FIGURE 1

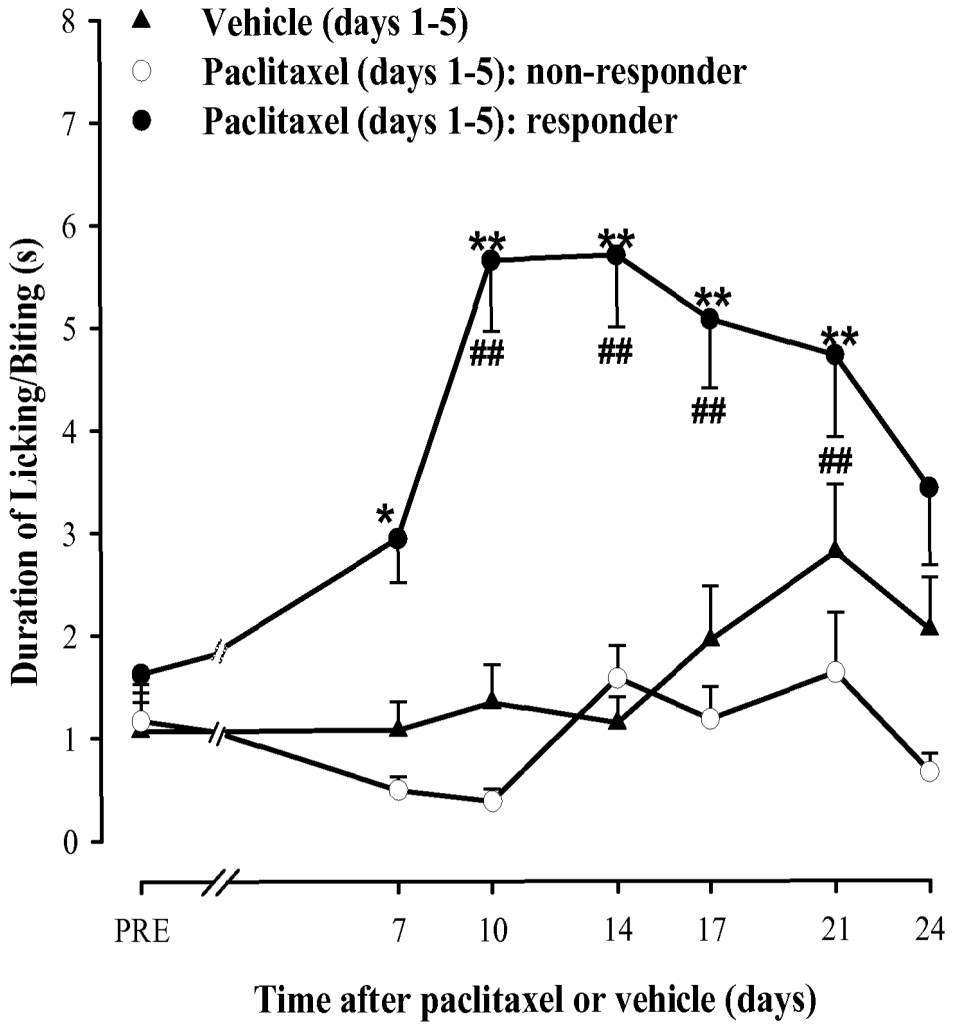

Vehicle (days 1-5)
Paclitaxel (days 1-5): non-responder
Paclitaxel (days 1-5): responder
Duration of Licking/Biting (s)
0
1
2
3
4
5
6
7
8
*
**
##
PRE
7
10
14
17
21
24
Time after paclitaxel or vehicle (days)

FIGURE 2

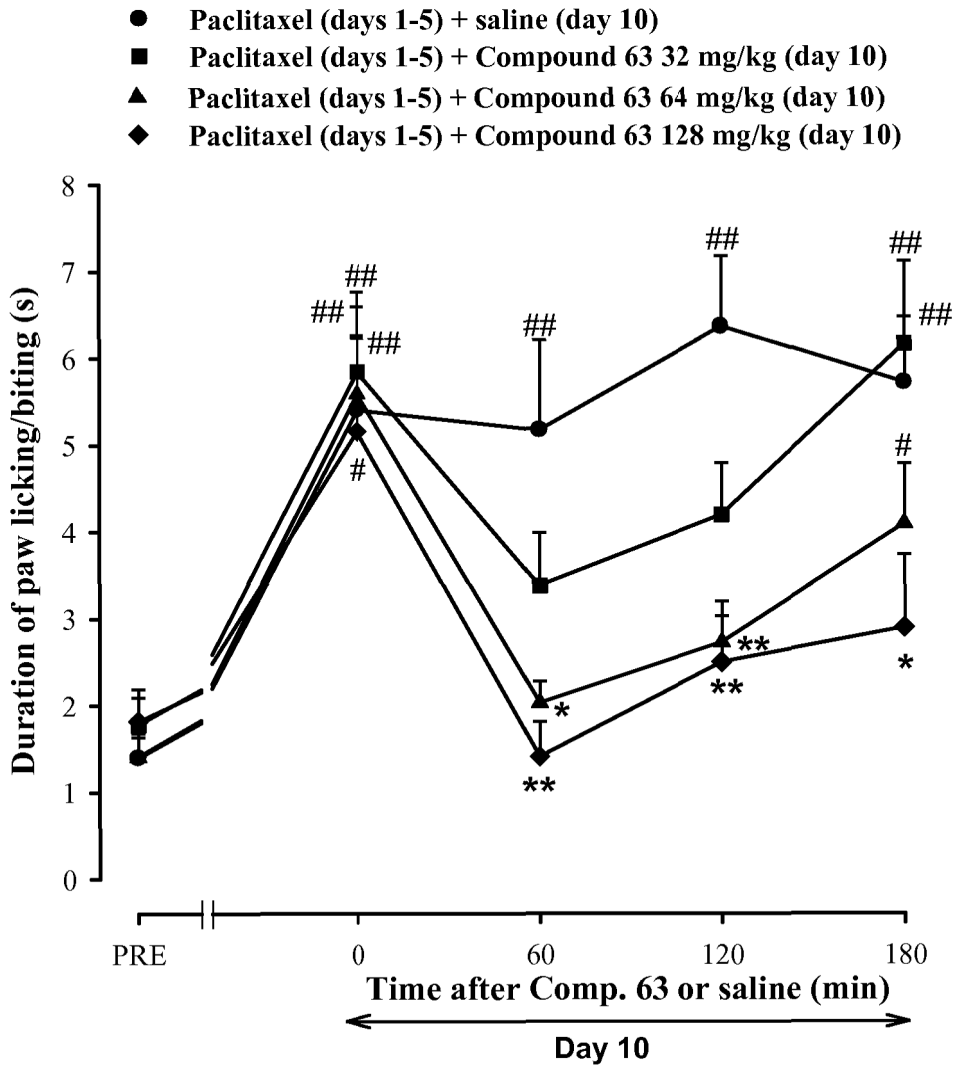

Paclitaxel (days 1-5) + saline (day 10)
Paclitaxel (days 1-5) + Compound 63 32 mg/kg (day 10)
Paclitaxel (days 1-5) + Compound 63 64 mg/kg (day 10)
Paclitaxel (days 1-5) + Compound 63 128 mg/kg (day 10)
Duration of paw licking/biting (s)
0
1
2
3
4
5
6
7
8
PRE
0
60
120
180
Time after Comp. 63 or saline (min)
Day 10

