For Research Use Only

AZD1080

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Catalog Number: CM04321

产品信息

Catalog Number:
CM04321

CAS号:
612487-72-6

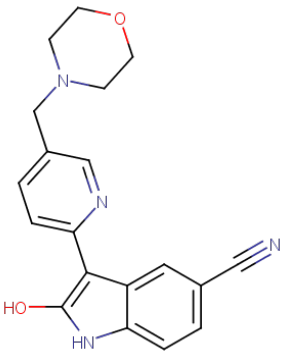
分子式:
$C_{19}H_{18}N_4O_2$

主要靶点:
GSK-3

主要通路:
PI3K/Akt/mTOR信号通路|干细胞

分子量:
334.37

溶解度:
DMSO:49 mg/mL (146.5 mM),Ethanol:<1 mg/mL



靶点活性

GSK-3β:31 nM|GSK-3α:6.9 nM

体外活性

AZD1080逆转小鼠的认知缺陷并拯救其功能失调的突触.口服AZD1080抑制大鼠脑中tau蛋白磷酸化,在峰浓度下脑/血浆暴露比率为0.5-0.8.急性口服AZD1080抑制外围GSK3的活性,剂量依赖性降低磷酸化糖原合成酶和总糖原合成酶的比率,在最高剂量为10mol/kg时达到平均最大抑制效果49%.

体内活性

AZD1080抑制表达人类tau的细胞中的tau磷酸化,IC50为324 nM。AZD1080抑制人GSK3α和GSK3β,Ki 值分别为6.9 nM和31 nM,对cdk2、cdk5、cdk1和Erk2表现出> 14倍的选择性。

细胞实验

3T3 fibroblasts are engineered to stably express four-repeat tau protein. These cells have high endogenous levels of GSK3 that is able to phosphorylate tau protein constitutively. This phosphorylation is inhibited by LiCl. After treatment with different compounds, cultures are washed twice with 5 mM MgCl2-PBS. Extracts for Western blot analysis are prepared by homogenizing cells in ice-cold extraction buffer consisting of 20 mM HEPES, pH 7.4, 100 mM NaCl, 10 mM NaF, 1% Triton X-100, 1 mM sodium orthovanadate, 10 mM EDTA, and protease inhibitors (2 mM phenylmethylsulfonyl fluoride, 10 μg/ml aprotinin, 10 μg/ml leupeptin, and 10 μg/ml pepstatin). The samples are homogenized at 4 °C, and protein content is determined by Bradford method. Total protein (25 μg) is electrophoresed on 10% SDS-PAGE gel and transferred to a nitrocellulose membrane. The experiments are performed using the following primary antibodies: tau Ser(P)-396, 1:1000; Tau5, 1:1000; and anti-GSK3β, 1:1000. The filters are incubated with the antibody at 4 °C overnight in 5% nonfat dried milk. A secondary antibody (1:5000), followed by ECL detection reagents are used for immunodetection. Quantitation of immunoreactivity is performed by densitometric scanning.(Only for Reference)

描述

AZD1080 is a selective, orally active, brain permeable GSK3 inhibitor.

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years