Capadenoson

Cat. No.: HY-14917

CAS No.: 544417-40-5

Molecular Formula: $C_{25}H_{18}ClN_5O_2S_2$

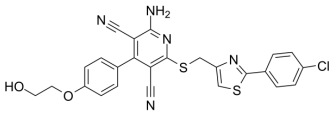
Molecular Weight: 520.03

Target: Adenosine Receptor

Pathway: GPCR/G Protein

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 : ≥ 50 mg/mL (96.15 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9230 mL	9.6148 mL	19.2297 mL
	5 mM	0.3846 mL	1.9230 mL	3.8459 mL
	10 mM	0.1923 mL	0.9615 mL	1.9230 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (4.81 mM); Suspended solution; Need ultrasonic and warming
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Capadenoson is a selective agonist of adenosine-A1 receptor.

IC_{50} & Target

Adenosine A1 receptor[1]

In Vitro

To further elucidate the pharmacological properties of Capadenson, GTP shift assays are performed with the standard full A1-agonist CCPA and the A1-antagonist 8-cyclopentyl-1,3-dipropylxanthine (DPCPX). CCPA shows a K_i value of 4.2 nM in the binding assay on rat cortical brain membranes. In the presence of 1 mM GTP this K_i value shifts to a value of 64 nM. Therefore the GTP shift for CCPA is 15. DPCPX shows a GTP shift of 1 with virtually identical K_i values in the absence and presence of GTP. Capadenson shows a K_i value of 24 nM in the binding assay. In the presence of 1 mM GTP this K_i value shifts to a value

	of 116 nM resulting in a GTP shift of 5 for Capadenoson[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In the in vivo experiments, Wistar rats and SHR are pre-treated with Capadenoson at a concentration of 0.15 mg/kg for 5 days. On day 5, a stress test (physical restraint) is performed for 2 hours. The plasma concentration of Capadenoson measured 3 hours after drug intake remains constant in the 5 days prior to the restraint stress test and averaged 7.63 μg/L on day 4 and 5, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Membranes from the human cortex are prepared. [^{35}S]GTPγS binding is measured. Briefly, 5 μg of membrane protein is incubated in a total volume of 160 μL for 2 hr at 25°C in a shaking water bath. [^{35}S]GTPγS binding in control incubations and in the presence of capadenoson showed a linear time course up to this incubation time. Binding buffer contained 50 mM Tris/HCl, pH 7.4, 2 mM triethanolamine, 1 mM EDTA, 5 mM $MgCl_2$, 10 μM GDP, 1 mM dithiothreitol, 100 mM NaCl, 0.2 units/mL adenosine deaminase, 0.2 nM [^{35}S]GTPγS, and 0.5% bovine serum albumin. Non-specific binding is determined in the presence of 10 μM GTPγS. Incubations are terminated through filtration of the samples over multiscreen FB glass fiber filters followed by two washes with binding buffer. The filters are dried, coated with scintillator and counted for radioactivity. Binding curves of [^{35}S]GTPγS are analyzed by nonlinear regression using GraphPad Prism[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] A total of 14 Wistar rats and 18 SHR (body weight 200-50 g, all female) underwent experiments to evaluate the exocytotic, stimulation-induced NE release during electrical field stimulation. Rats are killed by an injection of pentobarbital i.p. (0.5 mL/100 mg body weight), and hearts are rapidly excised, and placed in ice cold Krebs-Henseleit solution (KHL). They are quickly mounted on a Langendorff apparatus for retrograde perfusion with KHL. Perfusion rate is kept constant at 10 mL/min, the temperature is adjusted to 37°C, and the pH to 7.4 through bubbling with 5% CO_2/95% O_2. Via an inflow line desipramine at a concentration of 10^{-7} M is added to the perfusion buffer. After an equilibration period of 20 minutes, electrical field stimulation is commenced via two metal paddles adjacent to both sides of the beating heart for 1 minute (5V, 6 Hz). We collected the efflux in plastic tubes the minute before, during, and 3 minutes after the stimulation. These are rapidly frozen in liquid nitrogen and stored at −20°C till analysis. The NE release is calculated as the cumulative release induced by the electrical stimulation. After the first stimulation (S1), the study drug Capadenoson at concentrations of 30 μg/L (6×10^{-8} M) or 300 μg/L(6×10^{-7} M), or 2-chloro-N6-cyclopentyladenosine (CCPA, 10−6 M), respectively, are added via separate perfusion lines for 30 minutes. After this time a second stimulation (S2) is executed to determine the effect of the drugs on NE release compared to the first stimulation. The effect of each pharmacological intervention is analysed by calculating the ratio of NE release induced by the second and first stimulation (S2/S1 ratio). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Br J Pharmacol. 2020 Jan;177(2):346-359.
- Br J Pharmacol. 2019 Apr;176(7):864-878.
- Biochem Pharmacol. 2017 Jul 1;135:79-89.
- Biochem Pharmacol. 2016 Jan 1;99:101-12.
- Purinergic Signal. 2021 Jul 27.

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REFERENCES

[1]. Bott-Flügel L, et al. Selective attenuation of norepinephrine release and stress-induced heart rate increase by partial adenosine A1 agonism. PLoS One. 2011 Mar 28;6(3):e18048.

[2]. Bailey IR, et al. Optimization of Thermolytic Response to A1 Adenosine Receptor Agonists in Rats. J Pharmacol Exp Ther. 2017 Sep;362(3):424-430.

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