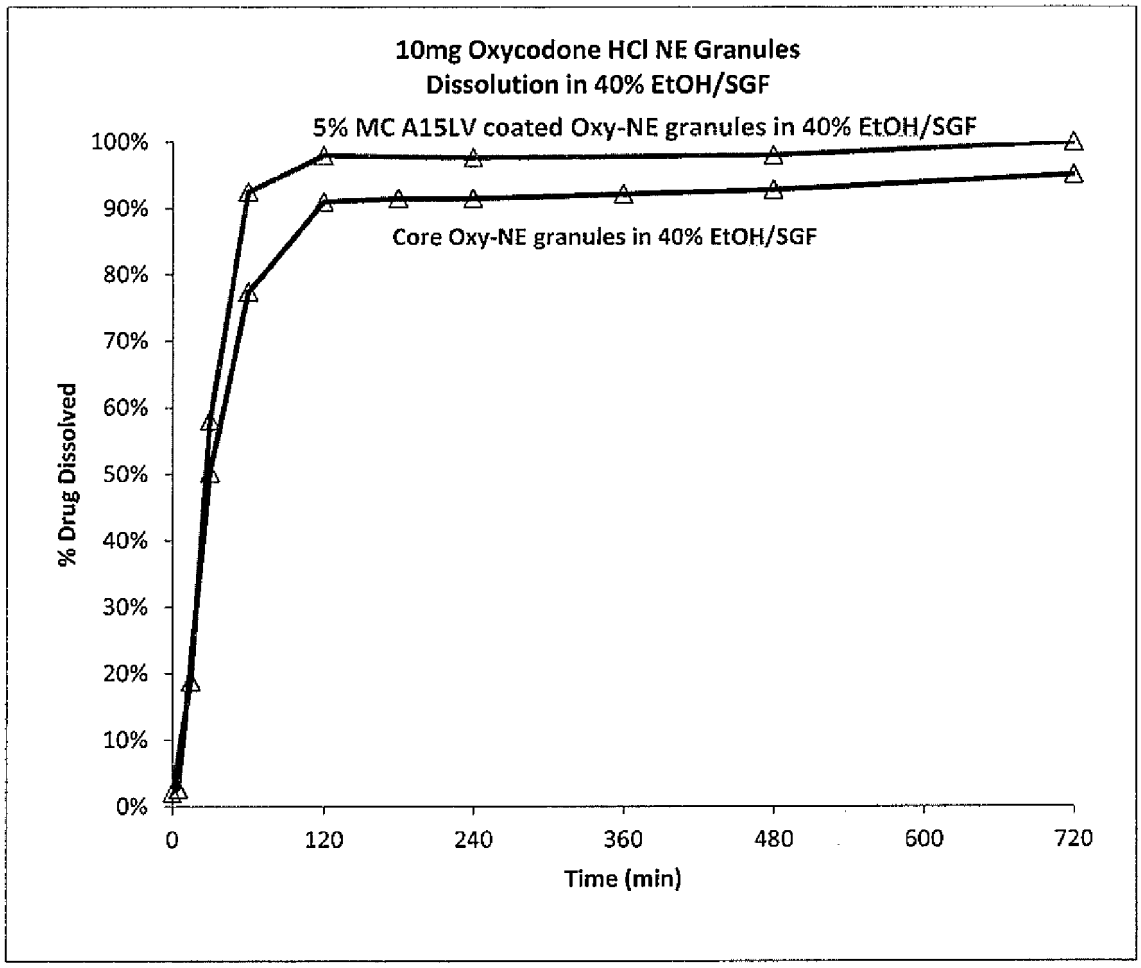

10mg Oxycodone HCl NE Granules
Dissolution in 40% EtOH/SGF
5% MC A15LV coated Oxy-NE granules in 40% EtOH/SGF
Core Oxy-NE granules in 40% EtOH/SGF
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)

FIGURE 6

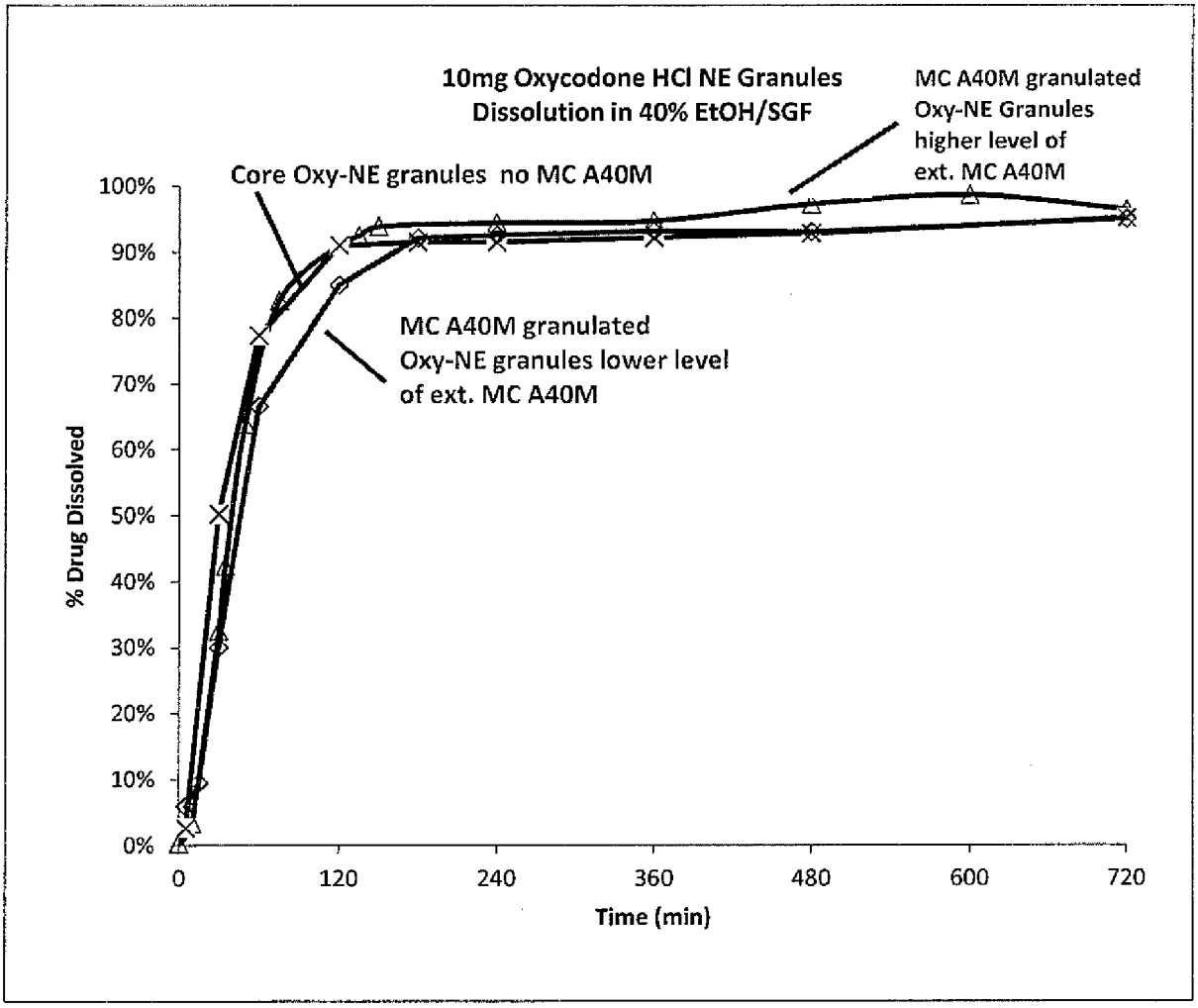

10mg Oxycodone HCl NE Granules
Dissolution in 40% EtOH/SGF
MC A40M granulated
Oxy-NE Granules
higher level of
ext. MC A40M
Core Oxy-NE granules no MC A40M
MC A40M granulated
Oxy-NE granules lower level
of ext. MC A40M
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)

