3. MATERIALS AND METHODS

Some changes due to improvement of the assays may occur between the writing of this study plan and testing. Validation of these changes will include verification that they do not affect assay results. The final study report will reflect the updated experimental conditions.

3.1. Experimental Conditions

3.1.1. *In Vitro* Pharmacology: Binding Assays

Assay	Source	Ligand	Conc.	Kd	Non Specific	Incubation	Detection Method	Bibl.
Receptors								
A_1*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]DPCPX	1 nM	1.7 nM	DPCPX (1 µM)	60 min RT	Scintillation counting	245
A_1*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]CCPA	1 nM	0.7 nM	CPA (10 µM)	60 min RT	Scintillation counting	198
A_{2A}*(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]CGS 21680	6 nM	27 nM	NECA (10 µM)	120 min RT	Scintillation counting	141
A_3*(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{125}I]AB-MECA	0.15 nM	0.22 nM	IB-MECA (1 µM)	120 min RT	Scintillation counting	206
α_1 (non-selective) (antagonist radioligand)	rat cerebral cortex	[^{3}H]prazosin	0.25 nM	0.09 nM	prazosin (0.5 µM)	60 min RT	Scintillation counting	88
α_{1A}*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]prazosin	0.1 nM	0.1 nM	epinephrine (0.1 mM)	60 min RT	Scintillation counting	897
α_{1B}*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]prazosin	0.15 nM	0.055 nM	phentolamine (10 µM)	60 min RT	Scintillation counting	701
α_{1D}*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]prazosin	0.2 nM	0.15 nM	phentolamine (10 µM)	60 min RT	Scintillation counting	760
α_2 (non-selective) (antagonist radioligand)	rat cerebral cortex	[^{3}H]RX 821002	0.5 nM	0.38 nM	(-)epinephrine (100 µM)	60 min RT	Scintillation counting	249
α_{2A} *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]RX 821002	1 nM	0.8 nM	(-)epinephrine (100 µM)	60 min RT	Scintillation counting	542
α_{2B}*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]RX 821002	2.5 nM	5 nM	(-)epinephrine (100 µM)	60 min RT	Scintillation counting	56
α_{2C} *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]RX 821002	2 nM	0.95 nM	(-)epinephrine (100 µM)	60 min RT	Scintillation counting	56
β_1 *(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H](-)CGP 12177	0.3 nM	0.39 nM	alprenolol (50 µM)	60 min RT	Scintillation counting	548
β_2 *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H](-)CGP 12177	0.3 nM	0.15 nM	alprenolol (50 µM)	120 min RT	Scintillation counting	794
AT_1 *(h)* (antagonist radioligand)	human recombinant (HEK-293 cells)	[^{125}I][Sar^1,Ile^8]-AT-II	0.05 nM	0.05 nM	angiotensin-II (10 µM)	120 min 37°C	Scintillation counting	776
AT_2 *(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{125}I]CGP 42112A	0.01 nM	0.01 nM	angiotensin-II (1 µM)	4 hr 37°C	Scintillation counting	248
APJ (apelin) *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I](Glp^{65},Nle^{75},Tyr^{77}) -apelin-13	0.03 nM	0.06 nM	apelin-13 (1 µM)	120 min RT	Scintillation counting	846
B_1*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]desArg^{10}-KD	0.35 nM	0.085 nM	desArg^9[Leu^8]-BK (10 µM)	60 min RT	Scintillation counting	525
B_2 *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]bradykinin	0.3 nM	0.32 nM	bradykinin (1 µM)	60 min RT	Scintillation counting	346