FIGURE 3

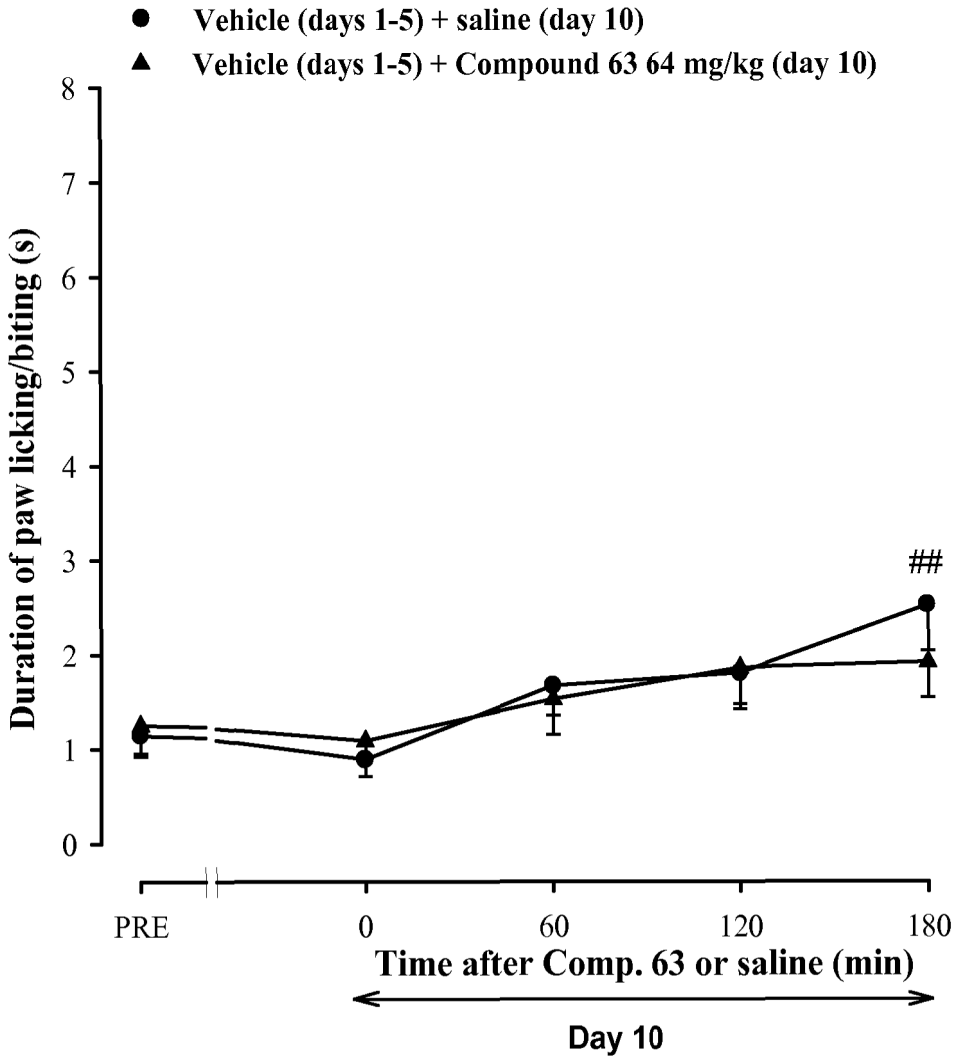

Vehicle (days 1-5) + saline (day 10)
Vehicle (days 1-5) + Compound 63 64 mg/kg (day 10)
Duration of paw licking/biting (s)
0
1
2
3
4
5
6
7
8
##
PRE
0
60
120
180
Time after Comp. 63 or saline (min)
Day 10

FIGURE 4

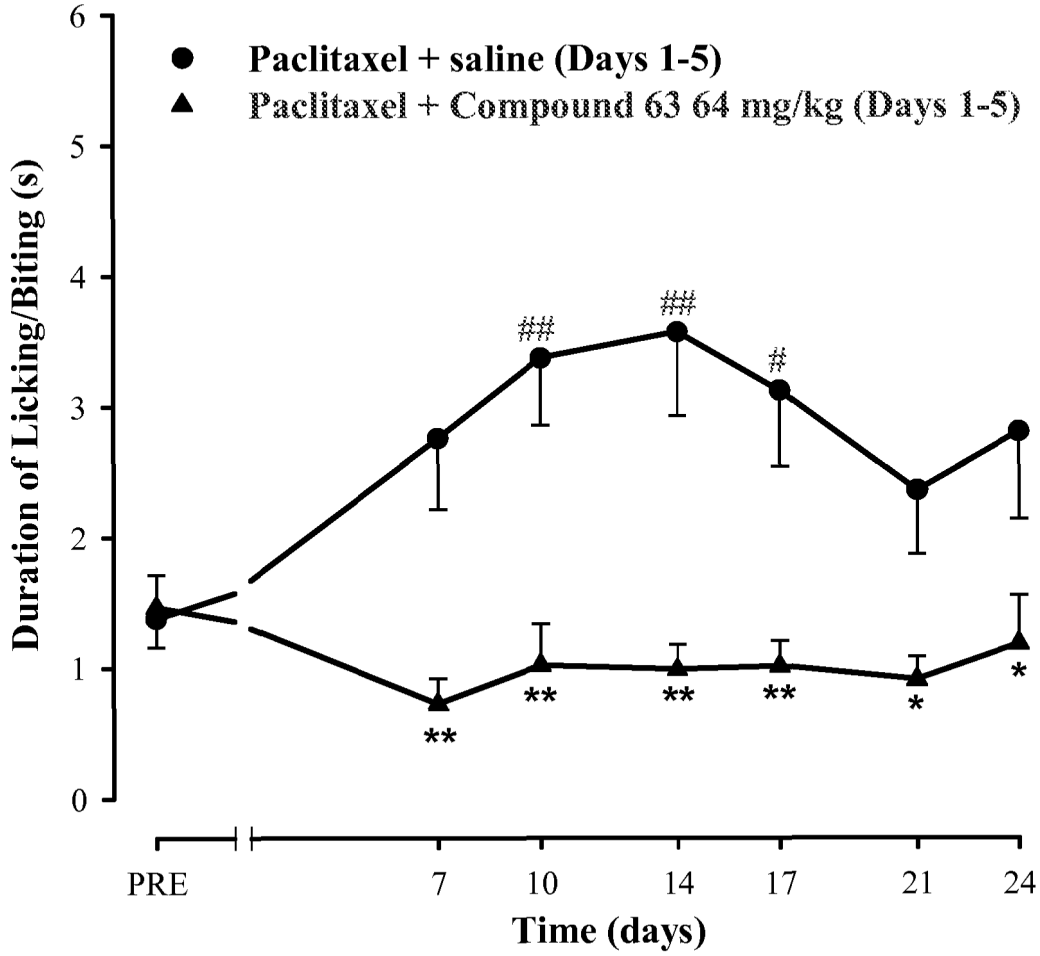

Paclitaxel + saline (Days 1-5)
Paclitaxel + Compound 63 64 mg/kg (Days 1-5)
Duration of Licking/Biting (s)
0
1
2
3
4
5
6
##
##
#
**
**
**
**
*
*
PRE
7
10
14
17
21
24
Time (days)

