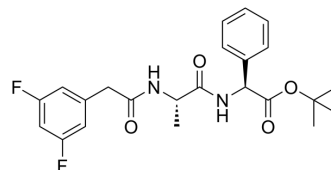


DAPT

| | | | |
|---------------------------|--|-------|----------|
| Cat. No.: | HY-13027 | | |
| CAS No.: | 208255-80-5 | | |
| Molecular Formula: | C ₂₃ H ₂₆ F ₂ N ₂ O ₄ | | |
| Molecular Weight: | 432.46 | | |
| Target: | γ-secretase; Autophagy; Apoptosis; Amyloid-β; Notch | | |
| Pathway: | Neuronal Signaling; Stem Cell/Wnt; Autophagy; Apoptosis | | |
| 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 : 62.5 mg/mL (144.52 mM; Need ultrasonic)
 Ethanol : 10 mg/mL (23.12 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent Concentration | Mass | | |
|---------------------------|-----------------------|-----------|------------|------------|
| | | 1 mg | 5 mg | 10 mg |
| | 1 mM | 2.3124 mL | 11.5618 mL | 23.1235 mL |
| | 5 mM | 0.4625 mL | 2.3124 mL | 4.6247 mL |
| | 10 mM | 0.2312 mL | 1.1562 mL | 2.3124 mL |

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

In Vivo

- Add each solvent one by one: corn oil
Solubility: 10 mg/mL (23.12 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 50% PEG300 >> 50% saline
Solubility: 5 mg/mL (11.56 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: 2.5 mg/mL (5.78 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution
- Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 1 mg/mL (2.31 mM); Clear solution

BIOLOGICAL ACTIVITY

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| Description | DAPT (GSI-IX) is a potent and orally active γ -secretase inhibitor with IC_{50} s of 115 nM and 200 nM for total amyloid- β ($A\beta$) and $A\beta_{42}$, respectively. DAPT inhibits the activation of Notch 1 signaling and induces cell differentiation. DAPT also induces autophagy and apoptosis. DAPT has neuroprotection activity and has the potential for autoimmune and lymphoproliferative diseases, degenerative disease and cancers treatment ^{[1][2]} . |
| IC_{50} & Target | IC_{50} : 115 nM ($A\beta$), 200 nM ($A\beta_{42}$) ^[5] |
| In Vitro | DAPT inhibits $A\beta$ production over 90%, effects only a modest reduction in APP β in the culture media. Although APP β is reduced by about 30% by DAPT treatment, this effect is not concentration-dependent and is reversed by the removal of DAPT ^[1] . CNE-2 cells are treated with increasing concentrations of DAPT (0, 25, 50 and 75 μ M), and the γ -secretase-generated Notch 1 fragment Val1744-NICD is decreased after 48 h in a dose-dependent manner ($P < 0.01$). The activation of γ -secretase is almost completely inhibited by DAPT at the concentration of 50 μ M ^[3] . MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| In Vivo | DAPT is administered to PDAPP mice (100 mg/kg s.c.) and the levels of DAPT and $A\beta$ are examined in the brain cortex. Peak DAPT levels of 490 ng/g are achieved in the brain 3 h after treatment, and levels greater than 100 ng/g (\sim 200 nM) are sustained throughout the first 18 h. These brain concentrations of DAPT are in excess of its IC_{50} for lowering $A\beta$ in neuronal cultures (115 nM), and results in a robust and sustains pharmacodynamic effect ^[1] . DAPT protects brain against cerebral ischemia by down-regulating the expression of Notch 1 and Nuclear factor kappa B in rats. Western blot analyses also show a significant decrease of Notch 1 and NF- κ B expression in DAPT (0.03 mg/kg) group ($P < 0.05$ vs. MCAO group) ^[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

PROTOCOL

| | |
|--|--|
| Cell Assay ^[1] | Human embryonic kidney cells, transfected with the gene for APP ₇₅₁ (HEK 293) are used for routine $A\beta$ reduction assays. Cells are plated in 96-well plates and allowed to adhere overnight in Dulbecco's modified Eagle medium (DMEM) supplemented with 10% heat-inactivated fetal bovine serum. Cells are pre-treated for 2 h at 37°C with DAPT (0, 0.4, 2, 10, 50 and 250 nM), media are aspirated off and fresh compound solutions applied. After an additional 2-h treatment period, conditioned media are drawn off and analyzed by a sandwich ELISA (266-3D6) specific for total $A\beta$. Reduction of $A\beta$ production is measured relative to control cells treated with 0.1% DMSO and expressed as a percentage inhibition. Data from at least six doses in duplicate are fitted to a four-parameter logistical model using XLfit software in order to determine potency ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| Animal Administration ^{[1][3]} | Mice ^[1] The three- to four-month-old heterozygous PDAPP transgenic mice overexpressing the APP _{V717F} mutant form of the amyloid precursor protein. Each treatment group (n=10) consists of equal numbers of age-matched male and female animals that are fasted overnight prior to treatment. Both treatment and control groups are dosed at a volume of 10 mL/kg with DAPT or vehicle alone. Tissues are processed and all $A\beta$ and APP measurements are made. After removal of the brain, the cortex from one hemisphere is homogenized, centrifuged, and the supernatant is used for $A\beta$ measurements. Cortex from the other hemisphere is snap frozen for analysis of compound levels. $A\beta$ levels are expressed as ng/g of wet tissue weight, and percentage reductions are calculated relative to the mean $A\beta$ level of tissue from vehicle-treated control animals. Data are analyzed with Mann-Whitney non-parametric statistics to assess significance. Rats ^[3] Male Sprague-Dawley rats (260-290 g) are used. DAPT solution is stereotactically injected into the lateral cerebral ventricle (LV) immediately after MCAO. The stereotactic injections into the LVs are performed at coordinates -0.8 mm anteroposterior, ± 1.5 mm mediolateral and -4.5 mm dorsoventral from the bregma. 30 rats are randomly assigned to three operating groups (10 rats in each group): sham-operated group that receive equal volume of PBS without MCAO operation; MCAO group that receive equal volume PBS after MCAO (MCAO); and DAPT group that receive DAPT as 0.03 mg/kg after MCAO. 24 h after operation the first neurological function is assessed and then 48 h after operation the second neurological |

function is assessed. Meanwhile, brain water content and infarction volume are measured and compared among different groups.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2022 Dec 2;378(6623):eabo5503.
- Nat Biotechnol. 2023 Jan 16.
- Mil Med Res. 2020 Sep 6;7(1):42.
- Neuro Oncol. 2023 Apr 21;noad079.
- J Clin Invest. 2018 Jan 2;128(1):483-499.

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- [3]. Li S, et al. DAPT protects brain against cerebral ischemia by down-regulating the expression of Notch 1 and nuclear factor κ B in rats. Neurol Sci. 2012 Dec;33(6):1257-64.
- [4]. Tanimizu N, et al. Intrahepatic bile ducts are developed through formation of homogeneous continuous luminal network and its dynamic rearrangement in mice. Hepatology. 2016 Jul;64(1):175-88.
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- [7]. Yixin Tao, et al. β -catenin activation in hair follicle dermal stem cells induces ectopic hair outgrowth and skin fibrosis. J Mol Cell Biol. 2018 May 16.

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

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