Assay	Source	Ligand	Conc.	Kd	Non Specific	Incubation	Detection Method	Bibl.
CB_1*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]CP 55940	0.5 nM	3.5 nM	WIN 55212-2 (10 µM)	120 min 37°C	Scintillation counting	657
CB_2*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]WIN 55212-2	0.8 nM	1.5 nM	WIN 55212-2 (5 µM)	120 min 37°C	Scintillation counting	165
CCK_1 (CCK_A) *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]CCK-8s	0.08 nM	0.24 nM	CCK-8s (1 µM)	60 min RT	Scintillation counting	562
CCK_2 (CCK_B) *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]CCK-8s	0.08 nM	0.054 nM	CCK-8s (1 µM)	60 min RT	Scintillation counting	134
CRF_1*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]sauvagine	0.075 nM	0.12 nM	sauvagine (0.5 µM)	120 min RT	Scintillation counting	557
D_1*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]SCH 23390	0.3 nM	0.2 nM	SCH 23390 (1 µM)	60 min RT	Scintillation counting	281
D_{2S}*(h)* (antagonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]methyl-spiperone	0.3 nM	0.15 nM	(+)butaclamol (10 µM)	60 min RT	Scintillation counting	87
D_{2S}*(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]7-OH-DPAT	1 nM	0.68 nM	butaclamol (10 µM)	60 min RT	Scintillation counting	87
D_{2L}*(h)* (antagonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]methyl-spiperone	0.3 nM	0.1 nM	butaclamol (10 µM)	60 min RT	Scintillation counting	659
D_3*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]methyl-spiperone	0.3 nM	0.085 nM	(+)butaclamol (10 µM)	60 min RT	Scintillation counting	145
$D_{4.4}$*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]methyl-spiperone	0.3 nM	0.19 nM	(+)butaclamol (10 µM)	60 min RT	Scintillation counting	252
D_5*(h)* (antagonist radioligand)	human recombinant (GH4 cells)	[^{3}H]SCH 23390	0.3 nM	0.25 nM	SCH 23390 (10 µM)	60 min RT	Scintillation counting	232
ET_A*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]endothelin-1	0.03 nM	0.03 nM	endothelin-1 (100 nM)	120 min 37°C	Scintillation counting	30
ET_B *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]endothelin-1	0.03 nM	0.04 nM	endothelin-1 (0.1 µM)	120 min 37°C	Scintillation counting	541
$GABA_{A1}$ *(h)* (α1,β2,γ2) (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]muscimol	15 nM	30 nM	muscimol (10 µM)	120 min RT	Scintillation counting	1096
mGluR5 (h) (agonist radioligand)	human recombinant (CHO cells)	[3H]Quisqualate	40nM	44nM	L-Glutamate (1mM)	120 min RT	Scintillation counting	1222
glycine (strychnine-sensitive) (antagonist radioligand)	rat spinal cord	[^{3}H]strychnine	2 nM	20 nM	strychnine (100 µM)	15 min 0°C	Scintillation counting	150
CXCR2 (IL-8B) *(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{125}I]IL-8	0.025 nM	0.022 nM	IL-8 (30 nM)	60 min RT	Scintillation counting	266
CCR1 *(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{125}I]MIP-1α	0.01 nM	0.02 nM	MIP-1α (100 nM)	120 min RT	Scintillation counting	172
H_1*(h)* (antagonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]pyrilamine	1 nM	1.7 nM	pyrilamine (1 µM)	60 min RT	Scintillation counting	492
H_2*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{125}I]APT	0.075 nM	2.9 nM	tiotidine (100 µM)	120 min RT	Scintillation counting	540
H_3*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]N$^{\alpha}$-Me-histamine	1 nM	0.32 nM	(R)α-Me-histamine (1 µM)	60 min RT	Scintillation counting	563
I_2 (antagonist radioligand)	rat cerebral cortex	[^{3}H]idazoxan (+ 1 µM yohimbine)	2 nM	4 nM	cirazoline (10 µM)	30 min RT	Scintillation counting	27