FIGURE 5

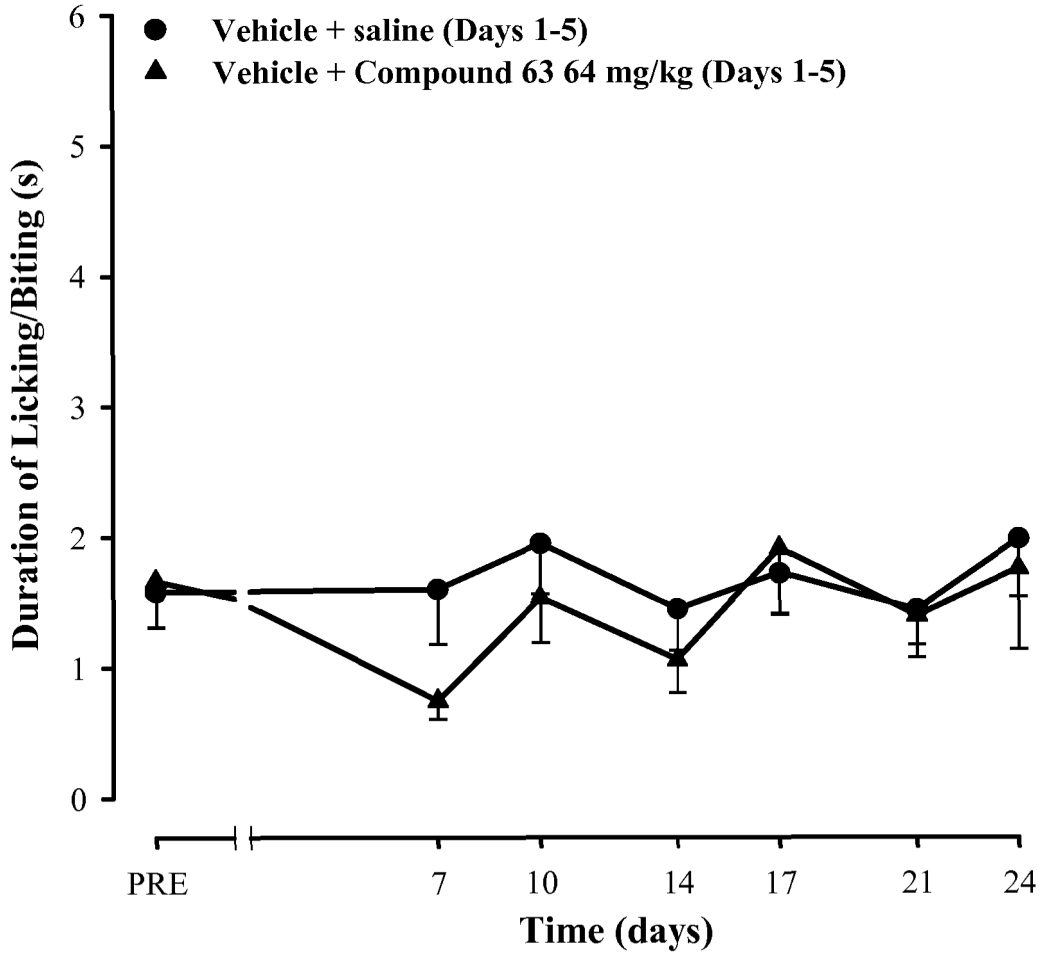

Vehicle + saline (Days 1-5)
Vehicle + Compound 63 64 mg/kg (Days 1-5)
Duration of Licking/Biting (s)
0
1
2
3
4
5
6
PRE
7
10
14
17
21
24
Time (days)

FIGURE 6

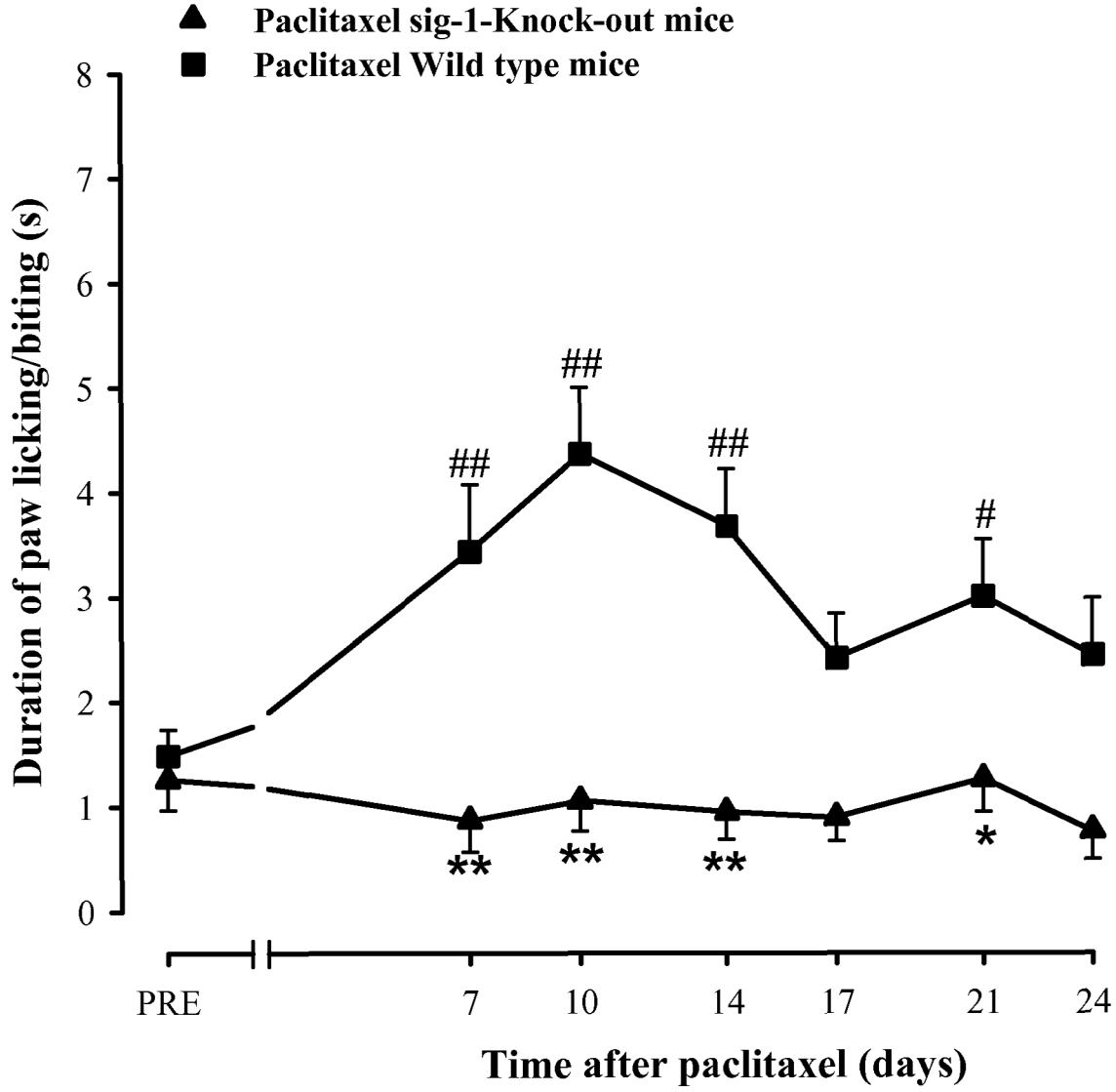

Paclitaxel sig-1-Knock-out mice
Paclitaxel Wild type mice
Duration of paw licking/biting (s)
0
1
2
3
4
5
6
7
8
##
##
##
#
**
**
**
*
PRE
7
10
14
17
21
24
Time after paclitaxel (days)

