PD153035 Hydrochloride

Cat. No.: HY-12013

CAS No.: 183322-45-4

Molecular Formula: $C_{16}H_{15}BrClN_3O_2$

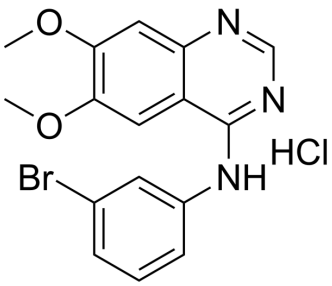
Molecular Weight: 396.67

Target: EGFR

Pathway: JAK/STAT Signaling; 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 : 5.125 mg/mL (12.92 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	2.5210 mL	12.6049 mL	25.2099 mL
5 mM	0.5042 mL	2.5210 mL	5.0420 mL
10 mM	0.2521 mL	1.2605 mL	2.5210 mL

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

BIOLOGICAL ACTIVITY

Description

PD153035 Hydrochloride (SU-5271 Hydrochloride) is a potent EGFR inhibitor with K_i and IC_{50} of 6 and 25 pM, respectively.

IC_{50} & Target

EGFR 6 pM (Ki)	EGFR 25 pM (IC_{50})

In Vitro

PD153035 inhibits EGF-stimulated receptor autophosphorylation in A431 human epidermoid carcinoma cells, with an IC_{50} of 14 nM[1]. PD153035 has little effect on PDGFR, FGFR, CSF-1 receptor, the insulin receptor, or on src tyrosine kinases at concentrations as high as 50 μM. PD153035 rapidly suppresses autophosphorylation of the EGF receptor at low nanomolar concentrations in fibroblasts or in human epidermoid carcinoma cells and selectively blocks EGF-mediated cellular processes including mitogenesis, early gene expression, and oncogenic transformation[2]. PD153035 causes a dose-dependent growth inhibition of EGF receptor-positive cell lines, beginning at less than micromolar concentrations, and the IC_{50} is less than 1 pM in most cases[3].

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

In Vivo

PD153035 levels in the plasma and tumor rise to 50 and 22 μM within 15 minutes following a single i.p. dose of 80 mg/kg. While the plasma levels of PD 153035 falls below 1 μM by 3 hours, in the tumors it remains at micromolar concentrations for

	at least 12 hours. The tyrosine phosphorylation of the EGF receptor is rapidly suppressed by 80-90% in the tumors[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Different EGF receptor-overexpressing cell lines (A43 1, Difi, MDA-MB-468, MDA-MB-231, DU145, SiHa, C4i, and MEl 80) are treated with PD153035 at increasing concentrations of 0.125-2.5 p.M. Growth inhibitory effect in monolayer cell culture is assessed[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice: Mice are injected with PD153035 (80 mg/kg) or vehicle and rumors are excised at 20 minutes and 180 minutes and extracts are prepared. Two mice are used for each time point and the experiment is repeated four times. Within each of the four experiments ANOVA is used to compare the inhibition by PD 153035 of the EGF-stimulation[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2018 Jun 5;9(1):2174.
- Elife. 2015 Feb 10;4:e05178.
- Cell Death Dis. 2022 Jul 25;13(7):647.
- Int J Stem Cells. 2022 Jun 30.
- Gen Comp Endocrinol. 2020 Dec 1;299:113616.

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REFERENCES

[1]. Bridges AJ, et al. Tyrosine kinase inhibitors. 8. An unusually steep structure-activity relationship for analogues of 4-(3-bromoanilino)-6,7-dimethoxyquinazoline (PD 153035), a potent inhibitor of the epidermal growth factor receptor. J Med Chem. 1996 Jan 5;39(1):267-76.

[2]. Fry DW, et al. A specific inhibitor of the epidermal growth factor receptor tyrosine kinase. Science. 1994 Aug 19;265(5175):1093-5.

[3]. Bos M, et al. PD153035, a tyrosine kinase inhibitor, prevents epidermal growth factor receptoractivation and inhibits growth of cancer cells in a receptor number-dependent manner. Clin Cancer Res. 1997 Nov;3(11):2099-106.

[4]. Kunkel MW, et al. Inhibition of the epidermal growth factor receptor tyrosine kinase by PD153035 in human A431 tumors in athymic nude mice. Invest New Drugs. 1996;13(4):295-302.

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