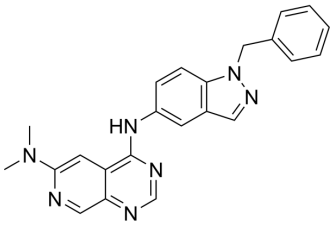
GW2974

Cat. No.:	HY-112293
CAS No.:	202272-68-2
Molecular Formula:	$C_{23}H_{21}N_7$
Molecular Weight:	395.46
Target:	EGFR
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (50.57 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5287 mL	12.6435 mL	25.2870 mL
	5 mM	0.5057 mL	2.5287 mL	5.0574 mL
	10 mM	0.2529 mL	1.2644 mL	2.5287 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

GW2974 is a potent dual inhibitor of EGFR and HER2 with IC_{50} value of 0.007 μM and 0.016 μM, respectively. GW2974 demonstrates in vitro inhibition of the EGFR and HER2 and inhibits the growth of tumor cell. GW2974 can be used for glioblastoma multiforme (GBM) disease research[1][2].

IC_{50} & Target

$EGFR^{L858R/T790M}$	HER2
0.007 μM (IC_{50})	0.016 μM (IC_{50})

In Vitro

GW2974 (0.5-50 μM, 3 h) has an obvious cytotoxicity appeared at 10 μM or above and inhibits cell proliferation of U87MG and U251MG cells at 0.5-5 μM after 24 h treatment[1].

GW2974 (0.5-5 μM, 24 h) has a dose-related role in GBM cell invasion and migration[1].

GW2974 (0.001-100 μM, 24 h) inhibits BT474, HN5, N87 cells growth[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	U87MG, U251MG

Concentration:	0.5-50 μM
Incubation Time:	3 h
Result:	Reduced U87MG and U251MG cells viability to 89.4% and 86.3% in 0.5 μM and 5 μM compared with control.

Cell Proliferation Assay[1]

Cell Line:	U87MG, U251MG
Concentration:	0.5-5 μM
Incubation Time:	24 h
Result:	Inhibited U87MG and U251MG cells proliferation in 0.5 μM and 5μM.

Cell Invasion Assay[1]

Cell Line:	U87MG, U251MG
Concentration:	0.5-5 μM
Incubation Time:	24 h
Result:	Reduced the percentage to 55.6% and 48.6% of U87MG and U251MG cells in 0.5 μM, respectively.

Cell Migration Assay [1]

Cell Line:	U87MG, U251MG
Concentration:	0.5-5 μM
Incubation Time:	24 h
Result:	Decreased the relative migration distances (percentage) of U87MG and U251MG cells to 40.2% and 51.6% in 0.5 μM, respectively. Resulted in a relative migration distances of U87MG and U251MG cells in 5 μM compared with control.

Cell Proliferation Assay[2]

Cell Line:	BT474, HN5, N87
Concentration:	0.001-100 μM
Incubation Time:	24 h
Result:	Inhibited cell growth by 50% at concentrations > 1.0 μM with IC_{50}s < 0.4 μM.

In Vivo

GW2974 (30 mg/kg, 100 mg/kg for Oral gavage, once a day) inhibits GBM growth, invasion, and angiogenesis in dose of 30 mg/kg but abrogated the inhibitory effect of low-dose GW2974 on tumor invasion in dose of 100 mg/kg in GBM xenograft mice model[1].

GW2974 (10 mg/kg, 30 mg/kg, Oral gavage, twice a day) inhibits the growth of tumor in CD-1 nude mice (HN5) and C.B-17 SCID mice (BT474) models in a dosed dependent manner[2].

Animal Model:	GBM xenograft mice model[1]
Dosage:	30 mg/kg, 100 mg/kg
Administration:	Oral gavage (p.o.)
Result:	Decelerated tumor growth at dose of 30 mg/kg and 100 mg/kg. Inhibited the invasion to peritumor areas of tumors in 30 mg/kg group but augmented tumor invasion in 100 mg/kg group of brain tissues. Inhibited angiogenesis in doses of 30 mg/kg and 100 mg/kg.

Animal Model:	CD-1 nude mice (HN5), C.B-17 SCID mice (BT474)[2]
Dosage:	10 mg/kg, 30 mg/kg
Administration:	Oral gavage (p.o.)
Result:	Inhibited tumor growth in the HN5 model by treatment dose with 30 mg/kg. Inhibited tumor growth in the HN5 model about 95% inhibition and BT474 model about 50% inhibition by treatment dose with 10 mg/kg.

REFERENCES

[1]. Wang L, et al. Differential effects of low- and high-dose GW2974, a dual epidermal growth factor receptor and HER2 kinase inhibitor, on glioblastoma multiforme invasion. J Neurosci Res. 2013 Jan;91(1):128-37.

[2]. Rusnak DW, et al. The characterization of novel, dual ErbB-2/EGFR, tyrosine kinase inhibitors: potential therapy for cancer. Cancer Res. 2001 Oct 1;61(19):7196-20.

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