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DATASHEET

JHU37160 dihydrochloride (DREADD ligand) (water soluble)

Product overview

Name JHU37160 dihydrochloride (DREADD ligand) (water soluble)

Cat No HB626

Alternative names J60 dihydrochloride

Purity >98%

DescriptionNovel DREADD agonist with high affinity and potency for hM3Dq and hM4Di. Active in vivo. Water

soluble.

Images



Biological Data

Biological description

Overview

JHU37160 is reported to be a novel DREADD agonist with high in vivo DREADD potency for CNS applications.

It has high affinity in vitro for hM3Dq and hM4Di (K_i values are 1.9 nM (hM3Dq) and 3.6 nM (hM4Di).

It selectively displaces [3 H]clozapine from DREADDs and not from other clozapine-binding sites at concentrations up to 10 nM when tested for in situ [3 H]clozapine displacement in brain tissue from WT and D $_{1}$ -DREADD mice.

JHU37160 activates hM3Dq and hM4Di with high potency and efficacy in fluorescent and BRET-based assays in HEK-293 cells (EC $_{50}$ values are 18.5 and 0.2 nM at hM3Dq and hM4Di respectively.

Occupancy

JHU37160 exhibits high in vivo DREADD occupancy and was not reported to be a P-gp substrate.

In vivo application

JHU37160 is reported to be a potent in vivo DREADD agonist, which selectively inhibits locomotor activity in D_1 -hM3Dq and D_1 -hM4Di mice without any significant locomotor effects observed in wild type (WT) mice (at doses ranging 0.01 - 1 mg/kg).

It also produces robust and selective increases in hM3Dq-stimulated locomotion in rats expressing

hM3Dq in tyrosine hydroxylase expressing neurons (at doses ranging 0.01 – 0.3 mg/kg).

In in vivo electrophysiology experiments in mice, JHU37160 produces rapid and potent hM4Di-driven inhibition of light-evoked neuronal activation (at a dose of 0.1 mg/kg).

While its selectivity is not ideal (i.e. comparable to clozapine), its high in vivo potency allows for dose adjustments with minimal off-target effects. The compound exhibits promising characteristics for DREADD use in monkeys.

Shows dose-dependent anxiogenic effect in male Wistar and Long-Evans rats, regardless of DREADD expression, with no impact on locomotor behvaiour suggesting that high doses (e.g. 1mg/kg) should be avoided in chemogenetic experiments designed to evaluate circuit manipulation on anxiety-like behavior in rats.

Freebase also available.

Sold under license from the NIH, US patent pending 62/627,527

Stability Studies

For more info on the stability of water-soluble DREADD ligands in solution, please see the following guides:

• Stability of Water-Soluble DREADD ligands in Solution: A Technical Review

Solubility & Handling

Solubility overview Storage instructions Handling Soluble in water (100mM). Always store solutions at -20°C.

-20°C

Storage of solid

- Store at -20°C.
- Please note that the compound is a hydroscopic solid and contact with air may cause material
 to become sticky. Product performance should not be affected but we recommend storing the
 material in a sealed jar.

Storage of solutions

- Make up solutions and use immediately.
- If storage of solutions is required, you should aliquot out the solution into tightly sealed vials and store at -20 °C and store these for up to one month.
- Allow the product to equilibrate to RT for at least one hour before opening and using.

Storage of solutions at room temperature

- We have found that this compound precipitates in aqueous solution at RT (~25°C)
- We therefore recommend that you make up solutions and use immediately.
- Always check that your product is completely dissolved before use.

Stable for ambient temperature shipping. Follow storage instructions on receipt.

This product is for RESEARCH USE ONLY and is not intended for therapeutic or diagnostic use. Not for human or veterinary use

Chemical Data

Shipping Conditions

Important

Chemical name Molecular Weight Chemical structure 8-chloro-11-(4-ethylpiperazin-1-yl)-4-fluoro-5H-dibenzo[b,e][1,4]diazepine dihydrochloride 431.76

C₁₉H₂₀CIFN₄ · 2HCl 2369979-68-8 (free base)

Molecular Formula CAS Number

PubChem identifier 0

SMILES CI.CI.CCN1CCN(CC1)C3=Nc4cc(CI)ccc4Nc2c3cccc2F

Source Synthetic

InChi InChi=1S/C19H20CIFN4.2CIH/c1-2-24-8-10-25(11-9-24)19-14-4-3-5-15(21)18(14)22-16-7-6-13(20)1

2-17(16)23-19;;/h3-7,12,22H,2,8-11H2,1H3;2*1H

InChiKey DHICOGMHOCAKOF-UHFFFAOYSA-N

Appearance Yellow solid

Licensing details Sold under license from the NIH, US patent pending 62/627,527

References

Chemogenetic ligands for translational neurotheranostics

Bonaventura et al (2018) bioRxiv doi: https://doi.org/10.1101/487

High-potency ligands for DREADD imaging and activation in rodents and monkeys.

Bonaventura et al (2019) Nat Commun. 10(1) **PubMedID** 31604917

0067 Humanized Chemogenetic Approach to Treat Sleep Apnea

Curado et al (2019) Sleep (42)

OP-01-02 Graft-host synaptic connectivity can be chemogenetically inhibited with clinically relevant activators to eliminate graft-induced dyskinesias (GID) without loosing anti-parkinsonian benefits of dopaminergic grafts

Subramanian et al (2019) World Congress On Parkinson's Disease And Related Disorders 2019 Poster Abstract

DREADDs: The Power of the Lock, the Weakness of the Key. Favoring the Pursuit of Specific Conditions Rather than Specific Ligands.

Goutaudier et al (2019) eNeuro 6

PubMedID 31562177

High dose administration of DREADD agonist JHU37160 produces increases in anxiety-like behavior in male rats.

Van Savage J et al (2023) Behavioural brain research 452

PubMedID 37352979