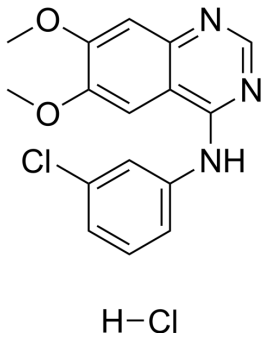
AG-1478 hydrochloride

Cat. No.:	HY-13524A
CAS No.:	170449-18-0
Molecular Formula:	$C_{16}H_{15}Cl_2N_3O_2$
Molecular Weight:	352.22
Target:	EGFR; HCV; Influenza Virus
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AG-1478 hydrochloride (Tyrphostin AG-1478 hydrochloride) is a selective EGFR tyrosine kinase inhibitor with IC_{50} of 3 nM. AG-1478 hydrochloride has antiviral effects against HCV and encephalomyocarditis virus (EMCV)[1][2][3][4].		
IC_{50} & Target	EGFR 3 nM (IC_{50})	HCV	EMCV
In Vitro	AG-1478 (AG1478) is irreversible for growth regulation of human lung (A549) and prostate (DU145) cancer cell lines, cultured in chemically defined DMEM/F12 medium. AG-1478 seems to be more effective at lower concentrations, but is unable to completely inhibit growth of A549 cells[1]. Inhibition of EGFR by specific tyrosine kinase inhibitor AG-1478 (AG1478) significantly decreases the angiotensin II-mediated synthesis of TGF-β and fibronectin by cardiac fibroblasts. EGFR is pharmacologically inhibited by small-molecule inhibitor AG-1478 with IC_{50} of 4 nM[2]. Both Polyfect (PF) and Superfect (SF) treatment lead to increased apoptosis in HEK 293 cells to a similar extent as assessed by flow cytometry. The antioxidant, tempol, significantly reduced dendrimer-mediated apoptosis for both PF and SF. AG-1478 (AG1478), at a 10-fold higher dose (100 μM) than used in signaling studies, is used as a positive control and significantly induced apoptosis in HEK 293 cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	Administration of AG-1478 (AG1478) significantly reduces myocardial inflammation, fibrosis, apoptosis, and dysfunction in both two obese mouse models. $ApoE^{-/-}$ mice are first fed with HFD for 8 weeks (ApoE-HFD), and then administrated with AG-1478 (10 mg/kg/day) or 542 (10 mg/kg/day) for another 8 weeks by oral gavage. AG-1478 or 542 treatment blocks HFD induced cardiac EGFR phosphorylation in vivo, without affecting the plasma level of low density lipoprotein (LDL) and total triglyceride (TG)[2]. Administration of EGF (10 nM) leads to a robust and reproducible elevation in EGFR phosphorylation that can be blocked by AG-1478 (AG1478), a known inhibitor of EGFR phosphorylation. Increasing doses of Polyfect (PF) result in a significant reduction in EGF-induced EGFR phosphorylation ($p<0.05$) but this is to a lesser extent than observed with AG1478 [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

CUSTOMER VALIDATION

- Adv Sci (Weinh). 2023 Apr 14;e2204824.
- Cell Death Dis. 2021 May 18;12(6):509.

- Cell Death Dis. 2020 Jun 15;11(6):459.
- Cell Death Dis. 2019 Sep 9;10(9):649.
- Oncogene. 2021 Jul;40(30):4884-4893.

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REFERENCES

[1]. Bojko A, et al. The effect of tyrphostins AG494 and AG1478 on the autocrine growth regulation of A549 and DU145 cells. Folia Histochem Cytobiol. 2012 Jul 5;50(2):186-95.

[2]. Li W, et al. EGFR Inhibition Blocks Palmitic Acid-induced inflammation in cardiomyocytes and Prevents Hyperlipidemia-induced Cardiac Injury in Mice. Sci Rep. 2016 Apr 18;6:24580.

[3]. Akhtar S, et al. Cationic Polyamidoamine Dendrimers as Modulators of EGFR Signaling In Vitro and In Vivo. PLoS One. 2015 Jul 13;10(7):e0132215.

[4]. Dorobantu CM, et al. Tyrphostin AG1478 Inhibits Encephalomyocarditis Virus and Hepatitis C Virus by Targeting Phosphatidylinositol 4-Kinase IIIα. Antimicrob Agents Chemother. 2016 Sep 23;60(10):6402-6.

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