FIGURE 1

EXPERIMETAL PROTOCOL N°1 (PERIOPERATIVE ADMINISTRATION)

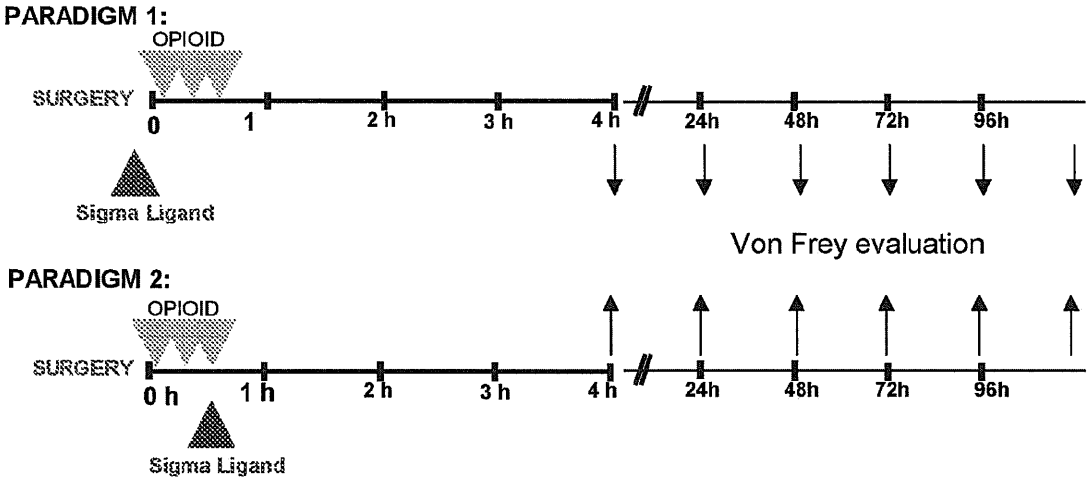


FIGURE 2

PARADIGM 1:

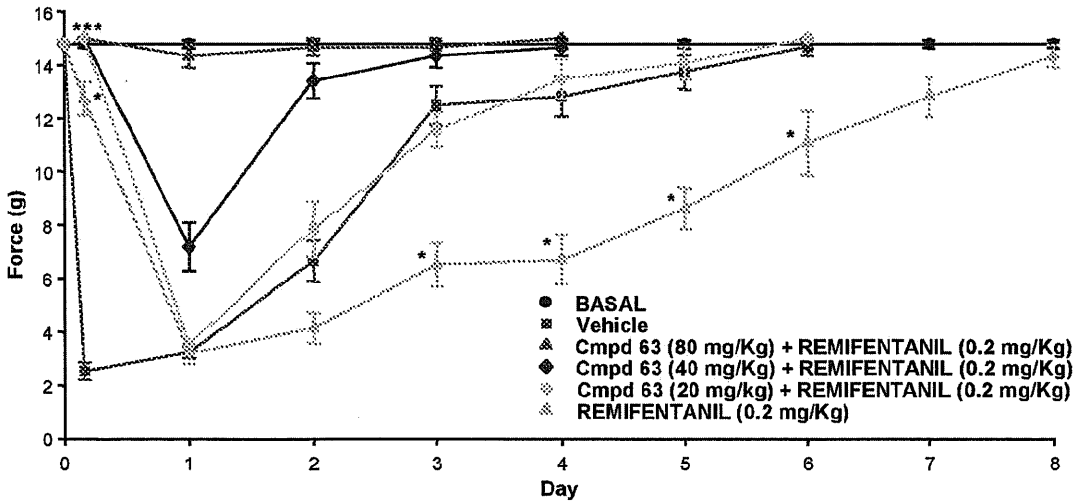


FIGURE 3

PARADIGM 2:

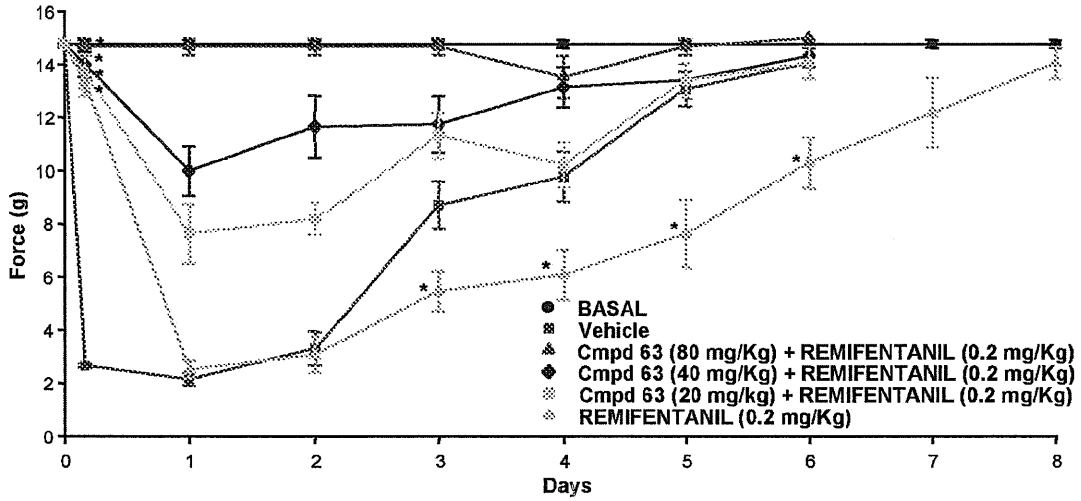


FIGURE 4

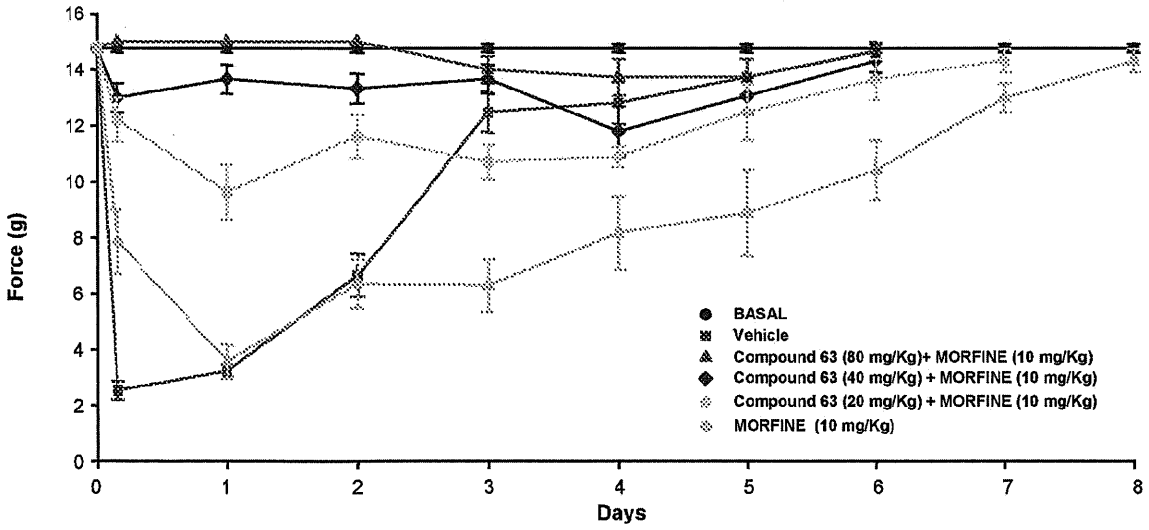


FIGURE 5

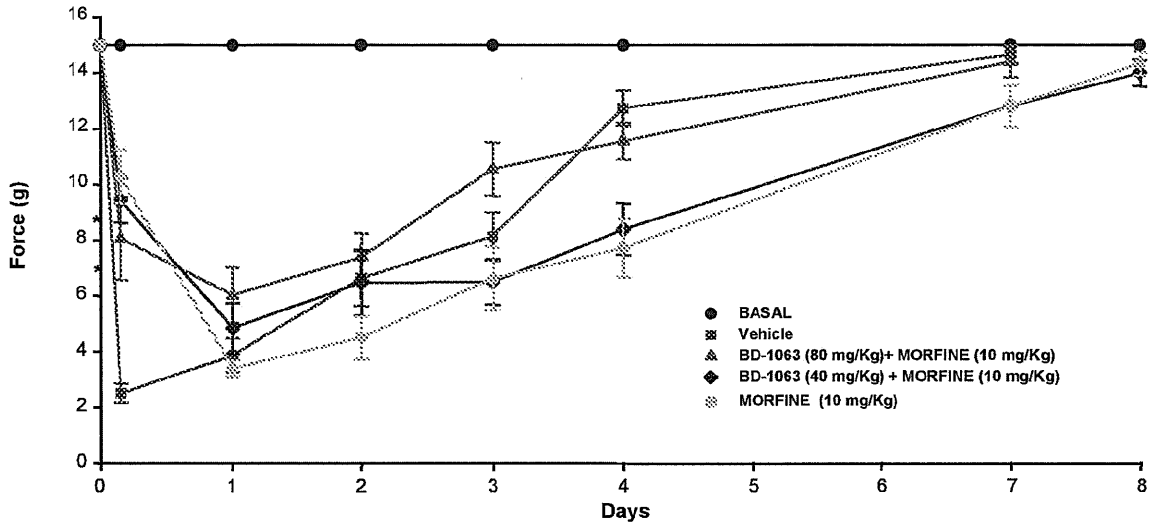


FIGURE 6

EXPERIMETAL PROTOCOL N°3 (COADMINISTRATION IN NAÏVE RATS)

