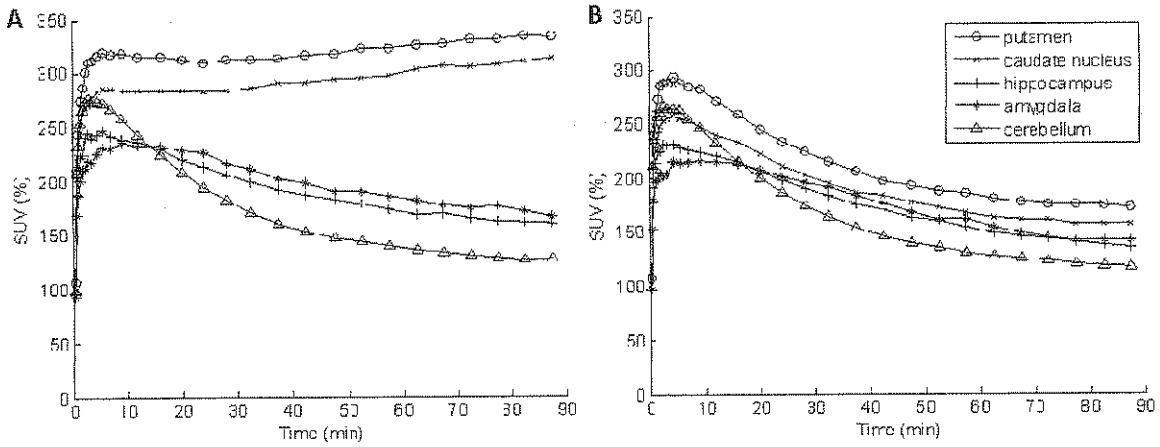

A
B
SUV (%)
Time (min)
putamen
caudate nucleus
hippocampus
amygdala
cerebellum

Figure 1

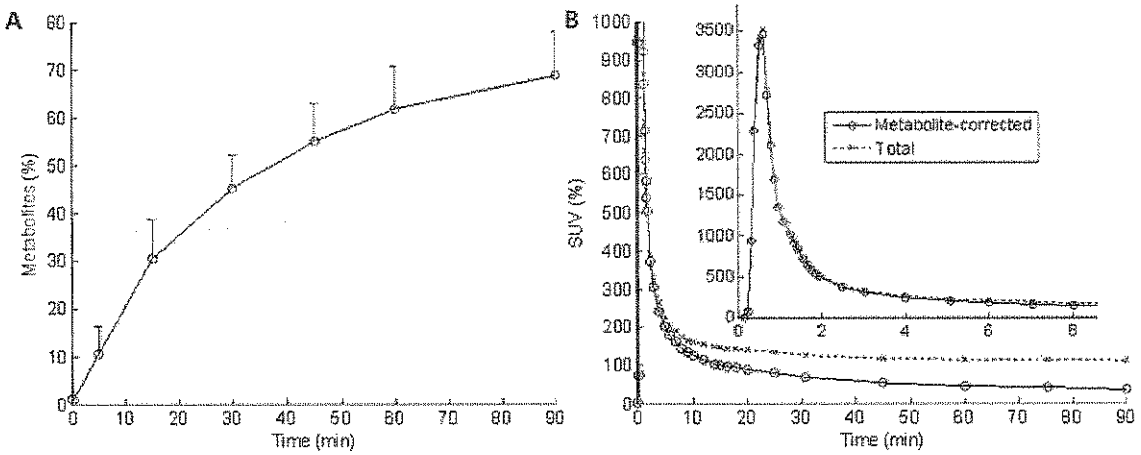

A
Metabolites (%)
Time (min)
B
SUV (%)
Time (min)
Metabolite-corrected
Total

Figure 2

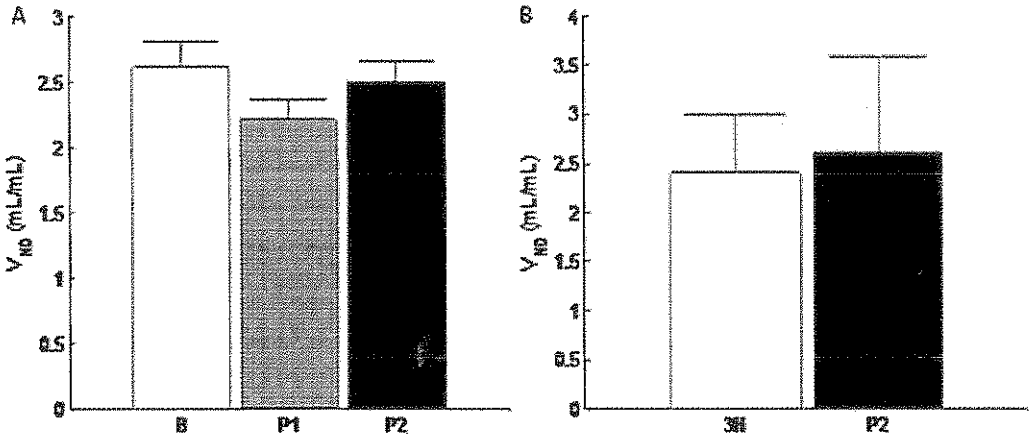


