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DATASHEET Deschloroclozapine (DCZ)

Product overview

| Name | Deschloroclozapine (DCZ) |
|-------------------|--|
| Cat No | HB8555 |
| Alternative names | DCZ |
| Biological action | Agonist |
| Purity | >98% |
| Description | Potent, selective and metabolically stable hM3Dq and hM4Di muscarinic DREADD actuator. |

Images



Biological Data

Biological description

<u>Overview</u>

Deschloroclozapine (DCZ) is reported to be a potent, selective and highly brain-penetrable muscarinic hM3Dq and hM4Di DREADD actuator with minimal off-target actions ($K_i = 6.3$ and 4.2 nM at hM3Dq and hM4Di respectively) and (EC₅₀ values are 0.13 and 0.081 nM at hM3Dq and hM4Di respectively in a BRET-based assay.

It represents a potent, selective, metabolically stable and fast acting DREADD agonist with utility in both mice and non-human primates for a variety of applications.

It shows 100-fold improved affinity and greater agonist potency for hM3Dq and hM4Di compared to Clozapine n-Oxide (CNO) or DREADD agonist 21 (C21) with reduced off-target binding compared with clozapine in vitro. It has lower affinity at D₁, D₂ and 5-HT_{2A} and 5-HT_{2C} receptors compared with clozapine.

PET studies demonstrate the compound is rapidly brain penetrable, is apparently selective and doses for DREADD occupancy are 20-fold and 60-fold lower than CNO or DREADD agonist 21 (C21) respectively.

Uses and applications

Systemic delivery of low doses of DCZ (1 or 3 μ g/kg) were shown to enhance neuronal activity via hM3Dq in mice and monkeys within minutes.

Intramuscular doses of 100 µg/kg reversibly induced spatial working memory deficits in hM4Di

expressing monkeys.

Deschloroclozapine dihydrochloride (water soluble) also available.

Solubility & Handling

Storage instructions Solubility overview Important Room temperature Soluble in DMSO (100 mM), and in ethanol (50 mM with warming) 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 Molecular Weight Chemical structure 6-(4-methylpiperazin-1-yl)-11H-benzo[b][1,4]benzodiazepine 292.38



Molecular Formula CAS Number PubChem identifier SMILES Source InChi

InChiKey Appearance H C₁₈H₂₀N₄ 1977-07-7 16103 CN1CCN(CC1)C2=NC3=CC=CC3NC4=CC=CC42 Synthetic InChI=1S/C18H20N4/c1-21-10-12-22(13-11-21)18-14-6-2-3-7-15(14)19-16-8-4-5-9-17(16)20-18/h2-9,19H,10-13H2,1H3 VQHITFFJBFOMBG-UHFFFAOYSA-N Yellow solid

References

Deschloroclozapine, a potent and selective chemogenetic actuator enables rapid neuronal and behavioral modulations in mice and monkeys

Nagai et al (2020) Nature Neuroscience 1157-1167PubMedID32632286

Chemogenetic actuator drugs impair prefrontal cortex-dependent working memory in rhesus monkeys Upright and Baxter (2019) bioRxiv https://doi.org/10.1101/864140

Binding of 5H-dibenzo[b,e][1,4]diazepine and chiral 5H-dibenzo[a,d]cycloheptene analogues of clozapine to dopamine and serotonin receptors.

Phillips et al (1994) J Med Chem 37(17)
PubMedID 8064797