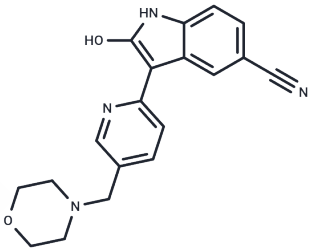
Data Sheet (Cat.No.T1741)

TargetMol

AZD1080

Chemical Properties



CAS No. : 612487-72-6

Formula: C19H18N4O2

Molecular Weight: 334.37

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	AZD1080 is a selective, orally active, brain permeable GSK3 inhibitor.
Targets(IC50)	GSK-3
In vitro	AZD1080 reverses cognitive deficits in mice and rescues their dysfunctional synapses. Oral administration of AZD1080 inhibits tau protein phosphorylation in the rat brain, with a peak brain/plasma exposure ratio of 0.5-0.8. Acute oral intake of AZD1080 suppresses peripheral GSK3 activity in a dose-dependent manner, reducing the phosphorylation ratio of glycogen synthase to total glycogen synthase, achieving an average maximum inhibition of 49% at the highest dose of 10mol/kg.
In vivo	AZD1080 inhibits tau phosphorylation in cells expressing human tau with an IC50 of 324 nM. It also inhibits human GSK3α and GSK3β with Ki values of 6.9 nM and 31 nM, respectively, demonstrating over 14-fold selectivity against cdk2, cdk5, cdk1, and Erk2.
Kinase Assay	Kinase Assay: GSK3 scintillation proximity assay is done. The competition experiments are carried out in duplicate with 10 concentrations of the inhibitor in clear-bottomed microtiter plates. The biotinylated peptide substrate biotin-AAEELDSRAGS(PO3H2)PQL, is added at a final concentration of 2 μM in an assay buffer containing 6 milliunits of recombinant human GSK3 (equal mix of both α and β), 12 mM MOPS, pH 7.0, 0.3 mM EDTA, 0.01% β-mercaptoethanol, 0.004% Brij 35, 0.5% glycerol, and 0.5 μg of bovine serum albumin/25 μl and preincubated for 10–15 min. The reaction is initiated by the addition of 0.04 μCi of [γ-33P]ATP and unlabeled ATP in 50 mM Mg(Ac)2 to a final concentration of 1 μM ATP and assay volume of 25 μl. Blank controls without peptide substrate are used. After incubation for 20 min at room temperature, each reaction is terminated by the addition of 25 μl of stop solution containing 5 mM EDTA, 50 μM ATP, 0.1% Triton X-100, and 0.25 mg of streptavidin-coated SPA beads corresponding to 35 pmol of binding capacity. After 6 h the radioactivity is determined in a liquid scintillation counter.
Cell Research	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)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 40 mg/mL (119.63 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.9907 mL	14.9535 mL	29.907 mL
5 mM	0.5981 mL	2.9907 mL	5.9814 mL
10 mM	0.2991 mL	1.4953 mL	2.9907 mL
50 mM	0.0598 mL	0.2991 mL	0.5981 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Georgievska B, et al. J Neurochem, 2013, 125(3), 446-456.
Hu S, Hu M, Liu J, et al. Phosphorylation of Tau and α-Synuclein Induced Neurodegeneration in MPTP Mouse Model of Parkinson's Disease. Neuropsychiatric Disease and Treatment. 2020, 16: 651.
Hu S, Hu M, Liu J, et al. Phosphorylation of Tau and α-Synuclein Induced Neurodegeneration in MPTP Mouse Model of Parkinson's Disease[J]. Neuropsychiatric Disease and Treatment. 2020, 16: 651.

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