Imatinib Mesylate

Cat. No.: HY-50946

CAS No.: 220127-57-1

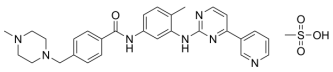
Molecular Formula: $C_{30}H_{35}N_7O_4S$

Molecular Weight: 589.71

Target: c-Kit; Bcr-Abl; PDGFR; Autophagy

Pathway: Protein Tyrosine Kinase/RTK; Autophagy

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (211.97 mM; Need ultrasonic)
H_2O : ≥ 50 mg/mL (84.79 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.6957 mL	8.4787 mL	16.9575 mL
5 mM	0.3391 mL	1.6957 mL	3.3915 mL
10 mM	0.1696 mL	0.8479 mL	1.6957 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (169.57 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.53 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.53 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.53 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Imatinib Mesylate (STI571 Mesylate) is a tyrosine kinases inhibitor that inhibits c-Kit, Bcr-Abl, and PDGFR (IC_{50}=100 nM) tyrosine kinases.

IC_{50} & Target

IC50: ~100 nM (c-Kit, Bcr-Abl, and PDGFR)[1]

In Vitro	Imatinib (STI571) Mesylate inhibits c-Kit autophosphorylation, activation of MAPK, and activation of Akt without altering total protein levels of c-kit, MAPK, or Akt. The concentration that produces 50% inhibition for these effects is approximately 100 nM[1]. Imatinib (STI571) mesylate is very effective (in vitro IC_{50} of 25 nM) against the chronic myeloid leukemia-causing kinase Bcr-Abl. Imatinib also efficiently inhibits Kit (in vitro IC_{50}, 410 nM) and PDGFR (in vitro IC_{50}, 380 nM)[2]. Imatinib (STI571) mesylate is a multi-target inhibitor of v-Abl, c-Kit and inhibits Bcr/Abl, v-Abl, Tel/Abl, the native PDGFβ receptor, and c-Kit, but it does not inhibit Src family kinases, c-Fms, Flt3, the EGFR or multiple other tyrosine kinases. Imatinib inhibits tyrosine phosphorylation and cell growth of Ba/F3 cells expressing Bcr/Abl, Tel/Abl, Tel/PDGFβR, and Tel/Arg with an IC_{50} of approximately 0.5 μM in each case, but it has no effect on untransformed Ba/F3 cells growing in IL-3 or on Ba/F3 cells transformed by Tel/JAK2[3]. Imatinib mesylate selectively inhibits the activity of Bcr/Abl, c-Kit and PDGFR kinases. Imatinib mesylate reveals distinct and rapid antileukemic activity in chronic myelogenous leukemia (CML) and Philadelphia-positive (Ph^+) acute lymphoblastic leukemia (ALL)[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Animals treated with Imatinib Mesylate show a decrease of mean body weight throughout the whole study. Body weight loss is noticeable in mice from groups that receive chemotherapy and the vitamin D analog combined treatment. The body weight decrease of mice treat with both combined Imatinib mesylate and PRI-2191 is the highest (15%) on Day 22 of the experiment, but after that day, mice start to recover[4]. In a rat Ischemia/reperfusion injury (IRI) model, Imatinib mesylate attenuates lung injury by an antipermeability and antiinflammatory effect. The delivery and function of Imatinib mesylate in the lung is also confirmed in this model[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [4]	Tested A549 cells are placed in 96-well flat-bottom plates at a density of 5×10^3 cells per well 24 h before the addition of the test compounds. The cells are incubated for 96 h with two different concentrations (10 and 100 nM) of PRI-2191 and concurrently with various concentrations of Imatinib mesylate (10, 100, 1000 and 10,000 ng/mL) and other cytostatic drugs (Docetaxel (DTX) or Idarubicin (ID) : 0.1, 1, 10, 100 ng/mL; Cisplatin (CIS): 1, 10, 100, 1000 ng/mL). The sulforhodamine B (SRB) assay is performed to evaluate the cytotoxic effect. As a result, IC_{50} is calculated for each separate experiment in Cheburator 0.4, Dmitry Nevozhay software[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4][5]	Mice[4] NOD/SCID female mice, 12-16 weeks old, body weight of 20-25 g, are used. Mice are subcutaneously (s.c.) inoculated in the right flank of the abdomen with A549 tumor cells suspension (5×10^6 cells in 0.2 mL of Hank's medium per mouse, Day 0) and then are randomized into groups receiving varied combinations of vitamin D analogs and chemotherapeutics. One out of two experimental protocols is applied in the respective experiments: 1. The treatment is started from Day 7 after inoculation of tumor cells (when tumors become palpable). Imatinib mesylate is administered intraperitoneally (i.p.) at a dose of 75 mg/kg/day, daily for 19 days (from Days 7-25). PRI-2191 is administered s.c. or by oral gavage at a dose of 2 μg/kg/day, 3 times a week (on Days 7, 12, 14, 16, 19, 21 and 23). 2. The treatment is started from Day 7 after inoculation of tumor cells (when tumors become palpable). Imatinib mesylate is administered intraperitoneally (i.p.) at a dose of 50 mg/kg/day, daily for 13 days (from Days 7-19). PRI-2191 and PRI-2205 are administered s.c. at doses of 1 or 10 μg/kg/day, respectively, 3 times a week (on Days 7, 10, 12, 14, 17, 19, 21, 24 and 26). At the end of the experiments, blood is collected under anesthesia; then, the mice are sacrificed. Rats[5] Male Lewis rats weighing 270 to 320 g are used in the experiments. Imatinib mesylate (50 mg/kg) is injected intraperitoneally in the Imatinib group (n=7), and 0.5 mL of 20% DMSO without Imatinib is administered in the vehicle group (n=7). The dose of 25 mg/kg is preliminarily tested, and it produces a little improvement in lung function without statistical significance. The dose of 50 mg/kg and intraperitoneal administration are adopted based on this result and past reports. The animals undergo left thoracotomy, and the left hilum is occluded with a small metallic clamp. The occlusion is performed 20 minutes after Imatinib or vehicle administration. During clamping, the tidal volume (TV) and respiratory rate (RR) are adjusted to 8 mL/kg and 80 breaths/min, respectively. After 90 minutes of ischemia, the clamp is removed and reperfusion is maintained for 120 minutes. During reperfusion, blood flow and ventilation are restored in the bilateral lung. In the sham