Figure 3

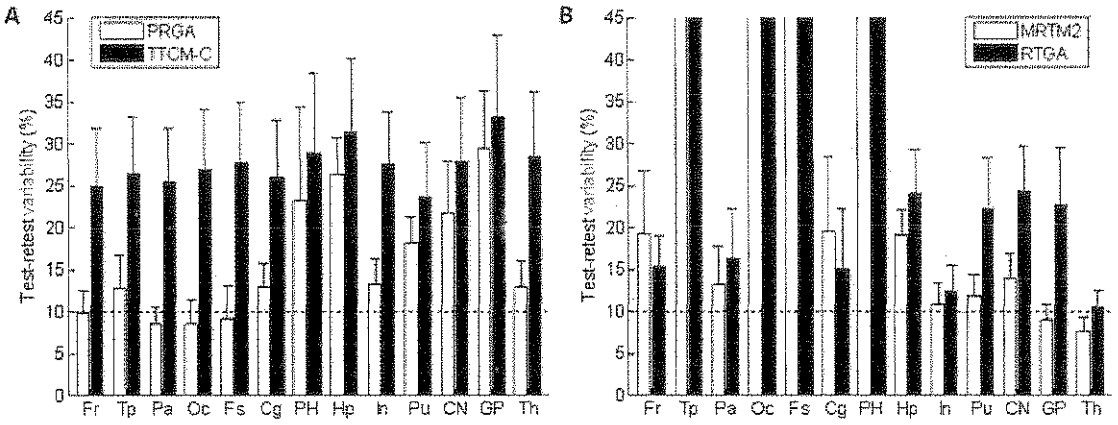

A
PRGA
TTCM-C
Test-retest variability (%)
0
5
10
15
20
25
30
35
40
45
Fr Tp Pa Oc Fs Cg PH Hp In Pu CN GP Th
B
MRTM2
RTGA
Test-retest variability (%)
0
5
10
15
20
25
30
35
40
45
Fr Tp Pa Oc Fs Cg PH Hp In Pu CN GP Th

