PF-562271 besylate

Cat. No.: HY-10458

CAS No.: 939791-38-5

Molecular Formula: $C_{27}H_{26}F_3N_7O_6S_2$

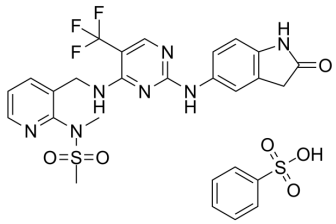
Molecular Weight: 665.66

Target: FAK; Pyk2

Pathway: Protein Tyrosine Kinase/RTK

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 : 21.4 mg/mL (32.15 mM; Need ultrasonic and warming)

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	1.5023 mL	7.5113 mL	15.0227 mL
5 mM	0.3005 mL	1.5023 mL	3.0045 mL
10 mM	0.1502 mL	0.7511 mL	1.5023 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: ≥ 1.67 mg/mL (2.51 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (2.51 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (2.51 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-562271 (VS-6062) besylate is a potent ATP-competitive, reversible inhibitor of FAK and Pyk2 kinase, with an IC_{50} of 1.5 nM and 13 nM, respectively[1].

IC_{50} & Target

IC50: 1.5 nM (FAK), 13 nM (Pyk2), 30 nM (CDK2), 47 nM (CDK3), 58 nM (CDK1), 97 nM (CDK7), 97 nM (Flt3)[1]

In Vitro

PF-562271 (VS-6062) besylate is a 30- to 120-nM (15.2 to 60.1 ng/mL) inhibitor of cdk2/E, cdk5/p35, cdk1/B, and cdk3/E in recombinant enzyme assays[1]. PF-562,271 blocks bFGF-stimulated blood vessel angiogenesis as performed in chicken chorioallantoic membrane assays[2]. Treatment of cells with PF-562,271 or knock-down of FAK by siRNA is observed to

	increase cell-cell adhesion strength[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PF-562,271 (33 mg/kg, p.o.) inhibits FAK phosphorylation in tumors in a dose- and time-dependent manner in tumor-bearing mice. FAK phosphorylation inhibition relative to total blood concentration of PF-562,271 results in a calculated EC_{50} of 93 ng/mL. PF-562,271 (25 mg/kg, p.o.) induces apoptosis 2-fold greater in treated tumors compared with vehicle-treated control tumors on day 3[1]. PF-562,271 (33 mg/kg, p.o.) and dasatinib extensively inhibit the movement of tumor cells in the animals. Inhibition of FAK kinase activity following treatment with PF-562,271 results in altered E-cadherin dynamics in vivo [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Briefly, purified-activated FAK kinase domain (amino acid 410-689) is reacted with 50 μM ATP and 10 μg per well of a random peptide polymer of Glu and Tyr, p(Glu/Tyr), in kinase buffer [50 mM HEPES (pH 7.5), 125 mM NaCl, and 48 mM $MgCl_2$] for 15 min. Phosphorylation of p(Glu/Tyr) is challenged with serially diluted compound at 1/2-Log concentrations starting at a top concentration of 1 μM. Each concentration is tested in triplicate. Phosphorylation of p(Glu/Tyr) is detected with a general antiphospho-tyrosine (PY20) antibody followed by horseradish peroxidase (HRP)-conjugated goat anti-mouse IgG antibody. HRP substrate is added, and absorbance readings at 450 nm are obtained after addition of stop solution (2mol/LH_2SO_4). IC_{50} values are determined using the Hill-Slope Model. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Exponentially growing cells are trypsinized and resuspended in sterile PBS and inoculated s.c. (1×10^6 cells per mouse in 200 μL) into the right flank of mice. Animals bearing tumors of appr 150 mm^3 in size are divided into groups receiving either vehicle (5% Gelucire) or PF-562,271 (diluted in vehicle), and dosed by p.o. gavage. Animal body weight and tumor measurements are obtained every 2 d. Tumor volume (mm^3) is measured with Vernier calipers and calculated. For all tumor growth inhibition experiments, 8 to 10 mice per dose group are used. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Clin Cancer Res. 2019 Jul 15;25(14):4552-4566.
- Cancer Res. 2013 May 1;73(9):2873-83.
- Int J Cancer. 2015 Oct 1;137(7):1549-59.
- Sci Rep. 2018 May 8;8(1):7228.

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REFERENCES

[1]. Roberts WG, et al. Antitumor activity and pharmacology of a selective focal adhesion kinase inhibitor, PF-562,271. Cancer Res, 2008, 68(6), 1935-1944.

[2]. Lim ST, et al. FERM control of FAK function: implications for cancer therapy. Cell Cycle, 2008, 7(15), 2306-2314.

[3]. Canel M, et al. Quantitative in vivo imaging of the effects of inhibiting integrin signaling via Src and FAK on cancer cell movement: effects on E-cadherin dynamics. Cancer Res, 2010, 70(22), 9413-9422.

Caution: Product has not been fully validated for medical applications. For research use only.

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