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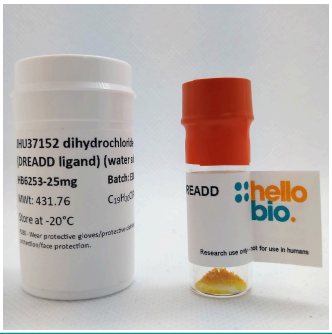
DATASHEET

JHU37152 dihydrochloride (DREADD ligand) (water soluble)

Product overview

Name	JHU37152 dihydrochloride (DREADD ligand) (water soluble)
Cat No	HB6253
Alternative names	J52 dihydrochloride
Purity	>98%
Description	Novel DREADD agonist with high affinity and potency for hM3Dq and hM4Di. Active in vivo. Water soluble.

Images



Biological Data

Biological description

Overview

JHU37152 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 1.8 nM (hM3Dq) and 8.7 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 [3H]clozapine displacement in brain tissue from WT and D_1-DREADD mice.

JHU37152 activates hM3Dq and hM4Di with high potency and efficacy in fluorescent and BRET-based assays in HEK-293 cells (EC_{50} values are 5 and 0.5 nM at hM3Dq and hM4Di respectively.

Occupancy

JHU37152 exhibits high in vivo DREADD occupancy and was not reported to be a P-gp substrate.

In vivo application

JHU37152 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).

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.

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

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

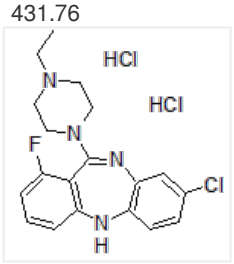
Storage of solutions at room temperature

- We recommend only keeping solutions at room temperature (25°C) for a few days as our studies have shown that after 96 hours the purity of the compound in solution drops to ~95% and will continue to drop over time.

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

Chemical Data

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



Molecular Formula $C_{19}H_{20}ClFN_4 \cdot 2HCl$
CAS Number 2369979-67-7 (free base)
PubChem identifier 0
SMILES Cl.Cl.CCN1CCN(CC1)C2=Nc4cc(Cl)ccc4Nc3cccc(F)c23
Source Synthetic
InChi InChI=1S/C19H20ClFN4.2ClH/c1-2-24-8-10-25(11-9-24)19-18-14(21)4-3-5-16(18)22-15-7-6-13(20)12-17(15)23-19;;/h3-7,12,22H,2,8-11H2,1H3;2*1H

Chemical name	8-chloro-11-(4-ethylpiperazin-1-yl)-1-fluoro-5H-dibenzo[b,e][1,4]diazepine dihydrochloride
InChiKey	FCMLDQBEZPOLPW-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