Figure 4

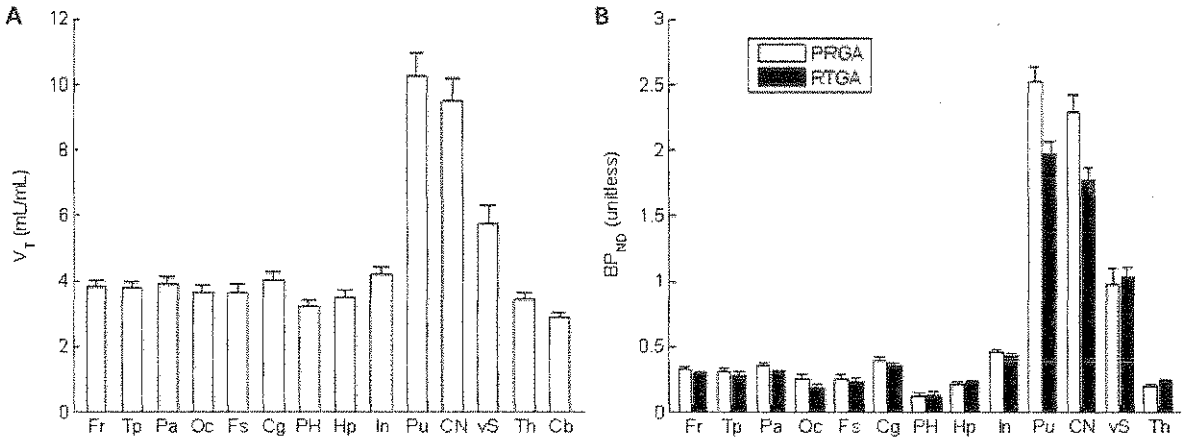

A
V_T (mL/mL)
0
2
4
6
8
10
12
Fr Tp Pa Oc Fs Cg PH Hp In Pu CN vS Th Cb
B
BP_{ND} (unitless)
0
0.5
1
1.5
2
2.5
3
PRGA
RTGA
Fr Tp Pa Oc Fs Cg PH Hp In Pu CN vS Th

Figure 5

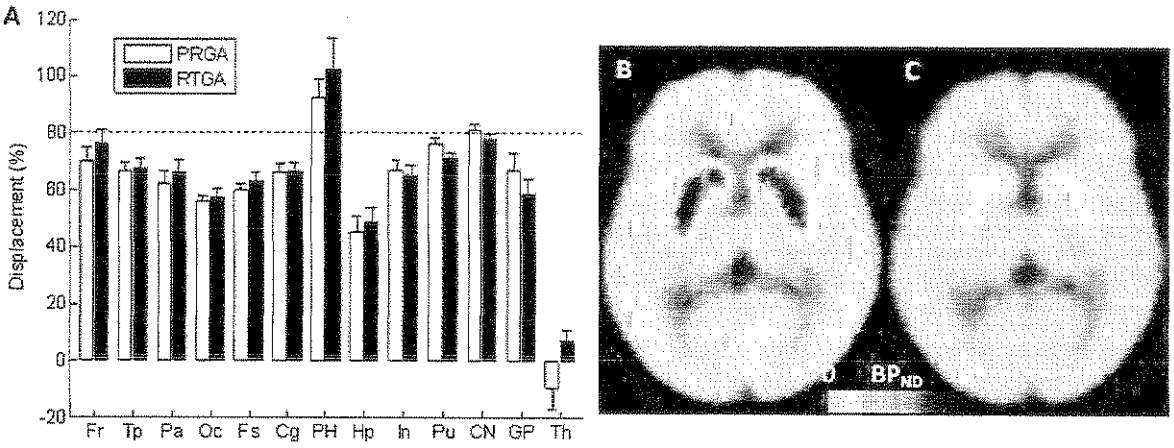

A
120
100
80
60
40
20
0
-20
Displacement (%)
PRGA
RTGA
Fr Tp Pa Oc Fs Cg PH Hp In Pu CN GP Th
B
C
BP ND

