Zardaverine

Cat. No.: HY-15485

CAS No.: 101975-10-4

Molecular Formula: $C_{12}H_{10}F_2N_2O_3$

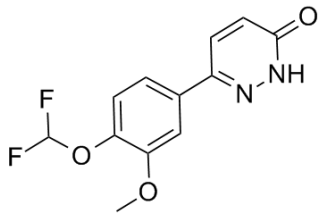
Molecular Weight: 268.22

Target: Phosphodiesterase (PDE)

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (93.21 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.7283 mL	18.6414 mL	37.2828 mL
	5 mM	0.7457 mL	3.7283 mL	7.4566 mL
	10 mM	0.3728 mL	1.8641 mL	3.7283 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: ≥ 2.08 mg/mL (7.75 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zardaverine is a newly developed dual-selective PDE3/4 inhibitor with IC50 values of 0.5 uM and 0.8 uM respectively. IC50 value: 0.5 uM (PDE3); 0.8 uM (PDE4)Target: PDE3; PDE4Zardaverine inhibited the cyclic GMP-inhibitable PDE III from human platelets and the rolipram-inhibitable PDE IV from canine trachea and human polymorphonuclear (PMN) cells with IC50-values of 0.58, 0.79 and 0.17 μM, respectively. The pyridazinone derivative affected the calmodulin-stimulated PDE I, the cyclic GMP-stimulated PDE II and the cyclic GMP-specific PDE V only marginally at concentrations up to 100μM. Zardaverine inhibits the ADP-induced aggregation of human platelets with an IC50 of 1.6 μM. This inhibition was synergistically increased by activators of adenylate cyclase such as PGE1 and forskolin. In human PMN cells, Zardaverine inhibited the zymosan-induced superoxide anion generation with an IC50 of 0.40 μM. Again, this effect was increased by activators of adenylate cyclase. Zardaverine acted in synergy with the adenylate cyclase activators prostaglandin E2 and CG 4203, a prostacyclin analog, and super-additive effects of combinations were observed. Zardaverine and dexamethasone prevent bronchial

eosinophilia and neutrophilia with similar dosage of 30 microM/kg orally, suggesting that this PDE III/IV inhibitor may be useful for both, bronchorelaxation and reduction of inflammation in asthma therapy.

REFERENCES

[1]. R.T. Schermuly, H. Leuchte, H.A. Ghofrani, et al. Zardaverine and aerosolised iloprost in a model of acute respiratoryfailure. ERJ, 2003 ,22 (2): 342-347.

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[3]. Schade FU, Schudt C. The specific type III and IV phosphodiesterase inhibitor zardaverine suppresses formation of tumor necrosis factor by macrophages. European Journal of Pharmacology.1993, 230(1):9-14.

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