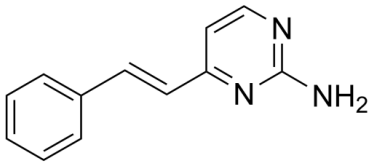
Data Sheet

Product Name:	TCN238
Cat. No.:	CS-6515
CAS No.:	125404-04-8
Molecular Formula:	C12H11N3
Molecular Weight:	197.24
Target:	mGluR
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : ≥ 150 mg/mL (760.49 mM)



BIOLOGICAL ACTIVITY:

TCN238 is a positive allosteric **mGlu4** receptor modulator with an **EC_{50}** of 1 μM. IC50 & Target: EC50: 1 μM (human or rat mGlu4)[1] **In Vitro:** In the rat mGlu4 PAM in vitro assay the EC_{50} of TCN238 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: TCN 238 is dissolved in isotonic NaCl solution supplemented with DMSO (30%). [2]Rat: 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].

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.

CAIndexNames:

2-Pyrimidinamine, 4-(2-phenylethenyl)-, (E)-

SMILES:

NC1=NC=CC(/C=C/C2=CC=CC=C2)=N1

Caution: Product has not been fully validated for medical applications. For research use only.

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