FIGURE 7

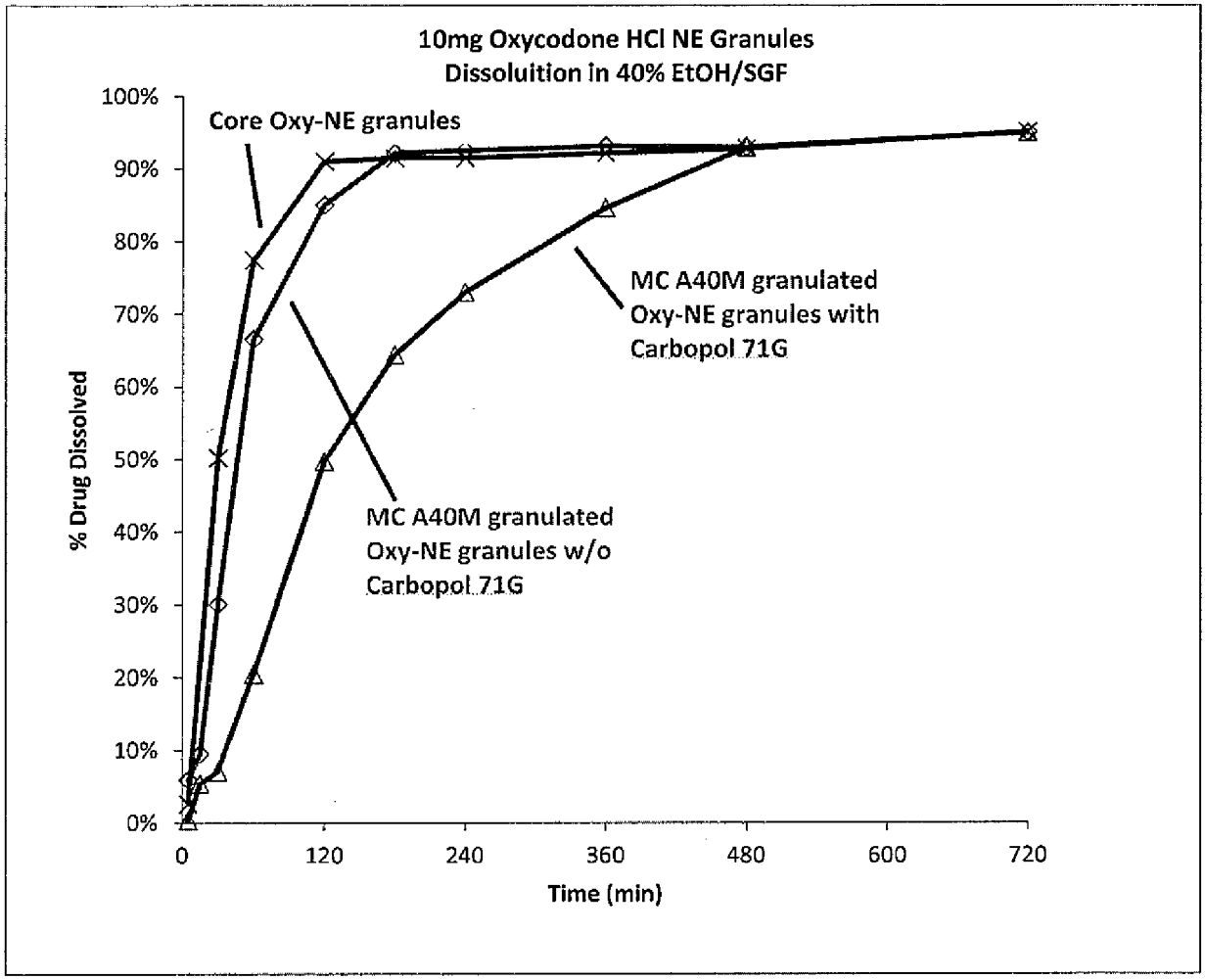

10mg Oxycodone HCl NE Granules
Dissoluition in 40% EtOH/SGF
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
% Drug Dissolved
Core Oxy-NE granules
MC A40M granulated
Oxy-NE granules with
Carbopol 71G
MC A40M granulated
Oxy-NE granules w/o
Carbopol 71G
0
120
240
360
480
600
720
Time (min)

FIGURE 8

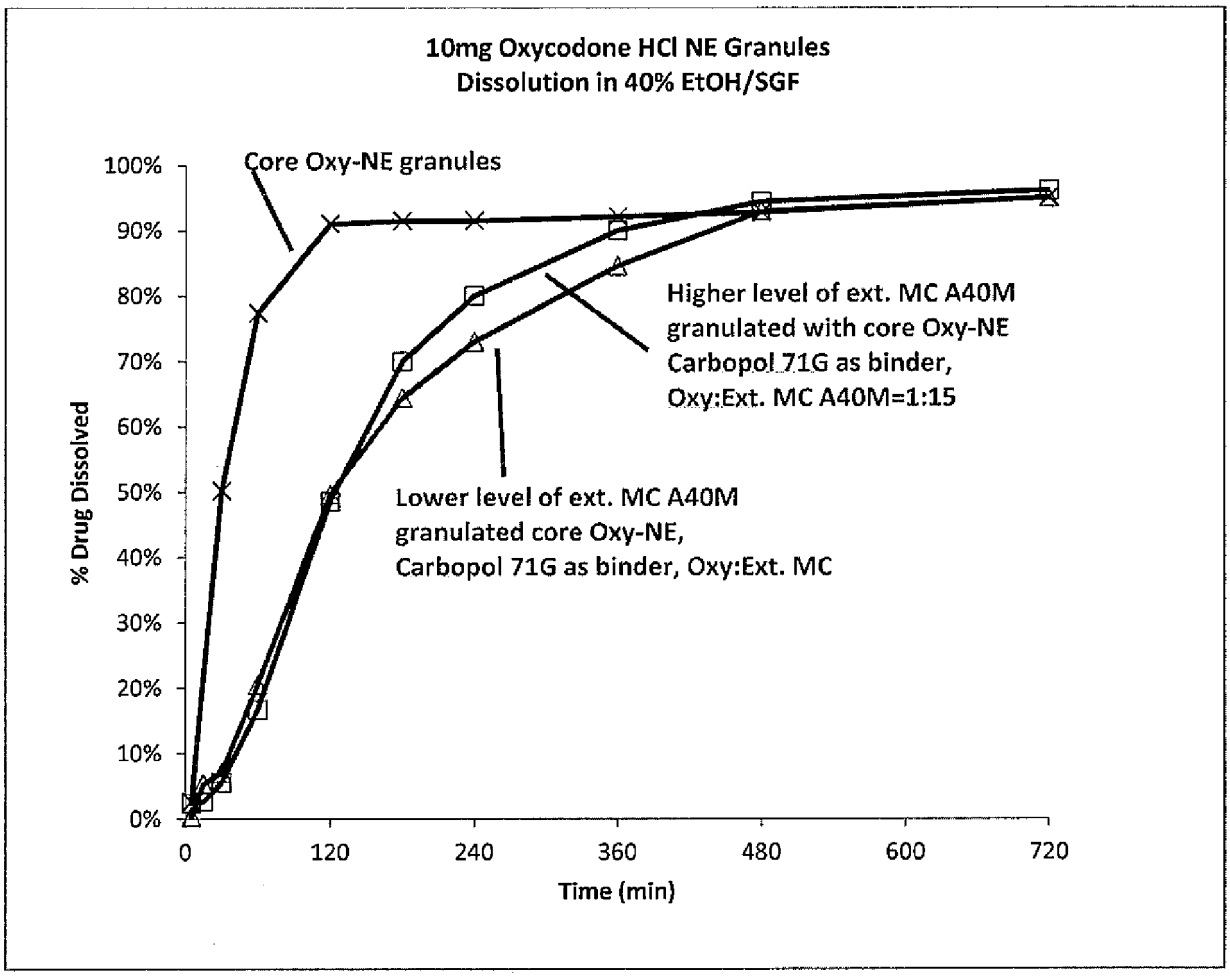

10mg Oxycodone HCl NE Granules
Dissolution in 40% EtOH/SGF
Core Oxy-NE granules
Higher level of ext. MC A40M granulated with core Oxy-NE Carbopol 71G as binder, Oxy:Ext. MC A40M=1:15
Lower level of ext. MC A40M granulated core Oxy-NE, Carbopol 71G as binder, Oxy:Ext. MC
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)

FIGURE 9

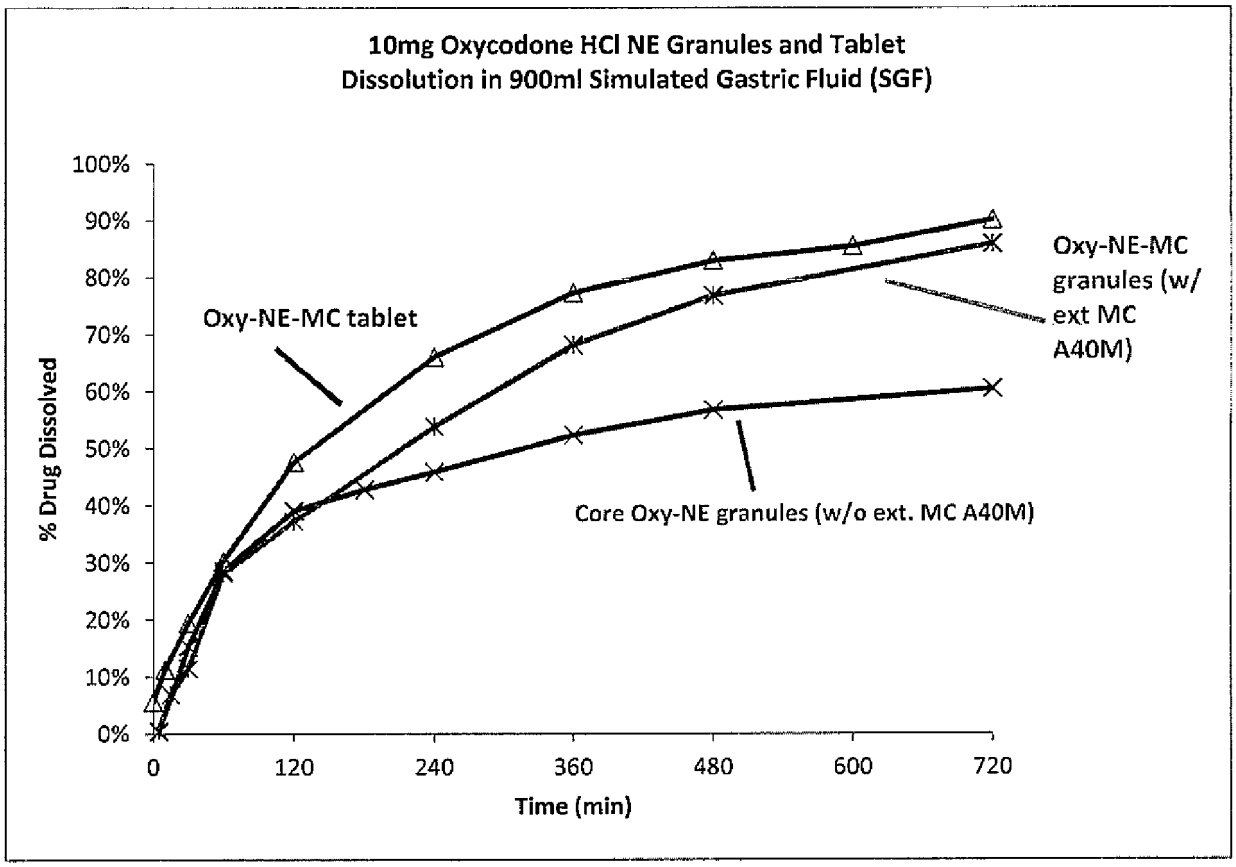

10mg Oxycodone HCl NE Granules and Tablet
Dissolution in 900ml Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)
Oxy-NE-MC tablet
Oxy-NE-MC granules (w/ ext MC A40M)
Core Oxy-NE granules (w/o ext. MC A40M)

