Data Sheet (Cat.No.T4695)

TargetMol

CP671305

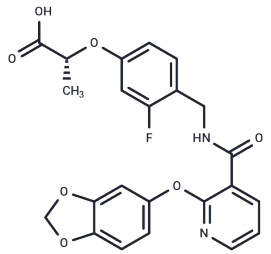
Chemical Properties

CAS No. : 445295-04-5

Formula: C23H19FN2O7

Molecular Weight: 454.4

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	CP671305 is an orally active, potent and selective inhibitor of phosphodiesterase-4-D.
Targets(IC50)	PDE
In vitro	CP-671,305 is a substrate of human OATP2B1 with a high affinity (Km=4 μM) but not a substrate for human OATP1B1 or OATP1B3. CP-671,305 is identified as a substrate of MRP2 and BCRP, but not MDR1. CP-671,305 displays high affinity (Km=12 μM) for rat hepatic Oatp1a4. CP-671,305 does not exhibit competitive inhibition of the five major cytochrome P450 enzymes, namely CYP1A2, 2C9, 2C19, 2D6 and 3A4 (IC50s >?50 μM). Likewise, no time-dependent inactivation of the five major cytochrome P450 enzymes is discernible with CP-671,305.
In vivo	The pharmacokinetics of CP-671,305 are largely unaltered, and compromised biliary clearance of CP-671,305 is compensated by increased urinary clearance. CP-671,305 demonstrates generally favourable pharmacokinetic properties, systemic plasma clearance after intravenous administration is low in Sprague-Dawley rats (9.60?±?1.16?mL/min/kg), beagle dogs (2.90?±?0.81?mL/min/kg) and cynomolgus monkeys (2.94?±?0.87?mL/min/kg) resulting in plasma half-lives >?5?h. Moderate to high bioavailability in rats (43-80%), dogs (45%) and monkeys (26%) is observed after oral dosing. In rats, oral pharmacokinetics are dose dependent over the dose range studied (10 and 25?mg/kg).
Animal Research	Jugular vein cannulated and bile duct-exteriorized male Sprague-Dawley rats (230-250 g) are used in the assay. All animals are fasted overnight before dosing, whereas access to water is provided ad libitum. Animals are fed following collection of the 2-h blood samples. CP-671,305 (3 mg/kg) in glycerol formal is administered intravenously (i.v.) via the jugular vein to three rats over 30 s, and serial plasma samples are collected before dosing and 0.033, 0.15, 0.5, 1, 2, 4, 6, 8, and 24 h after dosing. All plasma samples are kept frozen until analysis. In addition, an i.v. dose of 3 mg/kg is also given to bile duct-exteriorized rats (n=3), where plasma, bile, and urine samples are collected on ice for up to 24 h and stored at -20°C until analysis. For the DDI studies, cyclosporin A (20 mg/kg in glycerol formal) is administered i.v. 30 min before intravenous administration of CP-671,305. Rifampicin (50 mg/kg) in saline is administered i.v. 5 min before the administration of CP-671,305. Plasma samples from the various pharmacokinetic studies are generated by centrifugation at 3000 rpm for 10 min at 4°C. Samples are stored at -20°C, pending analysis by LC-MS/MS.

Solubility Information

Solubility	DMSO: > 150 mg/mL (330.11 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 (4.4 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	2.2007 mL	11.0035 mL	22.007 mL
5 mM	0.4401 mL	2.2007 mL	4.4014 mL
10 mM	0.2201 mL	1.1004 mL	2.2007 mL
50 mM	0.044 mL	0.2201 mL	0.4401 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

Kalgutkar AS, et al. Role of transporters in the disposition of the selective phosphodiesterase-4 inhibitor (+)-2-[4-({[2-(benzo[1,3]dioxol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-3-fluoro-phenoxy]-propionic acid in rat and human. Drug Metab Dispos. 2007 Nov;35(11):2111-8. Epub 2007 Aug 8.
Kalgutkar AS, et al. Disposition of CP-671, 305, a selective phosphodiesterase 4 inhibitor in preclinical species. Xenobiotica. 2004 Aug;34(8):755-70.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481