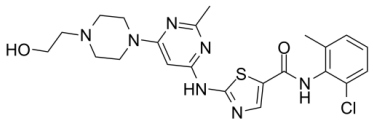
Data Sheet

Product Name:	Dasatinib
Cat. No.:	CS-0100
CAS No.:	302962-49-8
Molecular Formula:	C22H26ClN7O2S
Molecular Weight:	488.01
Target:	Apoptosis; Autophagy; Bcr-Abl; Src
Pathway:	Apoptosis; Autophagy; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 35.35 mg/mL (72.44 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

Dasatinib (BMS-354825) is a dual **Bcr-Abl** and **Src** family tyrosine kinase inhibitor with **IC_{50}**s of 0.6, 0.8, 79 and 37 nM for Abl, Src, c-Kit and c-Kit^{D816V}, respectively. IC50 & Target: IC50: 0.6 nM/0.8 nM (Abl^{WT}/Src)[1]
IC50: 79 nM/37 nM (c-Kit^{WT}/c-Kit^{D816V})[2] **In Vitro:** Dasatinib potently inhibits wild-type Abl kinase and all mutants except T315I over a narrow range (IC_{50}≤1.7 nM). Dasatinib (IC_{50}: 0.8 nM) displays 325-fold greater potency compared with STI571 against cells expressing wild-type Bcr-Abl in Ba/F3 cells[1]. **In Vivo:** Daily treatment with Dasatinib (50 mg/kg) is initiated on day 10. Using this approach, a significant inhibition of BCPAP orthotopic tumor growth is observed 6 days after treatment (day 16, P=0.014), which is sustained through days 23 and 29 (P=0.0003), compared with vehicle-treated mice[3]. Metabolism studies of Dasatinib (50 mg/kg) in rat suggested that Dasatinib is the major circulating component, whereas multiple metabolites contributed to the remaining 40-60% of the sample radioactivity at 4 h post dose[4].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Dasatinib is dissolved in DMSO (10 mM) and stored, and then diluted with appropriate media before use[1].[1]Ba/F3 cell lines are plated in triplicate and incubated with escalating concentrations of STI571, AMN107, or Dasatinib for 72 hours. Proliferation is measured using a methanethiosulfonate-based viability assay (CellTiter96 Aqueous One Solution Reagent). IC_{50} and IC_{90} values are reported as the mean of three independent experiments done in quadruplicate. The inhibitor concentration ranges for IC_{50} and IC_{90} determinations are 0 to 2,000 nM (STI571 and AMN107) or 0 to 32 nM (Dasatinib). The STI571 concentration range is extended to 6,400 nM for mutants with IC_{50}>2,000 nM. The Dasatinib concentration range is extended to 200 nM for mutant T315I. **Animal Administration:** Dasatinib is prepared in 80 mM sodium citratse buffer, pH 3.0 (Mice)[3].;Dasatinib is prepared in 0.5% methylcellulose (rats)[4].[3][4]Mice[3]
Male athymic nude mice (25 grams; 5-week old) are used. Dasatinib (50 mg/kg) is prepared for daily oral gavage (5 d/wk) in 80 mM sodium citrate buffer, pH 3.0. For the orthotopic murine model, mice are randomized on day 10 based on bioluminescence activity to receive drug or vehicle. In the metastatic murine model, mice receives dasatinib or vehicle, as described earlier, starting 2 days before intracardiac injection (pretreatment), or on day 11 following randomization (posttreatment).
Rats[4]
Dasatinib is dosed to male Wistar-Han (WH) rats at 50 mg/kg orally in 0.5% methylcellulose. The automated rat blood collection device is programmed to collect 200 µL of blood at predetermined intervals. At each time point, the accusampler is programmed to directly spot 20 µL of blood twice (two spots) onto the DBS card. The remaining 160 µL of liquid blood is collected into sodium EDTA-containing tubes. Plasma samples are obtained after immediate centrifugation of blood at 11,000 rpm for 5 min. The plasma samples are stored at −80°C until analyses. The DBS samples are dried under room temperature for a minimum of 2 h and stored in a plastic bag in the dessicator until sample analysis.

References:

[1]. O'Hare T, et al. In vitro activity of Bcr-Abl inhibitors AMN107 and BMS-354825 against clinically relevant STI571-resistant Abl kinase domain mutants. Cancer Res. 2005 Jun 1;65(11):4500-5.

[2]. Shah NP, et al. Dasatinib (BMS-354825) inhibits KITD816V, an STI571-resistant activating mutation that triggers neoplastic growth in most patients with systemic mastocytosis. Blood. 2006 Jul 1;108(1):286-91.

[3]. Chan CM, et al. Targeted inhibition of Src kinase with dasatinib blocks thyroid cancer growth and metastasis. Clin Cancer Res. 2012 Jul 1;18(13):3580-91.

[4]. Shen Z, et al. Metabolite profiling of dasatinib dosed to Wistar Han rats using automated dried blood spot collection. J Pharm Biomed Anal. 2012 Aug-Sep;67-68:92-7.

[5]. Weisberg E, et al. Using combination therapy to override stromal-mediated chemoresistance in mutant FLT3-positive AML: synergism between FLT3 inhibitors, dasatinib/multi-targeted inhibitors and JAK inhibitors. Leukemia. 2012 Oct;26(10):2233-44.

[6]. Kan He, et al. Protein kinase inhibitors. Patent. US20180099960A1.

CAIndexNames:

5-Thiazolecarboxamide, N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-

SMILES:

O=C(C1=CN=C(S1)NC2=NC(C)=NC(N3CCN(CC3)CCO)=C2)NC4=C(C=CC=C4Cl)C

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