FIGURE 7

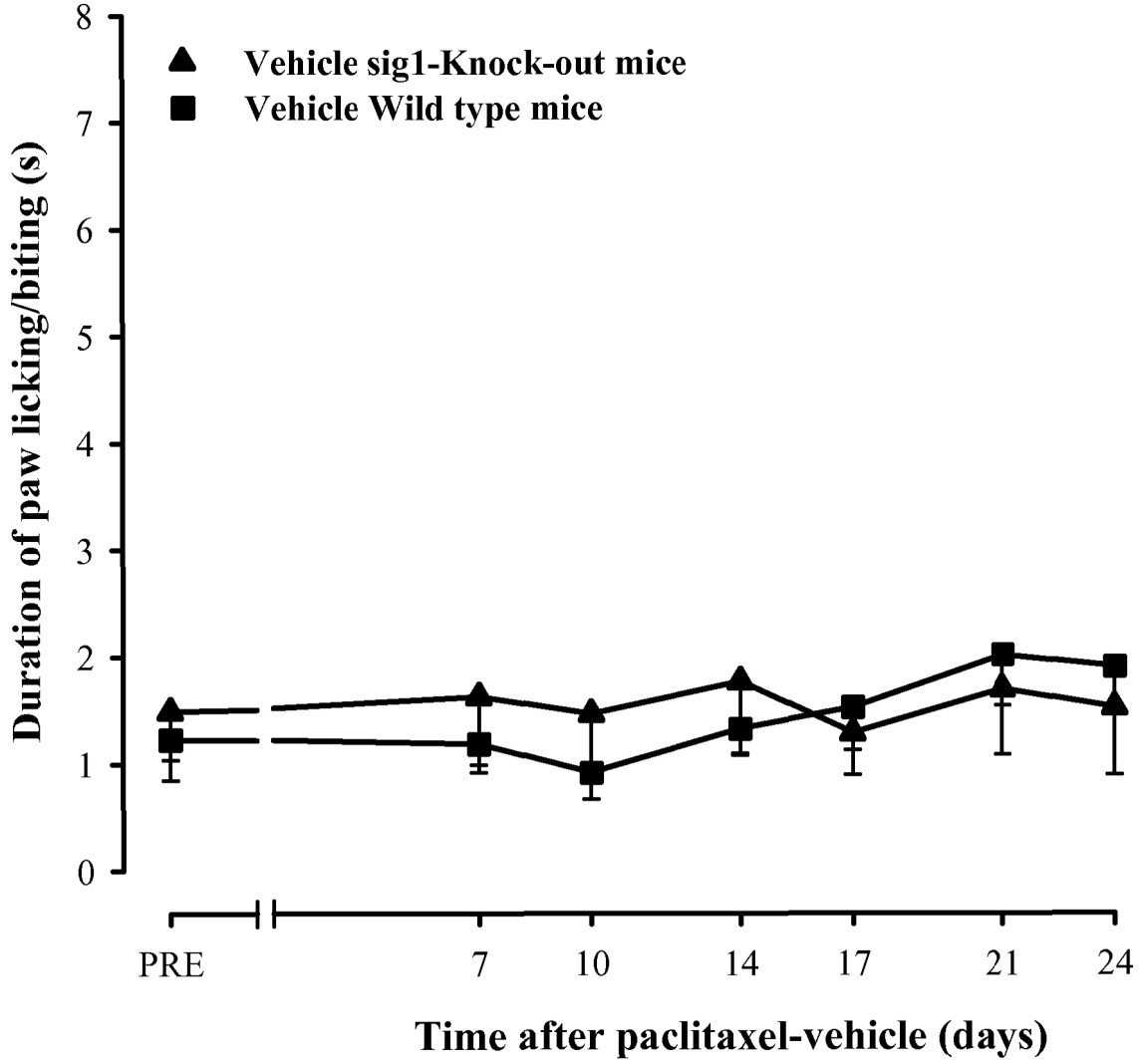

Vehicle sig1-Knock-out mice
Vehicle Wild type mice
Duration of paw licking/biting (s)
0
1
2
3
4
5
6
7
8
PRE
7
10
14
17
21
24
Time after paclitaxel-vehicle (days)

FIGURE 8

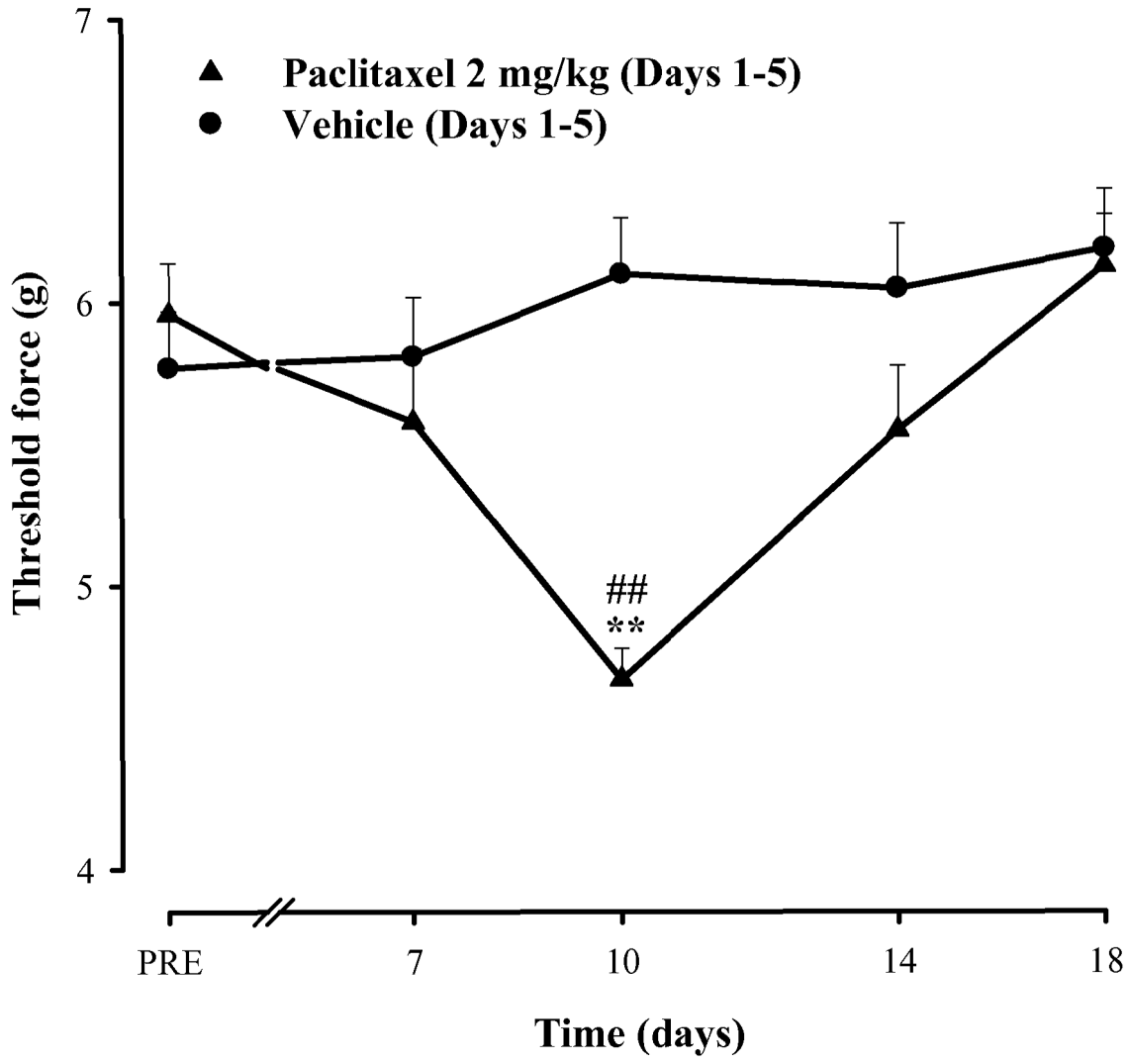

Paclitaxel 2 mg/kg (Days 1-5)
Vehicle (Days 1-5)
Threshold force (g)
7
6
5
4
##
**
PRE
7
10
14
18
Time (days)

