

Supporting Information

Discovery of Novel Aminotetralines and Aminochromanes as Selective and Competitive Glycine Transporter 1 (GlyT1) Inhibitors

Willi Amberg, Udo E. W. Lange, Michael Ochse, Frauke Pohlki, Berthold Behl, Ana Lucia Relo, Wilfried Hornberger, Carolin Hoft, Mario Mezler, Jens Sydor, Ying Wang, Hongyu Zhao, Jason T. Brewer, Justin Dietrich, Huanqiu Li, Irini Akritopoulou-Zanze, Yanbin Lao, Steven M. Hannick, Yi-Yin Ku, Anil Vasudevan*

AbbVie Deutschland GmbH & Co. KG, Neuroscience Research, Knollstrasse, 67061
Ludwigshafen, Germany

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CEREP Profile for Compound (7*S*,8*R*)-27a

Assay	Test Concentration (M)	% Inhibition of Control Specific Binding
A1 (h) (antagonist radioligand)	1.0E-05	-9
A2A (h) (agonist radioligand)	1.0E-05	15
A3 (h) (agonist radioligand)	1.0E-05	-8
alpha 1 (non-selective) (antagonist radioligand)	1.0E-05	15
alpha 2 (non-selective) (antagonist radioligand)	1.0E-05	0
beta 1 (h) (agonist radioligand)	1.0E-05	11
beta 2 (h) (agonist radioligand)	1.0E-05	4
AT1 (h) (antagonist radioligand)	1.0E-05	-25
AT2 (h) (agonist radioligand)	1.0E-05	-3
BZD (central) (agonist radioligand)	1.0E-05	4
BZD (peripheral) (antagonist radioligand)	1.0E-05	7
BB (non-selective) (agonist radioligand)	1.0E-05	-1
B2 (h) (agonist radioligand)	1.0E-05	6
CGRP (h) (agonist radioligand)	1.0E-05	-3
CB1 (h) (agonist radioligand)	1.0E-05	2
CCK1 (CCKA) (h) (agonist radioligand)	1.0E-05	-11
CCK2 (CCKB) (h) (agonist radioligand)	1.0E-05	-12
D1 (h) (antagonist radioligand)	1.0E-05	22
D2S (h) (antagonist radioligand)	1.0E-05	1
D3 (h) (antagonist radioligand)	1.0E-05	21
D4.4 (h) (antagonist radioligand)	1.0E-05	-3
D5 (h) (antagonist radioligand)	1.0E-05	17
ETA (h) (agonist radioligand)	1.0E-05	-15
ETB (h) (agonist radioligand)	1.0E-05	4
GABA (non-selective) (agonist radioligand)	1.0E-05	7
GAL1 (h) (agonist radioligand)	1.0E-05	0
GAL2 (h) (agonist radioligand)	1.0E-05	2
PDGF (agonist radioligand)	1.0E-05	5
CXCR2 (IL-8B) (h) (agonist radioligand)	1.0E-05	-8
TNF-alpha (h) (agonist radioligand)	1.0E-05	-2
CCR1 (h) (agonist radioligand)	1.0E-05	3
H1 (h) (antagonist radioligand)	1.0E-05	-1