	group (n=6), the animals are heparinized, thoracotomized, and ventilated for 210 minutes. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2023 Mar 1;8(1):90.
- Cell Metab. 2022 Feb 7;34(3):424-440.e7.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Sci Immunol. 2023 Mar 17;8(81):eade4656.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.

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REFERENCES

[1]. Heinrich MC, et al. Inhibition of c-kit receptor tyrosine kinase activity by STI 571, a selective tyrosine kinase inhibitor. Blood. 2000 Aug 1;96(3):925-32.

[2]. Guida T, et al. Sorafenib inhibits imatinib-resistant KIT and platelet-derived growth factor receptor beta gatekeeper mutants. Clin Cancer Res. 2007 Jun 1;13(11):3363-9.

[3]. Okuda K, et al. ARG tyrosine kinase activity is inhibited by STI571.Blood. 2001 Apr 15;97(8):2440-8

[4]. Maj E, et al. Vitamin D Analogs Potentiate the Antitumor Effect of Imatinib Mesylate in a Human A549 Lung Tumor Model. Int J Mol Sci. 2015 Nov 13;16(11):27191-207.

[5]. Tanaka S, et al. Protective Effects of Imatinib on Ischemia/Reperfusion Injury in Rat Lung. Ann Thorac Surg. 2016 Jul 23. pii: S0003-4975(16)30523-9

[6]. Meirson T, et al. Targeting invadopodia-mediated breast cancer metastasis by using ABL kinase inhibitors. Oncotarget. 2018 Apr 24;9(31):22158-22183.

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