FIGURE 9

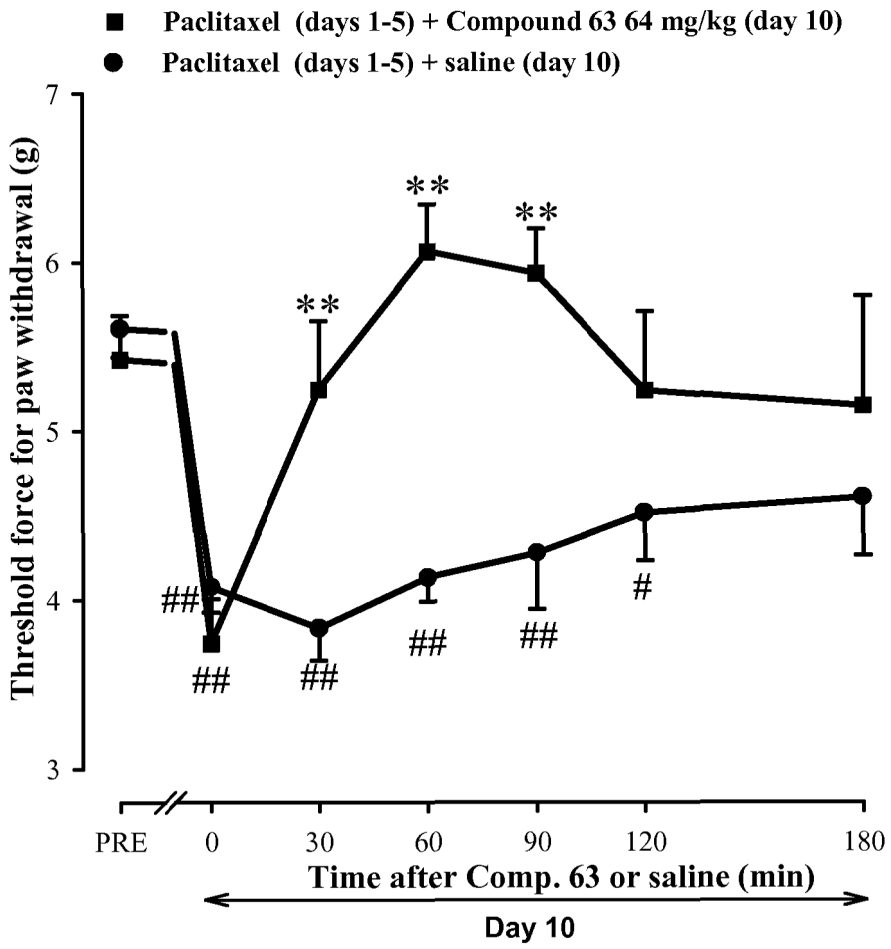

Paclitaxel (days 1-5) + Compound 63 64 mg/kg (day 10)
Paclitaxel (days 1-5) + saline (day 10)
Threshold force for paw withdrawal (g)
7
6
5
4
3
**
**
**
##
##
##
##
#
PRE
0
30
60
90
120
180
Time after Comp. 63 or saline (min)
Day 10

FIGURE 10

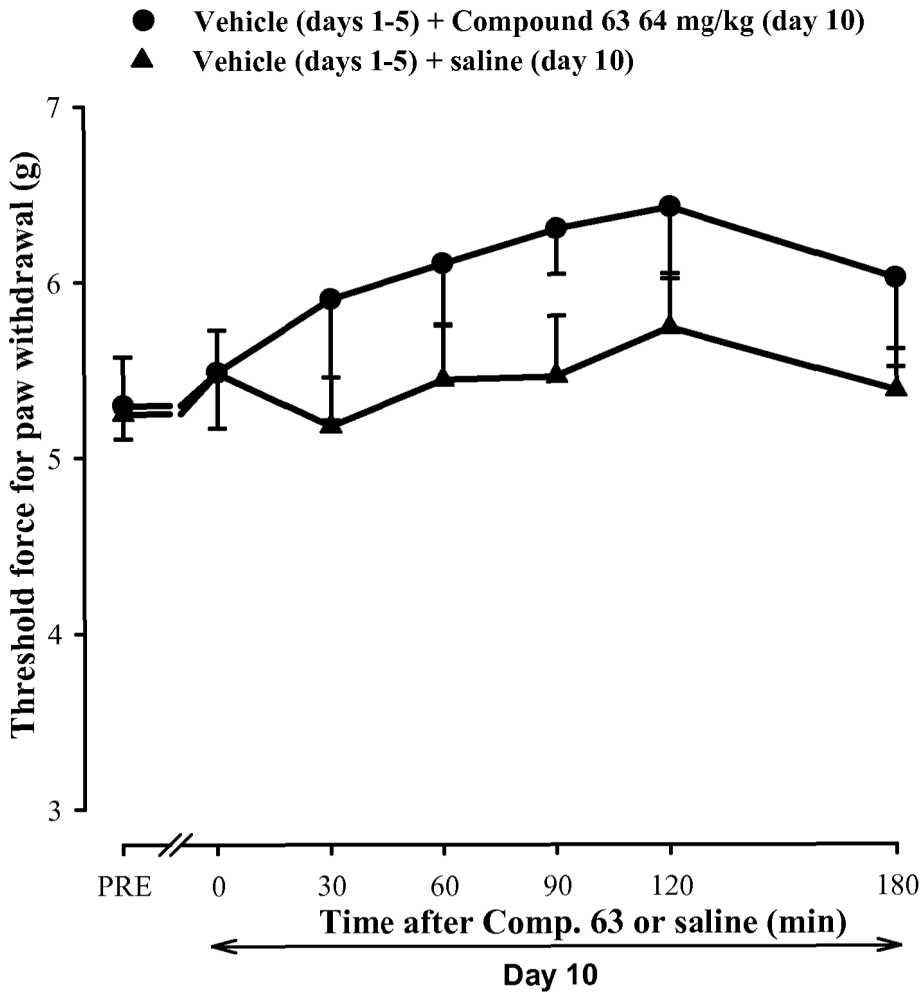

Vehicle (days 1-5) + Compound 63 64 mg/kg (day 10)
Vehicle (days 1-5) + saline (day 10)
Threshold force for paw withdrawal (g)
7
6
5
4
3
PRE
0
30
60
90
120
180
Time after Comp. 63 or saline (min)
Day 10

FIGURE 11

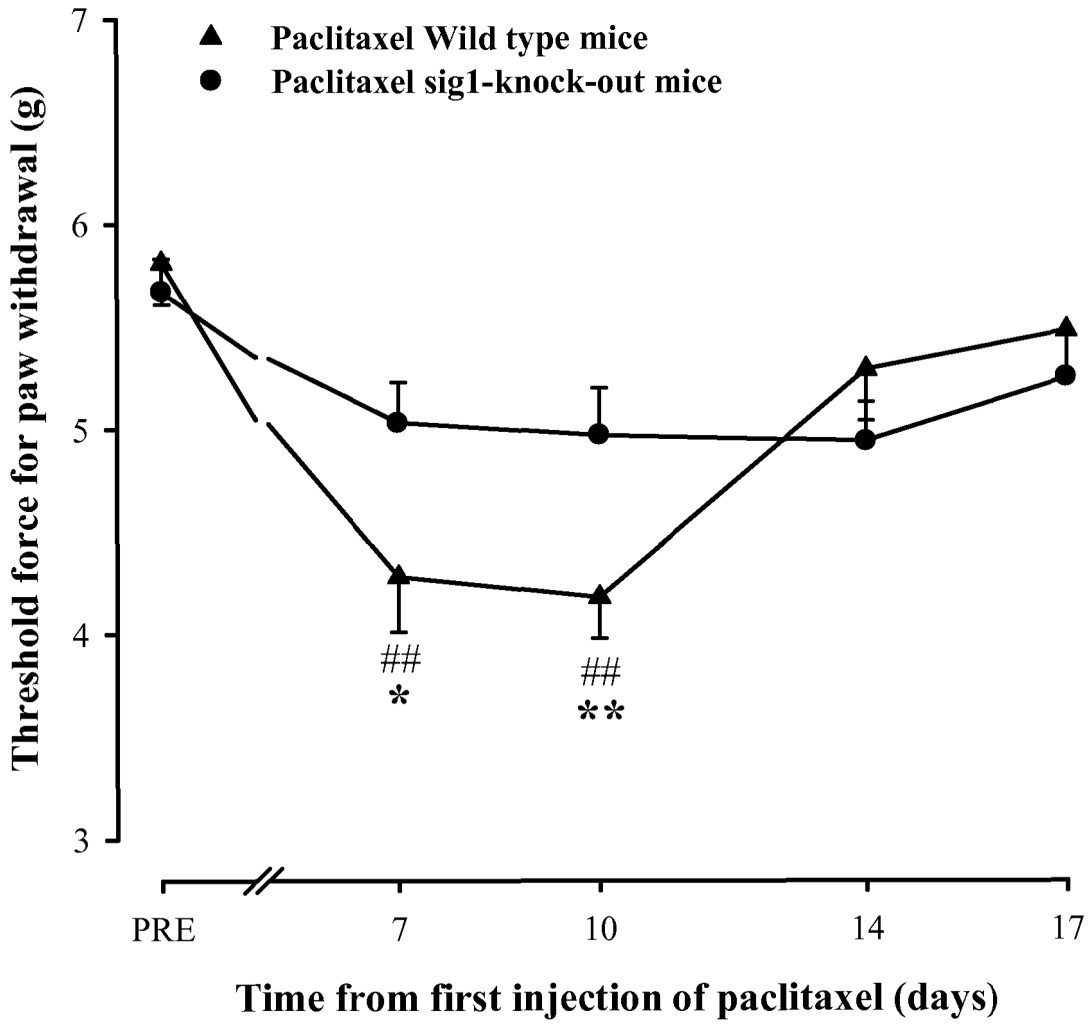

Paclitaxel Wild type mice
Paclitaxel sig1-knock-out mice
Threshold force for paw withdrawal (g)
7
6
5
4
3
##
*
##
**
PRE
7
10
14
17
Time from first injection of paclitaxel (days)