H2 (h) (antagonist radioligand)	1.0E-05	-10
MC4 (h) (agonist radioligand)	1.0E-05	7
MT1 (ML1A) (h) (agonist radioligand)	1.0E-05	-9
M1 (h) (antagonist radioligand)	1.0E-05	18
M2 (h) (antagonist radioligand)	1.0E-05	22
M3 (h) (antagonist radioligand)	1.0E-05	34
M4 (h) (antagonist radioligand)	1.0E-05	20
M5 (h) (antagonist radioligand)	1.0E-05	4
NK1 (h) (agonist radioligand)	1.0E-05	10
NK2 (h) (agonist radioligand)	1.0E-05	11
NK3 (h) (antagonist radioligand)	1.0E-05	9
Y1 (h) (agonist radioligand)	1.0E-05	-14
Y2 (h) (agonist radioligand)	1.0E-05	-8
NTS1 (NT1) (h) (agonist radioligand)	1.0E-05	-14
delta 2 (DOP) (h) (agonist radioligand)	1.0E-05	40
kappa (KOP) (agonist radioligand)	1.0E-05	81
	1.0E-06	27
mu (MOP) (h) (agonist radioligand)	1.0E-05	56
NOP (ORL1) (h) (agonist radioligand)	1.0E-05	3
PAC1 (PACAP) (h) (agonist radioligand)	1.0E-05	2
PPARgamma (h) (agonist radioligand)	1.0E-05	-6
PCP (antagonist radioligand)	1.0E-05	7
EP2 (h) (agonist radioligand)	1.0E-05	2
TP (h) (TXA2/PGH2) (antagonist radioligand)	1.0E-05	-2
IP (PGI2) (h) (agonist radioligand)	1.0E-05	-3
P2X (agonist radioligand)	1.0E-05	-9
P2Y (agonist radioligand)	1.0E-05	3
5-HT1A (h) (agonist radioligand)	1.0E-05	3
5-HT1B (antagonist radioligand)	1.0E-05	9
5-HT2A (h) (antagonist radioligand)	1.0E-05	4
5-HT2B (h) (agonist radioligand)	1.0E-05	11
5-HT2C (h) (antagonist radioligand)	1.0E-05	-9
5-HT3 (h) (antagonist radioligand)	1.0E-05	4
5-HT5a (h) (agonist radioligand)	1.0E-05	13
5-HT6 (h) (agonist radioligand)	1.0E-05	-2
5-HT7 (h) (agonist radioligand)	1.0E-05	9
sigma (non-selective) (agonist radioligand)	1.0E-05	14
sst (non-selective) (agonist radioligand)	1.0E-05	-16
GR (h) (agonist radioligand)	1.0E-05	2
VPAC1 (VIP1) (h) (agonist radioligand)	1.0E-05	-3
V1a (h) (agonist radioligand)	1.0E-05	14
Ca2+ channel (L, verapamil site) (phenylalkylamine) (antagonist radioligand)	1.0E-05	22
KV channel (antagonist radioligand)	1.0E-05	-3
SKCa channel (antagonist radioligand)	1.0E-05	-9
Na+ channel (site 2) (antagonist radioligand)	1.0E-05	16

Cl- channel (GABA-gated) (antagonist radioligand)	1.0E-05	2
norepinephrine transporter (h) (antagonist radioligand)	1.0E-05	5
dopamine transporter (h) (antagonist radioligand)	1.0E-05	-10
5-HT transporter (h) (antagonist radioligand)	1.0E-05	10

CEREP Profile for Compound (7S,8R)-51a

Assay	Test Concentration (M)	% Inhibition of Control Specific Binding
A1 (h) (antagonist radioligand)	1.0E-05	-5
A2A (h) (agonist radioligand)	1.0E-05	7
A3 (h) (agonist radioligand)	1.0E-05	2
alpha 1 (non-selective) (antagonist radioligand)	1.0E-05	7
alpha 2 (non-selective) (antagonist radioligand)	1.0E-05	4
beta 1 (h) (agonist radioligand)	1.0E-05	-8
beta 2 (h) (agonist radioligand)	1.0E-05	5
AT1 (h) (antagonist radioligand)	1.0E-05	-12
AT2 (h) (agonist radioligand)	1.0E-05	-2
BZD (central) (agonist radioligand)	1.0E-05	-10
BZD (peripheral) (antagonist radioligand)	1.0E-05	-6
BB (non-selective) (agonist radioligand)	1.0E-05	-15
B2 (h) (agonist radioligand)	1.0E-05	-10
CGRP (h) (agonist radioligand)	1.0E-05	-4
CB1 (h) (agonist radioligand)	1.0E-05	18
CCK1 (CCKA) (h) (agonist radioligand)	1.0E-05	-8
CCK2 (CCKB) (h) (agonist radioligand)	1.0E-05	-18
D1 (h) (antagonist radioligand)	1.0E-05	10
D2S (h) (antagonist radioligand)	1.0E-05	26
D3 (h) (antagonist radioligand)	1.0E-05	28
D4.4 (h) (antagonist radioligand)	1.0E-05	-6
D5 (h) (antagonist radioligand)	1.0E-05	8
ETA (h) (agonist radioligand)	1.0E-05	-6
ETB (h) (agonist radioligand)	1.0E-05	-25
GABA (non-selective) (agonist radioligand)	1.0E-05	4
GAL1 (h) (agonist radioligand)	1.0E-05	4
GAL2 (h) (agonist radioligand)	1.0E-05	-4
PDGF (agonist radioligand)	1.0E-05	-15
CXCR2 (IL-8B) (h) (agonist radioligand)	1.0E-05	-12
CCR1 (h) (agonist radioligand)	1.0E-05	-18
TNF-alpha (h) (agonist radioligand)	1.0E-05	-6

