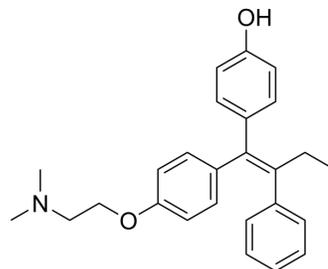


4-Hydroxytamoxifen

Cat. No.:	HY-16950		
CAS No.:	68047-06-3		
Molecular Formula:	C ₂₆ H ₂₉ NO ₂		
Molecular Weight:	387.52		
Target:	Estrogen Receptor/ERR		
Pathway:	Vitamin D Related/Nuclear Receptor		
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 : 50 mg/mL (129.03 mM; ultrasonic and warming and heat to 60°C)
 Ethanol : 20 mg/mL (51.61 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent		Mass		
	Concentration		1 mg	5 mg	10 mg
	1 mM		2.5805 mL	12.9026 mL	25.8051 mL
	5 mM		0.5161 mL	2.5805 mL	5.1610 mL
	10 mM		0.2581 mL	1.2903 mL	2.5805 mL

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

In Vivo

- Add each solvent one by one: 50% PEG300 >> 50% saline
Solubility: 5 mg/mL (12.90 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.08 mg/mL (5.37 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.08 mg/mL (5.37 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (5.37 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

4-Hydroxytamoxifen ((Z)-4-Hydroxytamoxifen) is an orally active, selective estrogen receptor modulator (SERM). 4-Hydroxytamoxifen ((Z)-4-Hydroxytamoxifen) induces CRISPR/Cas9 systems based on ER mediated nucleus translocation^[1] [2][3][4].

IC₅₀ & Target	Estrogen receptor 3.3 nM (IC ₅₀)	CRISPR/Cas9
In Vitro	<p>4-Hydroxytamoxifen (Monohydroxytamoxifen) is a selective oestrogen receptor antagonist, with an IC₅₀ of 3.3 nM for the [³H]oestradiol binding to oestrogen receptor. 4-Hydroxytamoxifen (10, 100 nM) enables to inhibit the binding of [³H]oestradiol to the human 8 S oestrogen receptor^[1].</p> <p>4-Hydroxytamoxifen activates intein-linked inactive Cas9, reduces off-target CRISPR-mediated gene editing. In human cells, conditionally active Cas9s modify target genomic sites with up to 25-fold higher specificity than wild-type Cas9^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>	
In Vivo	<p>4-Hydroxytamoxifen (0.2, 1 and 5 µg/day, p.o.) causes a dose-related decrease in uterine wet weight of immature rats^[1].</p> <p>4-Hydroxytamoxifen (6 µg/0.1 mL sesame oil/day, s.c.) effectively attenuates methamphetamine-induced nigrostriatal dopamine depletions in both sexes of intact and gonadectomized C57BL/6 J mice. 4-Hydroxytamoxifen does not alter the dopamine content levels in the striatum^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>	

PROTOCOL

Kinase Assay ^[1]

Cytosol (200 µL) is incubated for 30 min at 4°C with different concentrations of oestradiol, tamoxifen and (4-Hydroxytamoxifen) or dihydroxytamoxifen administered in 10 µL methanol. Control tubes are incubated with 10 µL methanol alone and non-specific binding is determined in a parallel incubation of cytosol (200 µL) with methanol (10 µL) containing DES (5 × 10⁶ M). [2,4,6,7-³H]Oestradiol solution (50 µL) in TED buffer is added to each tube to give a final concentration of 2 × 10⁻⁹ M. Incubation is continued for 4 h (4°C) and then 400 µL of a suspension of dextran-coated charcoal (250 mg % Norit A, 2.5 mg % dextran) in TED buffer are added and allowed to stand for 20 min. Tubes are centrifuged at 800 g for 10 min (4°C) and 400 µL samples of the supernatant are added to 10 mL tritium scintillator (6 g butyl PBD, 135 mL toluene, 720 ml dioxan, 100 g naphthalene, 45 mL absolute methanol). Samples are counted for 10 min in a liquid scintillation spectrometer. Counting efficiency is determined by external standardization (35-36 %). Results are represented as a percentage of the specifically bound radioactivity (c.p.m.) in the control tubes^[1].

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Animal Administration ^[3]

Mice^[3]

Animals of each sex are divided into two groups: one group receives 4-Hydroxytamoxifen [6 µg/0.1 mL sesame oil/day, subcutaneously (s.c.) starting at 06.00 h] injections for three consecutive days, while the other group receives an equivalent amount of sesame oil injection for 3 days. Four hours following the third injection, each group is then subdivided into two groups: one receives four cumulative doses of methamphetamine hydrochloride (10 mg/kg, s.c.), and the other receives a comparable volume of saline at 2-h intervals. Bilateral gonadectomy is performed under pentobarbital anesthesia (50 mg/kg, intraperitoneally). Five weeks after surgery, gonadectomized mice of each sex are randomly divided into six groups. Five groups of each sex receive three daily injections of various concentrations of 4-Hydroxytamoxifen (0, 1.5, 3.0, 6.0, and 12.0 µg/0.1 mL sesame oil/day). Four hours following the third injection, mice receive four doses of methamphetamine (MA, 10 mg/kg) at 2-h intervals. The remaining group of each sex receives sesame oil pretreatment for three consecutive days, followed by saline injections, and serves as the control group^[3].

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

CUSTOMER VALIDATION

- Nat Commun. 2018 Sep 25;9(1):3923.
- Mol Cell. 2020 Aug 6;79(3):425-442.e7.
- Acta Pharm Sin B. 2022 Sep;12(9):3618-3638.

- Cell Death Dis. 2021 May 18;12(6):509.
- Cell Death Dis. 2019 Sep 20;10(10):700.

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- [1]. Jordan VC, et al. A monohydroxylated metabolite of tamoxifen with potent antioestrogenic activity. *J Endocrinol.* 1977 Nov;75(2):305-16.
 - [2]. Davis KM, et al. Small molecule-triggered Cas9 protein with improved genome-editing specificity. *Nat Chem Biol.* 2015 May;11(5):316-8.
 - [3]. Kuo YM, et al. 4-Hydroxytamoxifen attenuates methamphetamine-induced nigrostriatal dopaminergic toxicity in intact and gonadectomized mice. *J Neurochem.* 2003 Dec;87(6):1436-43.
 - [4]. Zhang J, et al. Drug Inducible CRISPR/Cas Systems. *Comput Struct Biotechnol J.* 2019;17:1171-1177.
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Caution: Product has not been fully validated for medical applications. For research use only.

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