FIGURE 10

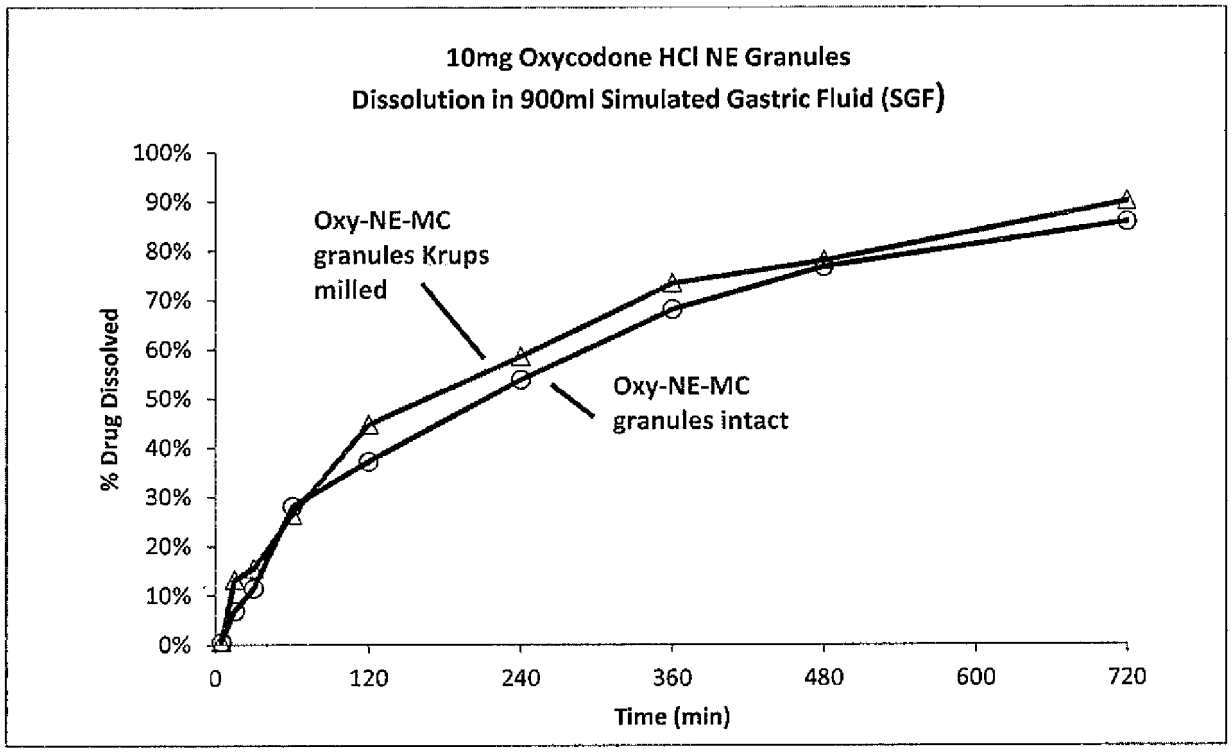

10mg Oxycodone HCl NE Granules
Dissolution in 900ml Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)
Oxy-NE-MC granules Krups milled
Oxy-NE-MC granules intact

FIGURE 11

Tamper Resistance-resistance to crushing- release from crushed granules in comparison to intact granules