Assay	Source	Ligand	Conc.	Kd	Non Specific	Incubation	Detection Method	Bibl.
CysLT$_1$ (LTD$_4$) *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]LTD$_4$	0.3 nM	0.24 nM	LTD$_4$ (1 µM)	60 min RT	Scintillation counting	618
MC$_1$ (agonist radioligand)	B16-F1 cells (endogenous)	[^{125}I]NDP-α-MSH	0.05 nM	0.05 nM	NDP-α-MSH (1 µM)	90 min RT	Scintillation counting	390
MC$_4$*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]NDP-α-MSH	0.05 nM	0.54 nM	NDP-α-MSH (1 µM)	120 min 37°C	Scintillation counting	211
MC$_5$*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]NDP-α-MSH	0.05 nM	0.7 nM	NDP-α-MSH (1 µM)	60 min 37°C	Scintillation counting	211
MT$_1$ (ML$_{1A}$) *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]2-iodomelatonin	0.01 nM	0.04 nM	melatonin (1 µM)	240 min RT	Scintillation counting	639
M (non-selective) (antagonist radioligand)	rat cerebral cortex	[^{3}H]QNB	0.05 nM	0.01 nM	atropine (1 µM)	120 min RT	Scintillation counting	195
M$_1$*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]pirenzepine	2 nM	13 nM	atropine (1 µM)	60 min RT	Scintillation counting	59
M$_3$ *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]4-DAMP	0.2 nM	0.5 nM	atropine (1 µM)	60 min RT	Scintillation counting	546
M$_4$*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]4-DAMP	0.2 nM	0.32 nM	atropine (1 µM)	60 min RT	Scintillation counting	59
M$_5$*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]4-DAMP	0.3 nM	0.3 nM	atropine (1 µM)	60 min RT	Scintillation counting	59
NK$_1$*(h)* (agonist radioligand)	U373MG uppsala	[^{125}I]-Substance P LYS3	0.05 nM	0.04 nM	[Sar^9,Met(O$_2$)^{11}]-SP (1 µM)	30 min RT	Scintillation counting	104
NK$_2$*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I]NKA	0.1 nM	0.12 nM	[Nleu^{10}]-NKA (4-10) (300 nM)	60 min RT	Scintillation counting	3
NK$_3$ *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]SR 142801	0.4 nM	0.47 nM	SB 222200 (10 µM)	120 min RT	Scintillation counting	741
Y (non-selective) (agonist radioligand)	rat cerebral cortex	[^{125}I]peptide YY	0.05 nM	0.1 nM	NPY (1 µM)	120 min RT	Scintillation counting	84
Y$_1$*(h)* (agonist radioligand)	SK-N-MC cells (endogenous)	[^{125}I]peptide YY	0.025 nM	0.06 nM	NPY (1 µM)	120 min 37°C	Scintillation counting	391
Y$_2$*(h)* (agonist radioligand)	KAN-TS cells	[^{125}I]peptide YY	0.015 nM	0.01 nM	NPY (1 µM)	60 min 37°C	Scintillation counting	77
N neuronal α4β2 *(h)* (agonist radioligand)	SH-SY5Y cells (human recombinant)	[^{3}H]cytisine	0.6 nM	0.3 nM	nicotine (10 µM)	120 min 4°C	Scintillation counting	1084
N neuronal α7 *(h)* (antagonist radioligand)	SH-SY5Y cells (human recombinant)	[^{125}I]α-bungarotoxin	0.05 nM	0.34 nM	α-bungarotoxin (1 µM)	120 min 37°C	Scintillation counting	347
N muscle-type *(h)* (antagonist radioligand)	TE671 cells (endogenous)	[^{125}I]α-bungarotoxin	0.5 nM	2 nM	α-bungarotoxin (5 µM)	120 min RT	Scintillation counting	524
opioid (non-selective) (antagonist radioligand)	rat cerebral cortex	[^{3}H]naloxone	1 nM	2.6 nM	naloxone (1 µM)	40 min RT	Scintillation counting	43
δ (DOP) *(h)* (agonist radioligand)	recombinant humain (Chem-1)	[^{3}H]DADLE	0.5 nM	0.6 nM	naltrexone (10 µM)	60 min RT	Scintillation counting	501
kappa (h) (KOP) (agonist radioligand)	RBL recombinant	[3H]U69593	0.5 nM	0.6 nM	naloxone (10µM)	60 min RT	Scintillation counting	222
µ (MOP) *(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]DAMGO	0.5 nM	0.35 nM	naloxone (10 µM)	120 min RT	Scintillation counting	260
NOP (ORL1) *(h)* (agonist radioligand)	recombinant humain	[^{3}H]nociceptin	0.06 nM	0.054 nM	nociceptin (1 µM)	60 min RT	Scintillation counting	1588
PPARγ *(h)* (agonist radioligand)	human recombinant (*E. coli*)	[^{3}H]rosiglitazone	5 nM	5.7 nM	rosiglitazone (10 µM)	120 min 4°C	Scintillation counting	567

