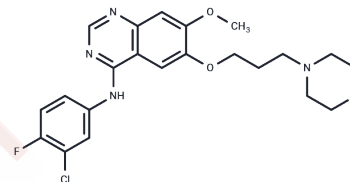


Gefitinib

Chemical Properties

CAS No. :	184475-35-2
Formula:	C ₂₂ H ₂₄ ClFN ₄ O ₃
Molecular Weight:	446.90
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



Biological Description

Description	Gefitinib (ZD1839) is an EGFR first-generation inhibitor with oral activity that inhibits the EGFR 19 Del and L858R mutations. Gefitinib has antitumor activity and is used for the treatment of EGFR-mutated non-small-cell lung cancers. Gefitinib administration RESULTS in the development of the EGFR C797S resistance mutation.
Targets(IC50)	Apoptosis,EGFR,Autophagy,Tyrosine Kinases
In vitro	<p>METHODS: Twenty-three tumor cells were treated with Gefitinib for 72 h, and cell viability was measured by MTT.</p> <p>RESULTS: Only the PC9 cell line had an IC₅₀ 1 μmol/L (highly sensitive), 14 cell lines had an IC₅₀ >10 μmol/L (resistant), and the remaining 8 cell lines had an IC₅₀ of 1-10 μmol/L (moderately sensitive). [1]</p> <p>METHODS: Tumor cells HT29, KB, Du145 and A549 were treated with Gefitinib (0.032-50 μM) for 2 h. EGF (0.1 μg/mL) was added five minutes prior to cell lysis, and the expression levels of target proteins were detected using Western Blot.</p> <p>RESULTS: Gefitinib produced a dose-dependent inhibition of EGFR autophosphorylation in all tumor cell lines. [2]</p>
In vivo	<p>METHODS: To detect anti-tumor activity in vivo, Gefitinib (3.125-200 mg/kg in 0.5% polysorbate 80) was administered orally to nude mice harboring tumors A431, Du145, or A549 once a day for seven to fifteen days.</p> <p>RESULTS: Gefitinib inhibited the growth of A431, Du145 or A549 tumors in a dose-dependent manner. [2]</p> <p>METHODS: To assay antitumor activity in vivo, Gefitinib (40 mg/kg once daily) or Gefitinib (200 mg/kg every five days) was administered by gavage for two weeks to athymic nude mice harboring the human lung cancer tumor H3255.</p> <p>RESULTS: Weekly treatment showed better inhibition than daily treatment. Compared with the daily dosing regimen, the weekly dosing regimen showed stronger inhibition of p-EGFR, p-ERK, and p-AKT. [3]</p>
Cell Research	The human NSCLC H1299, H1975, A549, H460, GLC82, H460, and CALU-3 cell lines were provided by the American Type Culture Collection and maintained in RPMI-1640 supplemented with 10% FBS in a humidified atmosphere with 5% CO ₂ . CALU-3 GEF-R is a cell line obtained in vitro as previously described. Briefly, over a period of 12 months, human CALU-3 lung adenocarcinoma cells were continuously exposed to increasing concentrations of gefitinib. The starting dose was the dose causing the inhibition of 50% of cancer cell growth (IC ₅₀ ; gefitinib, 1 μmol/L). The drug dose was progressively

A DRUG SCREENING EXPERT

Cell Research	increased to 15 $\mu\text{mol/L}$ in approximately 2 months, to 20 $\mu\text{mol/L}$ after other 2 months, to 25 $\mu\text{mol/L}$ after additional 2 months, and, finally, to 30 $\mu\text{mol/L}$ for a total of 12 months. The established resistant cancer cell lines were then maintained in continuous culture with the maximally achieved dose of each TKI that allowed cellular proliferation (30 $\mu\text{mol/L}$ for each drug) [2].
Animal Research	Four- to 6-week old female balb/c athymic (nu+/nu+) mice were purchased from Charles River Laboratories. Mice were acclimatized for 1 week before being injected with cancer cells and injected subcutaneously with 107 H1299 and CALU-3 GEF-R cells that had been resuspended in 200 μL of Matrigel. When established tumors of approximately 75 mm ³ in diameter were detected, mice were 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 consisted of 10 mice. Tumor volume was measured using the formula $\pi/6 \times \text{larger diameter} \times (\text{smaller diameter})^2$. Tumor tissues were collected from the xenografts and analyzed by Western blotting for the expression and activation of EGFR, AMPK, mitogen-activated protein kinase (MAPK), and S6 [2].

Solubility Information

Solubility	DMSO: 18.33 mg/mL (41.02 mM), Sonication is recommended. Ethanol: 4.50 mg/mL (10.07 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4.47 mg/mL (10.00 mM), Solution. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2376 mL	11.1882 mL	22.3764 mL
5 mM	0.4475 mL	2.2376 mL	4.4753 mL
10 mM	0.2238 mL	1.1188 mL	2.2376 mL
50 mM	0.0448 mL	0.2238 mL	0.4475 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

- Noro R, et al. Gefitinib (IRESSA) sensitive lung cancer cell lines show phosphorylation of Akt without ligand stimulation. *BMC Cancer*. 2006 Dec 6;6:277.
- Oeller M, Jaksch-Bogensperger H, Templin M, et al. Transcription Factors STAT3 and MYC Are Key Players of Human Platelet Lysate-Induced Cell Proliferation. *International Journal of Molecular Sciences*. 2022, 23(24): 15782.
- Shi J, Huang Y, Wen C, et al. Genome-wide identification and characterization of long non-coding RNAs involved in acquired resistance to gefitinib in non-small-cell lung cancer. *Computational Biology and Chemistry*. 2020, 87: 107288.
- Quan C, Chen Y, Wang X, et al. Loss of histone lysine methyltransferase EZH2 confers resistance to tyrosine kinase inhibitors in non-small cell lung cancer. *cancer letters*. 2020
- Zhao Deng, Chenbin Cui, Yanan Wang, Jiangjin Ni, et al. FSGHF3 and peptides, prepared from fish skin gelatin, exert a protective effect on DSS-induced colitis via the Nrf2 pathway. *Food & Function*. 2020
- Cao D, Chen D, Xia J N, et al. Artesunate promoted anti-tumor immunity and overcame EGFR-TKI resistance in non-small-cell lung cancer by enhancing oncogenic TAZ degradation. *Biomedicine & Pharmacotherapy*. 2022, 155: 113705.
- Liu Y, Luo Y, Yan S, et al. CRL2KLFDC3 mediates p14ARF N-terminal ubiquitylation degradation to promote non-small cell lung carcinoma progression. *Oncogene*. 2022: 1-14
- Kang J, Guo Z, Zhang H, et al. Dual Inhibition of EGFR and IGF-1R Signaling Leads to Enhanced Antitumor Efficacy against Esophageal Squamous Cancer. *International Journal of Molecular Sciences*. 2022, 23(18): 10382
- Teng J F, Qin D L, Mei Q, et al. Polyphyllin VI, a saponin from *Trillium tschonoskii* Maxim. induces apoptotic and autophagic cell death via the ROS triggered mTOR signaling pathway in non-small cell lung cancer. *Pharmacological Research*. 2019: 104396.
- Shang J, Ning S, Chen Y, et al. MDL-800, an allosteric activator of SIRT6, suppresses proliferation and enhances EGFR-TKIs therapy in non-small cell lung cancer. *Acta Pharmacologica Sinica*. 2021, 42(1): 120-131
- Zheng P, Huang Z, Tong D C, et al. Frankincense myrrh attenuates hepatocellular carcinoma by regulating tumor blood vessel development through multiple epidermal growth factor receptor-mediated signaling pathways. *World Journal of Gastrointestinal Oncology*. 2022, 14(2): 450
- Yu J, Zhang L, Peng J, et al. Dictamnine, a novel c-Met inhibitor, suppresses the proliferation of lung cancer cells by downregulating the PI3K/AKT/mTOR and MAPK signaling pathways. *Biochemical pharmacology*. 2022, 195: 114864.
- Yutang Huang, Yi Dai, Chunjie Wen, Shuai He, Jingjing Shi, Dezhong Zhao, Lanxiang Wu, Honghao Zhou circSETD3 Contributes to Acquired Resistance to Gefitinib in Non-Small-Cell Lung Cancer by Targeting the miR-520h/ABCG2 Pathway. *Molecular Therapy-Nucleic Acids*. 2020
- 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.
- He S, Shi J, Zhou H H, et al. Lnc-ABCA12-8 confers acquired resistance to gefitinib in non-small cell lung cancer by regulating the alternative splicing of fibronectin 1 in the IIIIS region. *Cancer Gene Therapy*. 2022, 29(11): 1686-1696.
- Liang J, Bi G, Sui Q, et al. Transcription factor ZNF263 enhances EGFR-targeted therapeutic response and reduces residual disease in lung adenocarcinoma. *Cell Reports*. 2024, 43(2).
- Shao J, Ye Z, Shen Z, et al. Chidamide improves gefitinib treatment outcomes in NSCLC by attenuating recruitment and immunosuppressive function of myeloid-derived suppressor cells. *Biomedicine & Pharmacotherapy*. 2024, 173: 116306.
- Hou X, Ai X, Liu Z, et al. Wheat germ agglutinin modified mixed micelles overcome the dual barrier of mucus/enterocytes for effective oral absorption of shikonin and gefitinib. *Drug Delivery and Translational Research*. 2024: 1-18.
- Zhang D, Tian X, Wang Y, et al. Polyphyllin I ameliorates gefitinib resistance and inhibits the VEGF/VEGFR2/p38 pathway by targeting HIF-1 α in lung adenocarcinoma. *Phytomedicine*. 2024: 155690.
- Wei X, Zhang G, Liu Q, et al. Almonertinib and alflutinib show novel inhibition on rare EGFR S768I mutant cells. *Clinical and Translational Oncology*. 2024: 1-16.
- Yan T, Zhang N, Liu F, et al. PCK2 induces gefitinib resistance by suppresses ferroptosis in non-small cell lung cancer. *Biochemical and Biophysical Research Communications*. 2024: 150200.

- Abdelaal N, Ragheb M A, Hassaneen H M, et al. Design, in silico studies and biological evaluation of novel chalcones tethered triazolo [3, 4-a] isoquinoline as EGFR inhibitors targeting resistance in non-small cell lung cancer. *Scientific Reports*. 2024, 14(1): 26647.
- Wen C, Li Y, Huang Y, et al. CircSETD3 mediates acquired resistance to gefitinib in non-small lung cancer cells by FXR1/ECT2 pathway. *The International Journal of Biochemistry & Cell Biology*. 2022: 106344.
- Zhang Q, et al. Effect of weekly or daily dosing regimen of Gefitinib in mouse models of lung cancer. *Oncotarget*. 2017 Aug 2;8(42):72447-72456.
- Tan J, et al. Tyrosine kinase inhibitors show different anti-brain metastases efficacy in NSCLC: A direct comparative analysis of icotinib, gefitinib, and erlotinib in a nude mouse model. *Oncotarget*. 2017 Oct 19;8(58):98771-98781.
- Hu L, Liu Y, Fu C, et al. The Tumorigenic Effect of the High Expression of Ladinin-1 in Lung Adenocarcinoma and Its Potential as a Therapeutic Target. *Molecules*. 2023, 28(3): 1103.
- Chen J, Lei C, Nie D, et al. Inorganic arsenic exposure promotes malignant progression by HDAC6-mediated down-regulation of HTRA1. *Journal of Applied Toxicology*. 2023
- Jiao D, Chen Y, Liu X, et al. Targeting MET endocytosis or degradation to overcome HGF-induced gefitinib resistance in EGFR-sensitive mutant lung adenocarcinoma. *Biochemical and Biophysical Research Communications*. 2023
- Dhar D, et al. Liver Cancer Initiation Requires p53 Inhibition by CD44-Enhanced Growth Factor Signaling. *Cancer Cell*. 2018 Jun 11;33(6):1061-1077.e6.
- Yang S, Yang S, Zhang H, et al. Targeting Na⁺/K⁺-ATPase by berbamine and ouabain synergizes with sorafenib to inhibit hepatocellular carcinoma. *British Journal of Pharmacology*. 2021
- Teng J F, Qin D L, Mei Q, et al. Polyphyllin VI, a saponin from *Trillium tschonoskii* Maxim. induces apoptotic and autophagic cell death via the ROS triggered mTOR signaling pathway in non-small cell lung cancer[J]. *Pharmacological Research*. 2019: 104396.
- Zhao X, Zhang N, Huang Y, et al. Lansoprazole Alone or in Combination With Gefitinib Shows Antitumor Activity Against Non-small Cell Lung Cancer A549 Cells in vitro and in vivo. *Frontiers in Cell and Developmental Biology*. 2021, 9: 947
- . circSETD3 Contributes to Acquired Resistance to Gefitinib in Non-Small-Cell Lung Cancer by Targeting the miR-520h/ABCG2 Pathway. *Molecular Therapy-Nucleic Acids*. 2020
- Wang L, Liu X X, Yang Y M, et al. RHBDF2 gene functions are correlated to facilitated renal clear cell carcinoma progression. *Cancer Cell International*. 2021, 21(1): 1-18.

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