4-Hydroxytamoxifen

Cat. No.: HY-16950

CAS No.: 68047-06-3

Molecular Formula: $C_{26}H_{29}NO_2$

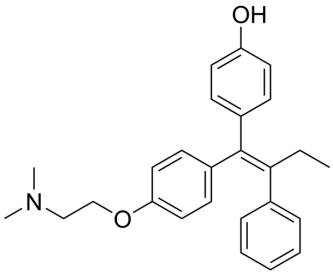
Molecular Weight: 387.52

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

1. 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
2. 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
3. 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].

IC_{50} & Target

Estrogen receptor 3.3 nM (IC_{50})	CRISPR/Cas9

In Vitro	4-Hydroxytamoxifen (Monohydroxytamoxifen) is a selective ostrogen receptor antagonist, with an IC_{50} of 3.3 nM for the [^{3}H]oestradiol binding to oestrogen receptor. 4-Hydroxytamoxifen (10, 100 nM) enables to inhibit the binding of [^{3}H]oestradiol to the human 8 S oestrogen receptor[1]. 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	4-Hydroxytamoxifen (0.2, 1 and 5 μg/day, p.o.) causes a dose-related decrease in uterine wet weight of immature rats[1]. 4-Hydroxytamoxifen (6 μg/0.1 mL sesame oil/day, s.c.) effectively attenuates methamphetamine-induced nigrostriatal dopamine depletions in bothsexes of intact and gonadectomized C57BL/6 J mice. 4-Hydroxytamoxifen does not alter the dopamine content levels in the striatum[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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 (5×10^6 M). [2,4,6,7-^{3}H]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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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 ofvarious 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

- Mol Cell. 2020 Aug 6;79(3):425-442.e7.
- Nat Commun. 2018 Sep 25;9(1):3923.
- Oncogene. 2023 Feb 2.
- Acta Pharm Sin B. 2022 Sep;12(9):3618-3638.
- Cell Death Dis. 2021 May 18;12(6):509.

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REFERENCES

[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 gonadetomized 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.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA