

The selectivity of α -adrenoceptor agonists for the human α 1A, α 1B and α 1D-adrenoceptors

Running title: α 1A, α 1B, α 1D-adrenoceptor agonist selectivity

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Supplementary Table 1

Ligands (arranged in alphabetical order), with supplier and catalogue number and maximum concentration used in functional assays. The response in CHO cells without any transfected receptors are given for intracellular calcium mobilisation, ERK1/2-phosphorylation, cAMP accumulation and forskolin-stimulated cAMP accumulation. Some compounds only stimulated a response at maximum concentration only. An EC₅₀ value was therefore not obtainable and % control values at the maximum concentration used are given. Values represent mean ± s.e.m. of n separate experiments. Ionomycin (10µM) stimulated a response 27.2 ± 1.2 fold over basal (n=6), PDBu (10µM) stimulated a response 7.5 ± 0.9 (n=7) and forskolin (10µM) stimulated a response 39.5 ± 3.2 (n=6) fold over basal.

CHO	Supplier and catalogue number	Maximum concentration	Intracellular calcium release		ERK1/2-phosphorylation			cAMP accumulation		cAMP accumulation (in presence of forskolin)			
			% ionomycin	n	Log EC ₅₀	% PDBu	n	% forskolin	n	Log EC ₅₀	% forskolin-stim cAMP	n	
A61603	Tocris – 1052	100µM	No response	4	No response			4	No response	5	No response		5
adrenaline	Sigma – E4642	100µM	No response	5	No response			5	No response	10	No response		10
allyphenyline	Sigma – SML1484	100µM	5.9 ± 1.0	3	100µM	12.7 ± 3.1	5	No response	5	No response		5	
amitraz	Sigma – 45323	10µM	No response	3	No response			4	ND		ND		
ARC 239	Sigma A5736	10µM	3.8 ± 2.5	3	No response			4	No response	5	No response		5
atipamezole	Sigma – A9611	10µM	No response	3	10µM	3.1 ± 1.9	6	No response	5	No response		5	
BHT920	Tocris - 2759	100µM	No response	3	100µM	3.8 ± 1.8	6	ND		ND			
BHT-933	Tocris -2758	100µM	1.4 ± 0.8	3	No response			5	ND		ND		
BMY7378	Sellakchem S2691	100µM	7.8 ± 2.2	3	No response			5	No response	5	No response		5
brimonidine	ARK - AK35795	100µM	No response	3	100µM	2.3 ± 1.7	5	No response	5	No response		5	
BRL 44408	Sigma – B4559	100µM	No response	3	100µM	17.6 ± 8.1	5	No response	5	100µM	77.6 ± 2.3	5	
bupirone	Sigma – B7148	100µM	3.1 ± 2.3	3	No response			5	No response	5	100µM	113.6 ± 5.2	5
CGP 12177	Sigma – C125	100µM	No response	3	-6.01 ± 0.41	22.8 ± 4.3	6	ND		ND			
chloroethylclonidine	Sigma – B003	100µM	3.3 ± 3.3	3	No response			4	ND		ND		
cirazoline	Sigma – C223	100µM	4.5 ± 0.8	3	100µM	33.4 ± 7.6	7	No response	5	100µM	82.4 ± 2.8	5	
clonidine	Sigma – C7897	100µM	1.6 ± 1.0	3	No response			6	No response	5	No response		5
detomidine	Sigma - 34265	100µM	4.3 ± 1.7	3	100µM	6.1 ± 4.0	7	No response	5	100µM	83.2 ± 4.9	5	
dexmedetomidine	Sigma – SML0956	100µM	6.3 ± 4.8	3	100µM	5.8 ± 2.2	7	No response	5	100µM	84.4 ± 4.7	5	
dihydroergotamine	Tocris - 0457	10µM	No response	3	-8.65 ± 0.06	35.9 ± 4.2	5	No response	5	10µM	77.4 ± 1.9	5	
dobutamine	Sigma – D0676	100µM	No response	4	10µM	16.4 ± 5.9	6	No response	5	No response		5	
dopamine	Sigma – H8502	100µM	No response	3	No response			4	No response	5	No response		5
eforaxan	Tocris - 0792	100µM	No response	3	No response			4	No response	5	No response		5
ephedrine	Sigma - 285749	1mM	5.3 ± 1.6	3	No response			5	No response	5	No response		5
etilefrine	ARK – AK390	100µM	No response	4	No response			4	No response	5	No response		5
fenoterol	Sigma – F1016	100µM	No response	3	No response			5	No response	5	No response		5
formoterol	Tocris – 1448	10µM	No response	3	No response			4	No response	5	No response		5
guanabenz	Sigma – G110	100µM	23.5 ± 7.4	3	100µM	8.5 ± 3.1	7	No response	5	No response		5	
guanfacine	Sigma – G1043	100µM	11.5 ± 2.9	3	100µM	2.5 ± 1.7	6	No response	5	No response		5	
idazoxan	Sigma - 16138	100µM	No response	3	No response			5	No response	5	No response		5
isoprenaline	Sigma - I5627	100µM	No response	3	100µM	5.1 ± 4.6	7	No response	5	No response		5	

