Dalmelitinib

Cat. No.: HY-147259

CAS No.: 1637658-98-0

Molecular Formula: $C_{22}H_{16}FN_7O_2S$

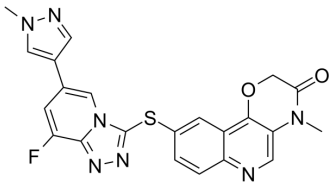
Molecular Weight: 461.47

Target: c-Met/HGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (216.70 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1670 mL	10.8349 mL	21.6699 mL
	5 mM	0.4334 mL	2.1670 mL	4.3340 mL
	10 mM	0.2167 mL	1.0835 mL	2.1670 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.42 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.42 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Dalmelitinib is an orally active selective c-Met kinase inhibitor (IC_{50}: 2.9 nM) that binds to the ATP-binding region of c-Met. Dalmelitinib induces the phosphorylation of MET, partially or completely inhibits the phosphorylation of AKT and ERK. Dalmelitinib potently inhibits cancer cell (c-Met oncogene amplification) proliferation, and is used for the research of cancers like human non-small cell lung cancer (NSCLC)[1].

In Vitro

Dalmelitinib (Compound 4 d) binds to the ATP-binding region of c-Met kinase, and shows slective inhibitory activity against c-Met with an IC_{50} value of 2.9 nM[1].

Dalmelitinib (0-1 μM approximately, 3 days) inhibits cell proliferation in various c-Met oncogene amplification cancer cell lines, with IC_{50} values ranging from 6 nM to 33 nM[1].

Dalmelitinib (0.1-1 μM, 6-24 h) significantly induces the phosphorylation of the tyrosine kinases (MET), partially or

completely inhibits the downstream phosphorylation of ERK and AKT in HCCLM3 cells[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	C-Met oncogene amplification cancer cell: SNU-5, HCCLM3, MHCC97-H, MHCC97-L, MKN-45, NCI-H1993. No C-Met oncogene amplification cancer cell: Huh-7, NCI-N87, NCI-1975, A549.
Concentration:	0-1 μM approximately.
Incubation Time:	3 days
Result:	IC_{50}: 33 nM (HCCLM3), 6 nM (MHCC97-H, MKN-45), 7 nM (MHCC97-L), 14 nM (NCI-H1993), 2 nM (SNU-5); Other cells: > 1000 nM.

Western Blot Analysis[1]

Cell Line:	C-Met oncogene amplification cancer cell: SNU-5, HCCLM3, MHCC97-H, MHCC97-L, MKN-45, NCI-H1993. No C-Met oncogene amplification cancer cell: Huh-7, NCI-N87, NCI-1975, A549.
Concentration:	0.1, 0.3, 1 μM
Incubation Time:	6-24 h
Result:	Significantly induced the phosphorylation of the tyrosine kinases (MET), partially inhibited the downstream phosphorylation of AKT, and completely inhibited the downstream phosphorylation of ERK.

In Vivo

Dalmelitinib (Compound 4 d, intragastric administration, 10-60 mg/kg) significantly inhibits the tumor growth in a dose-dependent manner in MKN-45 tumor xenograft nude mice[1].

Dalmelitinib (intragastric administration, 5 mg/kg for a single dose) shows a high plasma concentration, longer half-life and mean residence time, low clearance rates in BALB/c small nude mice[1].

Dalmelitinib shows a high level of No Observed Adverse Effect Level (NOAEL) in mice long-term toxicity (225 mg/kg/day) and acute toxicity (600 mg/kg/day)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MKN-45 tumor xenograft nude mice[1]
Dosage:	10, 30, 60 mg/kg
Administration:	Intragastric administration
Result:	Inhibited the tumor growth with the inhibitory rates of 29.5% (10 mg/kg), 34.2% (30 mg/kg), and 61.4% (60 mg/kg).

Animal Model:	BALB/c small nude mice (pharmacokinetic assay)[1]
Dosage:	5 mg/kg for a single dose
Administration:	Intragastric administration
Result:	Pharmacokinetic profile of Dalmelitinib (Compound 4 d)

Compound	Cmax (ng/mL)	AUC (ng/mL/h)	$t_{1/2}$ (h)	MRT (h)	CL/F (mL/min/kg)	Vz/F
Dalmelitinib	8628	122487	5.55	9.10	0.68	327

REFERENCES

[1]. Junjun Zhao, et al. Synthesis and biological evaluation of new [1,2,4]triazolo[4,3-a]pyridine derivatives as potential c-Met inhibitors. Bioorg Med Chem. 2016 Aug 15;24(16):3483-93.

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