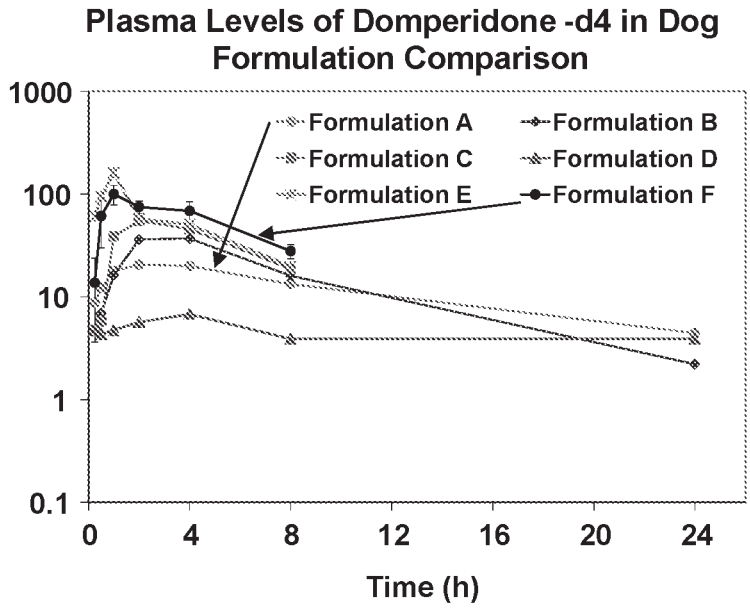
Plasma Levels of Domperidone -d4 in Dog
Formulation Comparison
1000
100
10
1
0.1
0
4
8
12
16
20
24
Time (h)
Formulation A
Formulation B
Formulation C
Formulation D
Formulation E
Formulation F

*FIG. 1*

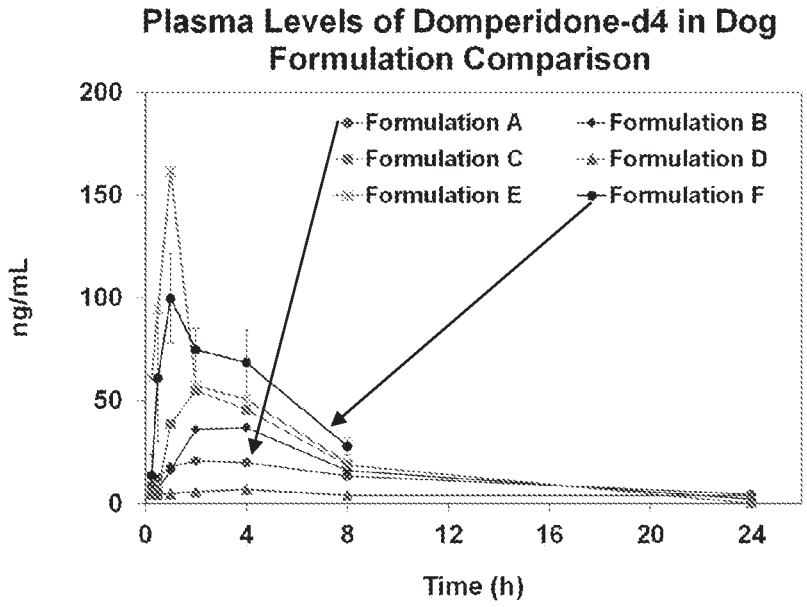
Plasma Levels of Domperidone-d4 in Dog
Formulation Comparison
200
150
100
50
0
ng/mL
0
4
8
12
16
20
24
Time (h)
Formulation A
Formulation B
Formulation C
Formulation D
Formulation E
Formulation F

