Mirodenafil dihydrochloride

Cat. No.: HY-14930A

CAS No.: 862189-96-6

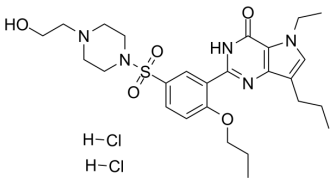
Molecular Formula: $C_{26}H_{39}Cl_2N_5O_5S$

Molecular Weight: 604.59

Target: Phosphodiesterase (PDE); Glucocorticoid Receptor; Wnt; β-catenin; Apoptosis

Pathway: Metabolic Enzyme/Protease; Immunology/Inflammation; Vitamin D Related/Nuclear Receptor; Stem Cell/Wnt; Apoptosis

Storage: 4°C, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (165.40 mM)

H_2O : 5 mg/mL (8.27 mM; ultrasonic and warming and heat to 60°C)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6540 mL	8.2701 mL	16.5401 mL
5 mM	0.3308 mL	1.6540 mL	3.3080 mL
10 mM	0.1654 mL	0.8270 mL	1.6540 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 (4.14 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.14 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.14 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mirodenafil (SK3530) dihydrochloride is an orally active, potent, reversible, and selective phosphodiesterase 5 (PDE5) inhibitor. Mirodenafil dihydrochloride is a glucocorticoid receptor (GR) modulator Mirodenafil dihydrochloride activates the Wnt/β-catenin signaling pathway by downregulating Dkk1 expression. Mirodenafil dihydrochloride can be used for the research of erectile dysfunction (ED), Alzheimer's disease (AD) and systemic sclerosis (SSc)[1][2][3].

IC_{50} & Target

PDE5

In Vitro

Mirodenafil dihydrochloride (0-40 μM, 24 h) exerts neuroprotective functions via activating the cGMP/PKG/CREB signaling pathway[2].
Mirodenafil dihydrochloride (0-40 μM, 24 h) enhances neuronal survival by protecting the mitochondrial membrane potential and inhibiting apoptosis[2].
Mirodenafil dihydrochloride (0-40 μM) inhibits GSK-3β signaling, resulting in reduced tau phosphorylation, decreased Aβ production by inhibiting amyloidogenesis and activating the autophagosomal pathway[2].
Mirodenafil dihydrochloride inhibits the transcriptional activity of the glucocorticoid receptor (GR), and inhibits homodimerization of GR in HT-22 cells[2].
Mirodenafil dihydrochloride (0-100 μM, 24 h) inhibits TGF-β-induced phosphorylation of Smad2/3 and mRNA expression of the fibrosis marker in fibroblasts[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	SH-SY5Y human neuroblastoma cells
Concentration:	0, 10, 20, 40 μM
Incubation Time:	24 h
Result:	Significantly increased cGMP levels by about 200% in a dose-dependent manner. Reversed the Aβ-induced decrease in phosphorylated CREB in a dose-dependent manner. $A\beta_{42}$ alone increased the levels of cleaved caspase-3 and cleaved PARP, whereas the combined treatment with mirodenafil markedly reduced the expression levels of both apoptotic markers.

RT-PCR[3]

Cell Line:	NIH3T3 mouse embryonic fibroblasts
Concentration:	0, 10, 100 μM
Incubation Time:	24 h
Result:	The mRNA expression of COL1A1, α-SMA, and CTGF were induced by treatment with TGF-β1, and Mirodenafil significantly reduced the expression of these profibrotic genes.

In Vivo

Mirodenafil dihydrochloride (4 mg/kg, IP, daily for 4 weeks) enhances the cognitive-behavioral performance in transgenic AD mice[2].
Mirodenafil dihydrochloride (0-10 mg/kg, Orally, daily for 3 weeks) ameliorates dermal fibrosis in a BLM-induced SSc mouse model by inhibiting the TGF-β signaling pathway, thereby suppressing the expression of collagen and profibrotic genes[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	APP-C105 transgenic mice (13-month-old, male, n=6)[2]
Dosage:	4 mg/kg
Administration:	IP, daily for 4 weeks
Result:	Improved cognitive function in the APP-C105 AD mice.

Animal Model:	Male BALB/c mice (8 weeks old, four groups, n=10/group)[3]
Dosage:	0, 5 or 10 mg/kg
Administration:	Orally, daily for 3 weeks

Result:	Ameliorated dermal fibrosis and downregulated the protein levels of fibrosis markers including COL1A1 and α-SMA in the BLM-induced SSc mouse model. Significantly decreased dermal thickness and collagen content.

REFERENCES

[1]. Park HJ, et al. Mirodenafil for the treatment of erectile dysfunction: a systematic review of the literature. World J Mens Health. 2014 Apr;32(1):18-27.

[2]. Kang BW, et al. Phosphodiesterase 5 inhibitor mirodenafil ameliorates Alzheimer-like pathology and symptoms by multimodal actions. Alzheimers Res Ther. 2022 Jul 8;14(1):92.

[3]. Roh JS, et al. Mirodenafil ameliorates skin fibrosis in bleomycin-induced mouse model of systemic sclerosis. Anim Cells Syst (Seoul). 2021 Nov 3;25(6):387-395.

Caution: Product has not been fully validated for medical applications. For research use only.

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