Product Data Sheet

Chemical Properties

**Product Name:** DAPT (GSI-IX)

**Cas No.:** 208255-80-5

**M.Wt:** 432.46

**Formula:** C23H26F2N2O4

**Synonyms:** gamma-Secretase Inhibitor IX, DAPT, GSI-IX

**Chemical Name:** tert-butyl (2S)-2-[[2S]-2-[2-(3,5-difluorophenyl)acetyl]amino]propanoyl]amino)-2-phenylacetate

**Canonical SMILES:** CC(C(=O)NC(C1=CC=CC=C1)C(=O)OC(C)(C)(C)C)NC(=O)CC2=CC(=CC(=C2\(\_\)2")F)F

**Solubility:** >21.6mg/mL in DMSO

**Storage:** Store at 4°C

**General tips:** For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

**Shopping Condition:** Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

**Targets:** Amyloid β

**Pathways:** Neuroscience >> Amyloid β

**Description:**

DAPT, N-[N-(3,5-Difluorophenacetyl]-L-alanyl]-S-phenylglycine t-butyl Ester, is a potent and specific inhibitor of \( \gamma \)-secretase, a multimeric membrane protein complex that catalyzes proteolytic cleavage of amyloid precursor protein (APP) resulting in the accumulation of amyloid-\( \beta \) (A\( \beta \)) peptides which is associated with early on-set of familial Alzheimer’s disease (AD). It directly
binds to the C-terminal fragment of the catalytic center of γ-secretase, presenilin (PS), especially within the transmembrane domain 7 or more C-terminal region, resulting in the synthesis of a photoactivable DAPT derivative. Through oral administration, DAPT dose-dependently reduced Aβ peptides levels in vivo in Plasma and cerebrospinal fluid in young (6 months old, plaque-free) and aged (17 months old, plaque-bearing) Tg2576 mice.

Reference:

Protocol

Cell experiment:

**Cell lines**
SHG -44 human glioma cell line

**Preparation method**
The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

**Reacting conditions**
5d; 1.0 μM

**Applications**
Cell viability in each group was detected by MTT. Compared with those in group A (control), proliferation of SHG -44 cells in group B (0.5 μM), C (1μM), D (5 μM) and E (10 μM) were inhibited by DAPT. For group B and A, the results were significantly different (P<0.05). However, cell viability of group B was significantly higher than those in group C, D and E (P<0.05). The results showed that increased inhibition effect was related to increased DAPT concentrations. However there was no difference among group C, D and E (P>0.05). It indicated that DAPT is a concentration-dependent inhibitor that may obviously inhibit SHG-44 cells proliferation. As concentration of DAPT higher than 1.0 μmol/L showed no more obvious disparities in cell inhibition, concentration of 1.0 μmol/L was our priority.

Animal experiment [3]:


<table>
<thead>
<tr>
<th>Animal models</th>
<th>Male Balb/C mice</th>
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</thead>
<tbody>
<tr>
<td>Dosage form</td>
<td>10 mg/kg/day; subcutaneously injected</td>
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<tr>
<td>Applications</td>
<td>CT26 colon adenocarcinoma cells (5 × 10^5 cells) in 500 μL of phosphate buffer solution (PBS) were inoculated subcutaneously into the dorsum of all mice. Administration of DAPT significantly reduced serum sVEGFR1, while could not change serum VEGF concentration in control mice. Immunohistochemical study of the tumors showed that CD31 positive cells were reduced after DAPT administration (280.6 ± 81 vs. 386 ± 59.9 CD31 positive cells/mm²), although it was not statistically significant.</td>
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<td>Other notes</td>
<td>Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.</td>
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**Reference:**


**Product Citations**

The result shows the level of Aβ40 and Aβ42 decreased as the DAPT concentration increased. Compared with Aβ42, the level of Aβ420 decreased more rapidly with increasing DAPT concentration.

The Neuro-2A cells (transfected with Klotho) were treated with DAPT for 16 h. The transfected Neuro-2A without DAPT treatment was assigned as control. Un-transfected Neuro-2A was assigned as wild type cells (wt). The protein levels of Klotho and Klotho (sub) from cells lysate were analyzed using Klotho and Flag antibody respectively. Gamma-secretase inhibitor DAPT could cleave Klotho stub. After treatment with DAPT, 5 kDa fragment was found in transfected cells, which was not seen in wt and control group.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

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