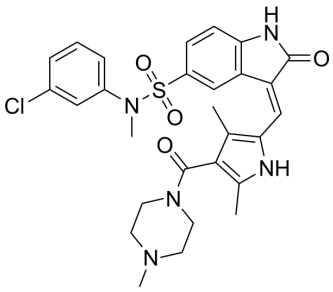
SU11274

Cat. No.:	HY-12014
CAS No.:	658084-23-2
Molecular Formula:	$C_{28}H_{30}ClN_5O_4S$
Molecular Weight:	568.09
Target:	c-Met/HGFR; Autophagy; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Autophagy; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (176.03 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7603 mL	8.8014 mL	17.6028 mL
5 mM	0.3521 mL	1.7603 mL	3.5206 mL
10 mM	0.1760 mL	0.8801 mL	1.7603 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 (4.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SU11274 is a selective Met inhibitor with IC_{50} of 10 nM, but has no effects on PGDFRβ, EGFR or Tie2.

IC_{50} & Target

IC50: 10 nM (Met)[1]

In Vitro

SU11274 exhibits greater than 50-fold selectivity for Met versus Flk and more than 500 times selectivity versus other tyrosine kinases such as FGFR-1, c-src, PDGFbR, and EGFR. SU11274 inhibits the phosphorylation of key regulators of the PI3K pathway, including AKT, FKHR, or GSK3β. SU11274 treatment inhibits the growth of TPR-MET-transformed BaF3 cells in a dose-dependent manner with IC_{50} of < 3 μM in the absence of interleukin 3, without growth inhibition of BaF3 cells transformed by other oncogenic tyrosine kinases, including BCR-ABL, TEL-JAK2, TEL-ABL, and TEL-PDGFβR. In addition to cell growth, SU11274 treatment significantly inhibits the migration of BaF3. TPR-MET cells by 44.8% and 80% at 1 μM and 5 μM, respectively. SU11274 inhibits HGF-dependent phosphorylation of Met as well as HGF-dependent cell proliferation and

motility with an IC_{50} of 1-1.5 μM. In H69 and H345 cells which have functional Met receptor, SU11274 inhibits the HGF-induced cell growth with IC_{50} of 3.4 μM and 6.5 μM, respectively. SU11274 induces G1 cell cycle arrest with cells in G1 phase increased from 42.4% to 70.6% at 5 μM, and induces caspase-dependent apoptosis by 24% at 1 μM[2]. SU11274 inhibits cell viability in c-Met-expressing non-small cell lung cancer (NSCLC) cells with IC_{50} values of 0.8-4.4 μM, and abrogates hepatocyte growth factor-induced phosphorylation of c-Met and its downstream signaling[3].

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

PROTOCOL

Kinase Assay [1]

A chimeric protein is constructed containing the cytoplasmic domain of human c-Met fused to Glutathione S-transferase (GST) and expressed in SF9 cells. The c-Met kinase GST-fusion protein is used for an ELISA-based Met biochemical assay using the random copolymer poly(Glu:Tyr) (4:1) immobilized on microtiter plates as a substrate. IC_{50} value is determined with various concentrations of SU11274 in a buffer containing 5 μM ATP and 10 mM $MnCl_2$, 50 mM HEPES (pH 7.5), 25 mM NaCl, 0.01% BSA, and 0.1 mM Na orthovanadate. The kinase reaction is performed for 5 minutes at room temperature. The extent of substrate phosphorylation is measured using horseradish peroxidase-conjugated anti-pTyr antibodies.

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

Cell Assay [2]

Cells are exposed to various concentrations of SU11274 in the presence or absence of HGF for 24, 48, and 72 hours. The number of viable cells is determined using the MTT assay or trypan blue exclusion. Cell Cycle and apoptosis are measured by fluorescence-activated cell sorter analysis via propidium iodide staining and Annexin V-positive staining, respectively.

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

CUSTOMER VALIDATION

- Cells. 2023 Oct 18, 12(20), 2481.
- Cancer Cell Int. 2019 Jul 24;19:192.
- Biochim Biophys Acta Mol Cell Res. 2023 Oct 31;1871(1):119623.
- Pediatr Surg Int. 2019 Dec;35(12):1369-1378.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Wang X, et al. Potent and selective inhibitors of the Met [hepatocyte growth factor/scatter factor (HGF/SF) receptor] tyrosine kinase block HGF/SF-induced tumor cell growth and invasion. Mol Cancer Ther, 2003, 2(11):1085-1092.

[2]. Sattler M, et al. A novel small molecule met inhibitor induces apoptosis in cells transformed by the oncogenic TPR-MET tyrosine kinase. Cancer Res, 2003, 63(17), 5462-5469.

[3]. Ma PC, et al. Functional expression and mutations of c-Met and its therapeutic inhibition with SU11274 and small interfering RNA in non-small cell lung cancer. Cancer Res, 2005, 65(4), 1479-1488.

Caution: Product has not been fully validated for medical applications. For research use only.

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