Assay	Source	Ligand	Conc.	Kd	Non Specific	Incubation	Detection Method	Bibl.
EP_2*(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]PGE_2	3 nM	3 nM	PGE_2 (10 µM)	120 min RT	Scintillation counting	781
IP (PGI_2) *(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]iloprost	6 nM	8 nM	iloprost (10 µM)	60 min RT	Scintillation counting	781
P2Y (agonist radioligand)	rat cerebral cortex	[^{35}S]dATPαS	10 nM	10 nM	dATPαS (10 µM)	60 min RT	Scintillation counting	298
5-HT_{1A}*(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]8-OH-DPAT	0.5 nM	0.5 nM	8-OH-DPAT (10 µM)	60 min RT	Scintillation counting	164
5-HT_{1B} (antagonist radioligand)	rat cerebral cortex	[^{125}I]CYP (+ 30 µM isoproterenol)	0.1 nM	0.16 nM	serotonin (10 µM)	120 min 37°C	Scintillation counting	111
5-HT_{2A}*(h)* (antagonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]ketanserin	0.5 nM	0.6 nM	ketanserin (1 µM)	60 min RT	Scintillation counting	20
5-HT_{2A}*(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{125}I](±)DOI	0.1 nM	0.3 nM	(±)DOI (1 µM)	60 min RT	Scintillation counting	288
5-HT_{2B}*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]mesulergine	2 nM	2.4 nM	SB206553 (10 µM)	60 min RT	Scintillation counting	678
5-HT_{2B}*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{125}I](±)DOI	0.2 nM	0.2 nM	(±)DOI (1 µM)	60 min RT	Scintillation counting	571
5-HT_{2C}*(h)* (antagonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]mesulergine	1 nM	0.5 nM	RS 102221 (10 µM)	120 min 37°C	Scintillation counting	543
5-HT_{2C}*(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{125}I](±)DOI	0.1 nM	0.9 nM	(±)DOI (10 µM)	60 min 37°C	Scintillation counting	288
5-HT_{4e}*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]GR 113808	0.3 nM	0.15 nM	serotonin (100 µM)	60 min 37°C	Scintillation counting	309
5-HT_{5a} *(h)* (agonist radioligand)	human recombinant (HEK-293 cells)	[^{3}H]LSD	1.5 nM	1.5 nM	serotonin (100 µM)	120 min 37°C	Scintillation counting	193
5-HT_6 *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]LSD	2 nM	1.8 nM	serotonin (100 µM)	120 min 37°C	Scintillation counting	161
5-HT_7 *(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]LSD	4 nM	2.3 nM	serotonin (10 µM)	120 min RT	Scintillation counting	217
sigma (non-selective) (h) (agonist radioligand)	Jurkat cells (endogenous)	[3H]DTG	10 nM	41 nM	Haloperidol (10 µM)	120 min RT	Scintillation counting	1136
GR *(h)* (agonist radioligand)	IM-9 cells (cytosol)	[^{3}H]dexamethasone	1.5 nM	1.5 nM	triamcinolone (10 µM)	6 hr 4°C	Scintillation counting	283
ER (non-selective) *(h)* (agonist radioligand)	MCF-7 cells (cytosol)	[^{3}H]estradiol	0.4 nM	0.2 nM	17-β-estradiol (6 µM)	20 hr 4°C	Scintillation counting	1070
Estrogen ER alpha (h) (agonist radioligand)	human recombinant (sf9 cells)	[3H] Estradiol	0.5 nM	0.20 nM	Diethylstilbestrol (1µM)	120 min RT	Scintillation counting	1280
PR *(h)* (agonist radioligand)	T47D cells (cytosol)	[^{3}H]progesterone	0.5 nM	2 nM	promegestone (1 µM)	20 hr 4°C	Scintillation counting	930
AR *(h)* (agonist radioligand)	LNCaP cells (cytosol)	[^{3}H]methyltrienolone	1 nM	0.8 nM	testostérone (1 µM)	24 hr 4°C	Scintillation counting	498
TRH_1*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]Me-TRH	2 nM	3.9 nM	TRH (10 µM)	120 min 4°C	Scintillation counting	709
V_{1a}*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]AVP	0.3 nM	0.5 nM	AVP (1 µM)	60 min RT	Scintillation counting	343
V_2*(h)* (agonist radioligand)	human recombinant (CHO cells)	[^{3}H]AVP	0.3 nM	0.76 nM	AVP (1 µM)	120 min RT	Scintillation counting	343