Figure 6

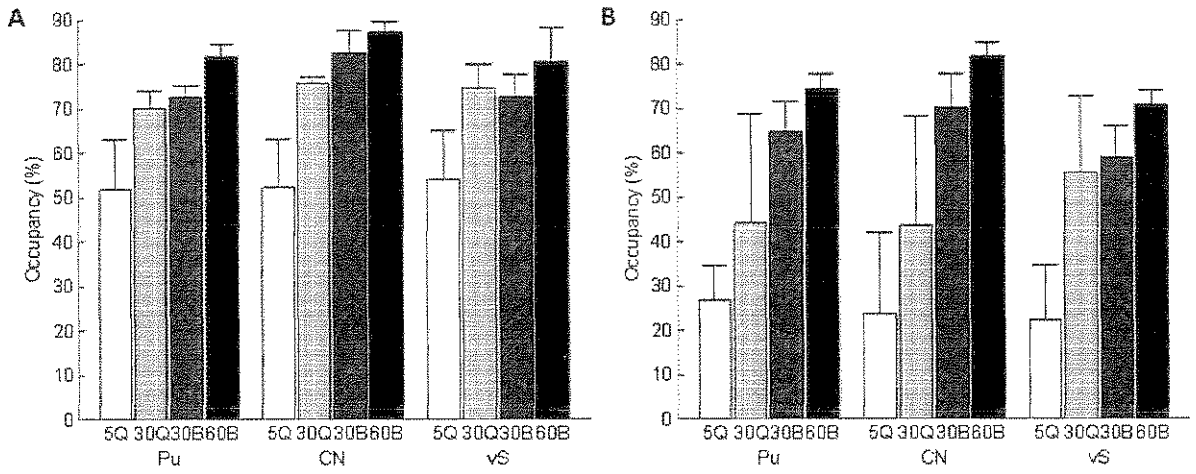


Figure 7

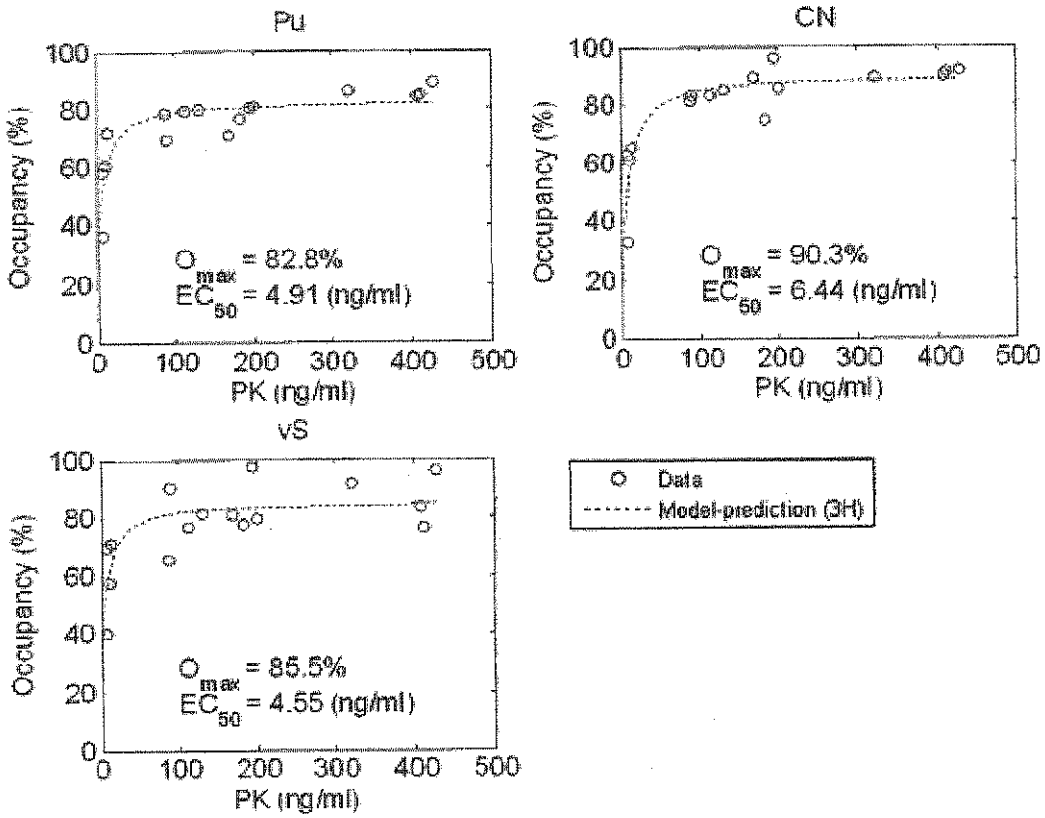

Pu
Occupancy (%)
PK (ng/ml)
O_{max} = 82.8%
EC_{50} = 4.91 (ng/ml)
CN
Occupancy (%)
PK (ng/ml)
O_{max} = 90.3%
EC_{50} = 6.44 (ng/ml)
vS
Occupancy (%)
PK (ng/ml)
O_{max} = 85.5%
EC_{50} = 4.55 (ng/ml)
Data
Model-prediction (3H)

Figure 8

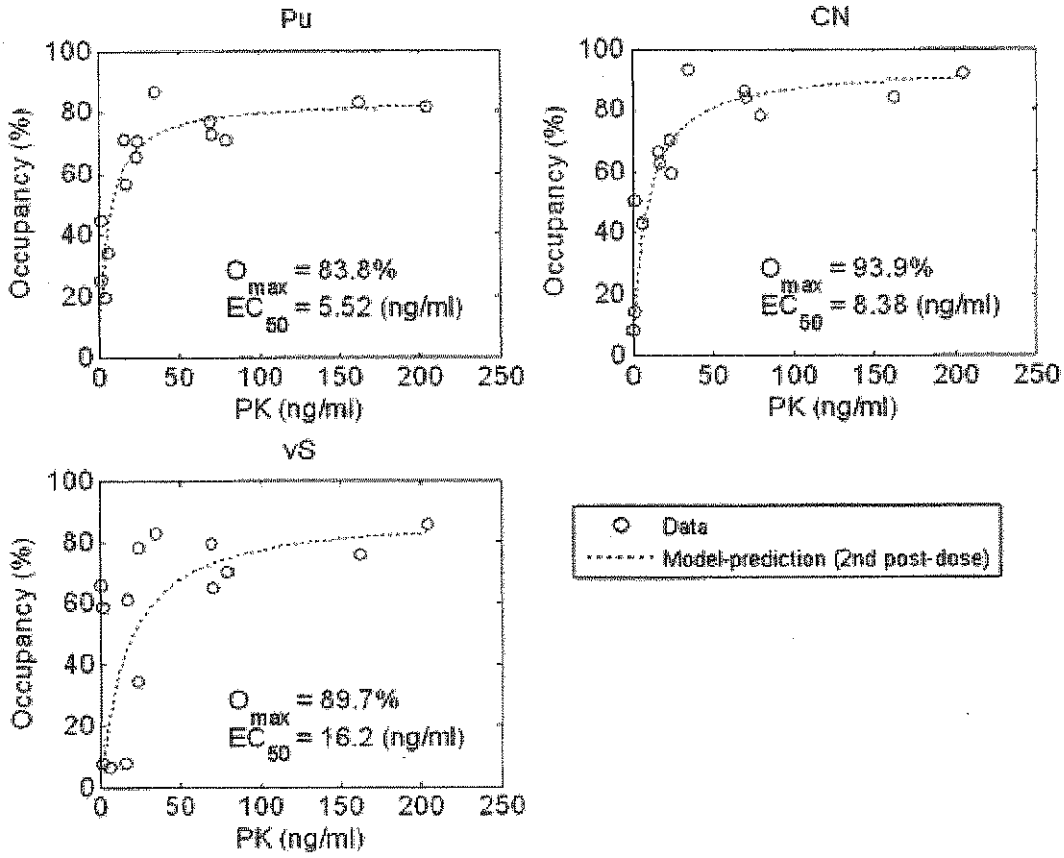

Pu
CN
vS
Occupancy (%)
PK (ng/ml)
O max = 83.8%
EC50 = 5.52 (ng/ml)
O max = 93.9%
EC50 = 8.38 (ng/ml)
O max = 89.7%
EC50 = 16.2 (ng/ml)
Data
Model-prediction (2nd post-dose)

