

S1 Table. *In vitro* Assay profile of Compound 4f in Eurofins Cerep Panlabs

- Enzyme and binding assay

Assay name	Species	Conc.	%Inh.
5-Lipoxygenase	hum	10 μ M	9
ATPase, Ca ²⁺ , Skeletal Muscle, Pig	pig	10 μ M	1
ATPase, Na ⁺ /K ⁺ , Heart, Pig	pig	10 μ M	0
Carbonic Anhydrase II	hum	10 μ M	-1
Catechol-O-Methyl Transferase (COMT)	pig	10 μ M	1
Cholinesterase, Acetyl, ACES	hum	10 μ M	-19
Cyclooxygenase COX-1	hum	10 μ M	11
Cyclooxygenase COX-2	hum	10 μ M	-10
HMG-CoA Reductase	hum	10 μ M	-5
Monoamine Oxidase MAO-B	hum	10 μ M	50
Nitric Oxide Synthase, Neuronal (nNOS)	rat	10 μ M	0
Nitric Oxide Synthetase, Inducible (iNOS)	mouse	10 μ M	5
Peptidase, Factor Xa	hum	10 μ M	-12
Peptidase, Matrix Metalloproteinase-1 (MMP-1)	hum	10 μ M	-5
Peptidase, Matrix Metalloproteinase-7 (MMP-7)	hum	10 μ M	4
Peptidase, Matrix Metalloproteinase-13 (MMP-13)	hum	10 μ M	3
Peptidase, Metalloproteinase, Neutral Endopeptidase	hum	10 μ M	0
Phosphodiesterase PDE10A2	hum	10 μ M	-13
Phosphodiesterase PDE3	hum	10 μ M	-3
Phosphodiesterase PDE4	hum	10 μ M	-5
Phosphodiesterase PDE4D2	hum	10 μ M	-1
Phosphodiesterase PDE5	hum	10 μ M	-10
Phosphodiesterase PDE6	bov	10 μ M	-9
Protein Serine/Threonine Kinase, PKC, Non-Selective	rat	10 μ M	-16
Protein Serine/Threonine Kinase, PRKACA (PKA)	hum	10 μ M	-23
Protein Serine/Threonine Kinase, ROCK1	hum	10 μ M	3
Protein Tyrosine Kinase, EGF Receptor	hum	10 μ M	1
Steroid 5 α -Reductase	rat	10 μ M	-2
Xanthine Oxidase	bov	10 μ M	6
Adenosine A ₁	hum	10 μ M	1
Adenosine A _{2A}	hum	10 μ M	-8

Items meeting criteria for significance ($\geq 50\%$ stimulation or inhibition) are highlighted.

Bov = bovine; gp = guinea pig; ham = hamster; hum = human; pig = porcine

%Inh.: % of inhibition

- Enzyme and binding assay (continued)

Assay name	Species	Conc.	%Inh.
Adenosine A _{2B}	hum	10 µM	16
Adrenergic α ₁ , Non-Selective	rat	10 µM	-2
Adrenergic α ₂ , Non-Selective	rat	10 µM	19
Adrenergic β ₁	hum	10 µM	-1
Adrenergic β ₂	hum	10 µM	2
Adrenergic β ₃	hum	10 µM	4
Androgen (Testosterone)	hum	10 µM	5
Angiotensin AT ₁	hum	10 µM	10
Angiotensin AT ₂	hum	10 µM	-4
Bradykinin B ₁	hum	10 µM	5
Bradykinin B ₂	hum	10 µM	9
Calcium Channel L-Type, Benzothiazepine	rat	10 µM	-10
Calcium Channel L-Type, Dihydropyridine	rat	10 µM	0
Calcium Channel L-Type, Phenylalkylamine	rat	10 µM	-10
Calcium Channel N-Type	rat	10 µM	4
Cannabinoid CB ₁	hum	10 µM	19
Cannabinoid CB ₂	hum	10 µM	5
Cholecystokinin CCK ₁ (CCK _A)	hum	10 µM	0
Cholecystokinin CCK ₂ (CCK _B)	hum	10 µM	11
Dopamine D ₁	hum	10 µM	-5
Dopamine D _{2L}	hum	10 µM	8
Dopamine D _{2S}	hum	10 µM	3
Dopamine D ₃	hum	10 µM	9
Dopamine D _{4.2}	hum	10 µM	3
Endothelin ET _A	hum	10 µM	1
Estrogen Receptor (non-selective)	hum	10 µM	-11
GABA _A , Chloride Channel, TBOB	rat	10 µM	-6
GABA _A , Flunitrazepam, Central	rat	10 µM	-11
GABA _A , Muscimol, Central	rat	10 µM	5
GABA _B , Non-Selective	rat	10 µM	0
GABA _{B1A}	hum	10 µM	4
GABA _{B1B}	hum	10 µM	13
Glucocorticoid	hum	10 µM	7
Glutamate, AMPA	rat	10 µM	-2
Glutamate, Kainate	rat	10 µM	2
Glutamate, NMDA, Agonism	rat	10 µM	7