*FIG. 2*

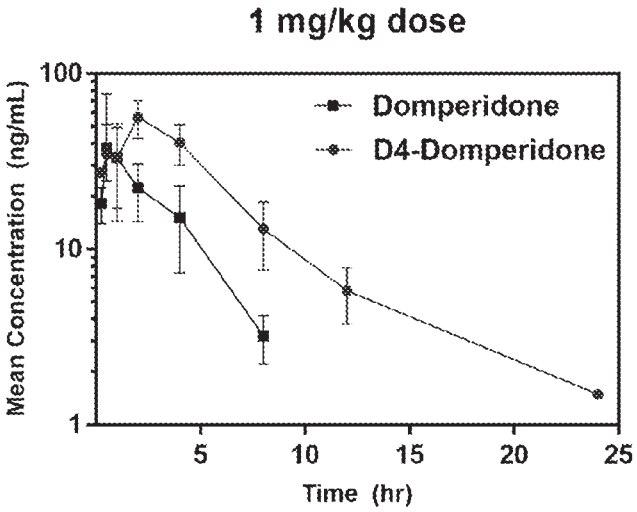
1 mg/kg dose
Mean Concentration (ng/mL)
100
10
1
5
10
15
20
25
Time (hr)
Domperidone
D4-Domperidone

*FIG. 3*

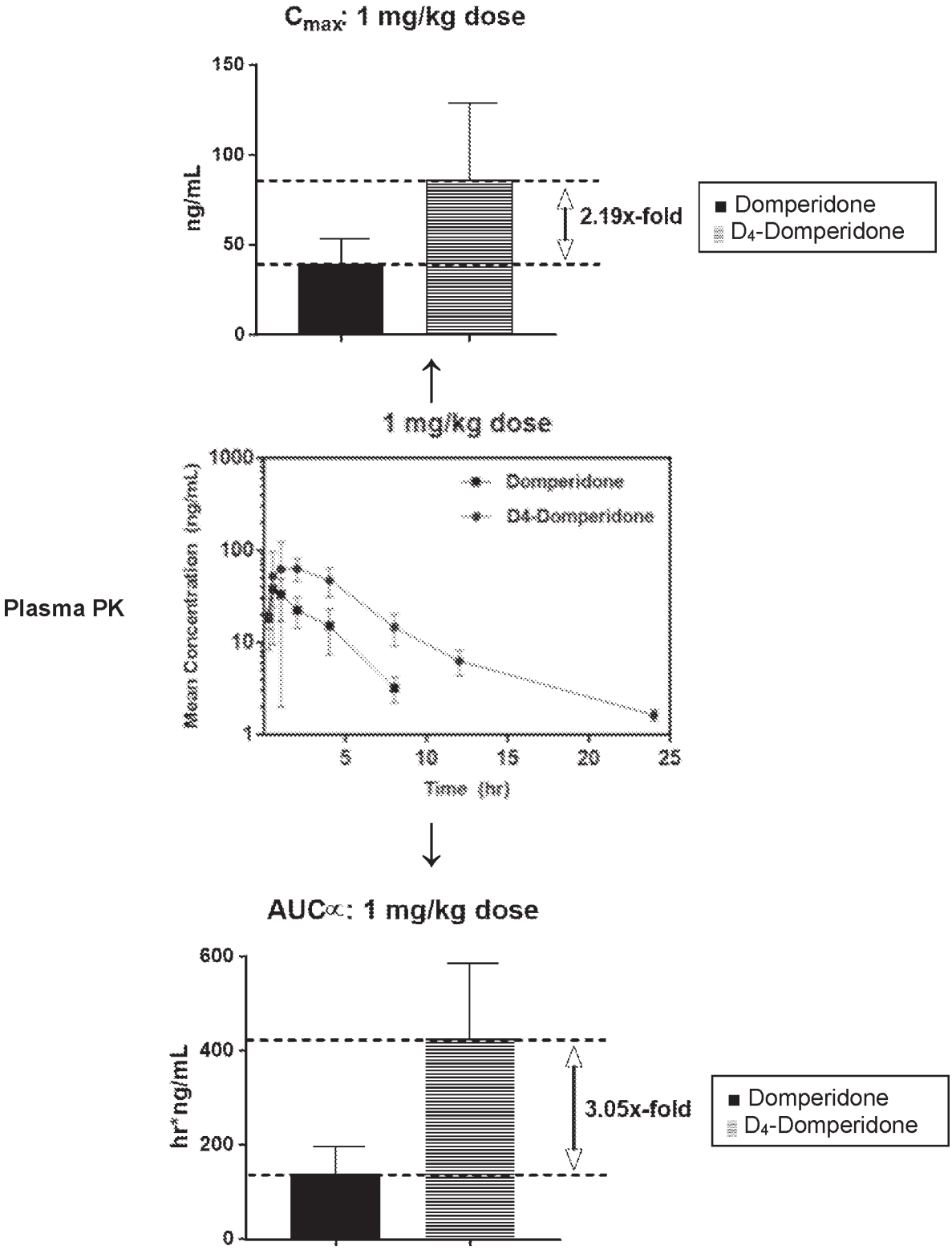
$C_{max}$: 1 mg/kg dose
150
100
50
0
ng/mL
2.19x-fold
Domperidone
D4-Domperidone
1 mg/kg dose
Plasma PK
1000
100
10
1
Mean Concentration (ng/mL)
Domperidone
D4-Domperidone
5
10
15
20
25
Time (hr)
AUC∞: 1 mg/kg dose
600
400
200
0
hr*ng/mL
3.05x-fold
Domperidone
D4-Domperidone

*FIG. 4*

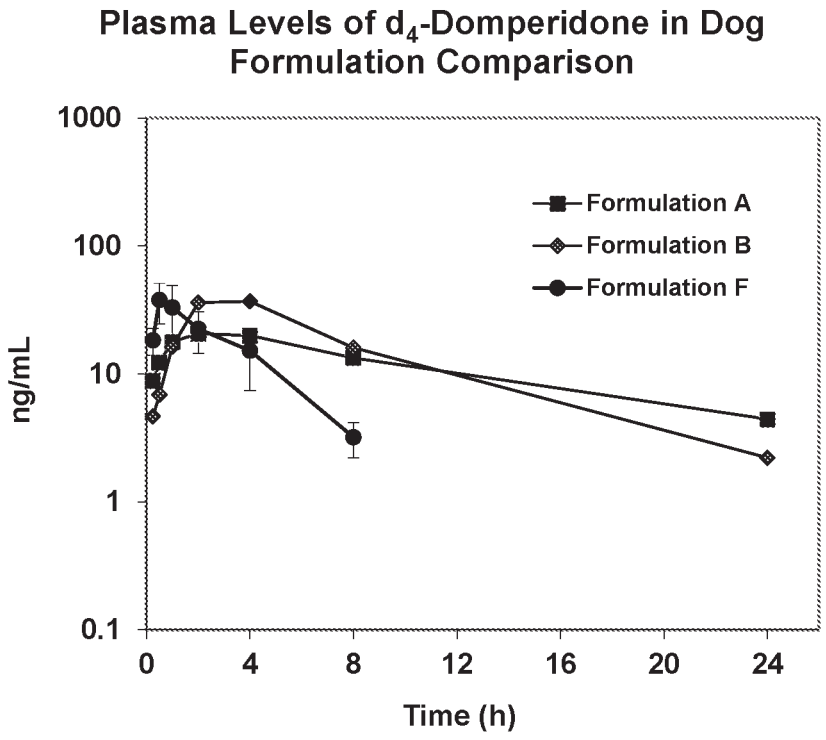
Plasma Levels of d4-Domperidone in Dog
Formulation Comparison
1000
100
10
1
0.1
ng/mL
0
4
8
12
16
20
24
Time (h)
Formulation A
Formulation B
Formulation F

*FIG. 5*

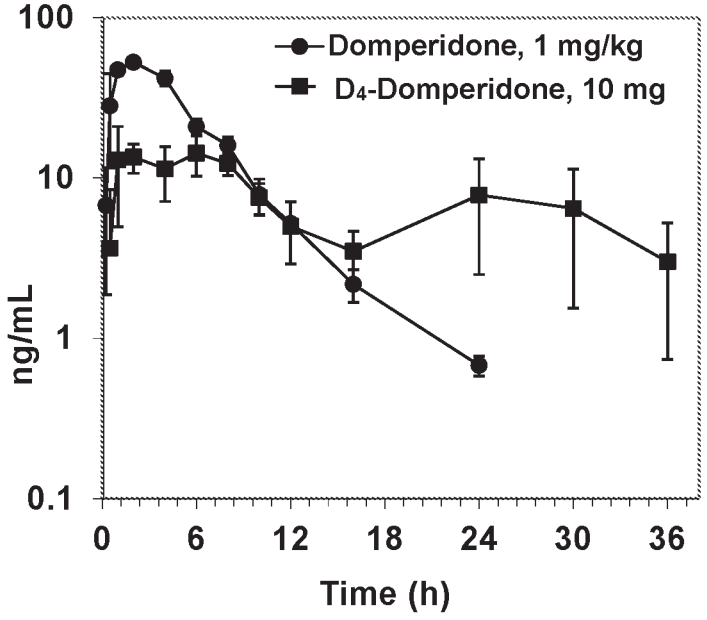
100
10
1
0.1
ng/mL
0
6
12
18
24
30
36
Time (h)
Domperidone, 1 mg/kg
D4-Domperidone, 10 mg

*FIG. 6*

| PLACEBO | ACTIVE |
|---|---|
| Medium chain triglycerides are dispensed in a suitable stainless steel container. | Medium chain triglycerides are dispensed in a suitable stainless steel container. |
| ↓ | ↓ |
| Butylated hydroxytoluene and butylated hydroxyanisole are weighed separately and transferred into the mixing vessel while mixing. Mixing is continued until all dissolved. MCT may be warmed to 35 ± 5 °C to dissolve the BHA / BHT. | Butylated hydroxytoluene and butylated hydroxyanisole are weighed separately and transferred into the mixing vessel while mixing. Mixing is continued until all dissolved. MCT may be warmed to 35 ± 5 °C to dissolve the BHA / BHT. |
| ↓ | ↓ |
| Pre-weighed Precirol ATO 5 is added to the MCT and mixed thoroughly using a bench top mixer (200-600 rpm) to achieve a homogenous suspension. | Pre-weighed Precirol ATO 5 is added to the MCT and mixed thoroughly using a bench top mixer (200-600 rpm) to achieve a homogenous suspension. |
| ↓ | ↓ |
| The final mixture should be homogenized for 15 ± 5 minutes to achieve a lump-free suspension. | The final mixture should be homogenized for 15 ± 5 minutes to achieve a lump-free suspension. |
| ↓ | ↓ |
| Once a homogenous suspension is achieved, the mixture is deaerated until it is free of air bubbles. | Pre-weighed $d_4$-domperidone is added to the suspension and mixed thoroughly using a bench top mixer (200-600 rpm) to achieve a homogenous suspension. |
| | ↓ |
| | Once a homogenous suspension is achieved, the mixture is deaerated until it is free of air bubbles. Collect a composite sample from middle of the medicine container for in-process assay testing. |

*FIG. 7*

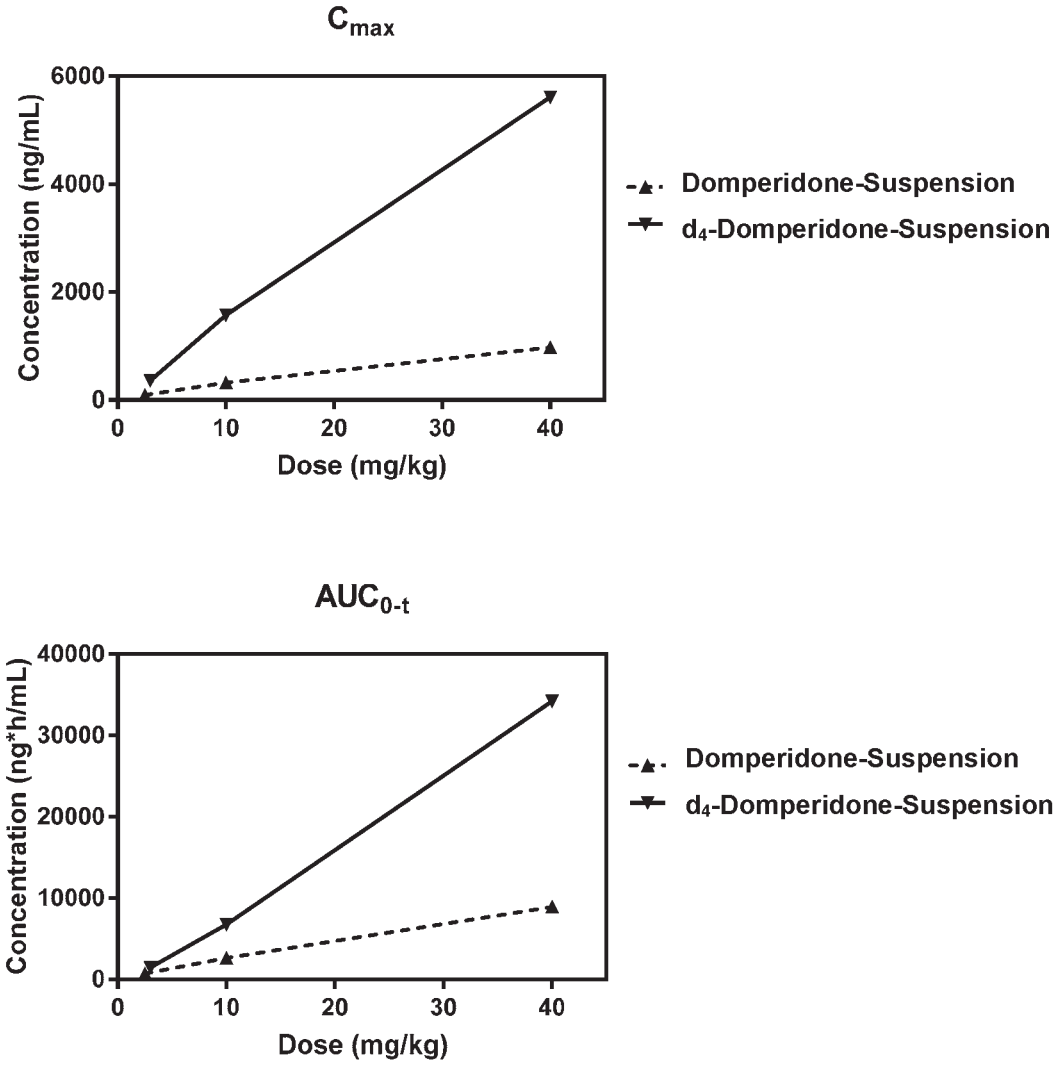
$C_{max}$
Concentration (ng/mL)
6000
4000
2000
0
0
10
20
30
40
Dose (mg/kg)
Domperidone-Suspension
$d_4$-Domperidone-Suspension
$AUC_{0-t}$
Concentration (ng*h/mL)
40000
30000
20000
10000
0
0
10
20
30
40
Dose (mg/kg)
Domperidone-Suspension
$d_4$-Domperidone-Suspension

*FIG. 8*

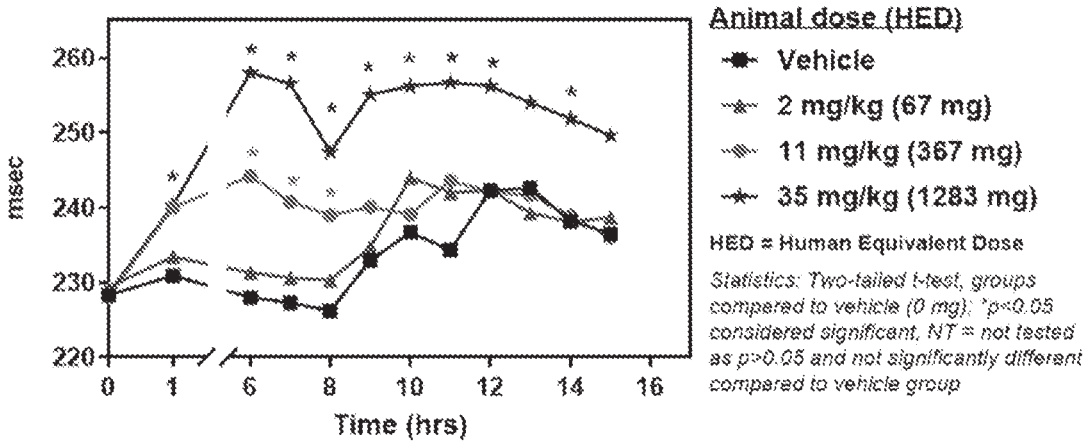
msec
260
250
240
230
220
0
1
6
8
10
12
14
16
Time (hrs)
Animal dose (HED)
Vehicle
2 mg/kg (67 mg)
11 mg/kg (367 mg)
35 mg/kg (1283 mg)
HED = Human Equivalent Dose
Statistics: Two-tailed t-test, groups compared to vehicle (0 mg); *p<0.05 considered significant, NT = not tested as p>0.05 and not significantly different compared to vehicle group