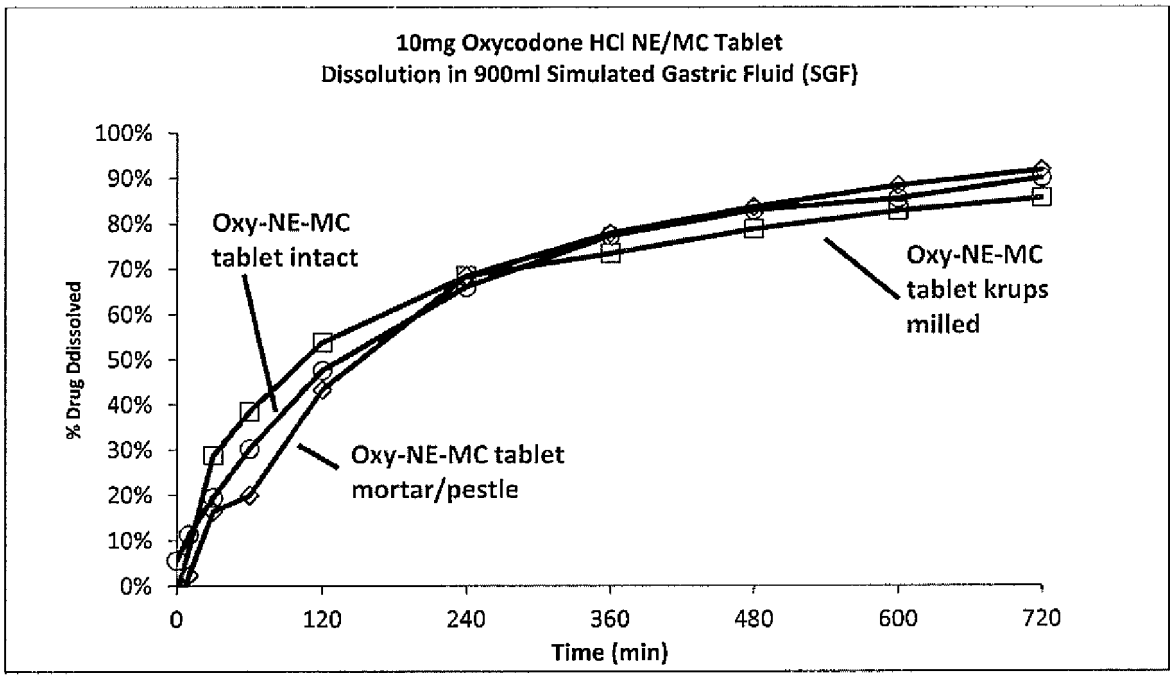


FIGURE 12A

Alcohol Resistance

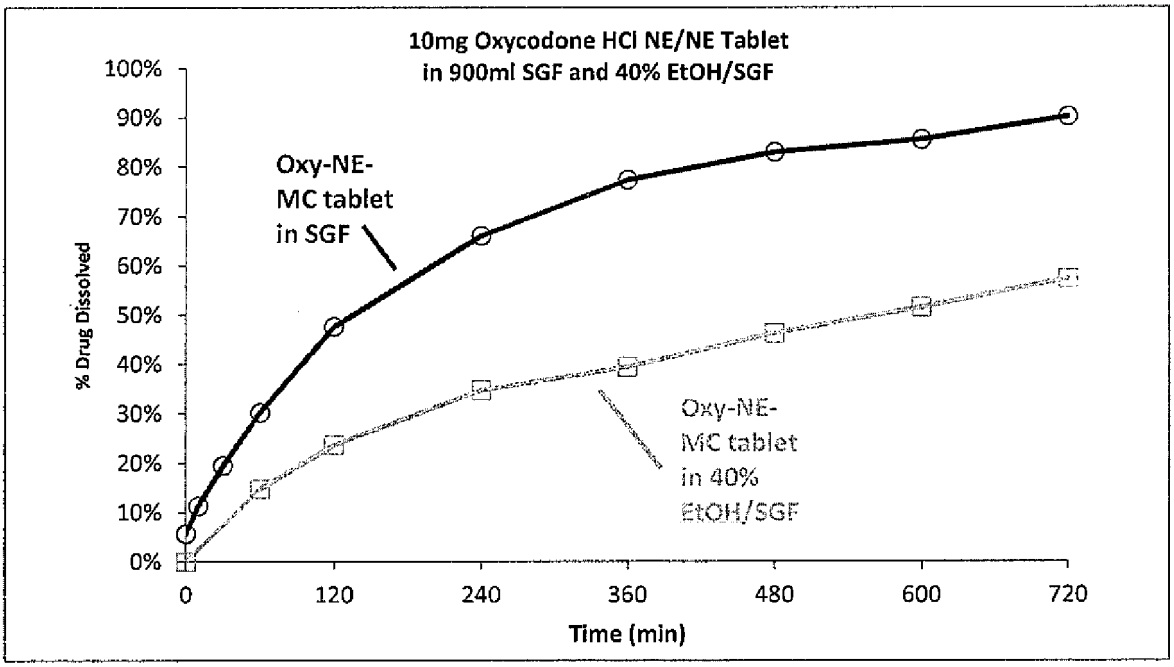


FIGURE 12B

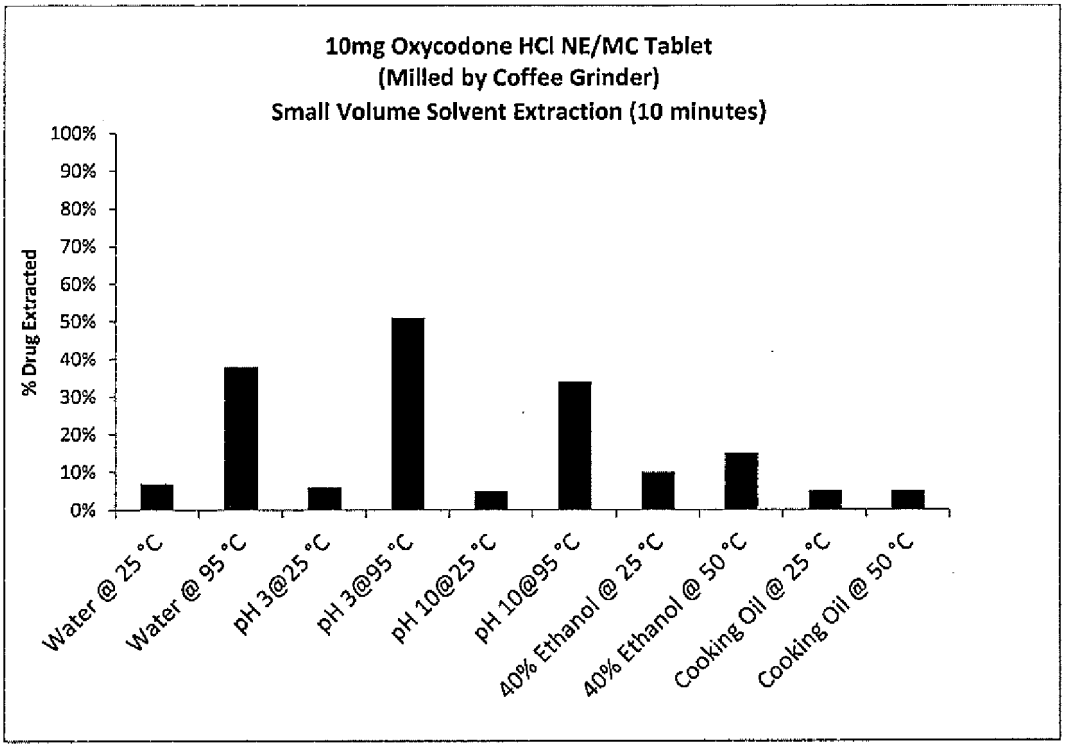


FIGURE 13A

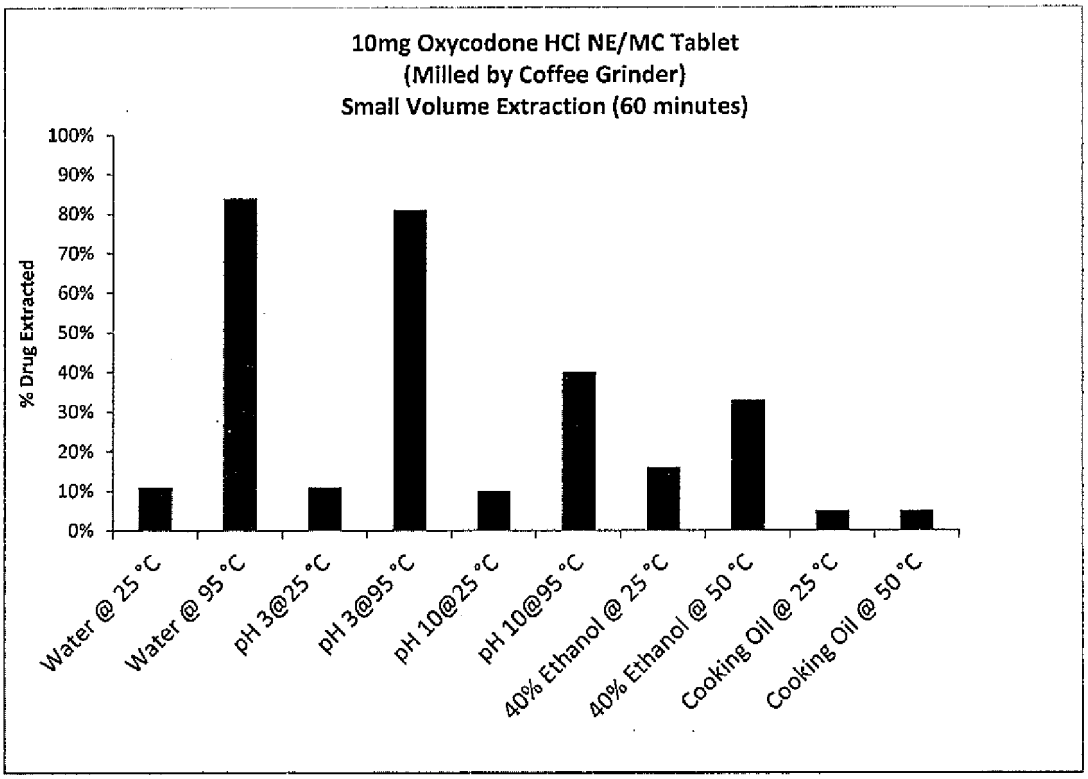


FIGURE 13B

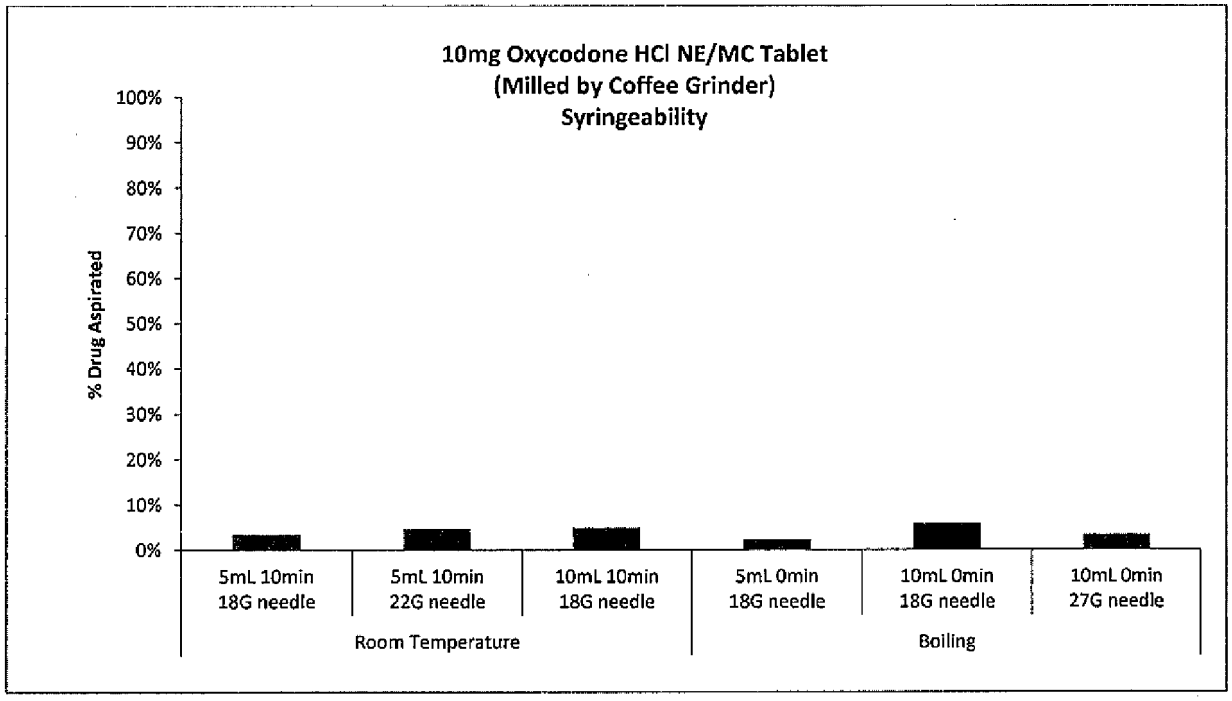

10mg Oxycodone HCl NE/MC Tablet
(Milled by Coffee Grinder)
Syringeability
% Drug Aspirated
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
5mL 10min 18G needle
5mL 10min 22G needle
10mL 10min 18G needle
5mL 0min 18G needle
10mL 0min 18G needle
10mL 0min 27G needle
Room Temperature
Boiling

