PF-431396

Cat. No.: HY-10460

CAS No.: 717906-29-1

Molecular Formula: $C_{22}H_{21}F_3N_6O_3S$

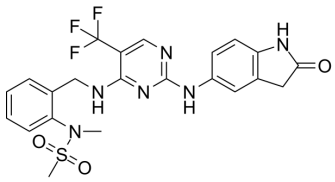
Molecular Weight: 506.5

Target: Pyk2; FAK

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 : ≥ 100 mg/mL (197.43 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9743 mL	9.8717 mL	19.7433 mL
5 mM	0.3949 mL	1.9743 mL	3.9487 mL
10 mM	0.1974 mL	0.9872 mL	1.9743 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: ≥ 2.5 mg/mL (4.94 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-431396 is an orally active dual focal adhesion kinase (FAK) and proline-rich tyrosine kinase 2 (PYK2) inhibitor, with IC_{50} values of 2 nM and 11 nM, respectively[1][2][3][4].

IC_{50} & Target

IC50: 2 nM (FAK); 11 nM (PYK2)[1].
Kd: 445 nM (BRD4)[1].

In Vitro

PF-431396 has a K_d value of 445 nM for BRD4[2].
PF-431396 appeares to selectively inhibit BCR-induced tyrosine phosphorylation of Pyk2 and FAK[3].
PF-431396 (2.5, 5 μM, 45 min) inhibits the phosphorylation of Pyk2 and FAK induced by clustering LFA-1 with plate-bound

Abs[3].

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

Western Blot Analysis[3]

Cell Line:	A20 cells ($(10^5$ cells in 0.5 ml of RPMI 1640 medium with 2% fetal calf serum and 50 μM 2-mercaptoethanol)).
Concentration:	0.15, 1, 2.5, 5 μM.
Incubation Time:	45 min.
Result:	The phosphorylation of Pyk2 and FAK induced by clustering LFA-1 with plate-bound Abs was also inhibited.

In Vivo

PF-431396 (10 or 30 mg/kg, orally) prevents bone loss induced by estrogen deficiency in rats primarily by stimulating bone formation, providing independent pharmacological confirmation for the function of PYK2 in regulating bone formation[4].

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

Animal Model:	Sprague–Dawley female rats (ovariectomized (OVX) Rats)[4].
Dosage:	10 or 30 mg/kg.
Administration:	Oral gavage, for 28 consecutive days.
Result:	Counteracted OVX-induced bone loss, completely preserving total bone content and total bone density. Promoted osteoblast recruitment and activity.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Mucosal Immunol. 2020 Nov;13(6):931-945.
- J Periodontal Res. 2015 Dec;50(6):855-863.
- Biomed Res Int. 2020 Oct 3;2020:2616930.
- bioRxiv. 2020 Jan.

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REFERENCES

[1]. Seungil Han, et al. Structural Characterization of Proline-rich Tyrosine Kinase 2 (PYK2) Reveals a Unique (DFG-out) Conformation and Enables Inhibitor Design. J Biol Chem. 2009 May 8; 284(19): 13193–13201.

[2]. Ciceri P, et al. Dual kinase-bromodomain inhibitors for rationally designed polypharmacology. Nat Chem Biol. 2014 Mar 2.

[3]. Tse KW, et al. B cell receptor-induced phosphorylation of Pyk2 and focal adhesion kinase involves integrins and the Rap GTPases and is required for B cell spreading. J Biol Chem. 2009 Aug 21;284(34):22865-77.

[4]. Leonard Buckbinder, et al. Proline-rich tyrosine kinase 2 regulates osteoprogenitor cells and bone formation, and offers an anabolic treatment approach for osteoporosis. Proc Natl Acad Sci U S A. 2007 Jun 19;104(25):10619-24.

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

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