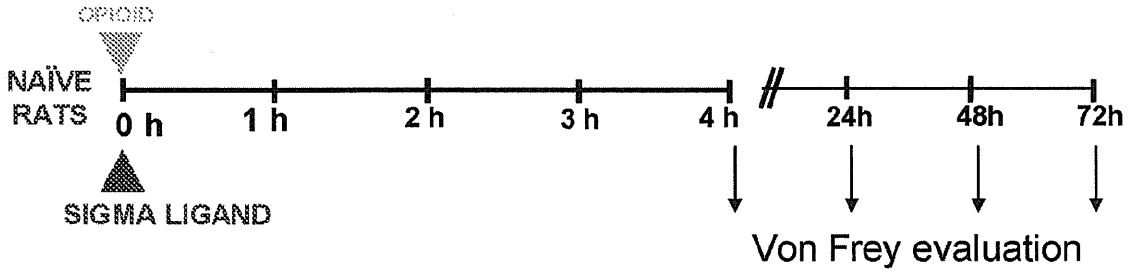


FIGURE 7

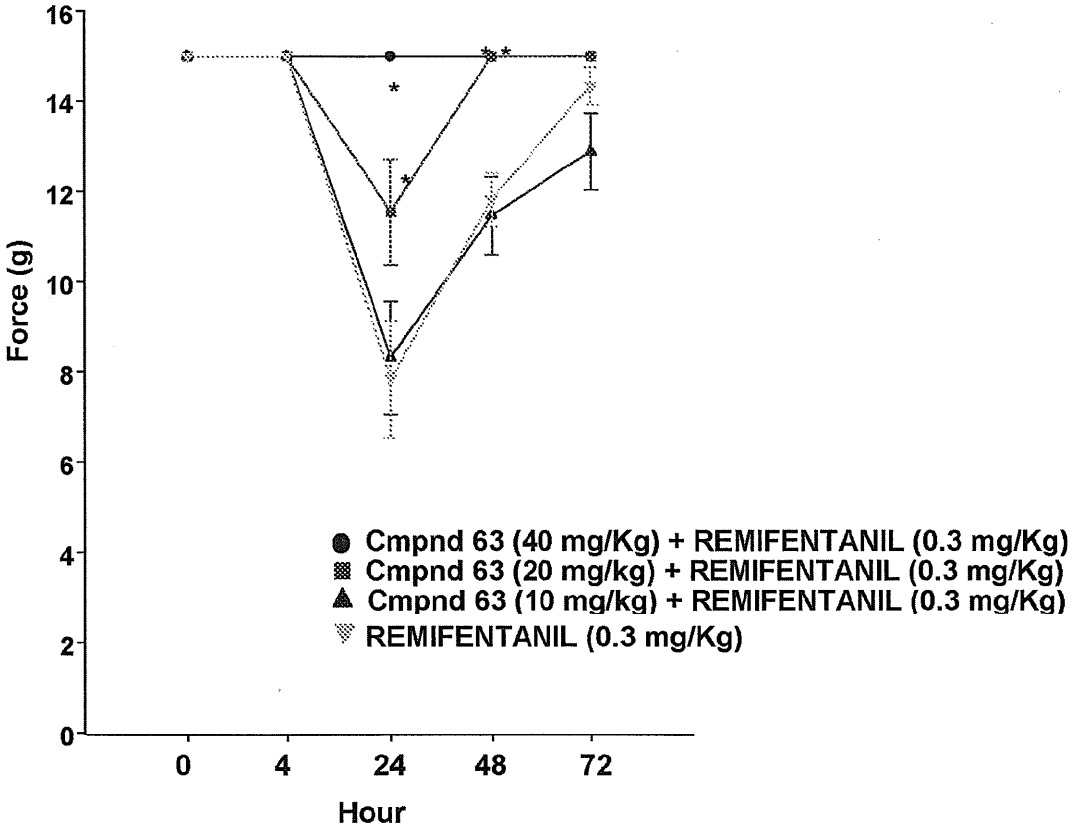

16
14
12
10
8
6
4
2
0
Force (g)
0
4
24
48
72
Hour
Cmpnd 63 (40 mg/Kg) + REMIFENTANIL (0.3 mg/Kg)
Cmpnd 63 (20 mg/kg) + REMIFENTANIL (0.3 mg/Kg)
Cmpnd 63 (10 mg/kg) + REMIFENTANIL (0.3 mg/Kg)
REMIFENTANIL (0.3 mg/Kg)

