MK-8033

Cat. No.: HY-13299

CAS No.: 1001917-37-8

Molecular Formula: $C_{25}H_{21}N_5O_3S$

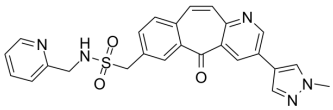
Molecular Weight: 471.53

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 : ≥ 46 mg/mL (97.55 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1208 mL	10.6038 mL	21.2076 mL
5 mM	0.4242 mL	2.1208 mL	4.2415 mL
10 mM	0.2121 mL	1.0604 mL	2.1208 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: ≥ 1 mg/mL (2.12 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (2.12 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MK-8033 is an orally active ATP competitive c-Met/Ron dual inhibitor (IC_{50}s: 1 nM (c-Met),7 nM (Ron)), with preferential binding to the activated kinase conformation. MK-8033 can be used in the research of cancers, such as breast and bladder cancers, non-small cell lung cancers (NSCLCs)[1][2].

IC_{50} & Target

Ron

7 nM (IC_{50})

In Vitro

MK-8033 (Compound 11r, 10 μM) displayed 31% inhibition of CYP3A4 (cytochrome P450 3A4)[1].

MK-8033 (1 μM, 2 h) inhibits phosphorylation of Y1349 of c-Met (IC_{50}: 0.03 μM) in the c-Met dependent gastric cancer cell line

GTL-16[1].
MK-8033 (1-10 μM, 72 h) inhibits GTL-16 cell proliferation (IC_{50}: 0.58 μM)[1].
MK-8033 binds more tightly to phosphorylated c-Met (K_d: 3.2 nM) than to its unphosphorylated counterpart (K_d: 10.4 nM), and inhibits oncogenic c-Met activation loop mutants with IC_{50}s ranging from 0.6 to 1 nM[1].
MK-8033 (0.1-10 μM, 2 h) reduces the phosphorylation of c-Met, ERK, and Akt in EBC-1 and H1993 cells[2].
MK-8033 (1 μM, 1 h) sensitizes EBC-1 and H1993 cells (high c-Met-expressing) to radiation[2].
MK-8033 (10 μM, 6 h) enhances γ-H2Ax levels in A549 cells compared to double irradiation and decreases in DNA repair[2].
MK-8033 (2 μM, 72 h) results in reduced cell proliferation, but modest induction of apoptosis in G-alpha protein mutant UM (uveal melanoma) cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	EBC-1, H1993 cells, A549 and H460 cells
Concentration:	0.1, 1, 10 μM
Incubation Time:	2 h
Result:	Reduced the phosphorylation of c-Met, ERK, and Akt in EBC-1 and H1993 cells in a dose-dependent manner.

In Vivo

MK-8033 (Compound 11r, oral administration, 3-100 mg/kg, twice daily for 21 days) inhibits tumor growth in GTL-16 c-Met amplified gastric tumor xenografts[1].
MK-8033 exhibits moderate clearance ($t_{1/2}$: 0.8 h for rats, 3.1 h for dog) and favorable bioavailability (35% for rats, 33% for dog)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Human GTL-16 c-Met amplified gastric tumor xenografts[1]
Dosage:	3, 10, 30, and 100 mg/kg
Administration:	Oral administration, twice daily for 21 days
Result:	Resulted in 22, 18, 57, and 86% tumor growth inhibition at 3, 10, 30, and 100 mg/kg, respectively. Inhibited c-Met (Y1349) phosphorylation.

CUSTOMER VALIDATION

- Nat Nanotechnol. 2021 Jul;16(7):830-839.
- Sci Rep. 2019 Dec 2;9(1):18101.

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REFERENCES

[1]. Chandrani Chattopadhyay, et al. Simultaneous inhibition of the HGF/MET and Erk1/2 pathways affect uveal melanoma cell growth and migration. PLoS One. 2014 Feb 13;9(2):e83957.

[2]. Northrup AB, et al, Discovery of 1-[3-(1-methyl-1H-pyrazol-4-yl)-5-oxo-5H-benzo[4,5]cyclohepta[1,2-b]pyridin-7-yl]-N-(pyridin-2-ylmethyl)methanesulfonamide (MK-8033): A Specific c-Met/Ron dual kinase inhibitor with preferential affinity for the activated

[3]. Bhardwaj V, et al. C-Met inhibitor MK-8003 radiosensitizes c-Met-expressing non-small-cell lung cancer cells with radiation-induced c-Met-expression. J Thorac Oncol. 2012 Aug;7(8):1211-7.

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