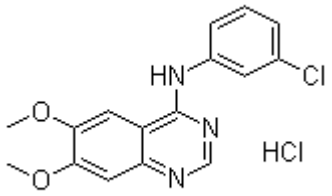
Product Introduction

AG-1478

AG-1478 (Tyrphostin AG-1478) is a selective EGFR inhibitor with IC50 of 3 nM

Technical Data:

Molecular Weight (MW):	352.22	
Formula:	$C_{16}H_{14}ClN_3O_2 \cdot HCl$	
Solubility (25 ℃) * <1 mg/ml means slightly soluble or insoluble:	DMSO 63 mg/mL	
	Water <1 mg/mL	
	Ethanol 13 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃ Powder	
	6 months-80℃ in DMSO	
CAS No.:	170449-18-0	

Biological Activity

AG-1478 is high selective over ErbB2 and PDGFR with IC50 of >100 μM.[1] AG-1478 preferentiallyinhibits U87MG cells expressing truncated EGFR with IC50 of 8.7 μM, compared to those expressingendogenous wt EGFR or overexpressing exogenous wt EGFR with IC50 of 34.6 μM and 48.4 μM,respectively, and inhibits the DNA synthesis with IC50 of 4.6 μM, 19.67 μM, and 35.2 μM, respectively.AG-1478 also preferentially inhibits the tyrosine kinase activity and autophosphorylation of the ΔEGFRcompared to endogenous or overexpressed exogenous wt EGFR.[2] AG-1478 (0.25 μM) abolishes theMAPK activation

induced by Ang II, a Ca2+ ionophore as well as EGF but not by a phorbol ester orplatelet-derived growth factor-BB in the VSMC.[3] AG-1478 inhibits EGF-induced mitogenesis of theBaF/ERX and LIM1215 cells with IC50 of 0.07 μM and 0.2 μM, respectively.[6] AG1478 is able to inhibitthe function of ATP-binding cassette (ABC) transporters such as ABCB1 and ABCG2, with a morepronounced effect on ABCG2.[7] Administration of AG-1478 blocks phosphorylation of the EGFR at the tumor site and inhibits the growthof A431 xenografts that overexpress the WT EGFR and glioma xenografts expressing the de2-7 EGFR.Even subtherapeutic doses of AG-1478 significantly enhance the efficacy of cytotoxic drugs, with thecombination of AG-1478 and temozolomide displaying synergistic antitumor activity against humanglioma xenografts. The combination of AG-1478 and an anti-EGFR antibody (mAb 806) displaysadditive and in some cases synergistic, antitumor activity against tumor xenografts overexpressing theEGFR.[4] The combination of AG-1478 (0.4 mg) with a single dose of 25 μCi 90Y-CHX-A''-DTPAhu3S193 results in a significant enhancement of efficacy compared with either agent alone.[5]

References

[1] Levitzki A, et al. Science, 1995, 267(5205), 1782-1788.

[2] Han Y, et al. Cancer Res, 1996, 56(17), 3859-3861.

[3] Eguchi S, et al. J Biol Chem, 1998, 273(15), 8890-8896.

[4] Johns TG, et al. Proc Natl Acad Sci U S A, 2003, 100(26), 15871-15876.

[5] Lee FT, et al. Clin Cancer Res, 2005, 11(19 Pt 2), 7080s-7086s.

[6] Ellis AG, et al. Biochem Pharmacol, 2006, 71(10), 1422-1434.