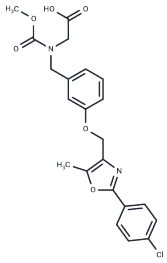
Data Sheet (Cat.No.T5532)

TargetMol

BMS-687453

Chemical Properties



CAS No. : 1000998-59-3

Formula: C22H21ClN2O6

Molecular Weight: 444.86

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	BMS-687453 is a potent and selective PPAR alpha agonist, demonstrating an EC(50) of 10 nM for human PPAR alpha and approximately 410-fold selectivity versus human PPAR gamma in PPAR-GAL4 transactivation assays.
Targets(IC50)	PPAR
In vitro	BMS-687453 is PPARα agonist, with an EC50 and IC50 of 10 nM and 260 nM for human PPARα and ~410-fold and more than 57-fold selectivity vs human PPARγ of 4100 nM and >15000 nM in PPAR-GAL4 transactivation assays. BMS-687453 exhibits high PPARα potency (EC50: 47 nM) with ~50-fold selectivity vs PPARγ (EC50: 2400 nM) in HepG2 cells. However, BMS-687453 shows less potent activities in rodent PPARα functional assays, with a moderate EC50 of 426 nM for mouse and 488 nM for hamster but remains a full PPARα agonist in both species [1].
In vivo	BMS 687453 (10-100 mg/kg) reduces plasma triglyceride levels and increases HDL levels in human ApoA1 transgenic mice. It also reduces serum triglyceride and LDL levels in hamsters fed a high-fat diet[2]
Kinase Assay	A homogeneous, fluorescent polarization PPARR and PPARγ binding assay was used as the primary screen for determining the PPARR and PPARγ binding affinity of compounds. The human functional activity of PPARR and PPARγ agonists was determined by using the GAL4-LBD assays as previously described. The in vitro hamster, rat, and mouse PPARR functional activities were tested in the chimeric GAL4/PPARR assay format described for human PPARR as above. The data are reported as an EC50 value calculated using XLfit 4 parameter fit and floating all parameters. Full-length human PPARR and PPARγ co-transfection assays in HepG2 cells were employed for further testing the leading compounds (BMS-687453) [1].
Animal Research	Male Syrian golden hamsters were acclimated to 12 h light/dark reverse light cycle for 7 days with high fat diet, then dosed daily by oral gavage for 21 days while on the same diet. At the end of the experiment, blood samples were drawn retro-orbitally after an 18 h fast and 24 h after the last dose for the determination of serum lipid levels. Livers were dissected out for mRNA analysis [1].

Solubility Information

Solubility	DMSO: 31 mg/mL (69.68 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 (4.5 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	2.2479 mL	11.2395 mL	22.479 mL
5 mM	0.4496 mL	2.2479 mL	4.4958 mL
10 mM	0.2248 mL	1.1239 mL	2.2479 mL
50 mM	0.045 mL	0.2248 mL	0.4496 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

Li J, et al. Discovery of an oxybenzylglycine based peroxisome proliferator activated receptor alpha selective agonist 2-((3-((2-(4-chlorophenyl)-5-methyloxazol-4-yl)methoxy)benzyl)(methoxycarbonyl)amino)acetic acid (BMS-687453). J Med Chem. 2010 Apr 8;53(7):2854-64.

Mukherjee R , Locke K T , Miao B , et al. Novel Peroxisome Proliferator-Activated Receptor ? Agonists Lower Low-Density Lipoprotein and Triglycerides, Raise High-Density Lipoprotein, and Synergistically Increase Cholesterol Excretion with a Liver X Receptor Agonist[J]. Journal of Pharmacology and Experimental Therapeutics, 2008, 327(3): 716-726.

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