FIGURE 8

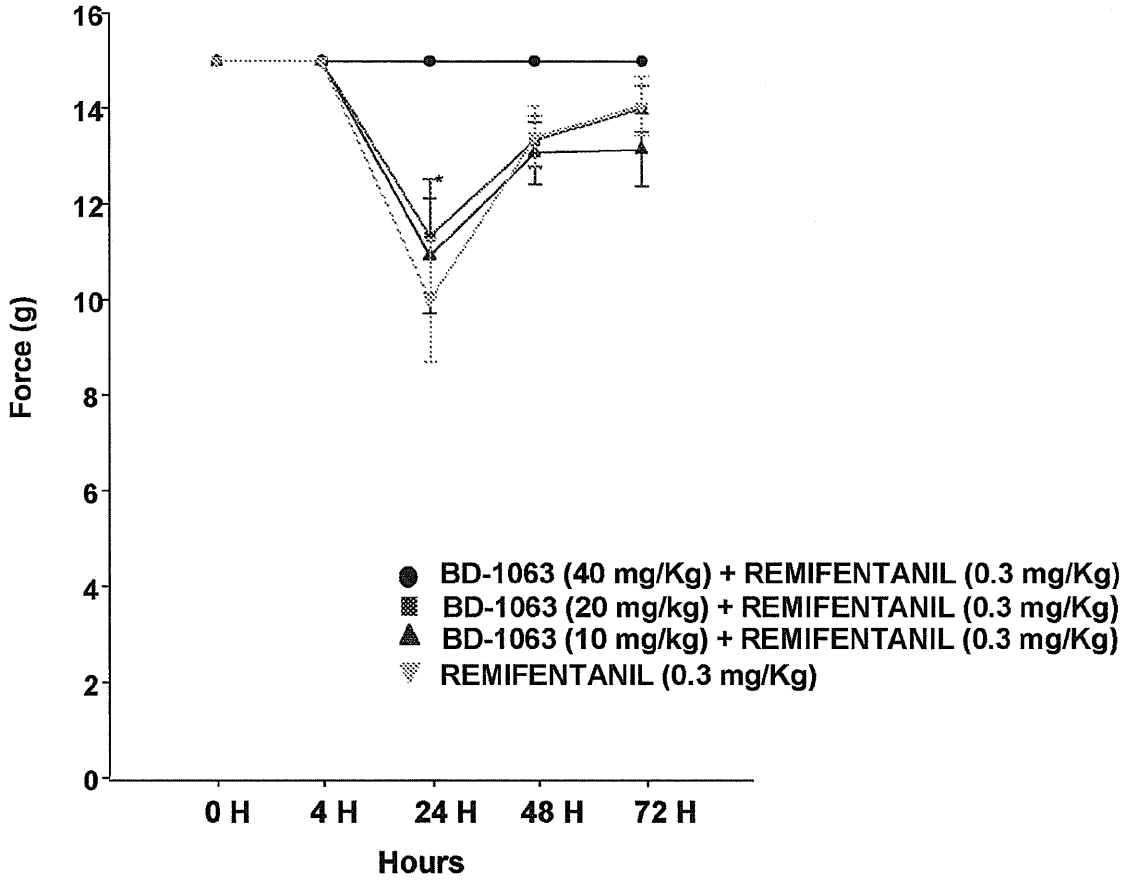

16
14
12
10
8
6
4
2
0
Force (g)
0 H
4 H
24 H
48 H
72 H
Hours
BD-1063 (40 mg/Kg) + REMIFENTANIL (0.3 mg/Kg)
BD-1063 (20 mg/kg) + REMIFENTANIL (0.3 mg/Kg)
BD-1063 (10 mg/kg) + REMIFENTANIL (0.3 mg/Kg)
REMIFENTANIL (0.3 mg/Kg)