*FIG. 9*

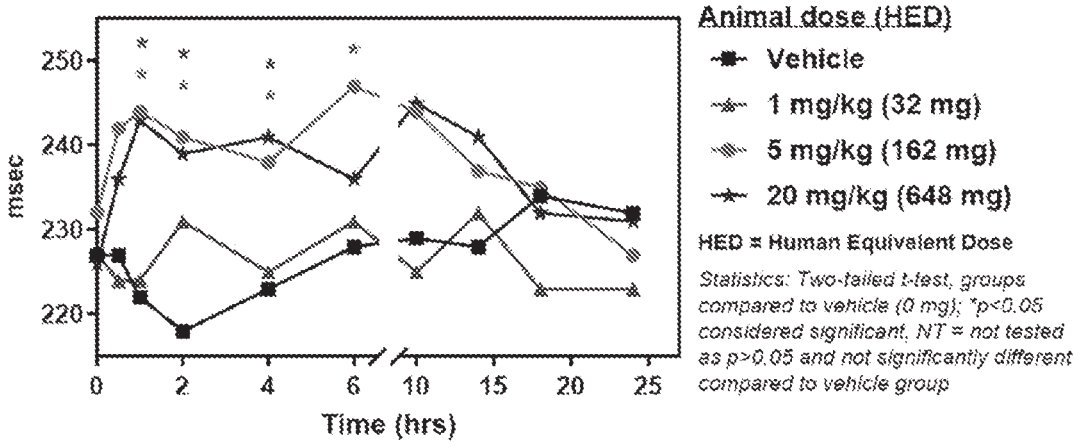
msec
250
240
230
220
0
2
4
6
10
15
20
25
Time (hrs)
Animal dose (HED)
Vehicle
1 mg/kg (32 mg)
5 mg/kg (162 mg)
20 mg/kg (648 mg)
HED = Human Equivalent Dose
Statistics: Two-tailed t-test, groups compared to vehicle (0 mg); *p<0.05 considered significant, NT = not tested as p>0.05 and not significantly different compared to vehicle group