Assay	Source	Ligand	Conc.	Kd	Non Specific	Incubation	Detection Method	Bibl.
Ion channels								
BZD (central) (agonist radioligand)	rat cerebral cortex	[^{3}H]flunitrazepam	0.4 nM	2.1 nM	diazepam (3 µM)	60 min 4°C	Scintillation counting	227
AMPA (agonist radioligand)	rat cerebral cortex	[^{3}H]AMPA	8 nM	82 nM	L-glutamate (1 mM)	60 min 4°C	Scintillation counting	166
kainate (agonist radioligand)	rat cerebral cortex	[^{3}H]kainic acid	5 nM	19 nM	L-glutamate (1 mM)	60 min 4°C	Scintillation counting	160
glycine (strychnine-insensitive) (antagonist radioligand)	rat cerebral cortex	[^{3}H]MDL 105,519	0.5 nM	5 nM	glycine (1 mM)	45 min 0°C	Scintillation counting	219
P2X (agonist radioligand)	rat urinary bladder	[^{3}H]α,β-MeATP	3 nM	2.6 nM	α,β-MeATP (10 µM)	120 min 4°C	Scintillation counting	17
5-HT$_3$*(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]BRL 43694	0.5 nM	1.15 nM	MDL 72222 (10 µM)	120 min RT	Scintillation counting	109
Ca^{2+} channel (L, dihydropyridine site) (antagonist radioligand)	rat cerebral cortex	[^{3}H]nitrendipine	0.1 nM	0.18 nM	nitrendipine (1 µM)	90 min RT	Scintillation counting	996
Ca^{2+} channel (L, diltiazem site) (benzothiazepines) (antagonist radioligand)	rat cerebral cortex	[^{3}H]diltiazem	15 nM	52 nM	diltiazem (10 µM)	120 min RT	Scintillation counting	212
Ca^{2+} channel (L, verapamil site) (phenylalkylamine) (antagonist radioligand)	rat cerebral cortex	[^{3}H]D888	3 nM	3 nM	D 600 (10 µM)	120 min RT	Scintillation counting	194
Ca^{2+} channel (N) (antagonist radioligand)	rat cerebral cortex	[^{125}I]ω-conotoxin GVIA	0.001 nM	0.0007 nM	ω-conotoxin GVIA (10 nM)	30 min RT	Scintillation counting	259
K_{ATP} channel (antagonist radioligand)	rat cerebral cortex	[^{3}H]glibenclamide	0.1 nM	0.05 nM	glibenclamide (1 µM)	60 min RT	Scintillation counting	6
Potassium Channel hERG (human)- [3H] Dofetilide	human recombinant (HEK-293 cells)	[3H]Dofetilide	3 nM	6.6 nM	Terfenadine (25 µM)	60 min RT	Scintillation counting	1398
K_V channel (antagonist radioligand)	rat cerebral cortex	[^{125}I]α-dendrotoxin	0.01 nM	0.04 nM	α-dendrotoxin (50 nM)	60 min RT	Scintillation counting	225
SK_{Ca} channel (antagonist radioligand)	rat cerebral cortex	[^{125}I]apamin	0.007 nM	0.007 nM	apamin (100 nM)	60 min 4°C	Scintillation counting	112
Na^+ channel (site 2) (antagonist radioligand)	rat cerebral cortex	[^{3}H]batrachotoxin	10 nM	91 nM	veratridine (300 µM)	60 min 37°C	Scintillation counting	28
Transporters								
adenosine transporter (antagonist radioligand)	guinea-pig cerebral cortex	[^{3}H]NBTI	0.15 nM	0.08 nM	NBTI (5 µM)	30 min RT	Scintillation counting	254
norepinephrine transporter *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]nisoxetine	1 nM	2.9 nM	desipramine (1 µM)	120 min 4°C	Scintillation counting	180
dopamine transporter *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]BTCP	4 nM	4.5 nM	BTCP (10 µM)	120 min 4°C	Scintillation counting	190
GABA transporter (antagonist radioligand)	rat cerebral cortex	[^{3}H]GABA (+ 10 µM isoguvacine) (+ 10 µM baclofen)	10 nM	4600 nM	GABA (1 mM)	30 min RT	Scintillation counting	214
choline transporter (CHT1) *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]hemicholinium-3	3 nM	3.9 nM	hemicholinium-3 (10 µM)	60 min RT	Scintillation counting	648
5-HT transporter *(h)* (antagonist radioligand)	human recombinant (CHO cells)	[^{3}H]imipramine	2 nM	1.7 nM	imipramine (10 µM)	60 min RT	Scintillation counting	566