FIGURE 14

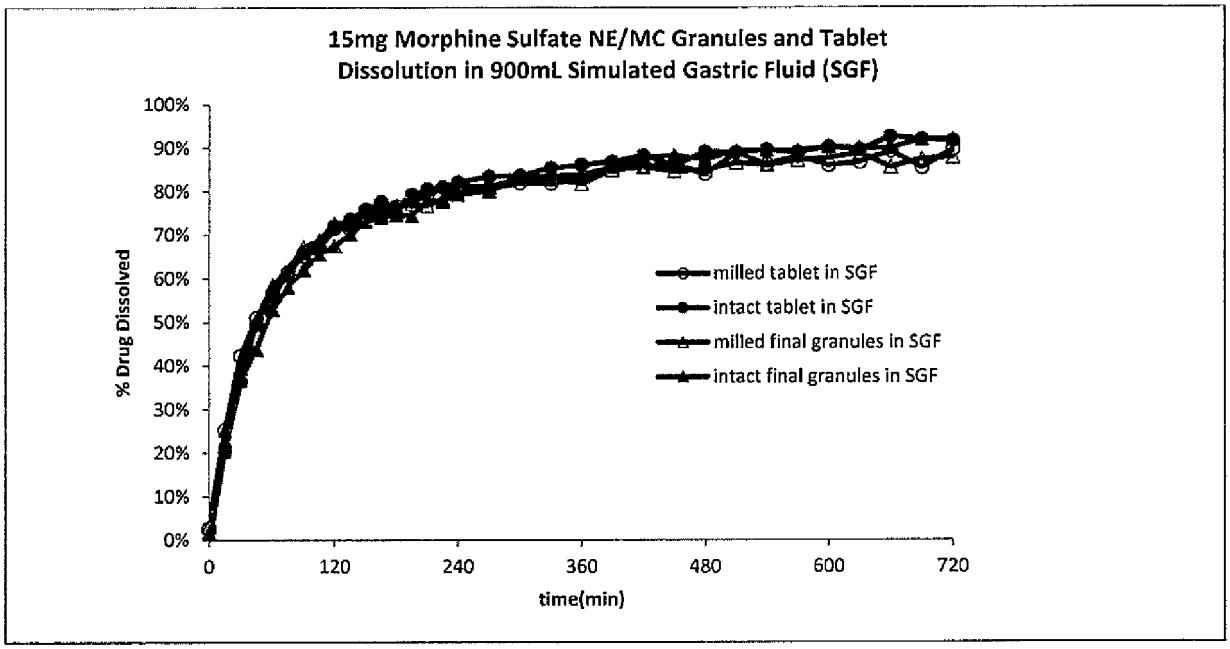


Figure 15A

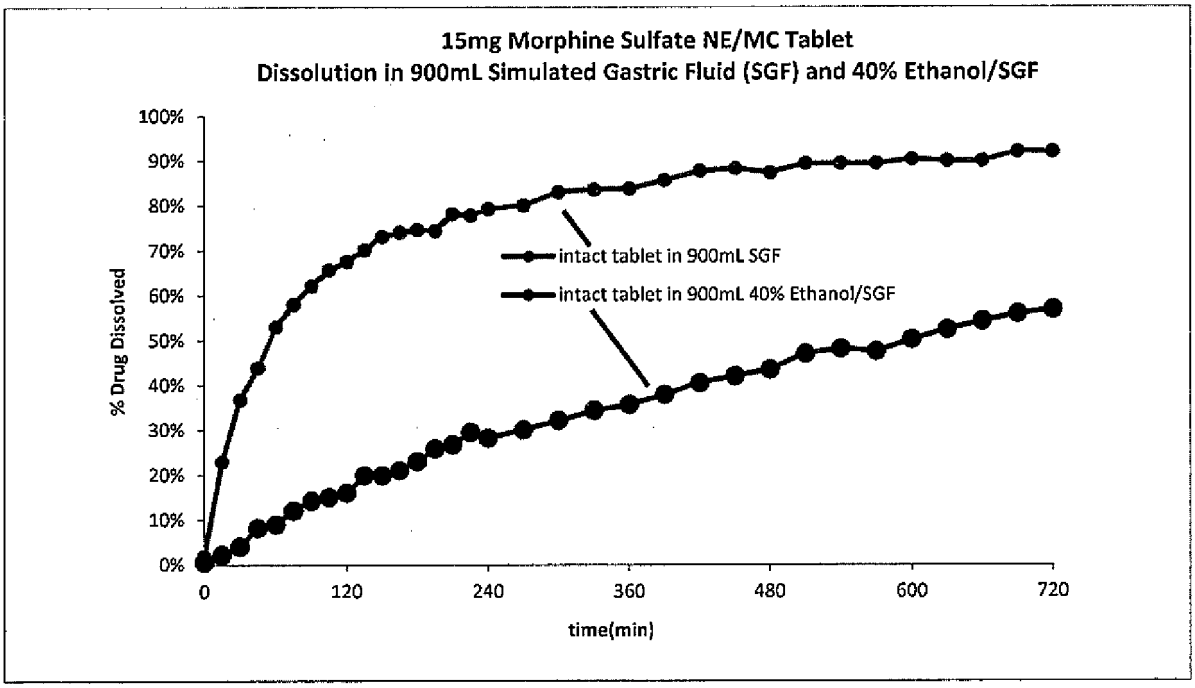


Figure 15B

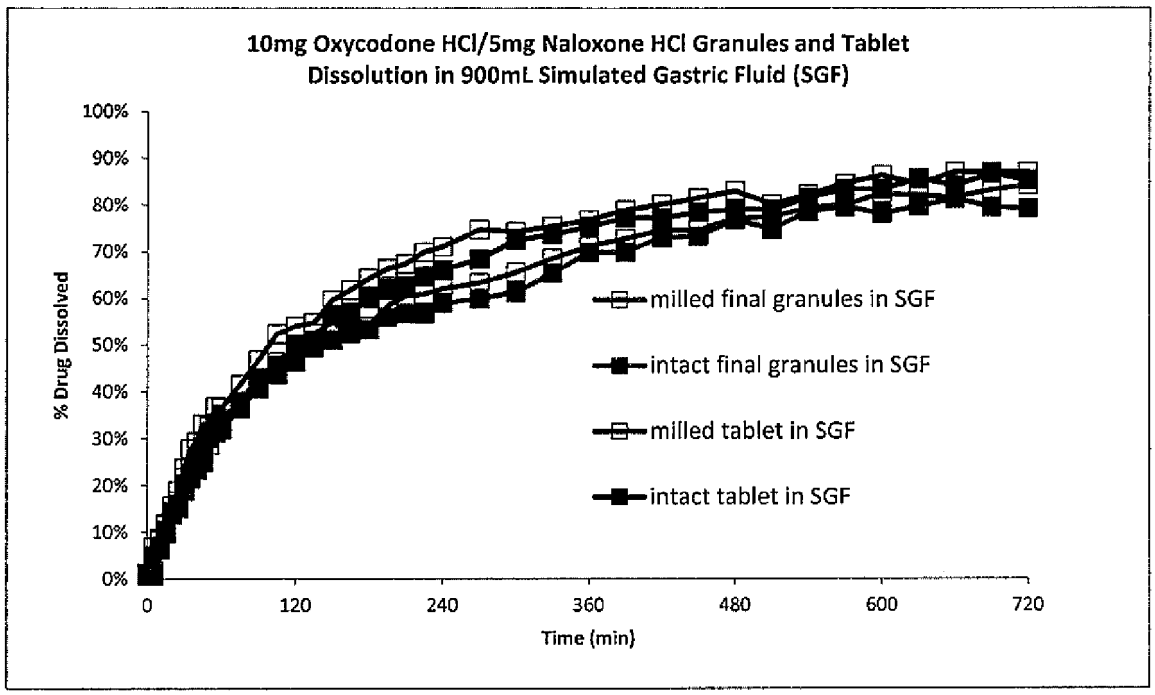

10mg Oxycodone HCl/5mg Naloxone HCl Granules and Tablet Dissolution in 900mL Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
Time (min)
milled final granules in SGF
intact final granules in SGF
milled tablet in SGF
intact tablet in SGF

Figure 16

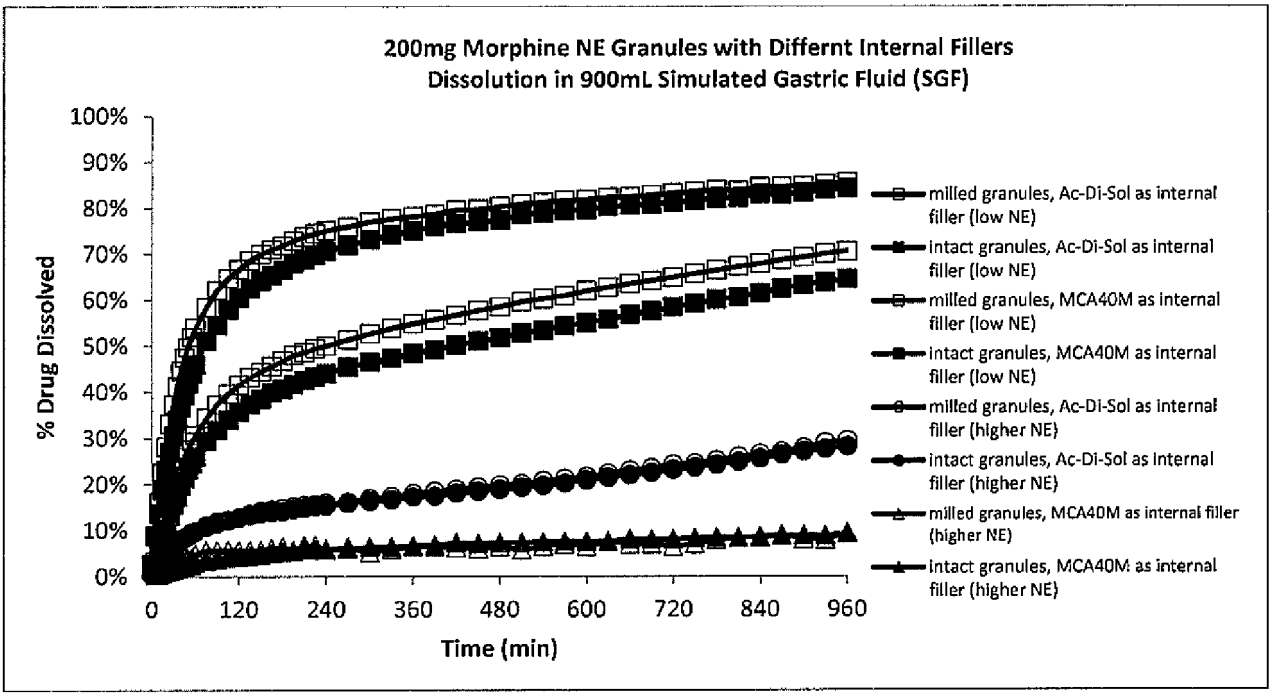

200mg Morphine NE Granules with Differnt Internal Fillers
Dissolution in 900mL Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
840
960
Time (min)
milled granules, Ac-Di-Sol as internal filler (low NE)
intact granules, Ac-Di-Sol as internal filler (low NE)
milled granules, MCA40M as internal filler (low NE)
intact granules, MCA40M as internal filler (low NE)
milled granules, Ac-Di-Sol as internal filler (higher NE)
intact granules, Ac-Di-Sol as internal filler (higher NE)
milled granules, MCA40M as internal filler (higher NE)
intact granules, MCA40M as internal filler (higher NE)