FIGURE 12

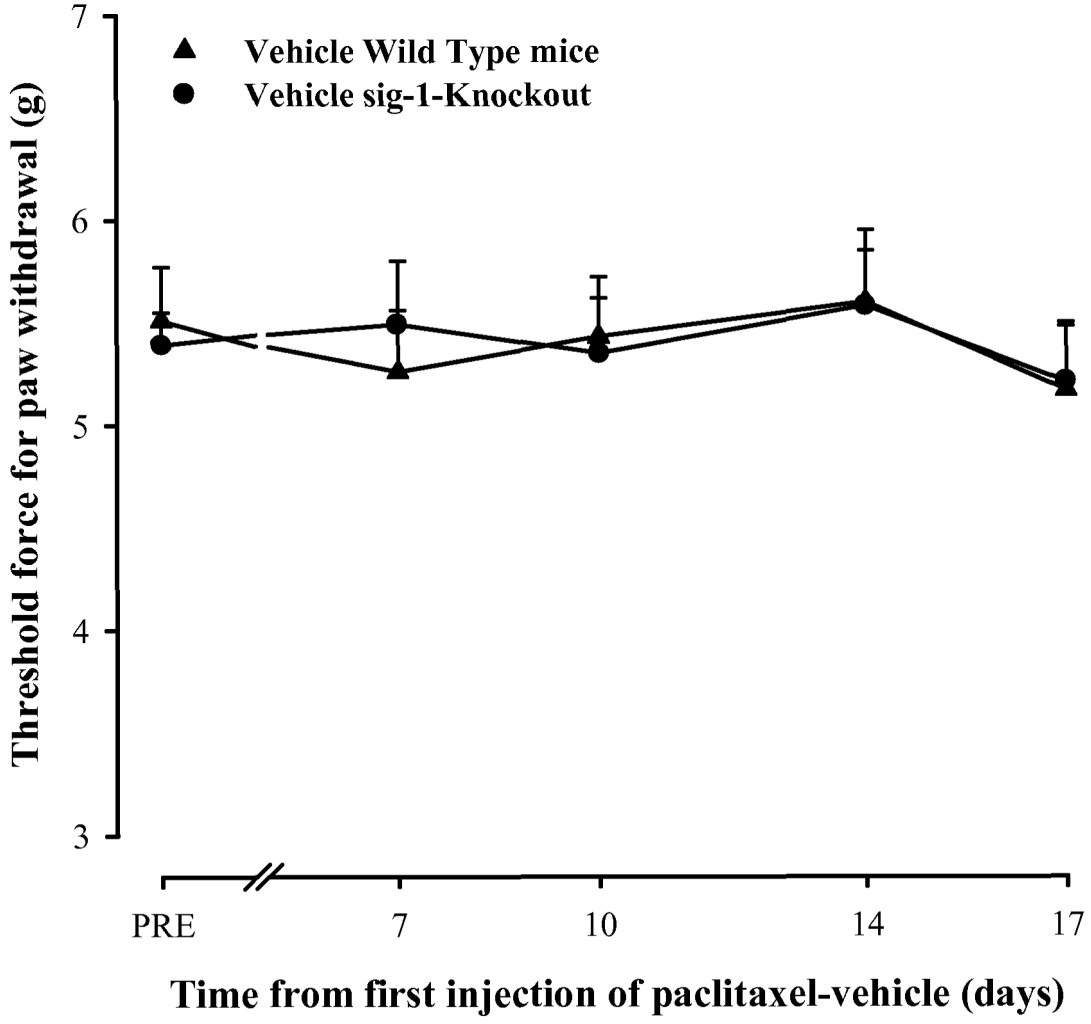

Vehicle Wild Type mice
Vehicle sig-1-Knockout
Threshold force for paw withdrawal (g)
7
6
5
4
3
PRE
7
10
14
17
Time from first injection of paclitaxel-vehicle (days)

FIGURE 13

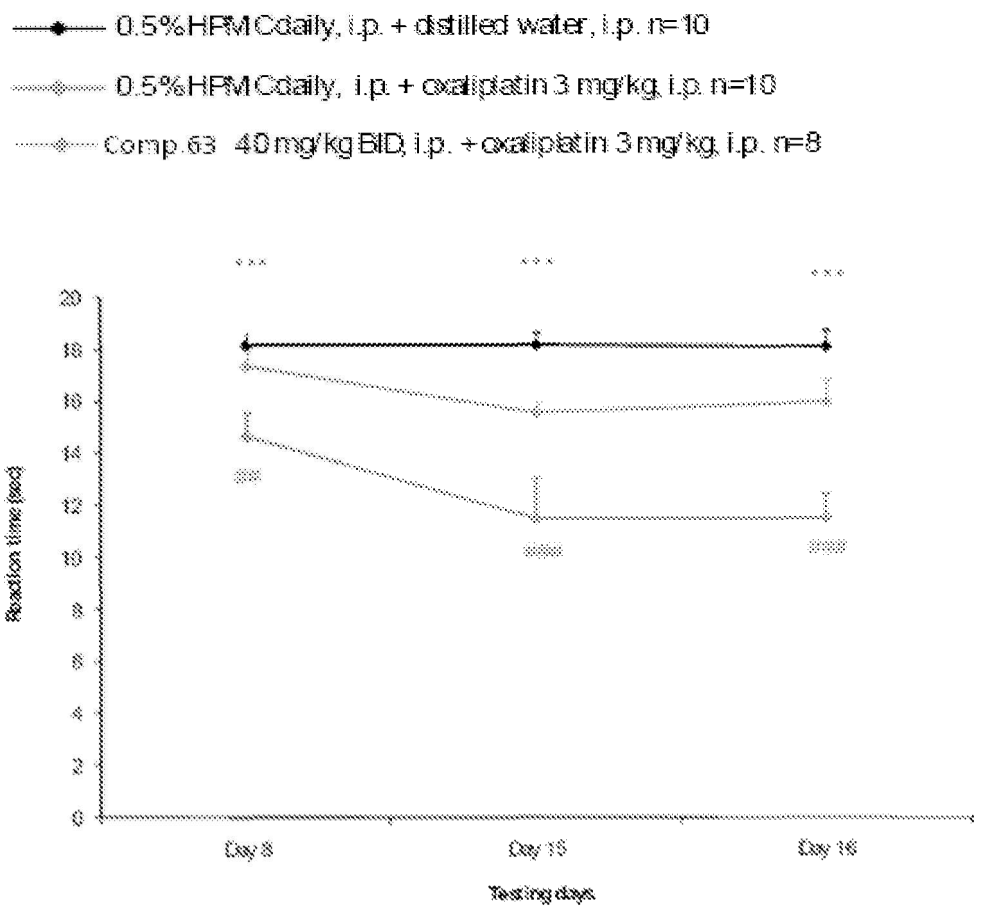

0.5%HPMC daily, i.p. + distilled water, i.p. n=10
0.5%HPMC daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp.63 40 mg/kg BID, i.p. + oxaliplatin 3 mg/kg, i.p. n=8
Reaction time (sec)
0
2
4
6
8
10
12
14
16
18
20
Day 8
Day 15
Day 16
Testing days

