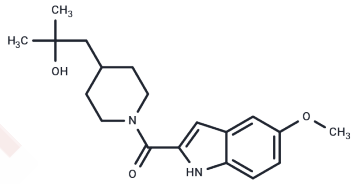
Data Sheet (Cat.No.T4529)

TargetMol

ASP-9521

Chemical Properties



CAS No. : 1126084-37-4

Formula: C19H26N2O3

Molecular Weight: 330.42

Storage: 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	ASP-9521 is a selective, potent and orally active indole-based AKR1C3 inhibitor with an IC50 of 11 nM for human AKR1C3.
Targets(IC50)	Others,Dehydrogenase,NADPH
In vitro	**METHODS**: H9c2 cells were preincubated in the presence of ASP9521 (25 μM) for 3 h. Then, DOX/DNR were added for the next 24 h. Cell viability was determined using the MTT assay. **RESULTS** The viability of H9c2 cells treated with DOX was 79%, while that of H9c2 cells preincubated with ASP9521 was 93%. ASP9521 almost completely protected cardiomyocytes from the toxic activity of DOX. [2] **METHODS**: Human lung cancer cell line A549 cells were treated with ASP9521 (0.1, 1, 10, 25, 50, 100 μM) and DNR (0.05–1 μM), and the IC50 of DNR alone or in combination with ASP9521 (25 μM) was calculated and compared. **RESULTS** The IC50 values obtained were 0.442 μM (DNR alone) and 0.379 μM (in combination with ASP9521). [2]
In vivo	ASP9521 inhibits the conversion of AD to T by recombinant human or cynomolgus monkey AKR1C3 in a concentration-dependent manner (IC50, human: 11 nM; IC50, monkey: 49 nM); ASP9521 is more than 100-fold more selective for AKR1C3 than for the isoform AKR1C2; a single oral dose of ASP9521 (3 mg/kg) inhibits AD-induced intratumoral T production in CWR22R xenografts, and this inhibitory effect persists for 24 hours; after oral administration, ASP9521 is rapidly eliminated from plasma, while its intratumoral concentration remains high; the bioavailability of oral ASP9521 (1 mg/kg) in rats, dogs, and monkeys is 35%, 78%, and 58%, respectively. [1]
Cell Research	LNCaP-AKR1C3 cells stably expressing human AKR1C3 are seeded in 96-well plates at 10000 cells/100 μL/well in RPMI-1640 medium supplemented with heat-inactivated charcoal-dextran-stripped FBS (1 % for the PSA expression assay and T measurement and 5 % for the cell proliferation assay). After 24 h incubation, AD is added to each well with or without ASP-9521 (0.3-100 nM). The cell culture media are collected 24 h after administration of AD to measure T concentration and 6 days after administration of AD to measure cell proliferation using Cell-Titer Glo assay.
Animal Research	ASP-9521 is prepared in 0.5 % methyl cellulose.Mice carrying HEK293 or HEK293-AKR1C3 tumors with similar sizes are selected and randomly divided into 5 groups (N=3 for each group). All groups are treated with ASP-9521 (single oral administration; 3 mg/kg).

Animal Research	Plasma (from the central vein) and tumor tissues are collected at 0.25, 0.5, 1, 2 and 4 h after administration of ASP-9521, and ASP-9521 concentrations are determined using the HPLCMS/MS method.

Solubility Information

Solubility	DMSO: 60 mg/mL (181.59 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 (6.05 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	3.0265 mL	15.1323 mL	30.2645 mL
5 mM	0.6053 mL	3.0265 mL	6.0529 mL
10 mM	0.3026 mL	1.5132 mL	3.0265 mL
50 mM	0.0605 mL	0.3026 mL	0.6053 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

Kikuchi A, et al. In vitro and in vivo characterisation of ASP9521: a novel, selective, orally bioavailable inhibitor of 17β-hydroxysteroid dehydrogenase type 5 (17βHSD5; AKR1C3).Invest New Drugs. 2014 Oct;32(5):860-70.

Jamrozik M, et al. In Silico and In Vitro Assessment of Carbonyl Reductase 1 Inhibition Using ASP9521-A Potent Aldo-Keto Reductase 1C3 Inhibitor with the Potential to Support Anticancer Therapy Using Anthracycline Antibiotics. Molecules. 2023 Apr 27;28(9):3767.

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