Figure 9

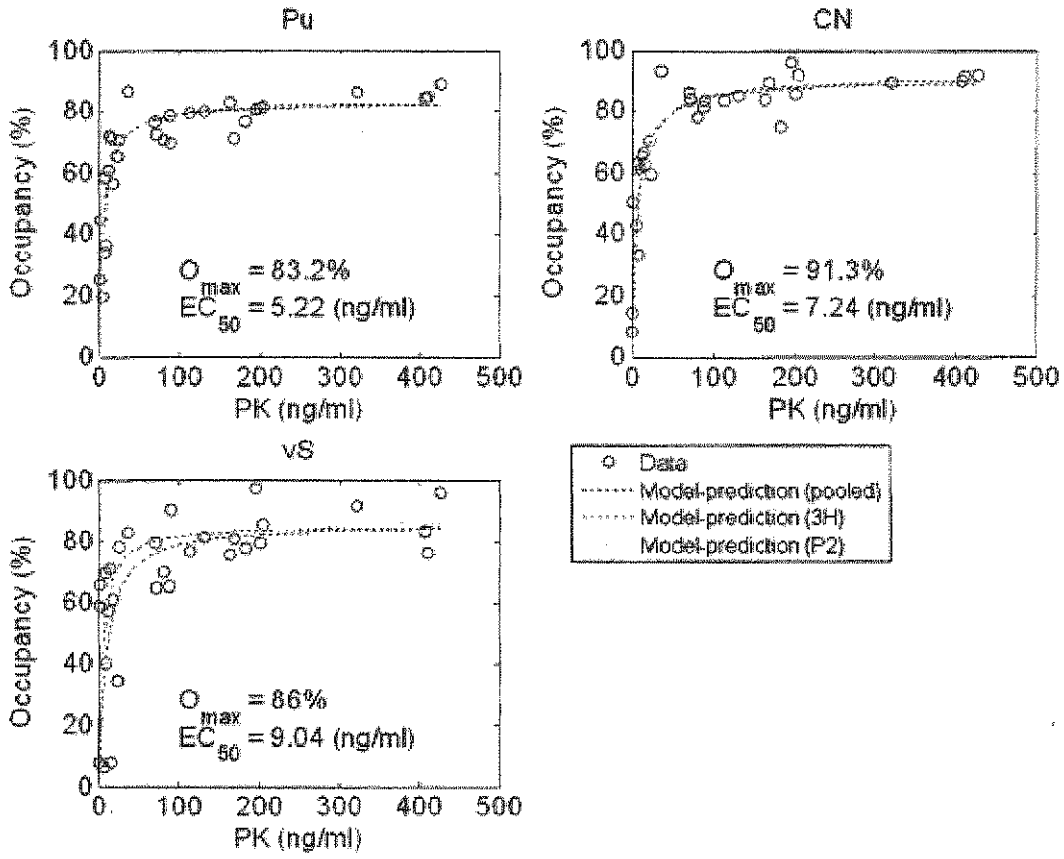

Pu
CN
vS
Occupancy (%)
PK (ng/ml)
O max = 83.2%
EC50 = 5.22 (ng/ml)
O max = 91.3%
EC50 = 7.24 (ng/ml)
O max = 86%
EC50 = 9.04 (ng/ml)
Data
Model-prediction (pooled)
Model-prediction (3H)
Model-prediction (P2)

Figure 10

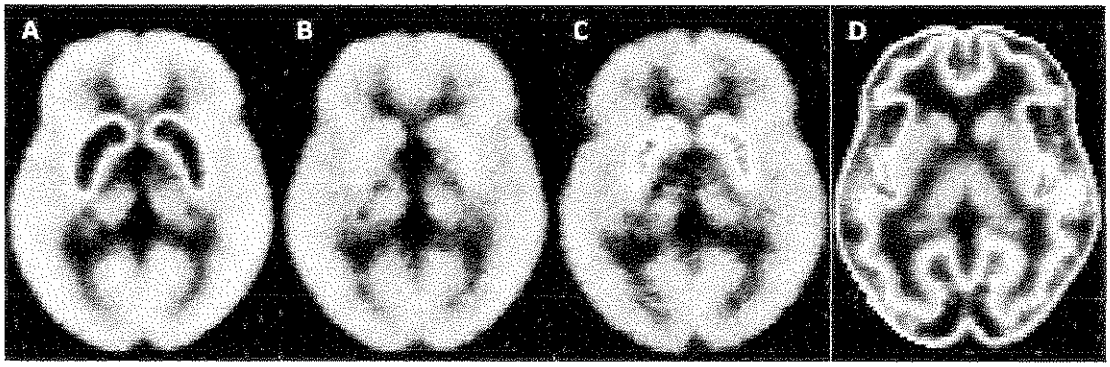


Figure 11

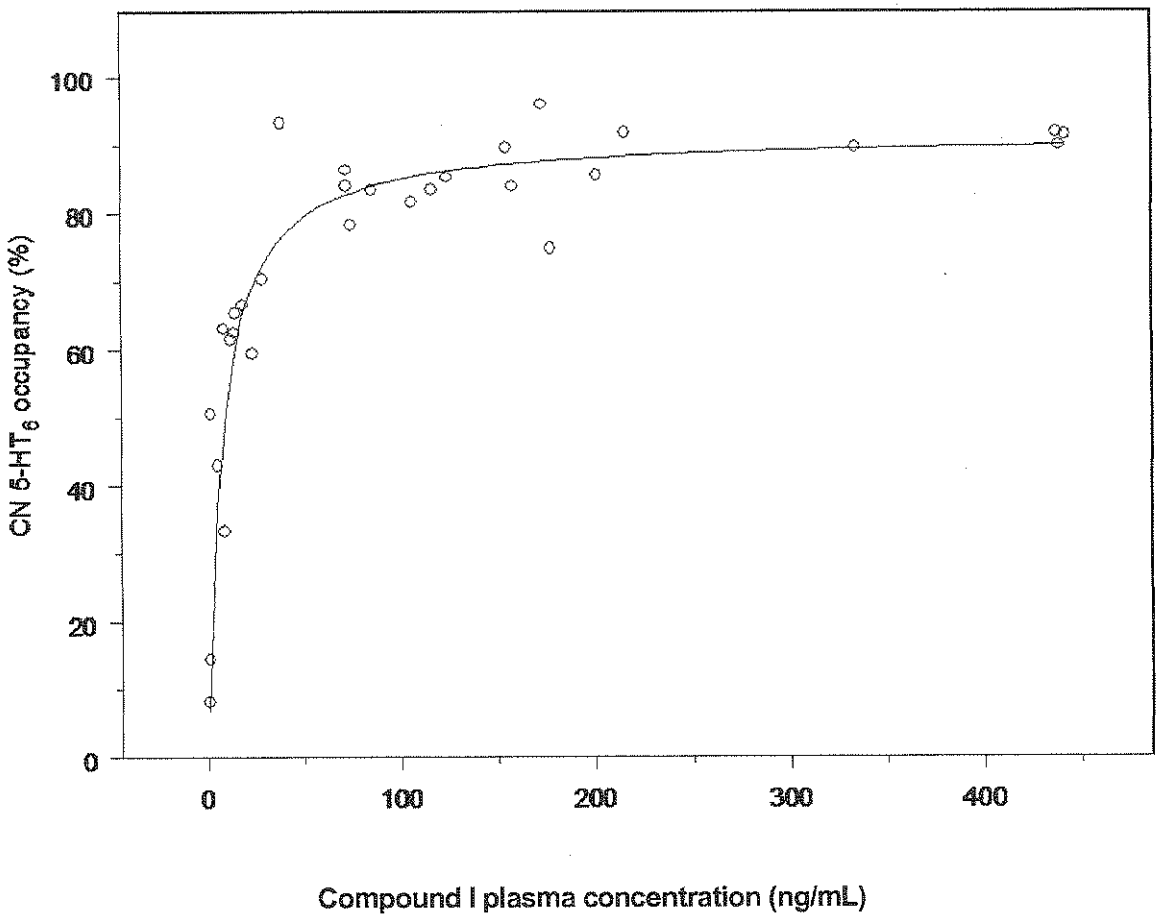

100
80
60
40
20
0
CN 5-HT6 occupancy (%)
0
100
200
300
400
Compound I plasma concentration (ng/mL)