H1 (h) (antagonist radioligand)	1.0E-05	4
H2 (h) (antagonist radioligand)	1.0E-05	-14
MC4 (h) (agonist radioligand)	1.0E-05	18
MT1 (ML1A) (h) (agonist radioligand)	1.0E-05	-1
M1 (h) (antagonist radioligand)	1.0E-05	34
M2 (h) (antagonist radioligand)	1.0E-05	34
M3 (h) (antagonist radioligand)	1.0E-05	36
M4 (h) (antagonist radioligand)	1.0E-05	38
M5 (h) (antagonist radioligand)	1.0E-05	15
NK1 (h) (agonist radioligand)	1.0E-05	3
NK2 (h) (agonist radioligand)	1.0E-05	28
NK3 (h) (antagonist radioligand)	1.0E-05	14
Y1 (h) (agonist radioligand)	1.0E-05	-34
Y2 (h) (agonist radioligand)	1.0E-05	16
NTS1 (NT1) (h) (agonist radioligand)	1.0E-05	-4
delta 2 (DOP) (h) (agonist radioligand)	1.0E-05	53
kappa (KOP) (agonist radioligand)	1.0E-05	37
mu (MOP) (h) (agonist radioligand)	1.0E-05	9
NOP (ORL1) (h) (agonist radioligand)	1.0E-05	4
PAC1 (PACAP) (h) (agonist radioligand)	1.0E-05	-17
PPARgamma (h) (agonist radioligand)	1.0E-05	-11
PCP (antagonist radioligand)	1.0E-05	-3
EP2 (h) (agonist radioligand)	1.0E-05	14
EP4 (h) (agonist radioligand)	1.0E-05	2
IP (PGI2) (h) (agonist radioligand)	1.0E-05	-3
P2X (agonist radioligand)	1.0E-05	12
P2Y (agonist radioligand)	1.0E-05	3
5-HT1A (h) (agonist radioligand)	1.0E-05	25
5-HT1B (antagonist radioligand)	1.0E-05	12
5-HT2A (h) (antagonist radioligand)	1.0E-05	4
5-HT2B (h) (agonist radioligand)	1.0E-05	1
5-HT2C (h) (antagonist radioligand)	1.0E-05	-5
5-HT3 (h) (antagonist radioligand)	1.0E-05	1
5-HT5a (h) (agonist radioligand)	1.0E-05	9
5-HT6 (h) (agonist radioligand)	1.0E-05	-19
5-HT7 (h) (agonist radioligand)	1.0E-05	-9
sigma (non-selective) (h) (agonist radioligand)	1.0E-05	53
sst (non-selective) (agonist radioligand)	1.0E-05	-18
GR (h) (agonist radioligand)	1.0E-05	-2
VPAC1 (VIP1) (h) (agonist radioligand)	1.0E-05	-10
V1a (h) (agonist radioligand)	1.0E-05	8
Ca2+ channel (L, verapamil site) (phenylalkylamine) (antagonist radioligand)	1.0E-05	41
KV channel (antagonist radioligand)	1.0E-05	-28
SKCa channel (antagonist radioligand)	1.0E-05	8
Na+ channel (site 2) (antagonist radioligand)	1.0E-05	38

Cl- channel (GABA-gated) (antagonist radioligand)	1.0E-05	-3
norepinephrine transporter (h) (antagonist radioligand)	1.0E-05	11
dopamine transporter (h) (antagonist radioligand)	1.0E-05	69
5-HT transporter (h) (antagonist radioligand)	1.0E-05	20