FIGURE 9

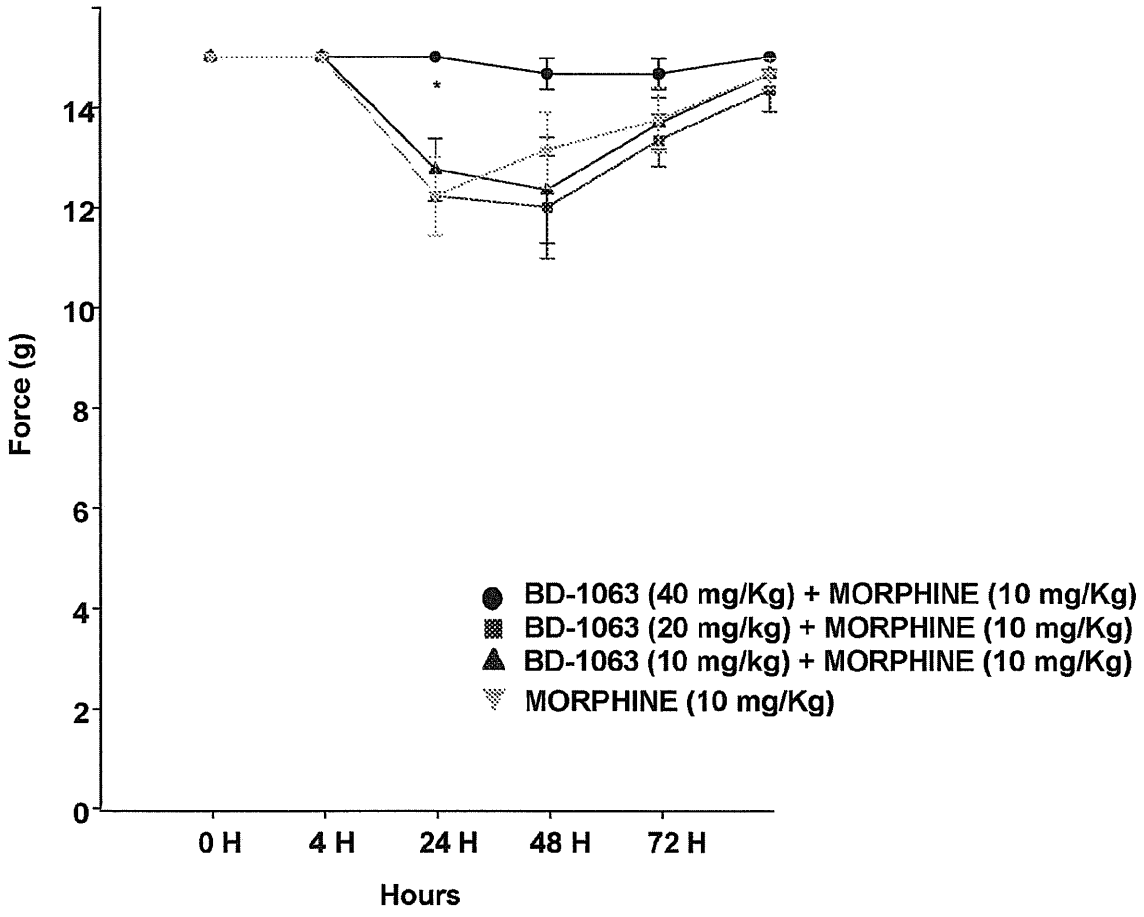

Force (g)
0
2
4
6
8
10
12
14
0 H
4 H
24 H
48 H
72 H
Hours
*
BD-1063 (40 mg/Kg) + MORPHINE (10 mg/Kg)
BD-1063 (20 mg/kg) + MORPHINE (10 mg/Kg)
BD-1063 (10 mg/kg) + MORPHINE (10 mg/Kg)
MORPHINE (10 mg/Kg)

FIGURE 10

PARADIGM 2:

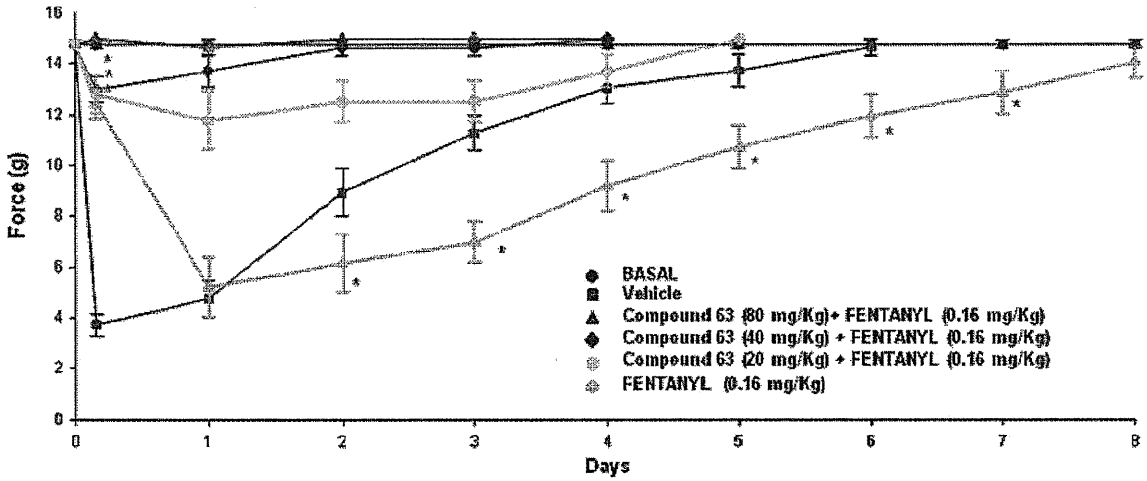


FIGURE 11

PARADIGM 2:

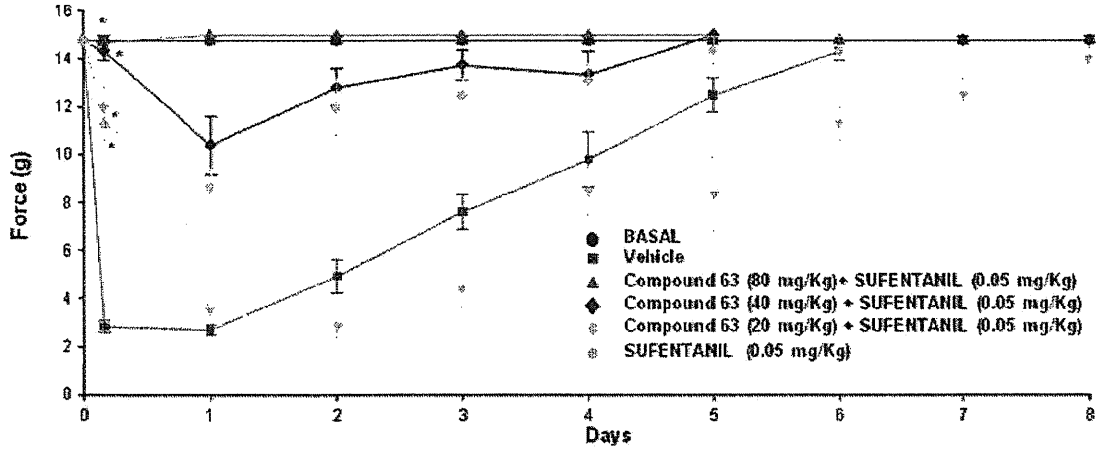


FIGURE 12

EXPERIMENTAL PROTOCOL N°2 (OIH precipitated by naloxone)