3.1.2. *In Vitro* Pharmacology: Cellular and Nuclear Receptor Functional Assays

Assay	Source	Stimulus	Incubation	Measured Component	Detection Method	Bibl.
Receptors						
CT (Calcitonin) *(h)* (agonist effect)	T47D cells (endogenous)	none (1 µM human calcitonin for control)	10 min RT	cAMP	HTRF	803
CT (Calcitonin) *(h)* (antagonist effect)	T47D cells (endogenous)	human calcitonin (30 nM)	10 min RT	cAMP	HTRF	803
GPR109A *(h)* (agonist effect)	**human recombinant (RBL cells)**	none (12 µM Nicotinic Acid Free Acid for control)	RT	intracellular [Ca^{2+}]	Fluorimetry	1528
GPR109A *(h)* (antagonist effect)	**human recombinant (RBL cells)**	Nicotinic Acid Free Acid (300 nM)	RT	intracellular [Ca^{2+}]	Fluorimetry	1528
P2Y11 *(h)* (agonist effect)	human recombinant (1321N1 cells)	none (1 mM of ATP for control)	RT	intracellular [Ca^{2+}]	Fluorimetry	1531
P2Y11 *(h)* (antagonist effect)	human recombinant (1321N1 cells)	ATP (60 µM)	RT	intracellular [Ca^{2+}]	Fluorimetry	1531

