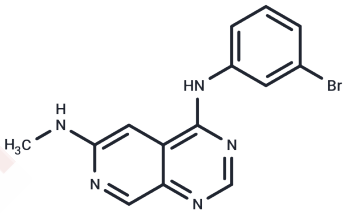
Data Sheet (Cat.No.T5410)

TargetMol

PD158780

Chemical Properties



CAS No. : 171179-06-9

Formula: C14H12BrN5

Molecular Weight: 330.18

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	PD 158780 reversibly inhibits auto and transphosphorylation of all four members of the ErbB receptor superfamily: EGFR, ErbB2, ErbB3, and ErbB4 (IC50s: 8μM, 49 nM, 52 nM, and 52 nM in cell assay).
Targets(IC50)	EGFR
In vitro	PD158780 inhibited EGF receptor autophosphorylation in A431 human epidermoid carcinoma with IC50 values of 13 nM. PD 158780 was highly specific for the EGF receptor in Swiss 3T3 fibroblasts, inhibiting EGF-dependent receptor autophosphorylation and thymidine incorporation at low nanomolar concentrations. PD 158780 inhibited heregulin-stimulated phosphorylation in the SK-BR-3 and MDA-MB-453 breast carcinomas with IC50 values of 49 and 52 nM, respectively [1].
Kinase Assay	Epidermal growth factor receptor was prepared from human A431 carcinoma cell shed membrane vesicles by immunoaffinity chromatography as previously described, and the assays were carried out as reported previously. The substrate used was based on a portion of phospholipase Cγ1, having the sequence Lys-His-Lys-Lys-LeuAla-Glu-Gly-Ser-Ala-Tyr472-Glu-Glu-Val. The reaction was allowed to proceed for 10 min at room temperature and then was stopped by the addition of 2 mL of 75 mM phosphoric acid. The solution was then passed through a 2.5 cm phosphocellulose disk which bound the peptide. This filter was washed with 75 mM phosphoric acid (5×), and the incorporated label was assessed by scintillation counting in an aqueous fluor. Control activity (no drug) gave a count of approximately 100 000 cpm. At least two independent dose-response curves were done and the IC50 values computed. The reported values are averages; variation was generally ±15% [1].
Cell Research	All cell lines were maintained as monolayers in dMEM/F12, 50:50 containing 10% fetal bovine serum. For growth inhibition assays, dilutions of the designated compound in 10 μL were placed in 24-well Linbro plates (1.7 x 1.6 cm, flat bottom) followed by the addition of cells (2 × 10^4) in 2 mL of medium. The plates were incubated for 72 hr at 37 °C in a humidified atmosphere containing 5% CO 2 in air. Cell growth was determined by counting cells with a Coulter model AM electronic cell counter. For clone formation in soft agar, cells were trypsinized, and 10,000 cells/mL were seeded into DMEM/F12 medium containing 10% fetal bovine serum, 0.4% agarose, and the designated concentration of compound. One milliliter of this solution was placed over a bottom layer of the same medium containing 0.8% agarose in a 35-mm Petri dish and incubated at 37 °C in a humidified atmosphere containing 5% CO 2 in air. After 3 weeks, colonies

Cell Research	were stained with p-iodonitrotetrazolium violet (INT) and quantitated with an image analyzer using the software NIH Image version 1.55. Incorporation of radiolabeled thymidine into cellular DNA was monitored by exposing compound-treated or control cells to [methyl)H]thymidine at a concentration of 1 μM and specific activity of 1 μCi/nmol. After 2 hr the cells were trypsinized and injected into 2 mL of ice-cold 15% trichloroacetic acid (TCA). The resulting precipitate was collected on glass fiber filters, washed five times with 2-mL aliquots of ice-cold 15% TCA, dried, and placed in scintillation vials plus 10 mL Ready gel [1].

Solubility Information

Solubility	Ethanol: 8 mg/mL (24.23 mM),Sonication is recommended. DMSO: 30 mg/mL (90.86 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: 1 mg/mL (3.03 mM),Sonication is recommended. *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.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.0287 mL	15.1433 mL	30.2865 mL
5 mM	0.6057 mL	3.0287 mL	6.0573 mL
10 mM	0.3029 mL	1.5143 mL	3.0287 mL
50 mM	0.0606 mL	0.3029 mL	0.6057 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

Fry DW, et al. Biochemical and antiproliferative properties of 4-[ar(alk)ylamino]pyridopyrimidines, a new chemical class of potent and specific epidermal growth factor receptor tyrosine kinase inhibitor. Biochem Pharmacol. 1997 Oct 15;54(8):877-87.

Rewcastle GW, et al. Tyrosine kinase inhibitors. 10. Isomeric 4-[(3-bromophenyl)amino]pyrido[d]-pyrimidines are potent ATP binding site inhibitors of the tyrosine kinase function of the epidermal growth factor receptor. J Med Chem. 1996 Apr 26;39(9):1823-35.