Dasatinib

Cat. No.: HY-10181

CAS No.: 302962-49-8

Molecular Formula: $C_{22}H_{26}ClN_7O_2S$

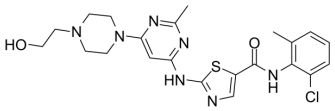
Molecular Weight: 488.01

Target: Bcr-Abl; Src; Autophagy; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Autophagy; Apoptosis

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 : 35.35 mg/mL (72.44 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0491 mL	10.2457 mL	20.4914 mL
	5 mM	0.4098 mL	2.0491 mL	4.0983 mL
	10 mM	0.2049 mL	1.0246 mL	2.0491 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.12 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.12 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.26 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.26 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.26 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Dasatinib (BMS-354825) is a highly potent, ATP competitive, orally active dual Src/Bcr-Abl inhibitor with potent antitumor activity. The K_is are 16 pM and 30 pM for Src and Bcr-Abl, respectively. Dasatinib inhibits Bcr-Abl and Src with IC_{50}s of <1.0 nM and 0.5 nM, respectively[1]. Dasatinib also induces apoptosis and autophagy.

IC_{50} & Target				
	Bcr-Abl 1.0 nM (IC_{50})	Src 0.5 nM (IC_{50})	lck 0.4 nM (IC_{50})	yes 0.5 nM (IC_{50})
	c-kit 5.0 nM (IC_{50})	PDGFRβ 28 nM (IC_{50})	p38 100 nM (IC_{50})	Her1 180 nM (IC_{50})
	Her2 710 nM (IC_{50})	FGFR-1 880 nM (IC_{50})	MEK 1700 nM (IC_{50})	

In Vitro

Dasatinib demonstrates significant activity against Bcr-Abl, Src, Lck, Yes, c-Kit, PDGFRβ, p38, Her1, Her2, FGFR-1, and MEK with IC_{50}s of <1.0, 0.50, 0.40, 0.50, 5.0, 28, 100, 180, 720, 880, and 1700 nM, respectively[1].

Dasatinib shows antiproliferative activities aversus K562 chronic myelogenous leukemia (CML), PC3 human prostate tumor, MDA-MB-231 human breast tumor, and WiDr human colon tumor cell lines with IC_{50}s of <1.0 nM, 9.4 nM, 12 nM, and 52 nM, respectively[1].

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

In Vivo

Dasatinib (5 mg/kg and 50 mg/kg, qd×10d, 5 on-2 off) possesses potent antitumor activity and a high safety margin in a K562 xenograft model of chronic myelogenous leukemia (CML), demonstrating complete tumor regressions and low toxicity at multiple dose levels[1].

Dasatinib (10 mg/kg) has a pharmacokinetic profile appropriate for continued advancement into in vivo efficacy studies. Dasatinib (10 mg/kg) demonstrates favorable half-lives ($t_{1/2}$s) of 3.3 and 3.1 h for i.v. and oral, respectively. The oral bioavailability (F_{po}) in this study is 27%[1].

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

Animal Model:	Nude mice bearing K562 xenografts
Dosage:	5 mg/kg and 50 mg/kg
Administration:	Oral administration on a 5 day on and 2 day off schedule.
Result:	Showed partial tumor regressions after one treatment cycle and complete disappearance of the tumor mass by the end of drug treatment. No toxicity (animal deaths, lack of weight gain) was observed.

Animal Model:	Sprague-Dawley Rats
Dosage:	10 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral and i.v.
Result:	C_{max} of 13.2 and 0.5 μM for i.v. and oral, respectively.

CUSTOMER VALIDATION

- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Pineal Res. 2019 Sep;67(2):e12588.
- Nat Commun. 2020 Apr 14;11(1):1790.
- Nat Commun. 2020 Apr 20;11(1):1913.

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REFERENCES

[1]. Lombardo LJ, et al. Discovery of N-(2-chloro-6-methyl- phenyl)-2-(6-(4-(2-hydroxyethyl)- piperazin-1-yl)-2-methylpyrimidin-4- ylamino)thiazole-5-carboxamide (BMS-354825), a dual Src/Abl kinase inhibitor with potent antitumor activity in preclinical assays. J Med Chem. 2004 Dec 30;47(27):6658-61.

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