3.1.3. *In Vitro* Pharmacology: Enzyme and Uptake Assays

Assay	Source	Substrate/Stimulus/Tracer	Incubation	Measured Component	Detection Method	Bibl.
Kinases						
Abl kinase *(h)*	human recombinant (insect cells)	ATP + Ulight-TK peptide (100 nM)	30 min RT	phospho-Ulight-TK peptide	LANCE	556
ERK_1*(h)*	human recombinant (*E. coli*)	ATP + Ulight-CFFKNIVTPRTPPPSQGK-amide (50 nM)	30 min RT	phospho-Ulight-CFFKNIVTPRTPPPSQGK-amide	LANCE	713
ERK_2*(h)* ($P42^{mapk}$)	human recombinant (*E. coli*)	ATP + Ulight-CFFKNIVTPRTPPPSQGK-amide (100 nM)	15 min RT	phospho-Ulight-CFFKNIVTPRTPPPSQGK-amide	LANCE	671
Fyn kinase *(h)*	human recombinant (insect cells)	ATP + biotinyl-βAβAβAYQAEENTYDEYEN (2 µM)	60 min RT	phospho-biotinyl-βAβAβAYQAEENTYDEYEN	HTRF	626
HER2/ErbB2 kinase *(h)*	human recombinant (insect cells)	ATP + biotinyl-βAβAβAAEEEEYFELVAKKK (600 nM)	10 min RT	phospho-biotinyl-βAβAβAAEEEEYFELVAKKK	HTRF	681
IRK *(h)* (InsR)	human recombinant	ATP + Ulight-Poly GAT[EAY(1:1:1)]n (50 nM)	10 min RT	phospho-Ulight-Poly GAT[EAY(1:1:1)]n	LANCE	467
JNK1 *(h)*	human recombinant (*E. coli*)	ATP + Ulight-CFFKNIVTPRTPPPSQGK-amide (100 nM)	60 min RT	phospho-Ulight-CFFKNIVTPRTPPPSQGK-amide	LANCE	611
JNK3 *(h)*	human recombinant (*E. coli*)	ATP + Ulight-CFFKNIVTPRTPPPSQGK-amide (100 nM)	30 min RT	phospho-Ulight-CFFKNIVTPRTPPPSQGK-amide	LANCE	680
Lck kinase *(h)*	human recombinant (insect cells)	ATP + Ulight-Poly GAT[EAY(1:1:1)]n (25 nM)	10 min RT	phospho-Ulight-Poly GAT[EAY(1:1:1)]n	LANCE	556
Lyn A kinase *(h)*	human recombinant (insect cells)	ATP + biotinyl-βAβAβAKVEKIGEGTYGVVYK (400 nM)	120 min RT	phospho-biotinyl-βAβAβAKVEKIGEGTYGVVYK	HTRF	41
p38α kinase *(h)*	human recombinant (*E. coli*)	ATP + Ulight-CFFKNIVTPRTPPPSQGK-amide (100 nM)	30 min RT	phospho-Ulight-CFFKNIVTPRTPPPSQGK-amide	LANCE	620
PKCα *(h)*	human recombinant (insect cells)	ATP + biotinyl-βAβAβAKIQASFRGHMARKK (60 nM)	10 min RT	phospho-biotinyl-βAβAβAKIQASFRGHMARKK	HTRF	628
Src kinase *(h)*	human recombinant (insect cells)	ATP + Ulight-Poly GAT[EAY(1:1:1)]n (5 nM)	10 min RT	phospho-Ulight-Poly GAT[EAY(1:1:1)]n	LANCE	41
Epigenetic enzymes and DNA-related enzymes						
Catechol O-methyltransferase (h)	human recombinant (E. coli)	Pyrocatechol (15 µM)/ SAM (10 µM)	15 min, 37°C	SAH	MS	1491
CENP-E *(h)*	human recombinant (*E. coli*)	ATP (100 µM)	5 min RT	inorganic phosphate	Photometry	853
Eg5 *(h)*	human recombinant	ATP (50 µM)	10 min RT	inorganic phosphate	Photometry	853
HDAC3 *(h)*	human recombinant	fluorogenic HDAC substrate (50 µM)	10 min RT	fluoro-lysine	Fluorimetry	896
HDAC4 *(h)*	human recombinant	fluorogenic HDAC substrate class 2a (20 µM)	30 min RT	fluoro-lysine	Fluorimetry	896
HDAC6 *(h)*	human recombinant	fluorogenic HDAC substrate (25 µM)	30 min RT	fluoro-lysine	Fluorimetry	896
HDAC11 *(h)*	human recombinant	fluorogenic HDAC substrate class 2a (50 µM)	30 min 37°C	fluoro-lysine	Fluorimetry	896
sirtuin 1 *(h)* (activator effect)	human recombinant (*E. coli*)	fluorogenic HDAC substrate (200 µM)	20 min RT	fluoro-lysine	Fluorimetry	976
sirtuin 2 *(h)* (inhibitor effect)	human recombinant (*E. coli*)	fluoro-lysine sirtuin 2 deacetylase substrate (150 µM)	60 min RT	fluoro-lysine	Fluorimetry	976

