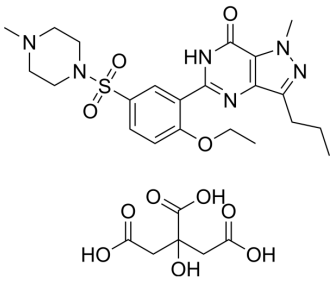
Sildenafil citrate

Cat. No.:	HY-15025A
CAS No.:	171599-83-0
Molecular Formula:	$C_{28}H_{38}N_6O_{11}S$
Molecular Weight:	666.7
Target:	Phosphodiesterase (PDE); Autophagy; Apoptosis; Bacterial
Pathway:	Metabolic Enzyme/Protease; Autophagy; Apoptosis; Anti-infection
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (75.00 mM; Need ultrasonic)
H_2O : 2 mg/mL (3.00 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.4999 mL	7.4996 mL	14.9992 mL
5 mM	0.3000 mL	1.4999 mL	2.9998 mL
10 mM	0.1500 mL	0.7500 mL	1.4999 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: ≥ 5 mg/mL (7.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (7.50 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (7.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Sildenafil citrate is a potent phosphodiesterase type 5 (PDE5) inhibitor with IC_{50} of 5.22 nM.
IC_{50} & Target	PDE5
In Vitro	Pretreatment with 1 μM Sildenafil citrate potentiates the phosphorylation of ERK1/ERK2, an increase in the percentage of cells in S phase and cell proliferation, compared with serotonin stimulation alone (P<0.05). Pretreatment with 1 μM Sildenafil citrate followed by serotonin stimulation leads to dramatic increase in OD value to 0.33, significantly different compared with serotonin stimulation alone (P<0.05). 1 μM Sildenafil obviously enhances the upregulation of ERK1/ERK2

	phosphorylation induced by serotonin[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In the dog model of erection, Sildenafil citrate significantly increases ICP and ICP/BP but shows no significant effect on BP compared with vehicle[1]. Sildenafil treatment significantly decreases the number of TL^+-cells at 10 but not 0.5 mg/kg. At this time point, cells positive for the M1-like marker $COX\text{-}2^+$ are found in the ischemic core in PBS-treated animals, whereas they are mostly observed in the penumbra in 10 mg/kg (but not 0.5 mg/kg) Sildenafil-treated animals. In contrast, 8 days after pMCAo the number of microglia/macrophages stained by Iba-1 are significantly reduced by Sildenafil treatment (0.5 and/or 10 mg/kg dose)[3]. Sildenafil citrate has been reported to decrease flap necrosis in preclinical animal models by increasing the secretion of growth factors (FGF and VEGF), and histologically is shown to be effective in rat cavernous nerve architecture[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cells at approximately 90% confluence are harvested with 0.1% trypsin/0.01% ethylene diamine tetraacetic acid (EDTA) solution and seeded into a 96-well plate at a density of 2×10^4 cells/well and grown in RPMI-1640 containing 10% FBS for three days, followed by serum starvation for three days. Cells are then incubated for different time with various concentration of serotonin or 1 μM Sildenafil followed by serotonin with or without U0126, as indicated. Control cells are treated in the same way except sterile PBS replaced the drug. After treatment, medium is changed to fresh medium, and cells are incubated with 5 g/L of MTT for four hours. MTT is then dissolved with 150 μL of 10% DMSO for 20 minutes. The optical densities (OD) in the 96-well plates are determined using a microplate reader at 570 nm[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3][4]	Mice[3] Ischemia is induced in C57Bl/6 mice on postnatal (P) day 9 by permanent middle cerebral artery occlusion (pMCAo), and followed by either PBS or Sildenafil intraperitoneal (i.p.) injections. In the first set of experiments, animals are randomly divided into five groups and treated with either PBS or a single dose of Sildenafil citrate (0.5, 2.5, 10, and 15 mg/kg), given intraperitoneally (i.p.) 5 min after pMCAo. In the second set of experiments, animals are randomly divided into three groups and treated with either PBS or a single dose of Sildenafil citrate (0.5 and 10 mg/kg, i.p.) 5 min after pMCAo. Rats[4] Thirty male Sprague-Dawley rats weighing between 210 and 240 g are used. Rats from all groups are anesthetized with xylazine + ketamine and then a crush injury is created by using a one-minute long vascular clamp to the right sciatic nerve. One day before the procedure, rats from Group 1 are started on a 28-day treatment consisting of a daily dose of 20 mg/kg body weight Sildenafil given orally via nasogastric tube, while the rats from Group 2 are started on an every-other-day dose of 10 mg/kg body weight Sildenafil citrate. Rats from Group 3 did not receive any drugs. Subjects in all 3 groups are fed ad libitum with normal rat chow and tap water. Forty-two days after the nerve damage is created, the rats underwent a static sciatic index (SSI) test, sedation and motor coordination tests, and accelerated rotarod tests. Rats are sacrificed under anesthesia and their sciatic nerves are removed surgically. Histopathologic analyses of the nerves and bone densitometry evaluation of the extremities are then performed. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Bioeng Transl Med. 2023 Jul 2.
- Biochim Biophys Acta Mol Basis Dis. 2024 Jan 5:167018.
- Int J Mol Sci. 2022 Jun 20;23(12):6860.
- Sci Rep. 2020 Oct 2;10(1):16383.

- ACS Omega. 2020 Nov 15;5(46):29935-29942.

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REFERENCES

[1]. Wang Z, et al. The Selectivity and Potency of the New PDE5 Inhibitor TPN729MA. J Sex Med. 2013 Nov;10(11):2790-7.

[2]. Li BB, et al. Sildenafil potentiates the proliferative effect of porcine pulmonary artery smooth muscle cells induced by serotonin in vitro. Chin Med J (Engl). 2011 Sep;124(17):2733-40.

[3]. Moretti R, et al. Sildenafil, a cyclic GMP phosphodiesterase inhibitor, induces microglial modulation after focal ischemia in the neonatal mouse brain. J Neuroinflammation. 2016 Apr 28;13(1):95.

[4]. Korkmaz MF, et al. The Effect of Sildenafil on Recuperation from Sciatic Nerve Injury in Rats. Balkan Med J. 2016 Mar;33(2):204-11.

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