PRX-08066

Cat. No.: HY-15472

CAS No.: 866206-54-4

Molecular Formula: $C_{19}H_{17}ClFN_5S$

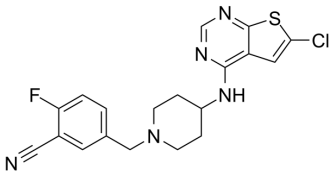
Molecular Weight: 401.89

Target: 5-HT Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

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 : 7 mg/mL (17.42 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4882 mL	12.4412 mL	24.8824 mL
	5 mM	0.4976 mL	2.4882 mL	4.9765 mL
	10 mM	0.2488 mL	1.2441 mL	2.4882 mL

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

BIOLOGICAL ACTIVITY

Description

PRX-08066 is a selective 5-hydroxytryptamine receptor 2B (5-HT2BR, IC50= 3.4 nM) antagonist that causes selective vasodilation of pulmonary arteries. IC50 value: 3.4 nM [1]Target: HT2B receptorin vitro: PRX-08066 inhibits 5-HT-induced mitogen-activated protein kinase activation with IC50 of 12 nM and markedly reduces thymidine incorporation with IC50 of 3 nM in Chinese hamster ovary cells expressing the human 5-HT2BR, which suggests that PRX-08066 can potentially inhibit the pathologic 5-HT-induced vascular muscularization associated with PAH [1]. PRX-08066 inhibits cell proliferation with IC50 of 0.46 nM and with a maximum inhibition of 20% and 5-HT secretion with IC50 of 6.9 nM with a maximum inhibition of 30% in the 5-HT(2B) expressing SI-NET cell line, KRJ-I. PRX-08066 inhibits isoproterenol-stimulated 5-HT release with IC50 of 1.25 nM and a maximum inhibition of 60% in NCI-H720 cells. PRX-08066 (0.5 nM) significantly inhibits ERK phosphorylation in KRJ-I cells. PRX-08066 inhibits TGFβ1, CTGF and FGF2 transcription and secretion in KRJ-I cells. PRX-08066 decreases level of transcripts for Ki67 (84%) as well as Ki67 protein (36.8%) associated with an increase in caspase 3 transcript levels in KRJ-I cells. PRX-08066 decreases level of transcripts of TGFβ1, FGF2 and TPH1 in KRJ-I cells. PRX-08066 significantly increases the number of dead cells (34%) compared with untreated controls in KRJ-I cells. PRX-08066 causes a significant increase in dead/caspase 3 positive cells (76%) and caspase 3 activity (52%) in HEK293 cells [2].in vivo: PRX-08066 (100 mg/kg) treated groups demonstrates less right ventricular hypertrophy and septal flattening than the monocrotaline control group in rats. PRX-08066 significantly reduces peak pulmonary artery pressure at 50 mg/kg and 100 mg/kg compared with monocrotaline

	control rats. PRX-08066 also significantly reduces right ventricle (RV)/body weight and RV/left ventricle + septum, compared with MCT-treated rats. PRX-08066 significantly attenuates the elevation in pulmonary artery pressure and RV hypertrophy and maintains cardiac function. PRX-08066 significantly reduces the hypoxia-dependent increase in right ventricular systolic pressure in both rats and mice without affecting the systemic mean arterial pressure in the animals [1]. PRX-08066 (100 mg/kg) significantly inhibits both right ventricular systolic pressure and right ventricular/left ventricular +septum weight elevations in rats. PRX-08066 (30 mg/kg) inhibits right ventricular systolic pressure and monocrotaline-induced ERK phosphorylation in whole lung homogenates in rats [3].
IC_{50} & Target	5-HT_{2B} Receptor 3.4 nM (IC_{50})

REFERENCES

[1]. Porvasnik SL, et al. PRX-08066, a novel 5-hydroxytryptamine receptor 2B antagonist, reduces monocrotaline-induced pulmonary arterial hypertension and right ventricular hypertrophy in rats. J Pharmacol Exp Ther. 2010 Aug;334(2):364-72.

[2]. Svejda B, et al. The 5-HT(2B) receptor plays a key regulatory role in both neuroendocrine tumor cell proliferation and the modulation of the fibroblast component of the neoplastic microenvironment. Cancer. 2010 Jun 15;116(12):2902-12.

[3]. Warburton R.R., et al. Online University.

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