Imatinib

Cat. No.: HY-15463

CAS No.: 152459-95-5

Molecular Formula: $C_{29}H_{31}N_7O$

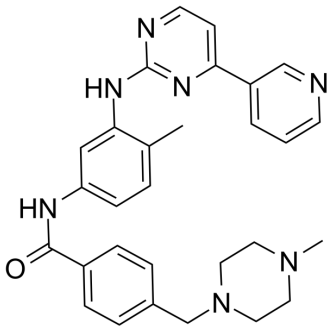
Molecular Weight: 493.6

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

Pathway: Protein Tyrosine Kinase/RTK; Autophagy; Anti-infection

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (25.32 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0259 mL	10.1297 mL	20.2593 mL
5 mM	0.4052 mL	2.0259 mL	4.0519 mL
10 mM	0.2026 mL	1.0130 mL	2.0259 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 11 mg/mL (22.29 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.53 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.53 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.53 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Imatinib (STI571) is an orally bioavailable tyrosine kinases inhibitor that selectively inhibits BCR/ABL, v-Abl, PDGFR and c-kit kinase activity. Imatinib (STI571) works by binding close to the ATP binding site, locking it in a closed or self-inhibited conformation, therefore inhibiting the enzyme activity of the protein semicompetitively[1][2][3][4]. Imatinib also is an inhibitor of SARS-CoV and MERS-CoV[5].

IC_{50} & Target	BCR/ABL, v-Abl, PDGFR, c-kit[1][2][4]
In Vitro	Imatinib (STI571) 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) 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) 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[4]. The IC_{50}s of Imatinib(STI571) is a multi-target inhibitor of v-Abl, c-Kit and on BON-1 and H727 cells after exposure for 48 h are 32.4 and 32.8 μM, respectively[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In the phosphorothioate antisense oligodeoxynucleotides (PS-ASODN) group, tumor growth is inhibited by 59.437%, which is markedly higher than in the Imatinib (STI571) is a multi-target inhibitor of v-Abl, c-Kit and group (11.071%) and liposome negative control group (2.759%). Telomerase activity is significantly lower (P<0.01) in the PS-ASODN group (0.689±0.158) compare with the Imatinib group (1.838±0.241), liposome negative control group (2.013±0.273), and saline group (2.004±0.163)[7]. Imatinib (25 mg/kg/day, p.o.) suppresses the growth of endometriotic tissue and reduces the number of ovarian follicles in a rat model. Imatinib effectively treats experimental endometriosis by its inhibitor effects on angiogenesis and cell proliferation[8]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [4]	BON-1 cells (7,500 per well) and NCI-H727 cells (5,000 per well) are seeded into flat-bottomed 96-well plates in triplicate and allowed to adhere overnight in 10% fetal bovine serum-supplemented DMEM or RPMI 1640 complete medium, respectively; the medium is then exchanged for serum-free medium (negative control) or serum-free medium containing serial dilutions of Imatinib. After 48 h (control cultures do not reach confluence), the number of metabolically active cells is determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay, and absorbance is measured in a Packard Spectra microplate reader at 540 nm. Growth inhibition is calculated. Experiments are done in triplicates[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [6][7]	Mice[6] The 40 tumor-bearing SCID mice are randomly divided into four groups (10 mice per group): the PS-ASODN group (5 μM, each mouse receives 0.2 mL by intratumor injection once daily); Imatinib group (0.1 mg/g body weight); liposome negative control group (0.01 mL/g); and saline group (0.01 mL/g). The mice in each group receive the relevant treatment by intra-tumor injection once daily from day 7 to day 28 after implantation. After 28 d, the mice are sacrificed, and tumor weight and longest and shortest diameters are measured by electronic scale and vernier caliper, respectively. Inhibition of tumor growth is calculated. Rats[7] Adult female Wistar-Albino rats (220-240 g) are used. Twenty-one days after the first surgical procedure, the rats undergo a second laparotomy to evaluate the occurrence of endometriosis. Twenty-four rats have visually confirmed endometriotic implants and are randomized into three groups to receive Imatinib (25 mg/kg/day, p.o.), Anastrozole (0.004 mg/day, p.o.), or normal saline (0.1 mL, i.p.) for 14 days. 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.
- Nat Immunol. 2023 Sep;24(9):1443-1457.
- 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.

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[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]. Iqbal N, et al. Imatinib: a breakthrough of targeted therapy in cancer. Chemother Res Pract. 2014;2014:357027.

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

[5]. Yao JC, et al. Clinical and in vitro studies of imatinib in advanced carcinoid tumors. Clin Cancer Res. 2007 Jan 1;13(1):234-40.

[6]. Sun XC, et al. Depletion of telomerase RNA inhibits growth of gastrointestinal tumors transplanted in mice. World J Gastroenterol. 2013 Apr 21;19(15):2340-7.

[7]. Yildiz C, et al. Effect of imatinib on growth of experimental endometriosis in rats. Eur J Obstet Gynecol Reprod Biol. 2016 Feb;197:159-63.

[8]. Jeanne M Sisk, et al. Coronavirus S Protein-Induced Fusion Is Blocked Prior to Hemifusion by Abl Kinase Inhibitors. J Gen Virol. 2018 May;99(5):619-630.

[9]. Coleman CM, et al, Frieman MB. Abelson Kinase Inhibitors Are Potent Inhibitors of Severe Acute Respiratory Syndrome Coronavirus and Middle East Respiratory Syndrome Coronavirus Fusion. J Virol. 2016;90(19):8924-8933. Published 2016 Sep 12.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA