Gefitinib hydrochloride

Cat. No.: HY-50895A

CAS No.: 184475-55-6

Molecular Formula: $C_{22}H_{25}Cl_2FN_4O_3$

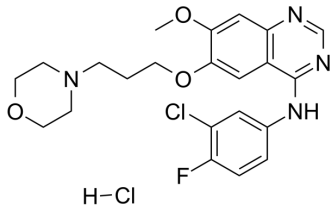
Molecular Weight: 483.36

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

H_2O : 6.25 mg/mL (12.93 mM; Need ultrasonic)

DMSO : 0.227 mg/mL (0.47 mM; Need ultrasonic and warming)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.0689 mL	10.3443 mL	20.6885 mL
5 mM	0.4138 mL	2.0689 mL	4.1377 mL
10 mM	0.2069 mL	1.0344 mL	2.0689 mL

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

BIOLOGICAL ACTIVITY

Description

Gefitinib hydrochloride (ZD1839 hydrochloride) is a potent, selective and orally active EGFR tyrosine kinase inhibitor with an IC_{50} of 33 nM. Gefitinib hydrochloride selectively inhibits EGF-stimulated tumor cell growth (IC_{50} of 54 nM) and that blocks EGF-stimulated EGFR autophosphorylation in tumor cells. Gefitinib hydrochloride also induces autophagy. Gefitinib hydrochloride has antitumour activity[1][2].

IC_{50} & Target

EGFR

In Vitro

Gefitinib (0.01-0.1 mM) results in increased phosphotyrosine load of the receptor, increased signalling to ERK and stimulation of proliferation and anchorage-independent growth, presumably by inducing EGFRvIII dimerisation in long-term exposure of EGFRvIII-expressing cells. On the other hand, gefitinib (1-2 mM) significantly decreases EGFRvIII phosphotyrosine load, EGFRvIII-mediated proliferation and anchorage-independent growth[1]. Gefitinib (ZD1839) inhibits the monolayer growth of these EGF-driven untransformed cells with IC_{50} of 20 nM[2]. Gefitinib leads to an inhibition of CALU-3 and GLC82 cell proliferation, with an IC_{50} of 2 μM[3].

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

In Vivo

Gefitinib (150 mg/kg, p.o.) in conbination with Metformin induces a significant reduction in tumor growth in nude mice

bearing H1299 or CALU-3 GEF-R cells that are grown subcutaneously as tumor xenografts[3]. In irradiated rats, Gefitinib treatment augmentes lung inflammation, including inflammatory cell infiltration and pro-inflammatory cytokine expression, while Gefitinib treatment attenuates fibrotic lung remodeling due to the inhibition of lung fibroblast proliferation[4].

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

PROTOCOL

Cell Assay [3]

Cancer cells are seeded in 96-well plates and are treated with different doses of Gefitinib (0.01-20 μM), Metformin or both for 72 hours. Cell proliferation is measured with the MTT assay. The IC_{50} values are determined by interpolation from the dose-response curves. Results represent the median of 3 separate experiments each conducted in quadruplicate. The results of the combined treatment are analyzed according to the method of Chou and Talalay by using the CalcuSyn software program[3].

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

Animal Administration [3][4]

Mice[3]

Four- to 6-week old female balb/c athymic (nu+/nu+) mice are acclimatized for 1 week before being injected with cancer cells and injected subcutaneously with 10^7 H1299 and CALU-3 GEF-R cells that has been resuspended in 200 μL of Matrigel. When established tumors of approximately 75 mm^3 in diameter are detected, mice are left untreated or treated with oral administrations of metformin (200 mg/mL metformin diluted in drinking water and present throughout the experiment), gefitinib (150 mg/kg daily orally by gavage), or both for the indicated time periods. Each treatment group consists of 10 mice. Tumor volume is measured using the formula π/6×larger diameter×(smaller diameter)^2.

Rats[4]

The rats are randomly assigned to 1 of 4 experimental groups: 1) the unirradiated rats treated with oral administration of vehicle (0.1% Tween 80) once daily; 2) the unirradiated rats treated with oral administration of gefitinib (50 mg/kg/day) once daily; 3) the irradiated rats treated with oral administration of vehicle once daily; 4) the irradiated rats treated with oral administration of gefitinib once daily. Each experimental group comprised 5-6 rats and all treatments are delivered for 14 days.

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

CUSTOMER VALIDATION

- Cancer Cell. 2018 Jun 11;33(6):1061-1077.e6.
- Cell Res. 2021 Jun;31(6):631-648.
- Cell Res. 2020 Oct;30(10):833-853.
- Signal Transduct Target Ther. 2019 Dec 13;4:60.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.

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REFERENCES

[1]. Pedersen MW, et al. Differential response to gefitinib of cells expressing normal EGFR and the mutant EGFRvIII. Br J Cancer. 2005 Oct 17;93(8):915-23.

[2]. Moasser MM, et al. The tyrosine kinase inhibitor ZD1839 ("Iressa") inhibits HER2-driven signaling and suppresses the growth of HER2-overexpressing tumor cells. Cancer Res. 2001 Oct 1;61(19):7184-8.

[3]. Morgillo F, et al. Synergistic effects of metformin treatment in combination with gefitinib, a selective EGFR tyrosine kinase inhibitor, in LKB1 wild-type NSCLC cell lines.

Clin Cancer Res. 2013 Jul 1;19(13):3508-19.

[4]. Miyake K, et al. Epidermal growth factor receptor-tyrosine kinase inhibitor (gefitinib) augments pneumonitis, but attenuates lung fibrosis in response to radiation injury in rats. J Med Invest. 2012;59(1-2):174-85.

[5]. Wakeling AE, et al. ZD1839 (Iressa): an orally active inhibitor of epidermal growth factor signaling with potential for cancer therapy. Cancer Res. 2002 Oct 15;62(20):5749-54.

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