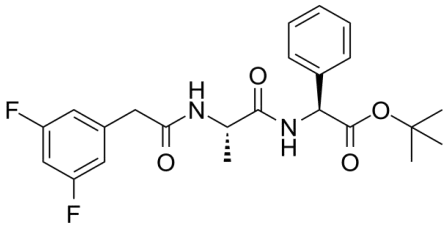
DAPT

Catalog Number: C208255

OrganRegen, INC.
Creating Solutions for Organoid Cultures

DESCRIPTION

Background	DAPT (GSI-IX) is a potent and orally active γ-secretase inhibitor with IC50s of 115 nM and 200 nM for total amyloid-β (Aβ) and Aβ42, 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].		
Alias	GSI-IX		
M. W t	432.46		
Formula	$C_{23}H_{26}F_2N_2O_4$		
CAS No	208255-80-5		
Storage	Powder	- 20°C	2 years
		- 80°C	3 years
	In solvent	- 80°C	12 months
		- 20°C	3 months
Solubility	DMSO	≥ 100 mg/mL(283.71 mM)	
	Ethanol	41 mg/mL(94.81 mM)	
	H2O	< 0.1 mg/mL(insoluble)	



$C_{23}H_{26}F_2N_2O_4$

BIOLOGICAL ALTIVITY

In Vitro

DAPT inhibits Aβ production over 90%, effects only a modest reduction in APPβ in the culture media. Although APPβ 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 μM), 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 μM[3].

In Vivo

DAPT is administered to PDAPP mice (100 mg/kg s.c.) and the levels of DAPT and Aβ 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 (~200 nM) are sustained throughout the first 18 h. These brain concentrations of DAPT are in excess of its IC50 for lowering Aβ 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-κB expression in DAPT (0.03 mg/kg) group (P<0.05 vs. MCAO group)[2].

REFERENCES

[1]. Dovey HF, et al. Functional gamma-secretase inhibitors reduce beta-amyloid peptide levels in brain. J Neurochem. 2001 Jan;76(1):173-81.

[2]. Li S, et al. DAPT protects brain against cerebral ischemia by down-regulating the expression of Notch 1 and nuclear factor κB in rats. Neurol Sci. 2012 Dec;33(6):1257-64.

[3]. Zhou JX, et al. γ-secretase inhibition combined with NSC 119875 enhances apoptosis of nasopharyngeal carcinoma cells.Exp Ther Med. 2012 Feb;3(2):357-361.