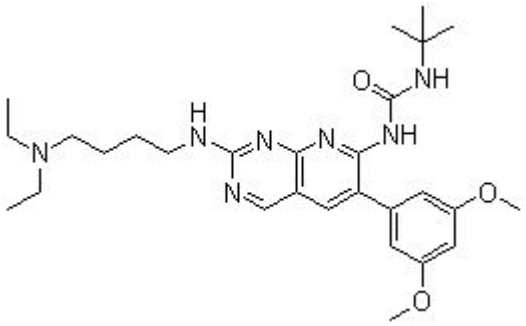
Product Introduction

PD173074

PD173074 is a potent FGFR1 inhibitor with IC50 of ~25 nM and also inhibits VEGFR2 with IC50 of 100-200 nM, ~1000-fold selective for FGFR1 than PDGFR and c-Src.

Technical Data:

Molecular Weight (MW):	523.67
Formula:	$C_{28}H_{41}N_7O_3$
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL
	Water <1 mg/mL
	Ethanol 100 mg/mL
Purity:	>98%
Storage:	3 years -20℃ Powder
	6 months-80℃ in DMSO
CAS No.:	219580-11-7



Biological Activity

PD173074 is an ATP-competitive inhibitor of FGFR1 with K_i of ~40 nM. PD173074 is also an effective inhibitor of VEGFR2. Compared to FGFR1, PD173074 weakly inhibits the activities of Src, InsR, EGFR, PDGFR, MEK, and PKC with 1000-fold or greater IC50 values. PD173074 inhibits autophosphorylation of FGFR1 and VEGFR2 in a dose-dependent manner with IC50 of 1-5 nM and 100-200 nM, respectively. [1] PD173074 inhibits FGF-2 promotion of granule neuron survival in a dose-dependent manner with IC50 of 12 nM, exhibiting 1,000-fold greater potency than that of SU 5402. [2] PD173074 specifically inhibits FGF-2-mediated effects on proliferation, differentiation, and MAPK activation in oligodendrocyte (OL) lineage cells. [3] PD173074 is active against the WT receptor and FGFR3 mutations

in multiple myeloma (MM) cell lines. PD173074 also potently inhibits autophosphorylation of FGFR3 in a dose-dependent manner with IC50 of ~5 nM. PD173074 treatment potently reduces viability of FGFR3-expressing KMS11 and KMS18 cells with IC50 of <20 nM. Inhibition of aFGF-stimulated MM cell growth by PD173074 is highly correlated with the expression of FGFR3. PD173074 treatment completely abolishes NIH 3T3 transformation mediated by Y373C FGFR3 but not by Ras V12, demonstrating that PD173074 specifically targets FGFR3-mediated cell transformation and lacks nonspecific cytotoxic effect. PD173074 also induces functional maturation of KMS11 and KMS18 cells. [4]

Administration of PD173074 at 1 mg/kg/day or 2 mg/ka/day in mice can effectively block angiogenesis induced by either FGF or VEGF in a dose-dependent manner with no apparent toxicity. [1] PD173074 inhibits in vivo growth of mutant FGFR3-transfected NIH 3T3 cells in nude mice. Inhibition of FGFR3 by PD173074 delays tumor growth and increases survival of mice in a KMS11 xenograft myeloma model. [4] In the H-510 xenograft, oral aministration of PD173074 blocks tumor growth similar to that seen with single-agent cisplatin administration, increasing median survival compared with control sham-treated animals. In H-69 xenografts, PD173074 induces complete responses lasting >6 months in 50% of mice. These effects are correlated with increased apoptosis in excised tumors, but not a consequence of disrupted tumor vasculature. [5]

References

[1] Mohammadi M, et al. EMBO J, 1998, 17(20), 5896-5904.

[2] Skaper SD, et al. J Neurochem, 2000, 75(4), 1520-1527.

[3] Bansal R, et al. J Neurosci Res, 2003, 74(4), 486-493.

[4] Trudel S, et al. Blood, 2004, 103(9), 3521-3528.

[5] Pardo OE, et al. Cancer Res, 2009, 69(22), 8645-8651.

[6] Byron SA, et al. Int J Gynecol Cancer, 2012, 22(9), 1517-1526.

Note： Products protected by valid patents are not offered for sale in countries where the sale of such products constitutes a patent infringement and its liability is at buyer’s risk. This item is only for R&D purpose not for commercial business in kilos. Buyers should overview the patent issue in their countries.