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产品名称: **TCN 238**
产品别名: **TCN 238**

生物活性:

Description	TCN238 is a positive allosteric mGlu4 receptor modulator with an EC ₅₀ of 1 μM.				
IC ₅₀ & Target	EC50: 1 μM (human or rat mGlu4)[1]				
In Vitro	In the rat mGlu4 PAM <i>in vitro</i> 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].				
Solvent&Solubility	<i>In Vitro:</i> DMSO : ≥ 150 mg/mL (760.49 mM) * "≥" means soluble, but saturation unknown.				
		<div><div>Solvent</div><div>Mass</div><div>Concentration</div></div>	1 mg	5 mg	10 mg
	Preparing	1 mM	5.0700 mL	25.3498 mL	50.6997 mL
	Stock Solutions	5 mM	1.0140 mL	5.0700 mL	10.1399 mL
		10 mM	0.5070 mL	2.5350 mL	5.0700 mL
*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液; 一旦配成溶液, 请分装保存, 避免反复冻融造成的产品失效。 储备液的保存方式和期限: -80°C, 6 months; -20°C, 1 month。 -80°C 储存时, 请在 6 个月内使用, -20°C 储存时, 请在 1 个月内使用。					
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. <i>Bioorg Med Chem Lett</i> . 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. <i>Life Sci</i> . 2016 May 15;153:50-4.				
实验参考:					
	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				



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Animal Administration	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	<p>[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.</p> <p>[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.</p>



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