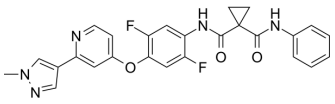
c-Kit-IN-1

Cat. No.:	HY-15240
CAS No.:	1225278-16-9
Molecular Formula:	$C_{26}H_{21}F_2N_5O_3$
Molecular Weight:	489.47
Target:	c-Kit; c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
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 (204.30 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0430 mL	10.2151 mL	20.4303 mL
5 mM	0.4086 mL	2.0430 mL	4.0861 mL
10 mM	0.2043 mL	1.0215 mL	2.0430 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 (5.11 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

c-Kit-IN-1 is a potent inhibitor of c-Kit and c-Met with IC_{50}s of <200 nM.

IC_{50} & Target

IC50: <200 nM (c-Met), <200 nM (c-Kit), <2 μM (KDR), <10 μM (PDGFRα), <10 μM (PDGFRβ)[1]

In Vitro

c-Kit-IN-1 is a c-Kit and c-Met inhibitor extracted from patent 2010051373A1, compound example 45, has an IC_{50} of <200 nM. c-Kit-IN-1 also inhibits KDR, PDGFR α and β with IC_{50}s of <2 μM, <10 μM and <10 μM, respectively[1].

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

PROTOCOL

Kinase Assay [1]	Activity of c-KIT kinase is determined by following the production of ADP from the kinase reaction through coupling with the pyruvate kinase/lactate dehydrogenase system. In this assay, the oxidation of NADH (thus the decrease at A340nm) is continuously monitored spectrophometrically. The reaction mixture (100 µL) contained c-KIT (cKIT residues T544-V976, from ProQinase, 5.4 nM), polyE4Y (1 mg/mL), $MgC1_2$ (10 mM), pyruvate kinase (4 units), lactate dehydrogenase (0.7 units), phosphoenol pyruvate (1 mM), and NADH (0.28 mM) in 90 mM Tris buffer containing 0.2 % octyl-glucoside and 1% DMSO, pH 7.5. Test compounds (e.g., c-Kit-IN-1) are incubated with c-KIT and other reaction reagents at 22°C for <2 min before ATP (200 µM) is added to start the reaction. The absorption at 340 nm is monitored continuously for 0.5 hours at 30°C on Polarstar Optima plate reader (BMG). The reaction rate is calculated using the 0 to 0.5 h time frame. Percent inhibition is obtained by comparison of reaction rate with that of a control (i.e. with no test compound). IC_{50} values are calculated from a series of percent inhibition values determined at a range of inhibitor concentrations using software routines as implemented in the GraphPad Prism software package[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	A serial dilution of test compounds (e.g., c-Kit-IN-1) are dispensed into a 96-well black clear bottom plate. For each cell line, five thousand cells are added per well in 200 µL complete growth medium. Plates are incubated for 67 hours at 37 degrees Celsius, 5% CO_2, 95% humidity. At the end of the incubation period 40 µL of a 440 µM solution of resazurin in PBS is added to each well and incubated for an additional 5 hours at 37 degrees Celsius, 5% CO_2, 95% humidity. Plates are read on a Synergy2 reader using an excitation of 540 nM and an emission of 600 nM. Data is analyzed using Prism software to calculate IC_{50} values[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Daniel L. Flynn, et al. Cyclopropane amides and analogs exhibiting anti-cancer and anti-proliferative activities. WO 2010051373 A1

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