TCN238

Cat. No.: HY-14419

CAS No.: 125404-04-8

Molecular Formula: $C_{12}H_{11}N_3$

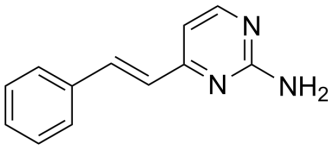
Molecular Weight: 197.24

Target: mGluR

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 150 mg/mL (760.49 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	5.0700 mL	25.3498 mL	50.6997 mL
5 mM	1.0140 mL	5.0700 mL	10.1399 mL
10 mM	0.5070 mL	2.5350 mL	5.0700 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

TCN238 is an orally bioavailable mGlu4 receptor positive allosteric modulator (PAM) with an EC_{50} of 1 μM[1].

IC_{50} & Target

mGlu4 Receptor
1 μM (EC50)

In Vitro

In the rat mGlu4 PAM in vitro assay the EC_{50} of TCN238 (Compound 11) is 1 μM which is comparable to the human assay. TCN238 is screened in rat and human mGlu5 assays, the IC_{50} of 11 is >30 μM on human mGlu5and >10 μM on rat mGlu5. TCN238 is run in a receptor screening panel of 68 targets and no activity is observed at ≥50% at 10 μM for any of the receptors. In CaCo-2 cells, TCN238 is found to have good permeability with no apparent efflux issue[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

TCN238 is highly CNS penetrant with a concentration of 33.8 μM in the brain. The plasma protein binding in rats is measured as 90% bound. The metabolic stability of TCN238 is assessed in rat and human microsomes and found to be 62% and 83% hepatic blood flow. The limited stability translated into a high in vivo clearance in rats of 75 mL/min/kg and TCN238 has a

moderate volume of distribution (2.7 L/kg) with a short mean residence time (0.6 h) when dosed at 2 mg/kg via intravenous injection. TCN238 is orally bioavailable and 30 min following administration of a30 mg/kg dose, the plasma concentration is found to be 11.6 μM[1]. TCN 238 does not affect the performance of the learned task. However, the expression level of GRM4 in the hippocampus is reliable down-regulated five days after treatment with TCN 238. In addition, the expression level of GABRA1, encoding GABAA α-subunit is downregulated five days after the treatment in the frontal cortex[2].

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PROTOCOL

Animal Administration [2]

Rats: TCN 238 is administered subcutaneously at a dose of 2 mg/kg (volume of 0.5 mL) four times in two days (morning and evening). Retrieval of the task is tested 30min after the first and third injections of TCN 238, and 5 days after the last injection of the substance. During the retrieval test the animals are placed to the start box, the door is opened, and the latent period of response is registered.[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. East SP, et al. An orally bioavailable positive allosteric modulator of the mGlu4 receptor with efficacy in an animal model of motor dysfunction. Bioorg Med Chem Lett. 2010 Aug 15;20(16):4901-5.

[2]. Pershina EV, et al. Subacute activation of mGlu4 receptors causes the feedback inhibition of its gene expression in rat brain. Life Sci. 2016 May 15;153:50-4.

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