Figure 17

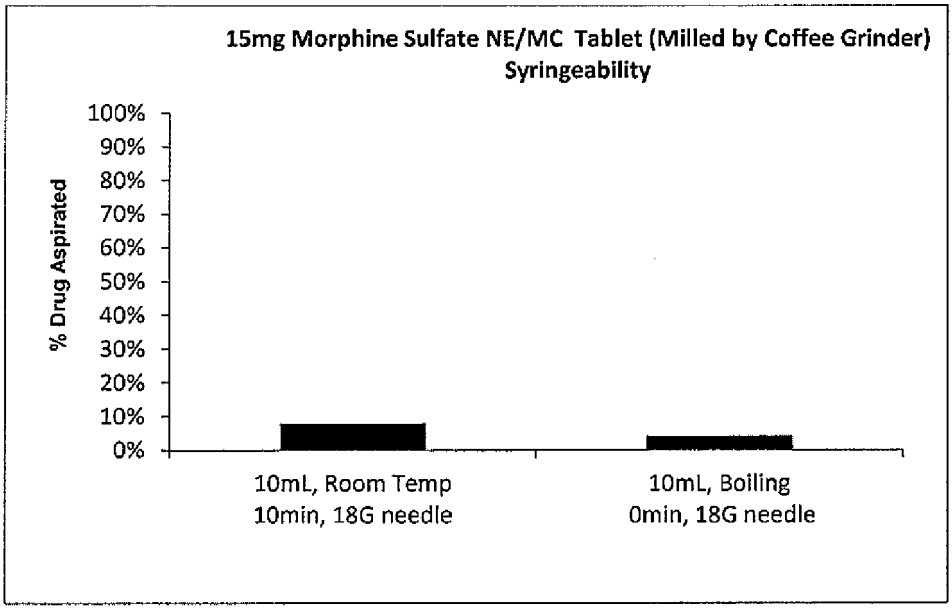


Figure 18A

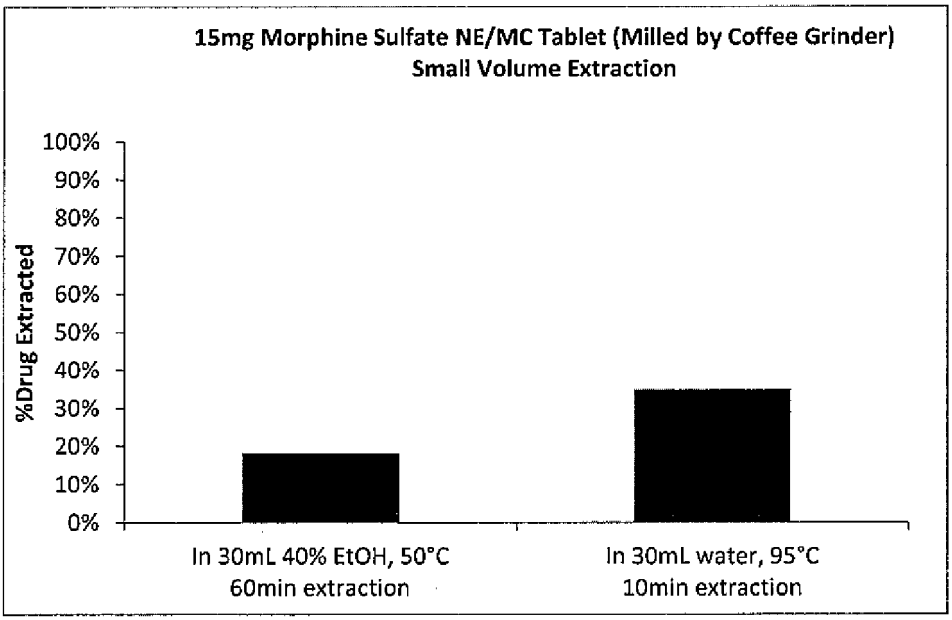


Figure 18B

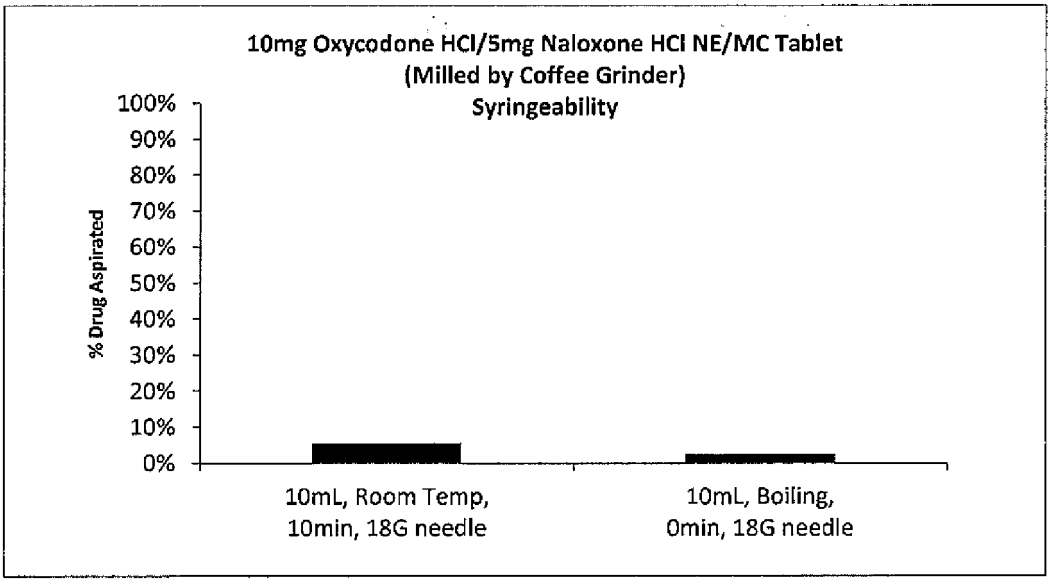


Figure 19A

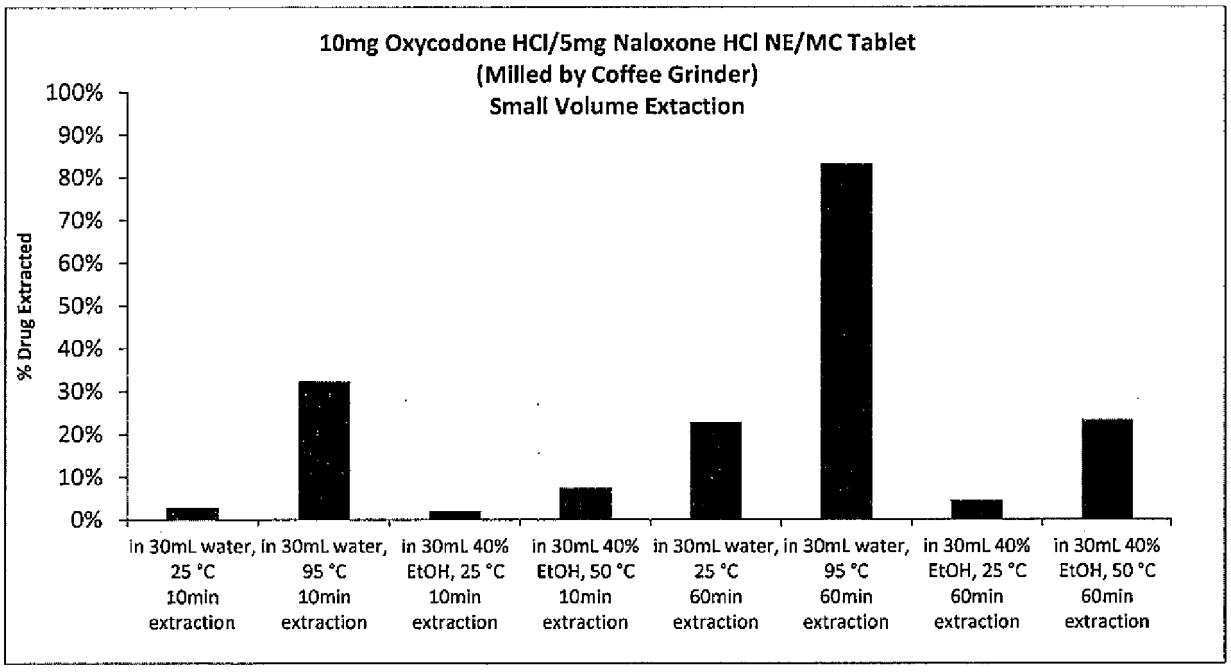


Figure 19B

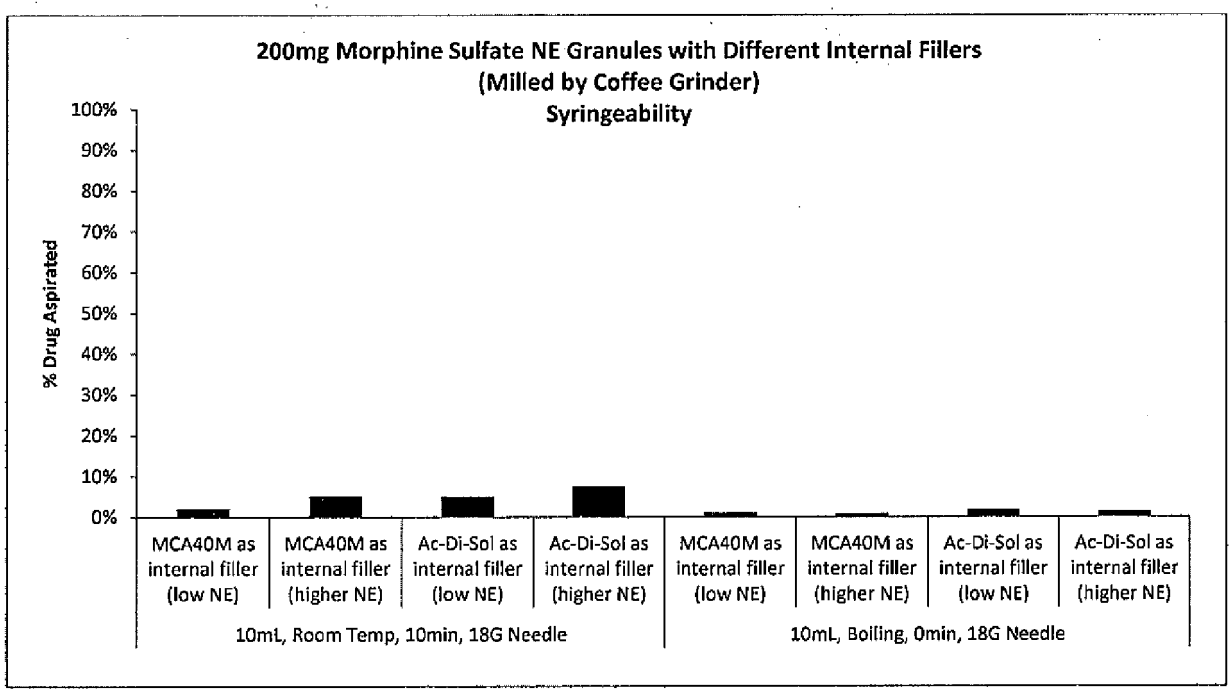


Figure 20A

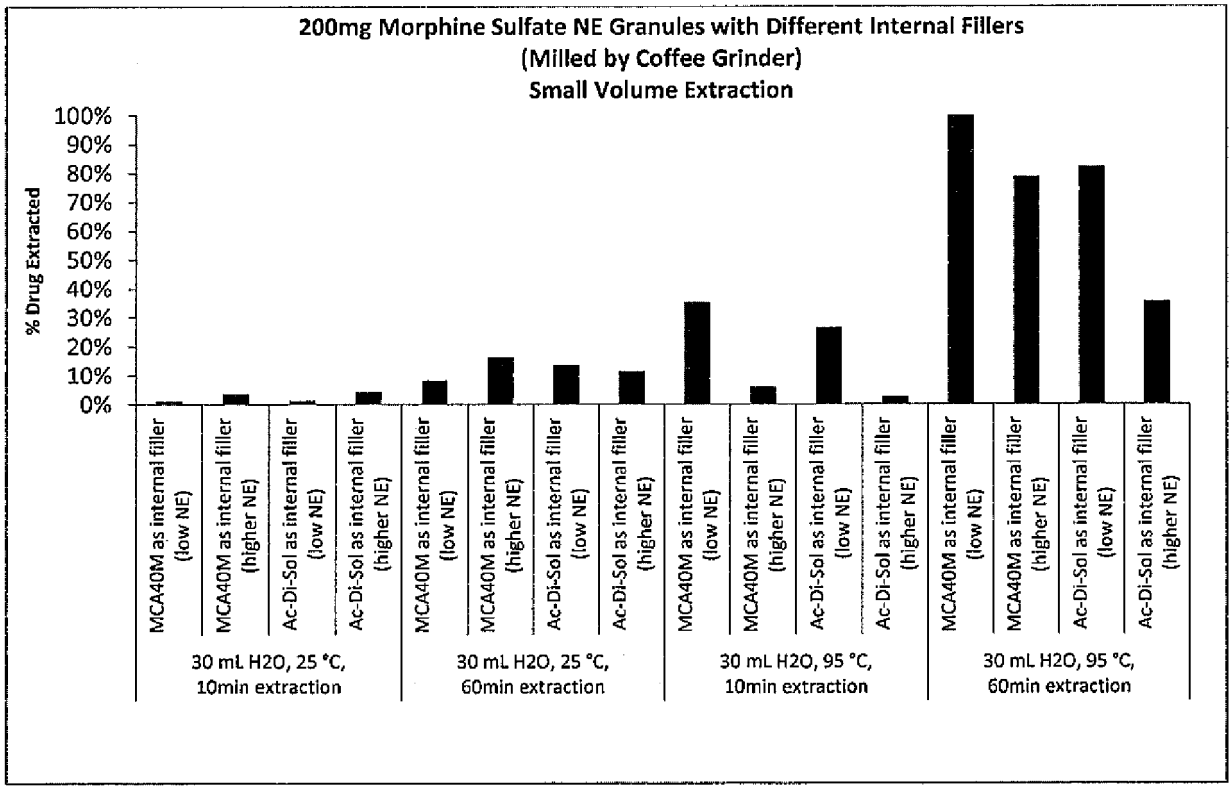


Figure 20B

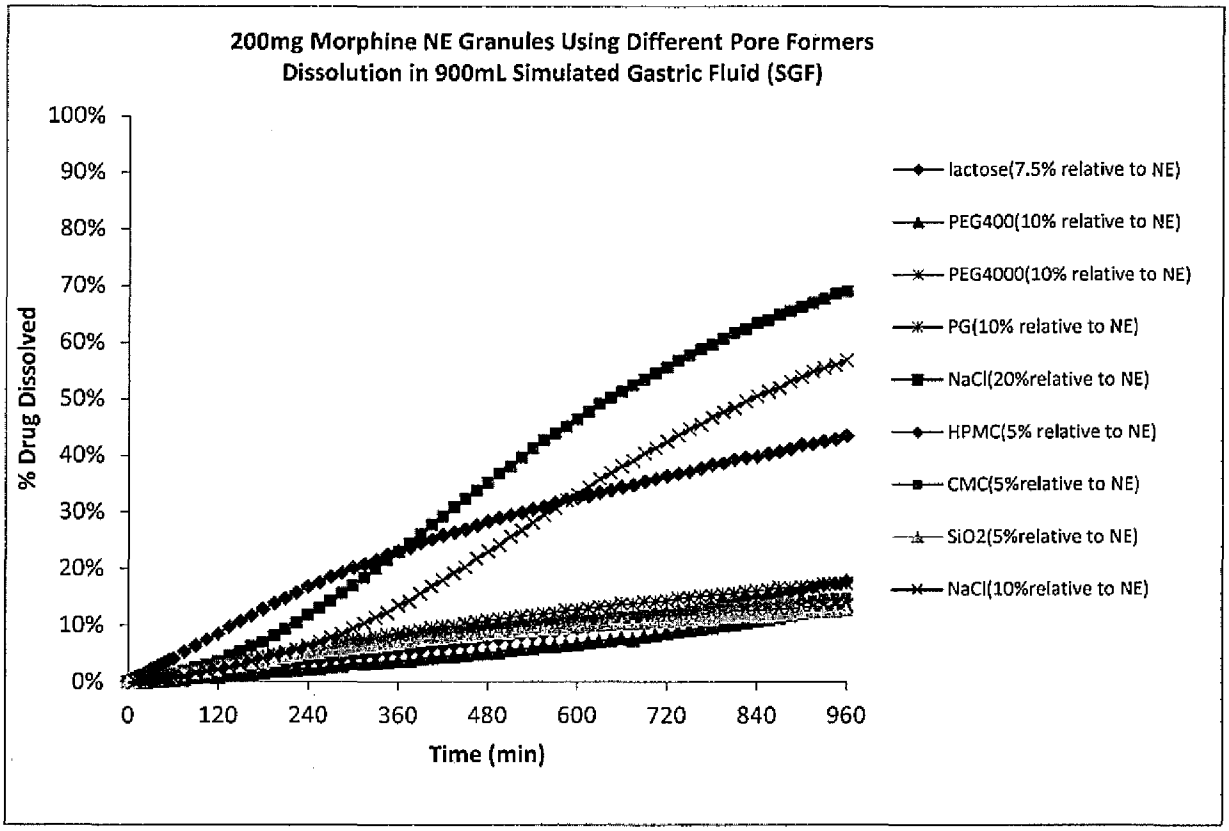

200mg Morphine NE Granules Using Different Pore Formers
Dissolution in 900mL Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
840
960
Time (min)
lactose(7.5% relative to NE)
PEG400(10% relative to NE)
PEG4000(10% relative to NE)
PG(10% relative to NE)
NaCl(20%relative to NE)
HPMC(5% relative to NE)
CMC(5%relative to NE)
SiO2(5%relative to NE)
NaCl(10%relative to NE)

Figure 21

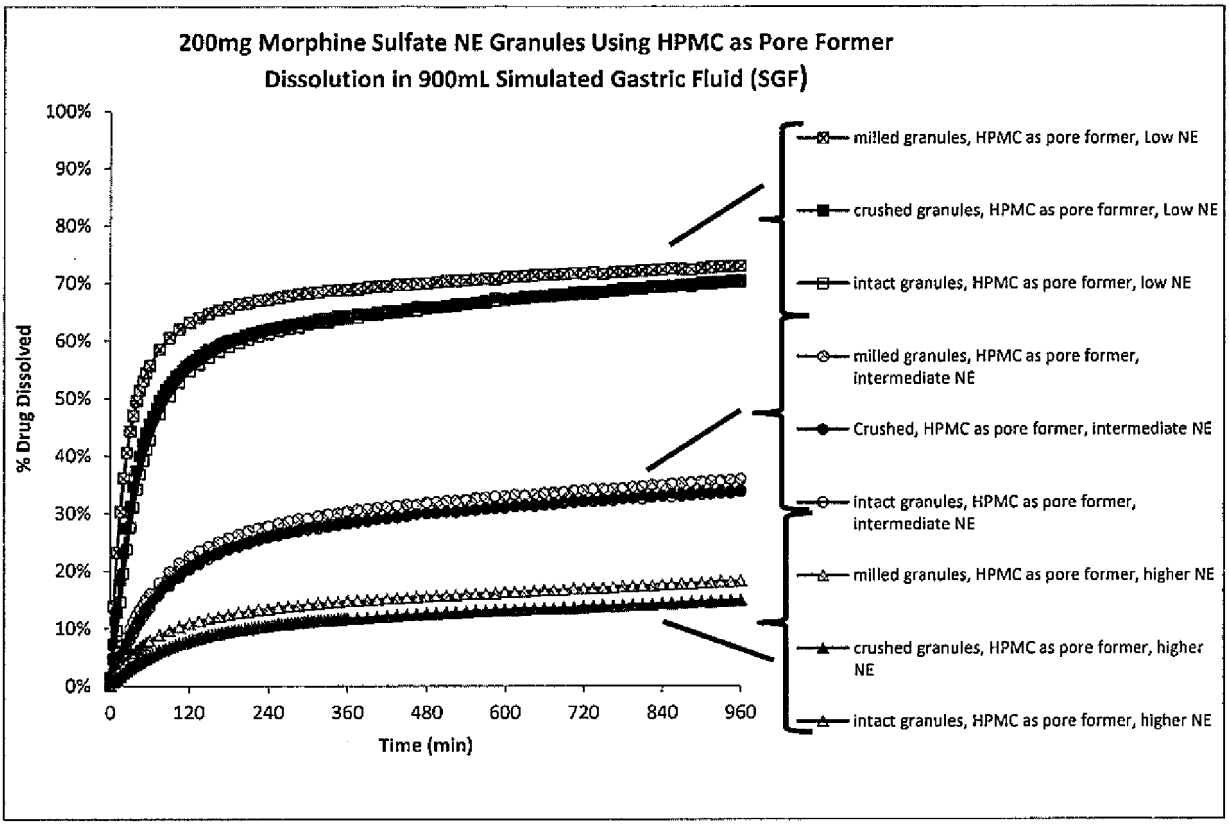

200mg Morphine Sulfate NE Granules Using HPMC as Pore Former
Dissolution in 900mL Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
840
960
Time (min)
milled granules, HPMC as pore former, Low NE
crushed granules, HPMC as pore formrer, Low NE
intact granules, HPMC as pore former, low NE
milled granules, HPMC as pore former, intermediate NE
Crushed, HPMC as pore former, intermediate NE
intact granules, HPMC as pore former, intermediate NE
milled granules, HPMC as pore former, higher NE
crushed granules, HPMC as pore former, higher NE
intact granules, HPMC as pore former, higher NE