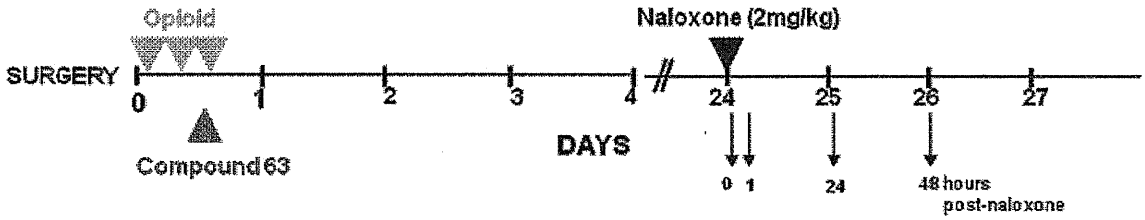


FIGURE 13

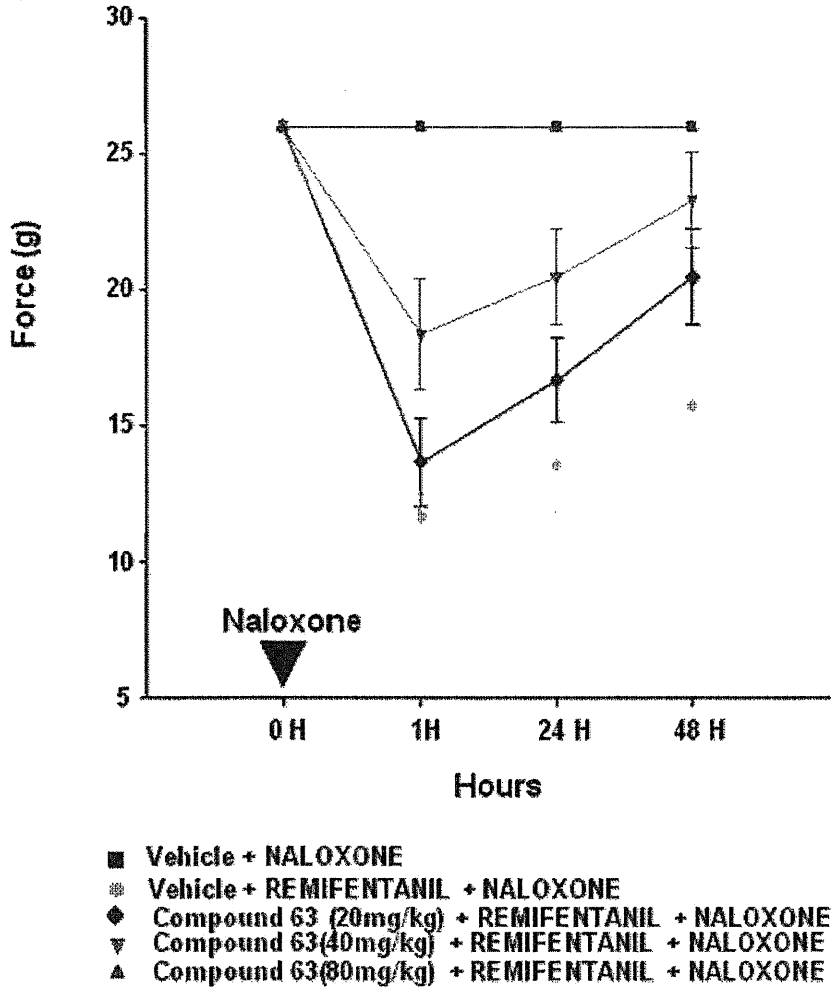


FIGURE 14

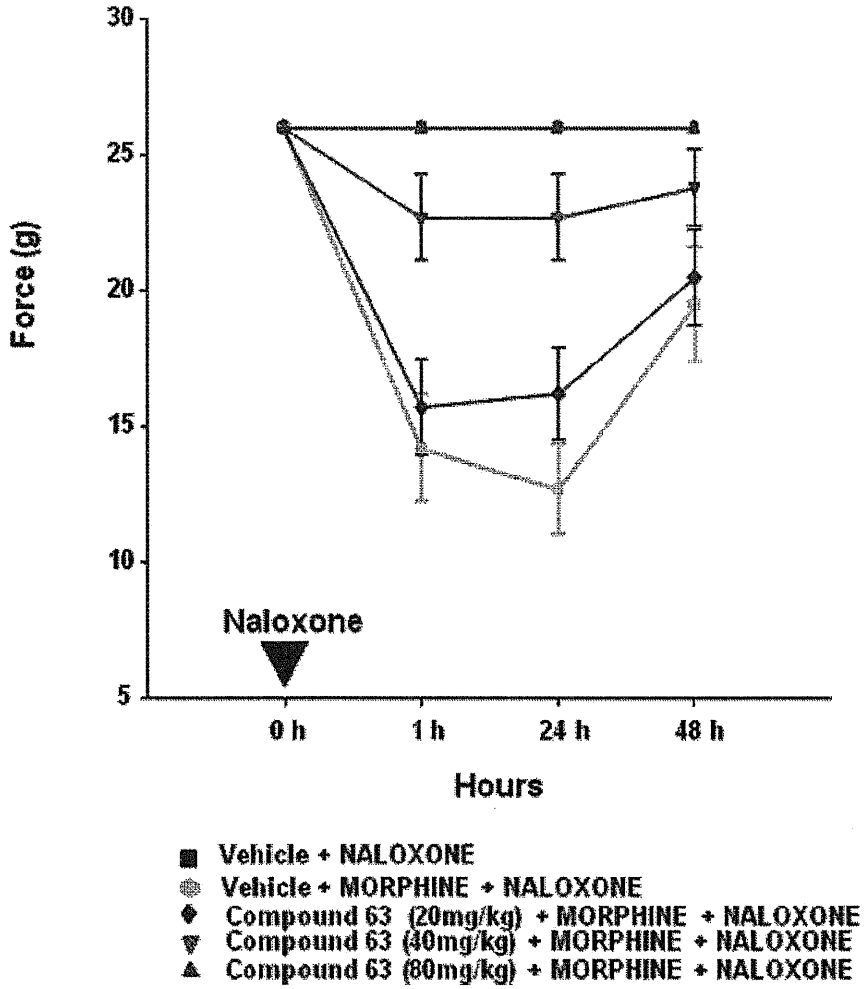

30
25
20
15
10
5
Force (g)
Naloxone
0 h
1 h
24 h
48 h
Hours
Vehicle + NALOXONE
Vehicle + MORPHINE + NALOXONE
Compound 63 (20mg/kg) + MORPHINE + NALOXONE
Compound 63 (40mg/kg) + MORPHINE + NALOXONE
Compound 63 (80mg/kg) + MORPHINE + NALOXONE

