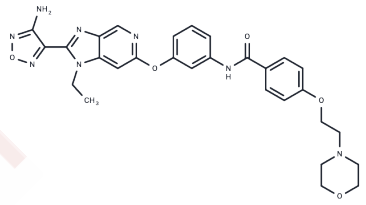
Data Sheet (Cat.No.T3518)

TargetMol

GSK269962A

Chemical Properties



CAS No. : 850664-21-0

Formula: C29H30N8O5

Molecular Weight: 570.6

Storage: Store under nitrogen
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	GSK269962A (GSK269962A HCl) is a selective ROCK(Rho-associated protein kinase) inhibitor with IC50 values of 1.6 and 4 nM for ROCK1 and ROCK2, respectively.
Targets(IC50)	ROCK,S6 Kinase
In vitro	GSK269962A completely abolished the actin stress fiber formation induced by angiotensin II in human smooth muscles. Such suppressive effect on actin fiber formation was observed beginning at around 1 μM GSK269962A. GSK269962A induced vasorelaxation in preconstricted rat aorta(tissue baths) with an IC50 of 35 nM. the relaxation induced by GSK269962A is reversible. GSK269962A suppressed IL-6 mRNA transcription and reduced LPS-induced IL-6 and TNF-α protein production in macrophages
In vivo	Oral administration of GSK269962A produced a profound dose-dependent reduction of systemic blood pressure in spontaneously hypertensive rats. The reduction of blood pressure was acute and substantial. The maximal effect on blood pressure was observed approximately 2 h after oral gavages. The reduction of blood pressure was accompanied by an acute, dose-dependent increase in heart rate, presumably due to the activation of baroreflex mechanism. ROCK inhibition with the use of GSK 269962 in the 10 mg/kg dose, in turn, triggered an increase in VV(voided volume), PVR(post-void residual), VT(volume threshold), VE(voiding efficiency), ICI(intercontraction interval), BC (bladder compliance), and VTNVC(volume threshold to elicit NVC).
Kinase Assay	The enzyme activity and kinetics of the purified ROCK1(3-543) are determined using scintillation proximity assay. In this assay, purified ROCK1 is incubated with peptide substrate (Biotin-Ahx-AKRRLSSLRA-CONH2), and 33ATP and the subsequent incorporation of 33P into the peptide is quantified by streptavidin bead capture. For IC50 determination, test compounds are dissolved at 10 mM in 100% DMSO, with subsequent serial dilution in 100% DMSO. Compounds are typically assayed over an 11-point dilution range with a concentration in the assay of 10 μM to 0.2 nM in 3-fold dilutions. For dose-response curves, data are normalized and expressed as percentage inhibition using the formula 100×[(U-C1)/(C2-C1)], where U is the unknown value, C1 is the average of the high signal (0%) control wells, and C2 is the average of the low signal (100%) control wells. Curve fitting is performed The results for each compound are recorded as pIC50 values[1].

Cell Research	Human primary smooth muscle cells were serum-starved(cells were grown on coverslips, and at approximately 50% confluence, they were serum-starved overnight) and stimulated with AngII (100 nM) for 2 h. ROCK inhibitors (3 μM for SB-772077-B or GSK269962A) were added 30 min before AngII stimulation, and cells were fixed and stained with rhodamine phalloidin. Confocal images of actin stain were obtained.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 6 mg/mL (10.52 mM),Sonication is recommended. DMSO: 57.1 mg/mL (100.07 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.51 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7525 mL	8.7627 mL	17.5254 mL
5 mM	0.3505 mL	1.7525 mL	3.5051 mL
10 mM	0.1753 mL	0.8763 mL	1.7525 mL
50 mM	0.0351 mL	0.1753 mL	0.3505 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Doe C, et al. J Pharmacol Exp Ther. 2007, 320(1):89-98.
Xu Q, Fu Q, Li Z, et al. Procyanidin C1 is a natural agent with senolytic activity against aging and age-related diseases. EMBO Molecular Medicine. (2021)13:e12716
Andrzej Wróbel, et al. Neurourology and Urodynamics. 2016.
Mondal T, Shivange G N, Tihagam R G T, et al. Unexpected PD-L1 immune evasion mechanism in TNBC, ovarian, and other solid tumors by DR5 agonist antibodies. EMBO Molecular Medicine. 2021 Mar 5;13(3):e12716. doi: 10.15252/emmm.202012716. Epub 2021 Feb 15.
Xu Q, Fu Q, Li Z, et al. Procyanidin C1 is a natural agent with senolytic activity against aging and age-related diseases[J]. bioRxiv. 2021
Mondal T, Shivange G N, Tihagam R G T, et al. Unexpected PD-L1 immune evasion mechanism in TNBC, ovarian, and other solid tumors by DR5 agonist antibodies. EMBO Molecular Medicine. 2021: e12716.

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