Supporting Information

Utilization of an active site mutant receptor for the identification of potent and selective atypical 5-HT_{2C} receptor agonists

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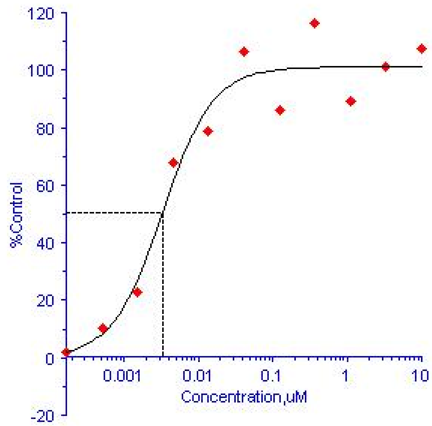
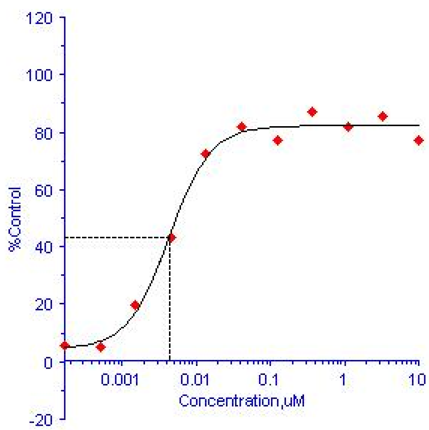
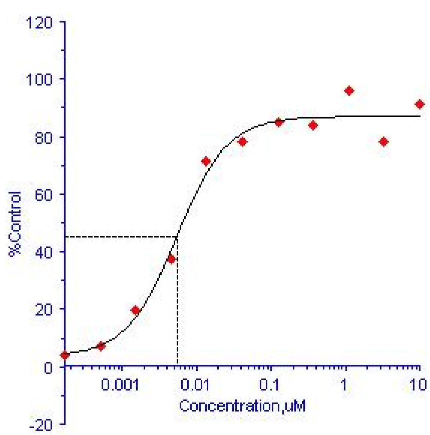
Representative 5-HT_{2C} concentration response curves for **69**



HFMAX	0.003285521 uM
SLOPE	1.283981
Y@MAXCONC	107.25
YMAX	101.1215
YMAXOBS	116.46
YMIN	-0.1324447

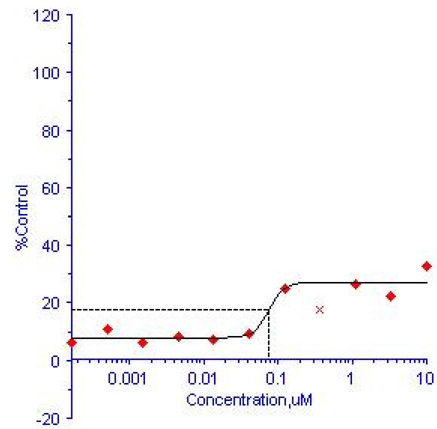


HFMAX	0.004317973 uM
SLOPE	1.554821
Y@MAXCONC	76.91
YMAX	82.26083
YMAXOBS	86.92
YMIN	4.436282

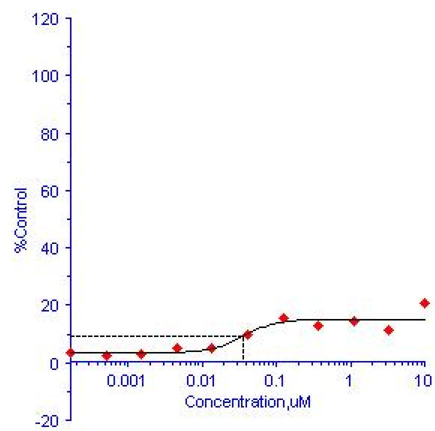


HFMAX	0.005448022 uM
SLOPE	1.27414
Y@MAXCONC	91.19
YMAX	86.99547
YMAXOBS	95.71
YMIN	3.55873

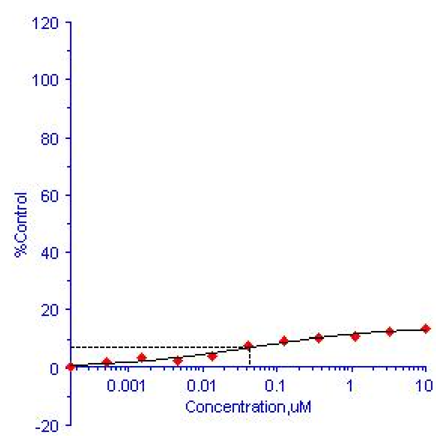
Representative 5-HT_{2B} concentration response curves for **69**



HFMAX	0.07543992 uM
SLOPE	4.357378
Y@MAXCONC	32.61
YMAX	27.05246
YMAXOBS	32.61
YMIN	7.861752

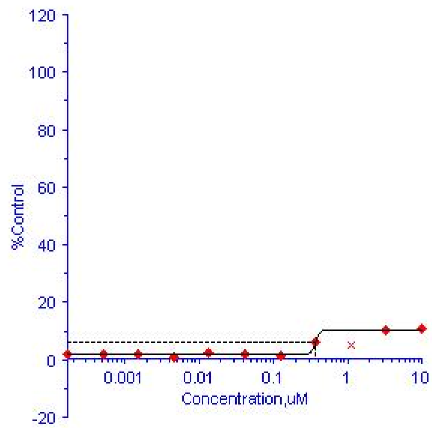


HFMAX	0.03653839 uM
SLOPE	1.930395
Y@MAXCONC	21
YMAX	15.24632
YMAXOBS	21
YMIN	3.412802

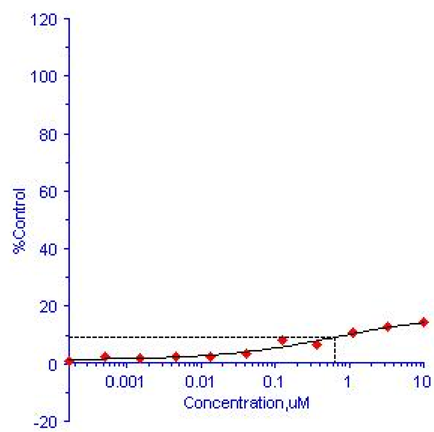


HFMAX	0.04405194 uM
SLOPE	0.4807289
Y@MAXCONC	13.46
YMAX	14.12605
YMAXOBS	13.46
YMIN	0

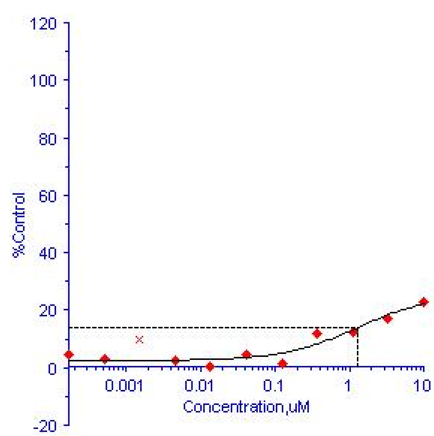
Representative 5-HT_{2A} concentration response curves for **69**



HFMAX	0.3715875 uM
SLOPE	17.0195
Y@MAXCONC	10.69
YMAX	10.37
YMAXOBS	10.69
YMIN	1.848572



HFMAX	0.6328486 uM
SLOPE	0.5621735
Y@MAXCONC	14.22
YMAX	17.05994
YMAXOBS	14.22
YMIN	1.4033



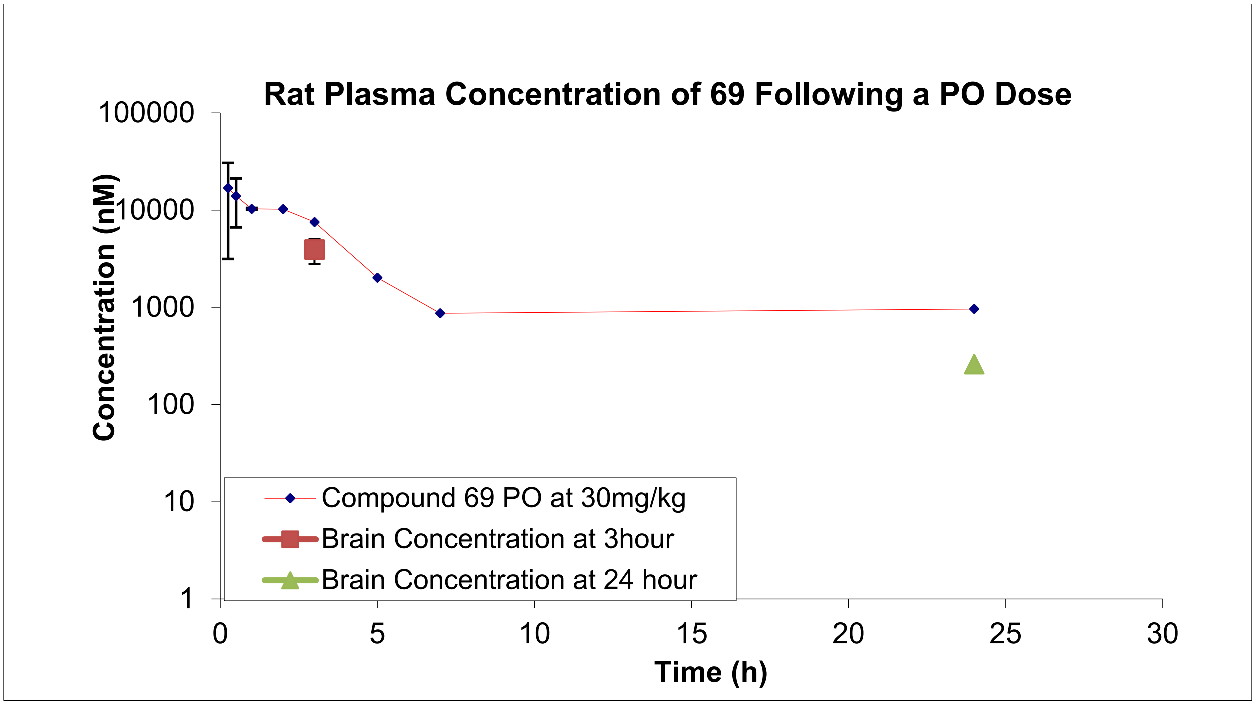
HFMAX	1.310347 uM
SLOPE	0.8654485
Y@MAXCONC	22.86
YMAX	25.52854
YMAXOBS	22.86
YMIN	2.471489

Rat pharmacokinetic data for **69**

Dosing Vehicle (PO):	10% CREMOPHOR-EL; 10% DIMETHYL ACETAMIDE (DMAC); 10% ETHANOL; 70% WATER				
	Compound 69 PO at 30 mg/kg				
Time (h)	**A**	**B**	**C**	**Mean**	**SD**
0.25	5469.6	13022.0	32080.3	**16857**	13714
0.5	2616.9	9325.2	29817.7	**13920**	14171
1	568.6	4327.1	25983.6	**10293**	13718
2	1582.2	3778.8	25306.2	**10222**	13109
3	1986.5	4868.5	15774.4	**7543**	7273
5	489.2	1164.9	4392.7	**2016**	2086
7	738.5	730.3	1136.8	**869**	232
24	39.7	<LLQ(5 nM)	1884.4	**962**	1304
Dose (nmole/kg)	94826	94826	94826	**94826**	0
Cmax (nM)	5470	13022	32080	**16857**	13714
Tmax (h)	0.3	0.3	0.3	**0**	0
AUClast (nM*h)	12610.2	23061.4	119785.0	**51819**	59092
AUCtot (nM*h)	12848.8	24601.3	140835.3	**59428**	70745
%AUCextra	2	6.3	14.9	**8**	7
thalf (h)	4	1.5	7.7	**4**	3
Brain/Plasma Ratio 3h	**1.6**	**0.7**	**0.3**	**0.87**	0.64
Brain/Plasma Ratio 24h	**0.5**	**NA**	**0.4**	**0.43**	

Sample Type: Brain	Compound 69 PO at 30 mg/kg				
TimePoint (Hrs)	**A (nM)**	**B (nM)**	**C (nM)**		
3h	1039	1137	1745		
24h	6	3	252	Mean	SD
Calculated Value 3h	3116	3411	5234	3920	1147
Calculated Value 24h	18	8	756	260.5	428.8

The brain sample were 1:2(vol:weight) diluted with water before homogenization. The dilution factor is 3.


Rat Plasma Concentration of 69 Following a PO Dose
100000
10000
1000
100
10
1
Concentration (nM)
0
5
10
15
20
25
30
Time (h)
Compound 69 PO at 30mg/kg
Brain Concentration at 3hour
Brain Concentration at 24 hour