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%Inh.: % of inhibition

- Enzyme and binding assay (continued)

Assay name	Species	Conc.	%Inh.
Glutamate, NMDA, Glycine	rat	10 µM	1
Glutamate, NMDA, Phencyclidine	rat	10 µM	9
Glycine, Strychnine-Sensitive	rat	10 µM	6
Growth Hormone Secretagogue (GHS, Ghrelin)	hum	10 µM	6
Histamine H ₁	hum	10 µM	-6
Histamine H ₂	hum	10 µM	-14
Imidazoline I ₂ , Central	rat	10 µM	24
Insulin	rat	10 µM	3
IP (PGI ₂)	hum	10 µM	8
Melatonin MT ₁	hum	10 µM	-4
Muscarinic M ₁	hum	10 µM	8
Muscarinic M ₂	hum	10 µM	0
Muscarinic M ₃	hum	10 µM	4
Nicotinic Acetylcholine	hum	10 µM	-5
Opiate δ ₁ (OP ₁ , DOP)	hum	10 µM	8
Opiate κ (OP ₂ , KOP)	hum	10 µM	6
Opiate μ (OP ₃ , MOP)	hum	10 µM	2
Potassium Channel [K _{ATP}]	ham	10 µM	11
Potassium Channel [SK _{CA}]	rat	10 µM	-6
Progesterone PR-B	hum	10 µM	8
Serotonin (5-Hydroxytryptamine) 5-HT _{1A}	hum	10 µM	5
Serotonin (5-Hydroxytryptamine) 5-HT _{2A}	hum	10 µM	2
Serotonin (5-Hydroxytryptamine) 5-HT _{2B}	hum	10 µM	81
Serotonin (5-Hydroxytryptamine) 5-HT _{2C}	hum	10 µM	10
Serotonin (5-Hydroxytryptamine) 5-HT ₃	hum	10 µM	4
Serotonin (5-Hydroxytryptamine) 5-HT ₄	gp	10 µM	-2
Sigma, Non-Selective	gp	10 µM	62
Sodium Channel, Site 2	rat	10 µM	10
Tachykinin NK ₁	hum	10 µM	3
Tachykinin NK ₂	hum	10 µM	0
Tachykinin NK ₃	hum	10 µM	4
Transporter, Dopamine (DAT)	hum	10 µM	30
Transporter, GABA	rat	10 µM	-12
Transporter, Norepinephrine (NET)	hum	10 µM	20
Transporter, Serotonin (5-Hydroxytryptamine) (SERT)	hum	10 µM	9

Items meeting criteria for significance (≥50% stimulation or inhibition) are highlighted.

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%Inh.: % of inhibition

- Enzyme and binding assay (continued)

Assay name	Species	Conc.	%Inh.
Transporter, Vesicular Monoamine (Non-Selective)	hum	10 μ M	-8
Vasopressin V _{1A}	hum	10 μ M	-1
Vasopressin V ₂	hum	10 μ M	6

Items meeting criteria for significance ($\geq 50\%$ stimulation or inhibition) are highlighted.

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%Inh.: % of inhibition

- Cellular functional assay

Assay name	Species	Conc.	%Cont.
Neurotensin-1 (NT1) (agonistic effect)	hum	10 μ M	6.5
5-HT7 (agonistic effect)	hum	10 μ M	-1.5
TRPV1 (agonistic effect)	hum	10 μ M	14.6
TRMP8 (antagonistic effect)	hum	10 μ M	-27.3

Results are expressed as a percent of control agonist response or inverse agonist response.

%Cont.: % of control