

Product Data Sheet

Product Name: ASP2905

Cat. No.: GC61960

Chemical Properties

Cas. No. 792184-90-8

SMILES FC1=CC=C(NC2=NC(NC3=CC=CC=C3)=NC(NCC4=NC=CC=N4)=N2)C=C1

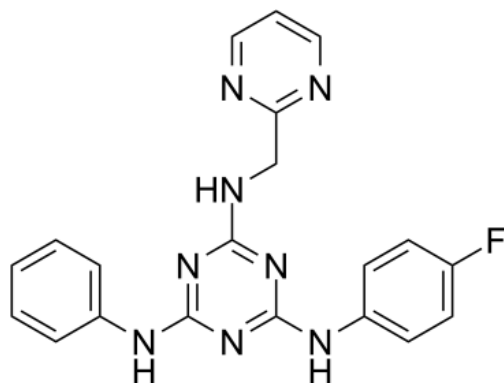
Formula $C_{20}H_{17}FN_8$ M.Wt 388.4

Solubility DMSO : 100 mg/mL (257.47 mM; Need ultrasonic) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines HEK293 cells (human embryonic kidney 293 cell line)

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HEK293 cells were co-transfected with an EGFP-riboswitch plasmid containing the aptamer AC17-4 integrated into a circularly-permuted pistol (CPP) ribozyme Preparation Method scaffold (a8-AC17-4-CPP) in the 3' UTR, and an mCherry-expressing plasmid as a transfection control. Cells were cultured in the absence or presence of ASP2905 (0.1–10 μ M).

Reaction
Conditions 0.1–10 μ M; 2 day.

Applications ASP2905 significantly activated gene expression from the riboswitch construct, leading to an approximately 10-fold upregulation of EGFP fluorescence compared to the no-ligand control.

Animal experiment [2]:

Animal models ddY mice, juvenile stroke-prone spontaneously hypertensive rats (SHRSP)

For the water finding task, normal ddY mice were orally administered ASP2905 (0.0313 and 0.0625mg/kg) 30 minutes before a training trial. Mice were then Preparation Method water-deprived until the test trial on the following day. For the five-trial passive avoidance task, juvenile SHRSP rats (4 weeks old) were administered ASP2905 (0.1 and 0.3mg/kg; orally) 30 minutes before the acquisition trials.

Dosage form 0.0313-0.3mg/kg; p.o.; Single administration 30 minutes before behavioral testing.

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Applications ASP2905 significantly shortened the finding latency (an index of latent learning/attention) of mice in the water finding task. ASP2905 significantly prolonged the cumulative latency of juvenile SHRSP rats (a model of ADHD) in the five-trial passive avoidance task, indicating an improvement in attention deficits and impulsivity.

References:

- [1] Fukunaga K, Dhamodharan V, Miyahira N, et al. Small-Molecule Aptamer for Regulating RNA Functions in Mammalian Cells and Animals. J Am Chem Soc. 2023 Apr 12;145(14):7820-7828.
- [2] Takahashi S, Ohmiya M, Honda S, et al. The KCNH3 inhibitor ASP2905 shows potential in the treatment of attention deficit/hyperactivity disorder. PLoS One. 2018 Nov 21;13(11):e0207750.

Background

ASP2905 is a novel, orally active potassium channel KCNH3 inhibitor. ASP2905 can cross the blood-brain barrier to exert antipsychotic effects, while also improving neuropsychiatric symptoms by enhancing cognitive function. ASP2905 is applicable for research in attention-deficit/hyperactivity disorder and schizophrenia^[1-2].

In vitro, ASP2905 (0.1–10 μ M) was applied to HEK293 cells for approximately 2 days. ASP2905 bound to aptazyme- and exon skipping-based riboswitches, significantly upregulating the expression of the reporter gene EGFP, with no significant effect on the viability of HEK293 cells^[3]. ASP2905 (0.1–1 μ M) was administered to primary cultured rat hippocampal neurons for 4 minutes. ASP2905 significantly decreased both the frequency and mean amplitude of spontaneous inhibitory postsynaptic currents (sIPSCs)^[4].

In vivo, ASP2905 (0.0313–0.3 mg/kg; orally) was administered to normal ddY mice and juvenile stroke-prone spontaneously hypertensive rats (SHRSP). ASP2905 significantly shortened the finding latency in mice, prolonged the cumulative latency in rats, and concurrently increased the extracellular levels of dopamine and acetylcholine in the medial prefrontal cortex of rats, as well as the alpha band power in electroencephalograms^[5]. ASP2905 (0.03–0.3mg/kg; oral administration) was used to treat a mouse model of schizophrenia. ASP2905 significantly reversed the prolonged immobility time in the

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forced swim test, shortened the finding latency in neonatal mice, and markedly ameliorated the hyperlocomotor activity in mice^[6].

References:

- [1] Nomura Y, Kim N, Zhu B, et al. Optimization of Exon-Skipping Riboswitches and Their Applications to Control Mammalian Cell Fate. ACS Synth Biol. 2024 Oct 18;13(10):3246-3255.
- [2] Ishii Y, Fukunaga K, Cooney A, et al. Switchable and orthogonal gene expression control inside artificial cells by synthetic riboswitches. Chem Commun (Camb). 2024 Jun 4;60(46):5972-5975.
- [3] Fukunaga K, Dhamodharan V, Miyahira N, et al. Small-Molecule Aptamer for Regulating RNA Functions in Mammalian Cells and Animals. J Am Chem Soc. 2023 Apr 12;145(14):7820-7828.
- [4] Takahashi S, Inamura K, Yarimizu J, et al. Neurochemical and neuropharmacological characterization of ASP2905, a novel potent selective inhibitor of the potassium channel KCNH3. Eur J Pharmacol. 2017 Sep 5;810:26-35.
- [5] Takahashi S, Ohmiya M, Honda S, et al. The KCNH3 inhibitor ASP2905 shows potential in the treatment of attention deficit/hyperactivity disorder. PLoS One. 2018 Nov 21;13(11):e0207750.
- [6] Takahashi S, Okamura A, Yamazaki M, et al. ASP2905, a specific inhibitor of the potassium channel Kv12.2 encoded by the Kcnh3 gene, is psychoactive in mice. Behav Brain Res. 2020 Jan 27;378:112315.

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