Figure 22

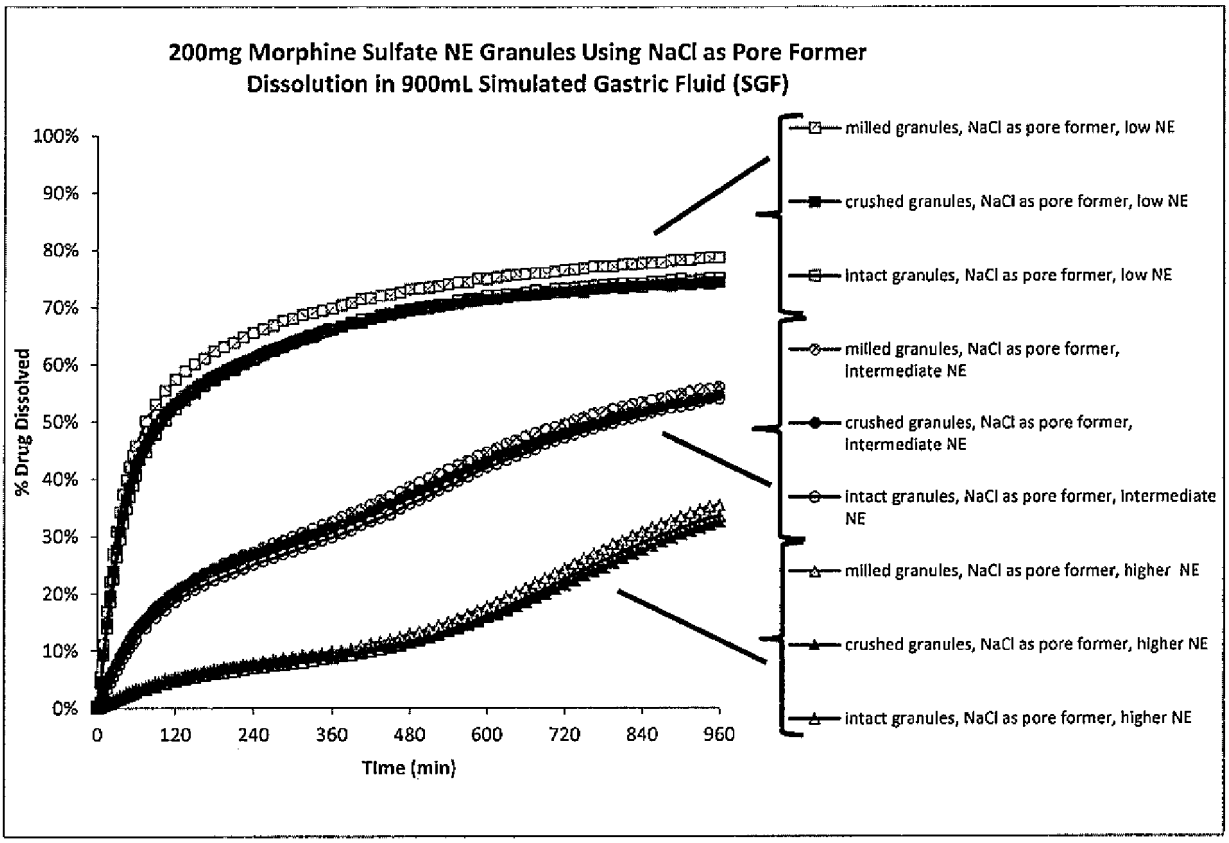

200mg Morphine Sulfate NE Granules Using NaCl as Pore Former
Dissolution in 900mL Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
840
960
Time (min)
milled granules, NaCl as pore former, low NE
crushed granules, NaCl as pore former, low NE
intact granules, NaCl as pore former, low NE
milled granules, NaCl as pore former, intermediate NE
crushed granules, NaCl as pore former, intermediate NE
intact granules, NaCl as pore former, intermediate NE
milled granules, NaCl as pore former, higher NE
crushed granules, NaCl as pore former, higher NE
intact granules, NaCl as pore former, higher NE

Figure 23

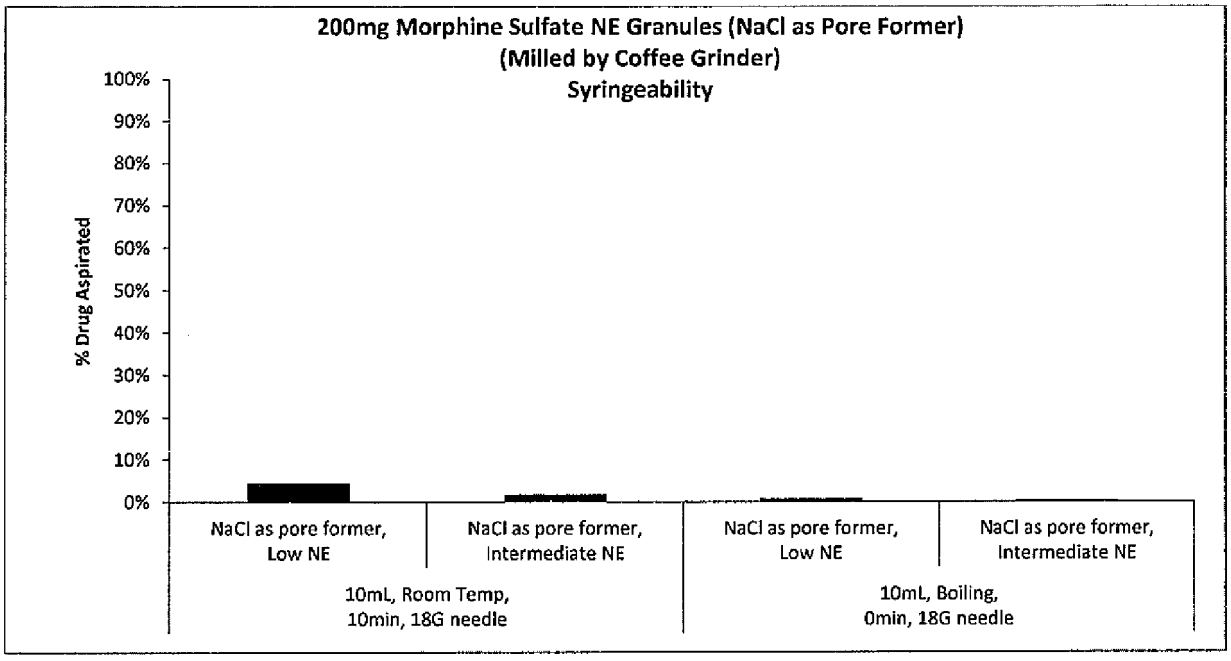


Figure 24A

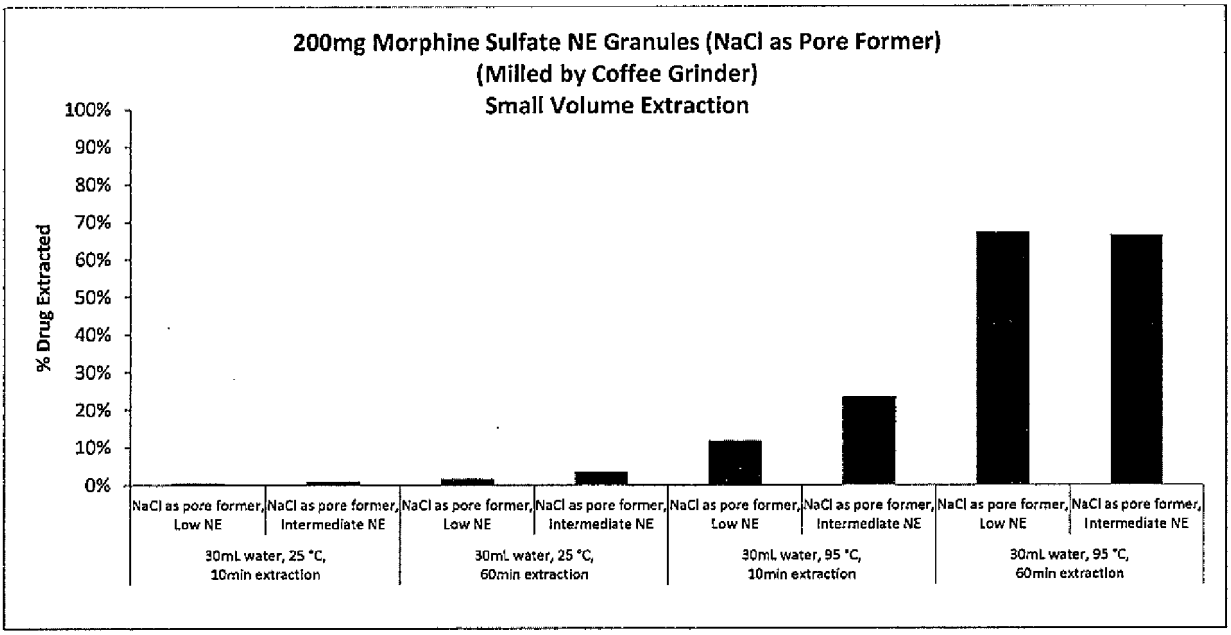


Figure 24B

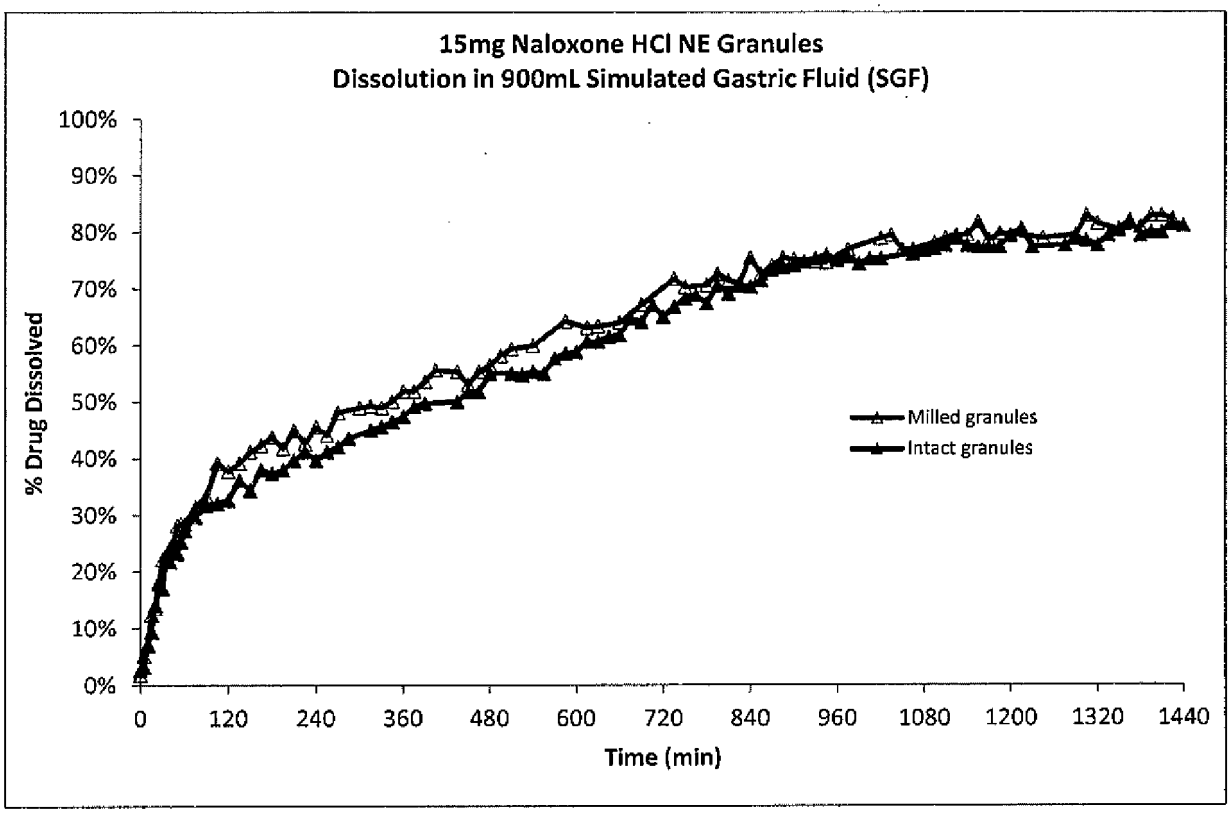

15mg Naloxone HCl NE Granules
Dissolution in 900mL Simulated Gastric Fluid (SGF)
% Drug Dissolved
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
120
240
360
480
600
720
840
960
1080
1200
1320
1440
Time (min)
Milled granules
Intact granules

Figure 25