*FIG. 10*

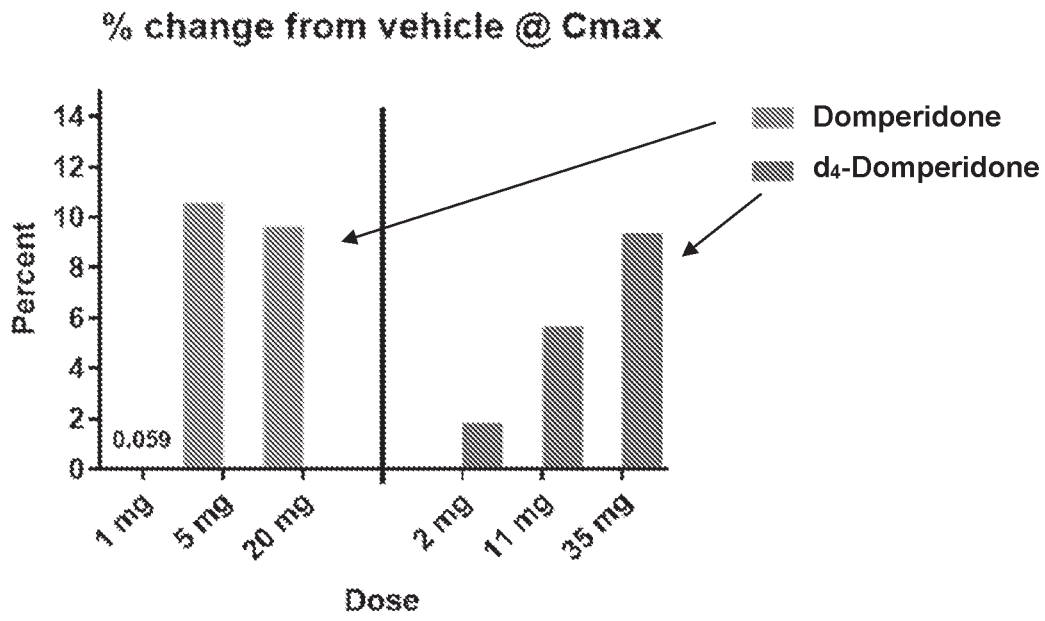
% change from vehicle @ Cmax
Domperidone
d4-Domperidone
Percent
14
12
10
8
6
4
2
0
0.059
1 mg
5 mg
20 mg
2 mg
11 mg
35 mg
Dose

*FIG. 11*

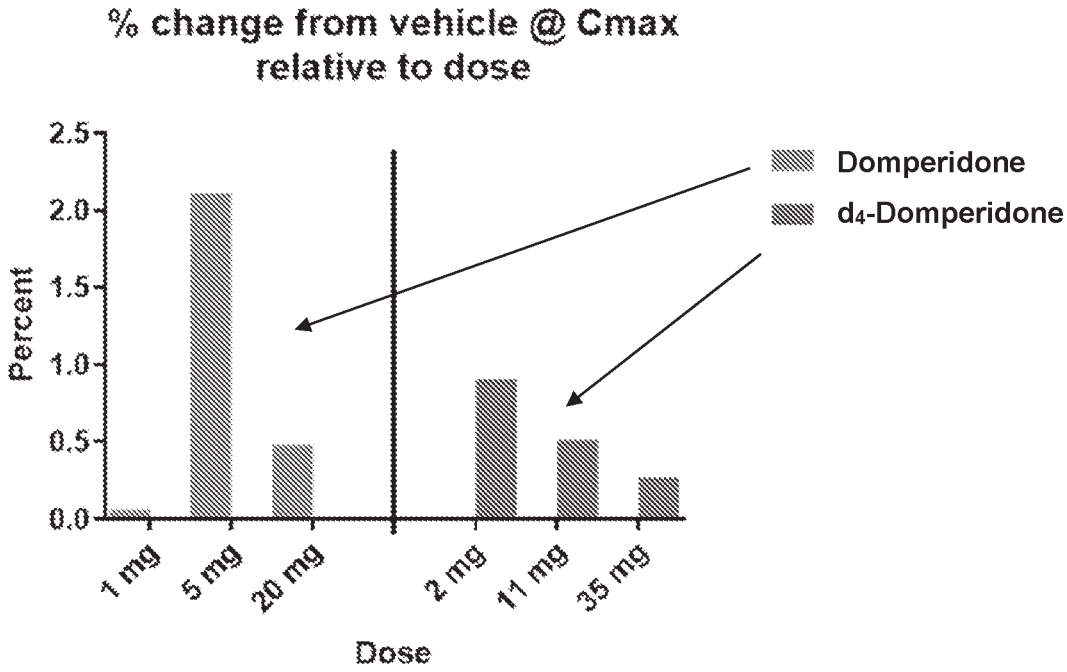
% change from vehicle @ Cmax
relative to dose
Domperidone
d4-Domperidone
Percent
2.5
2.0
1.5
1.0
0.5
0.0
1 mg
5 mg
20 mg
2 mg
11 mg
35 mg
Dose

*FIG. 12*