FIGURE 15

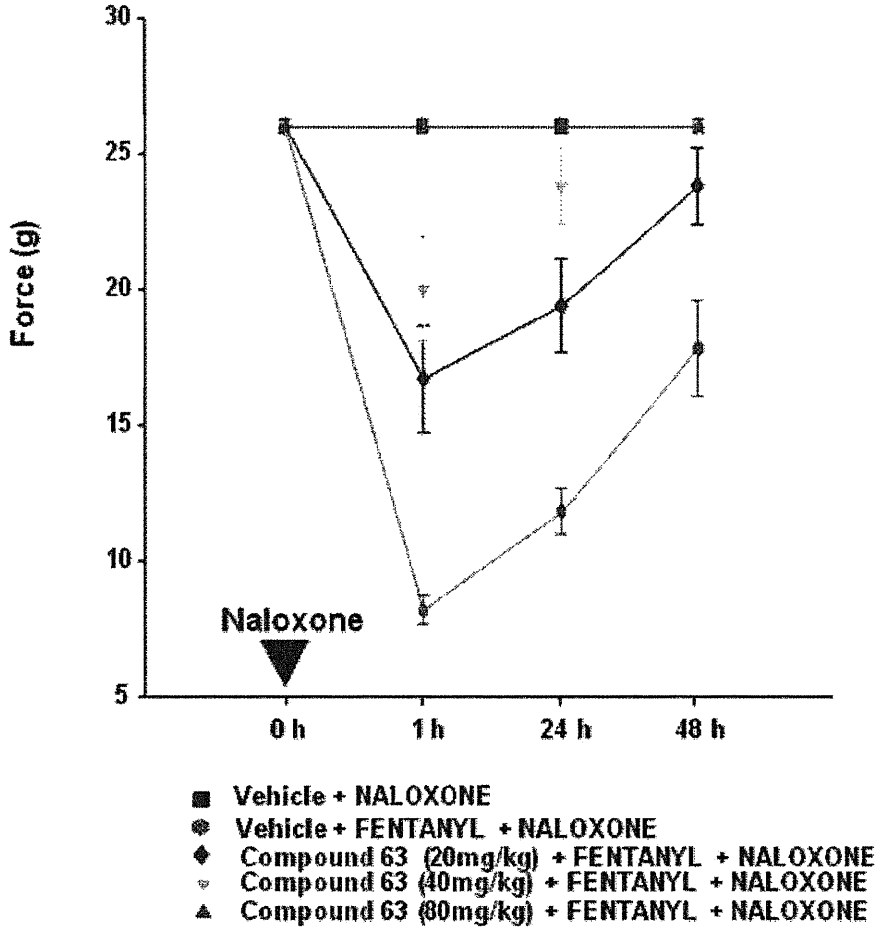
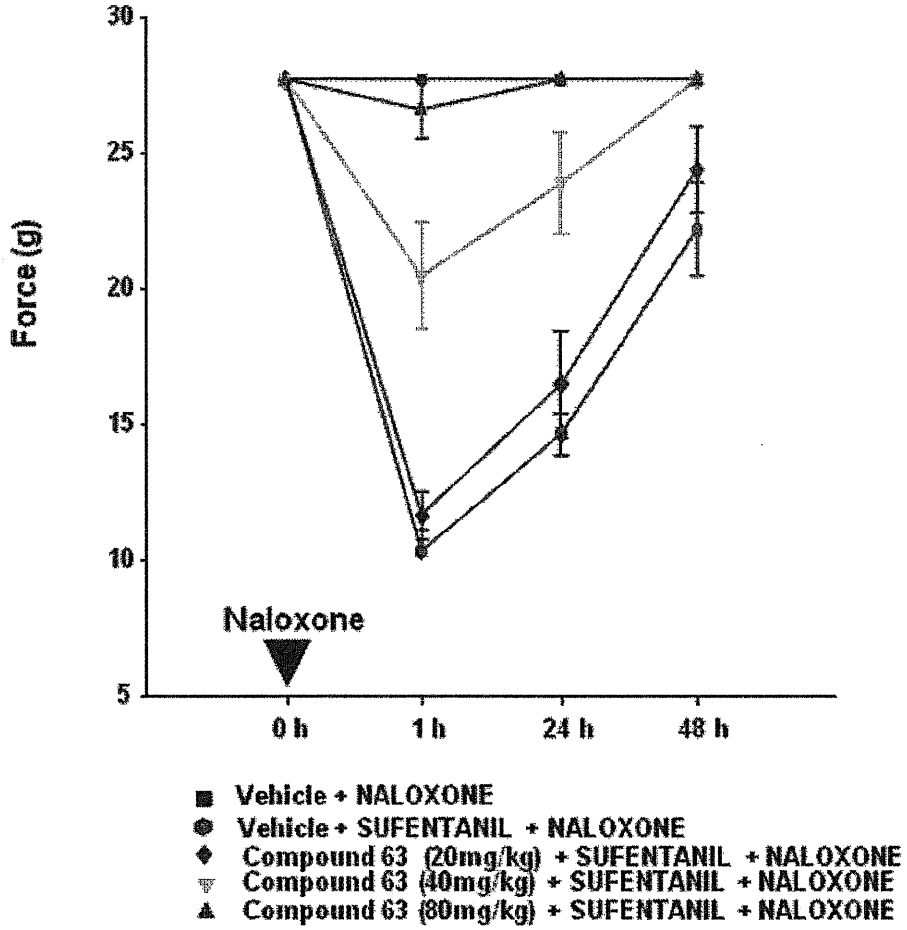

30
25
20
15
10
5
Force (g)
Naloxone
0 h
1 h
24 h
48 h
Vehicle + NALOXONE
Vehicle + FENTANYL + NALOXONE
Compound 63 (20mg/kg) + FENTANYL + NALOXONE
Compound 63 (40mg/kg) + FENTANYL + NALOXONE
Compound 63 (80mg/kg) + FENTANYL + NALOXONE

FIGURE 16


30
25
20
15
10
5
Force (g)
Naloxone
0 h
1 h
24 h
48 h
Vehicle + NALOXONE
Vehicle + SUFENTANIL + NALOXONE
Compound 63 (20mg/kg) + SUFENTANIL + NALOXONE
Compound 63 (40mg/kg) + SUFENTANIL + NALOXONE
Compound 63 (80mg/kg) + SUFENTANIL + NALOXONE