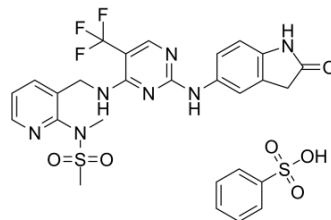


PF-562271 besylate

Cat. No.:	HY-10458		
CAS No.:	939791-38-5		
Molecular Formula:	C ₂₇ H ₂₆ F ₃ N ₇ O ₆ S ₂		
Molecular Weight:	665.66		
Target:	FAK; Pyk2		
Pathway:	Protein Tyrosine Kinase/RTK		
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 : 21.4 mg/mL (32.15 mM; Need ultrasonic and warming)

Concentration	Mass		
	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

- 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
- 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
- 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 besylate is a potent ATP-competitive, reversible inhibitor of FAK and Pyk2 kinase, with an IC₅₀ of 1.5 nM and 13 nM, respectively^[1].

IC₅₀ & 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-562,271 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 EC₅₀ 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 MgCl₂] 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/LH₂SO₄). IC₅₀ 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. (1×10⁶ cells per mouse in 200 μL) into the right flank of mice. Animals bearing tumors of appr 150 mm³ 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 (mm³) 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.

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

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