labetolol	Sigma - L1011	100µM	10.3 ± 3.1	3	-5.62 ± 0.04	25.9 ± 3.4	5	No response	5	No response		5
lisuride	Tocris - 4052	10µM	No response	3	-6.47 ± 0.16	41.0 ± 6.4	6	No response	5	10µM	85.2 ± 5.0	5
medetomidine	Tocris - 5160	100µM	11.7 ± 2.4	3	100µM	7.9 ± 3.8	7	No response	5	100µM	88.4 ± 3.2	5
metaraminol	Sigma – M4778	100µM	No response	4	No response		5	No response	5	No response		5
methoxamine	Sigma – M6524	100µM	No response	3	No response		4	No response	5	No response		5
methyl dopa	Tocris – 0584	10µM	No response	3	No response		4	ND		ND		
α-methylnorepinephrine	Sigma – SML0675	100µM	No response	3	No response		4	No response	5	No response		5
midodrine	Sigma – M8277	100µM	No response	3	No response		4	ND		ND		
moxonidine	Sellakchem – S2066	100µM	No response	3	100µM	3.1 ± 1.9	5	ND		ND		
2-MPMDQ	Tocris - 0661	10µM	No response	3	No response		5	No response	5	No response		5
3-MPPI	Tocris – 0581	10µM	No response	3	No response		5	No response	5	No response		5
naphazoline	Sigma – 70170	100µM	No response	3	100µM	9.2 ± 3.3	7	No response	5	No response		5
noradrenaline	Sigma – A0937	100µM	No response	3	No response		4	No response	5	No response		5
octopamine	Tocris – 2242	100µM	No response	4	100µM	2.9 ± 1.8	6	No response	5	No response		5
oxymetazoline	Tocris - 1142	100µM	3.1 ± 0.9	6	-7.96 ± 0.16	46.7 ± 6.0	10	No response	5	*-7.71 ± 0.15	18.1 ± 2.2%	5
Para-amino-clonidine	Sigma – A0779	10µM	No response	3	No response		5	No response	5	No response		5
PF3774076	Sigma – PZ0263	10µM	No response	3	No response		5	No response	5	No response		5
2-PMDQ	Tocris – 0627	10µM	No response	3	No response		7	No response	5	No response		5
rilmnidine	Tocris - 0790	100µM	No response	3	No response		4	ND		ND		
R-phenylephrine	Tocris - 2838	100µM	No response	3	No response		5	No response	5	No response		5
RWJ52353	Tocris - 3935	10µM	No response	3	No response		4	ND		ND		
salbutamol	Sigma – S5013	100µM	No response	4	100µM	3.5 ± 2.0	7	#ND		ND		
salmeterol	Tocris – 1660	10µM	3.2 ± 1.4	4	No response		4	#ND		ND		
ST-91	Tocris – 2638	100µM	No response	3	100µM	5.7 ± 3.1	6	No response	5	100µM	82.5 ± 1.6	5
sunepitron	Sigma – PZ0279	100µM	No response	3	100µM	4.1 ± 2.7	6	ND		ND		
synephrine	Sigma – S0752	100µM	No response	3	No response		7	No response	5	No response		5
T-CG 1000	Tocris – 5021	10µM	No response	3	100µM	12.3 ± 3.5	6	ND		ND		
tetrahydrozoline	Sigma – T4264	100µM	No response	3	No response		4	No response	5	No response		5
tizanidine	Sellakchem – S1437	100µM	No response	3	100µM	6.7 ± 3.3	5	No response	5	No response		5
UK14304	Tocris – 0425	10µM	No response	3	No response		5	No response	5	No response		5
xylazine	Sigma – X1251	100µM	2.3 ± 0.3	3	No response		6	ND		ND		
xylometazoline	Sigma – X6000	100µM	15.8 ± 2.7	5	-7.05 ± 0.17	56.2 ± 5.9	10	No response	5	*-7.18 ± 0.20	21.0 ± 2.4%*	5
ziprasidone	Sellakchem – S1444	10µM	No response	3	No response		5	ND		ND		

ND not determined

*oxymetazoline and xylometazoline cause a decrease in forskolin-stimulated cAMP accumulation. The data give are log IC₅₀ and % inhibition of forskolin-stimulated cAMP as both compounds caused a decrease in cAMP accumulation (as in supplementary figure 1).

#not determined here but no cAMP response was seen in untransfected cells in Baker 2010