Assay	Source	Substrate/Stimulus/Tracer	Incubation	Measured Component	Detection Method	Bibl.
Other enzymes						
Cholinesterase Butyryl CHLE (h)	human serum	S butyrylthiocholine (0.56 mM)	120 min RT	5 thio 2 nitro benzoic acid	Photometry	1218
COX1(h)	human recombinant	Arachidonic acid (3µM) + ADHP (25 µM)	3 min RT	Resorufin (oxydized ADHP)	Fluorimetry	1480
COX2(h)	human recombinant (Sf9 cells)	arachidonic acid (1.2 µM)+ ADHP (25 µM)	5 min RT	Resorufin (oxydized ADHP)	Fluorimetry	1480
5-lipoxygenase *(h)*	human recombinant (Sf9 cells) (cytosol)	arachidonic acid (25 µM)	20 min RT	rhodamine 123	Fluorimetry	1068
PDE1B *(h)*	human recombinant (Sf9 cells)	[3H]cGMP + cGMP (1.5 µM)	20 min RT	[3H]5'GMP	Scintillation counting	1399
PDE2A1 *(h)*	human recombinant (Sf9 cells)	[3H]cAMP + cAMP (2µM)	20 min RT	[3H]5'AMP	Scintillation counting	1399
PDE3A *(h)*	human recombinant (Sf9 cells)	[3H]cAMP + cAMP (0.5µM)	20 min RT	[3H]5'AMP	Scintillation counting	1399
PDE4A1A *(h)*	human recombinant (Sf9 cells)	[3H]cAMP + cAMP (0.5µM)	20 min RT	[3H]5'AMP	Scintillation counting	1399
PDE4B1 *(h)*	human recombinant (Sf9 cells)	[3H]cAMP + cAMP (0.5µM)	20 min RT	[3H]5'AMP	Scintillation counting	1399
PDE4D2 *(h)*	human recombinant (Sf9 cells)	[3H]cAMP + cAMP (0.5µM)	20 min RT	[3H]5'AMP	Scintillation counting	1399
PDE5 *(h)* (non-selective)	human platelets	[^{3}H]cGMP + cGMP (1 µM)	60 min RT	[^{3}H]5'GMP	Scintillation counting	263
ACE *(h)*	human recombinant	Abz-FRK(Dnp)-P-OH (15 µM)	30 min 37°C	Abz-Phe-Arg	Fluorimetry	1128
elastase *(h)*	human neutrophil	MeOSAAPV-pNa (0.4 mM)	30 min 37°C	pNa	Photometry	2
cathepsin G *(h)*	human leukocytes	N-SAAPF-pNa (1 mM)	15 min 37°C	pNa	Photometry	169
MMP-1 *(h)*	human recombinant (*E. coli*)	DNP-Pro-Cha-Gly-Cys(Me)-His-Ala-Lys(n-Me-Abz)-NH_2 (10 µM)	20 min 37°C	Cys(Me)-His-Ala-Lys(n-Me-Abz)-NH_2	Fluorimetry	342
MMP-9 *(h)*	human recombinant	NFF-2 (10 µM)	45 min 37°C	Mca-Arg-Pro-Lys-Pro-Tyr-Ala	Fluorimetry	297
adenylyl cyclase (activator effect)	CHO cells	none (100 µM forskolin for control)	10 min RT	cAMP	HTRF	1109
guanylyl cyclase *(h)* (activator effect)	human recombinant	GTP (10 µM) (100 µM SNP for control)	10 min RT	cGMP	HTRF	1076
phosphatase 1B *(h)* (PTP1B)	human recombinant (*E. coli*)	DIFMUP (10 µM)	30 min RT	DIFMU	Fluorimetry	928
acetylcholinesterase *(h)*	human recombinant (HEK-293 cells)	Acetylthiocholine (400 µM)	30 min RT	5 thio 2 nitrobenzoic acid	Photometry	63
MAO-A *(h)*	human placenta	kynuramine (0.15 mM)	20 min RT	4-OHquinoline	Photometry	265
MAO-B *(h)* recombinant enzyme	human recombinant	D-Luciferin derivative (4 µM)	60 min 37°C	methyl ester luciferin	Luminescence	1134
tyrosine hydroxylase	rat striatum	[^{3}H]tyrosine (10 µM)	20 min 37°C	[^{3}H]H_2O	Scintillation counting	168
ATPase (Na^+/K^+)	porcine cerebral cortex	ATP (2 mM)	60 min 37°C	Pi	Photometry	71

Assay	Source	Substrate/Stimulus/Tracer	Incubation	Measured Component	Detection Method	Bibl.

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