FIGURE 14

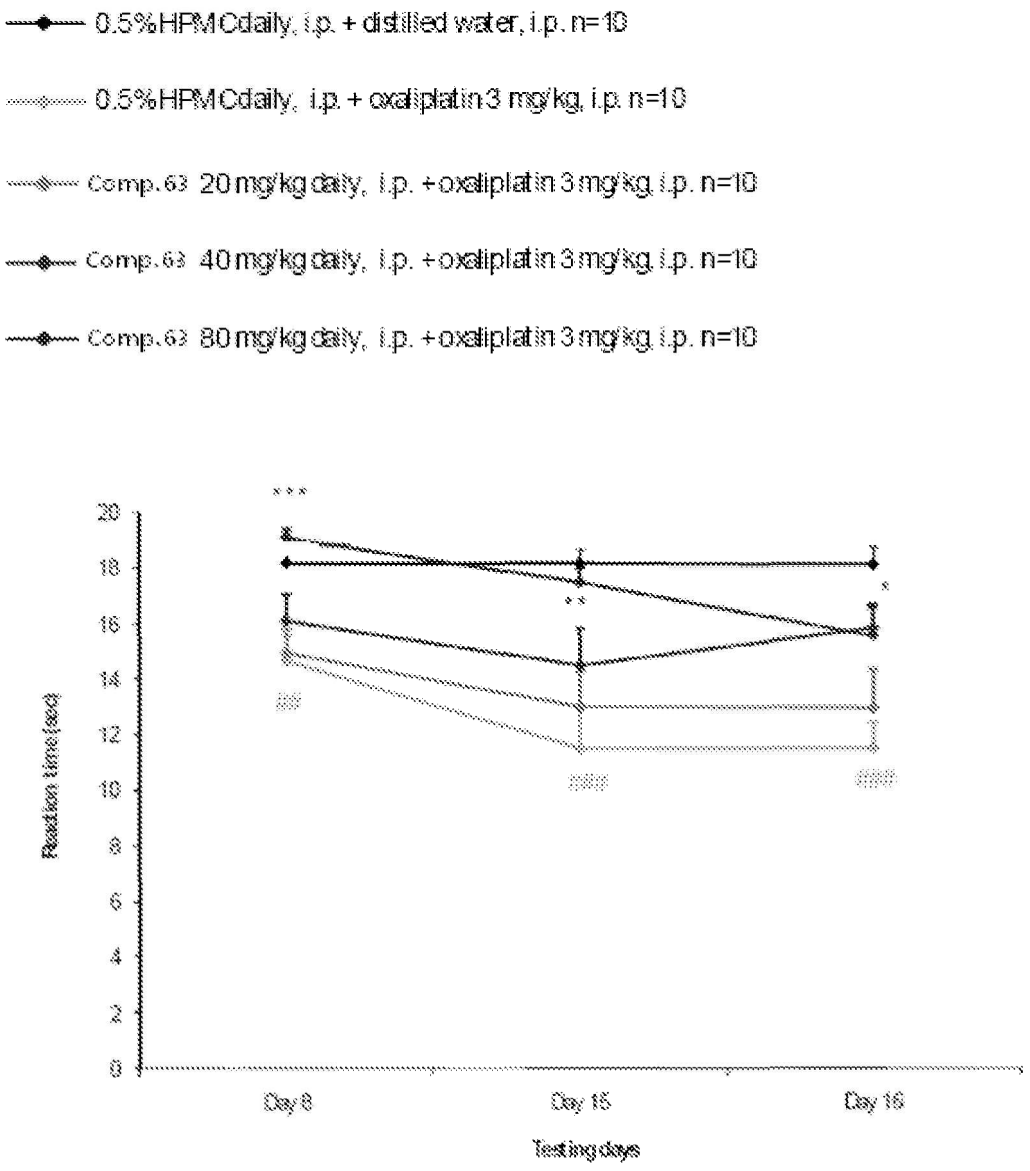

0.5% HPMC daily, i.p. + distilled water, i.p. n=10
0.5% HPMC daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp. 63 20 mg/kg daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp. 63 40 mg/kg daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp. 63 80 mg/kg daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Reaction time (sec)
20
18
16
14
12
10
8
6
4
2
0
Day 8
Day 15
Day 16
Testing days

FIGURE 15

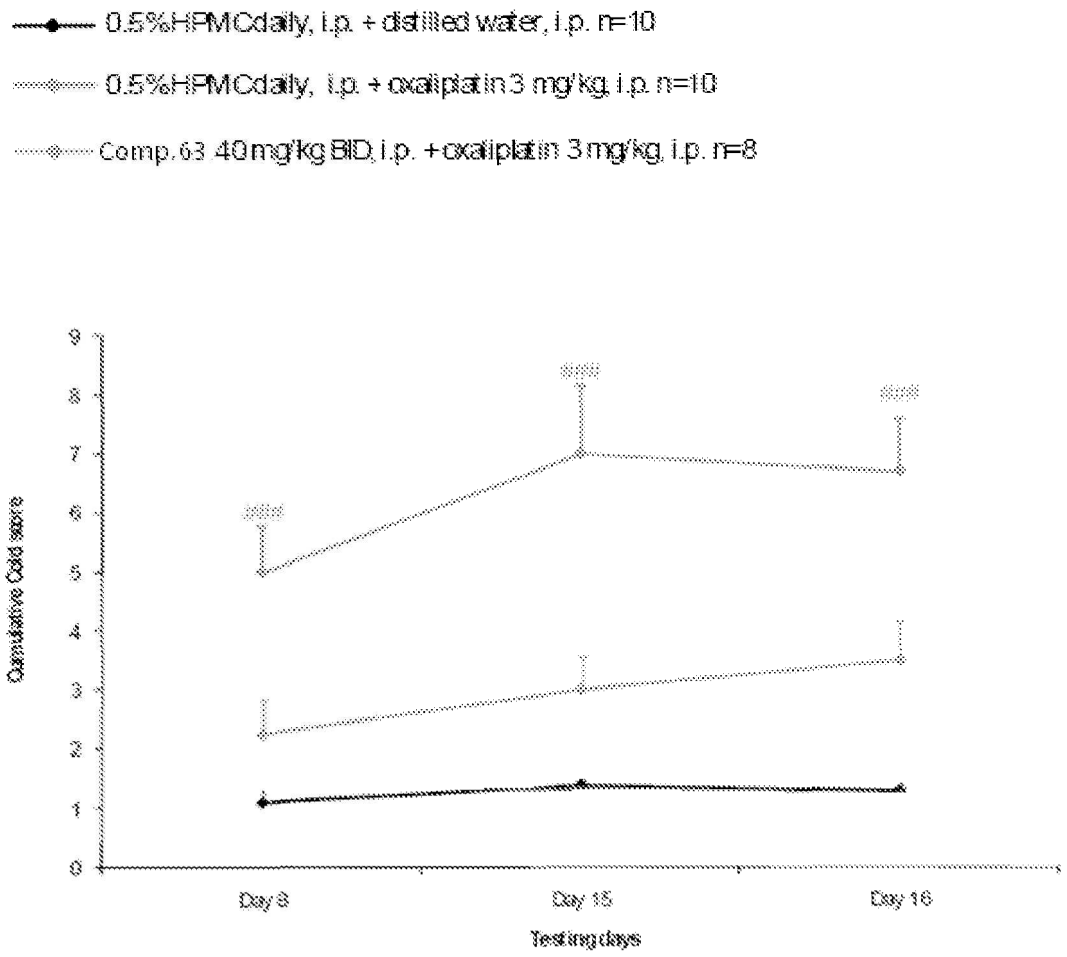

0.5%HPMCdaily, i.p. + distilled water, i.p. n=10
0.5%HPMCdaily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp.63 40mg/kg BID, i.p. +oxaliplatin 3mg/kg, i.p. n=8
Cumulative Cold score
0
1
2
3
4
5
6
7
8
9
Day 8
Day 15
Day 16
Testing days