Figure 12

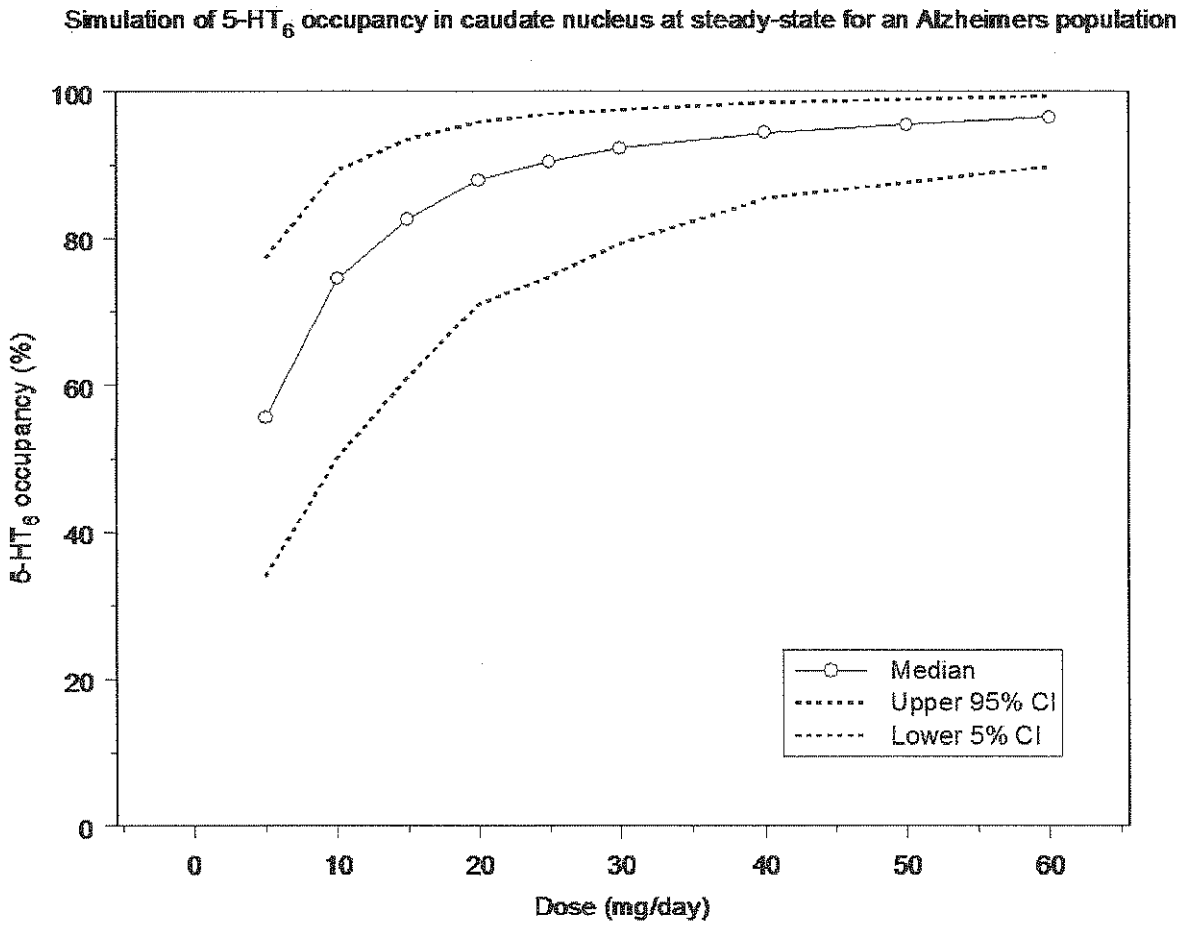

Simulation of 5-HT6 occupancy in caudate nucleus at steady-state for an Alzheimers population
5-HT6 occupancy (%)
100
80
60
40
20
0
0
10
20
30
40
50
60
Dose (mg/day)
Median
Upper 95% CI
Lower 5% CI

Figure 13