FIGURE 16

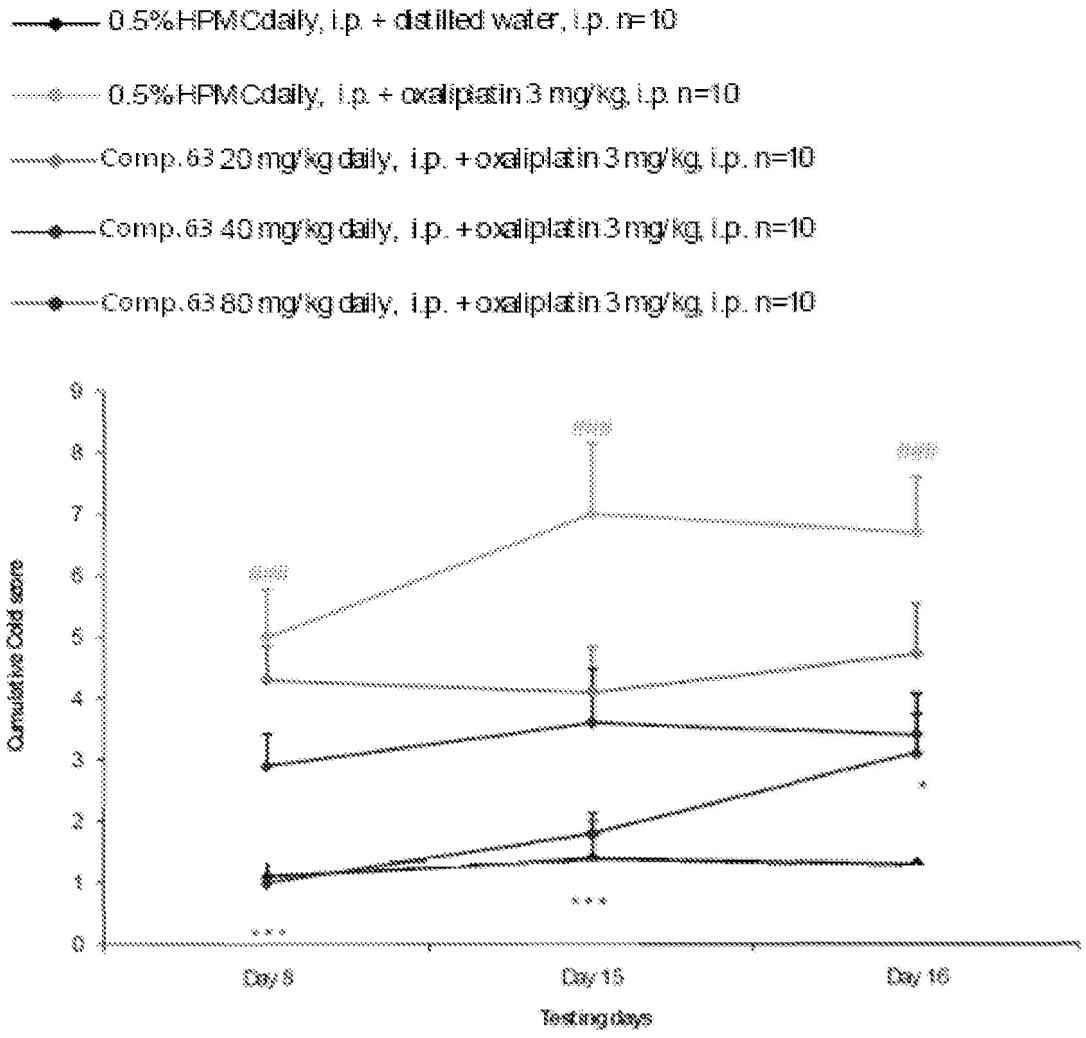

0.5% HPMC daily, i.p. + distilled water, i.p. n=10
0.5% HPMC daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp. 63 20 mg/kg daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp. 63 40 mg/kg daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Comp. 63 80 mg/kg daily, i.p. + oxaliplatin 3 mg/kg, i.p. n=10
Cumulative Cold score
0
1
2
3
4
5
6
7
8
9
Day 8
Day 15
Day 16
Testing days

FIGURE 17

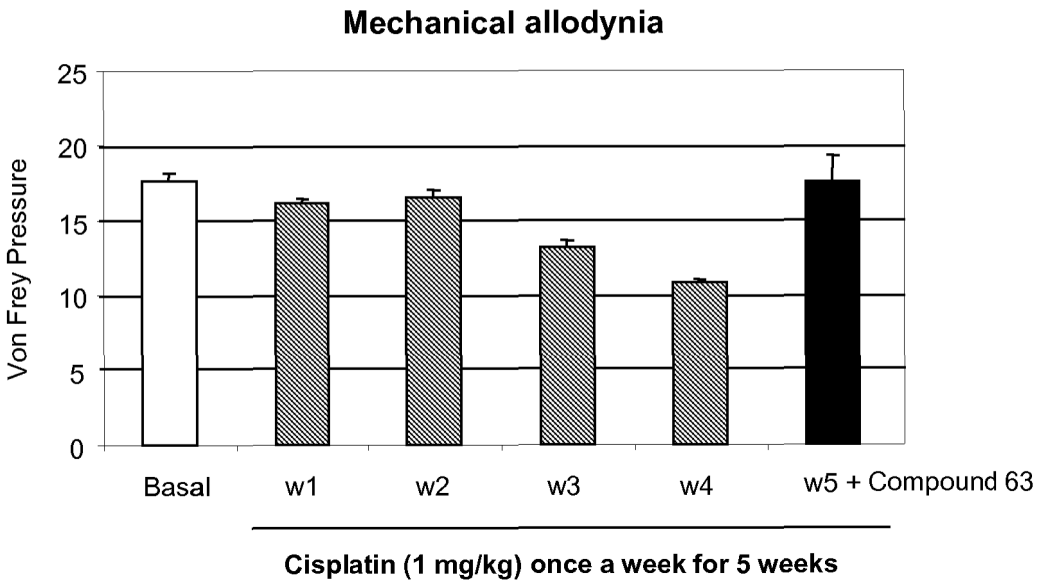
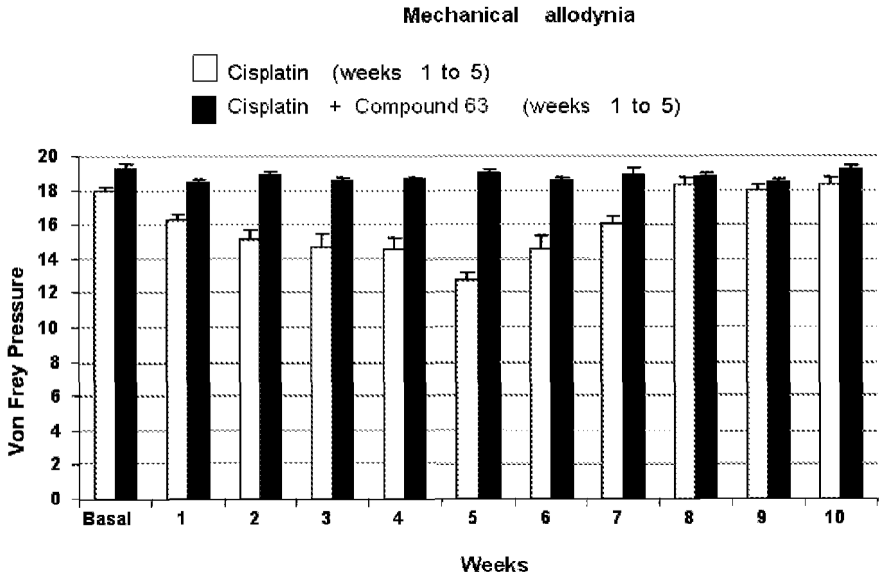

Mechanical allodynia
Von Frey Pressure
25
20
15
10
5
0
Basal
w1
w2
w3
w4
w5 + Compound 63
Cisplatin (1 mg/kg) once a week for 5 weeks

FIGURE 18


Mechanical allodynia
Cisplatin (weeks 1 to 5)
Cisplatin + Compound 63 (weeks 1 to 5)
Von Frey Pressure
0
2
4
6
8
10
12
14
16
18
20
Basal
1
2
3
4
5
6
7
8
9
10
Weeks