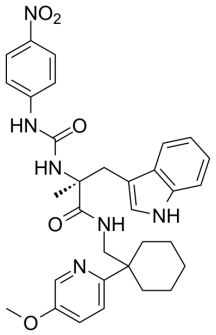
PD176252

Cat. No.:	HY-103286
CAS No.:	204067-01-6
Molecular Formula:	$C_{32}H_{36}N_6O_5$
Molecular Weight:	584.67
Target:	Bombesin Receptor
Pathway:	GPCR/G Protein
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 115 mg/mL (196.69 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7104 mL	8.5518 mL	17.1037 mL
	5 mM	0.3421 mL	1.7104 mL	3.4207 mL
	10 mM	0.1710 mL	0.8552 mL	1.7104 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 5.75 mg/mL (9.83 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5.75 mg/mL (9.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PD176252 is a potent antagonist of neuromedin-B preferring (BB_1) and gastrin-releasing peptide-preferring (BB_2) receptor with K_is of 0.17 nM and 1 nM for human BB_1 and BB_2 receptors, and 0.66 nM, 16 nM for Rat BB_1 and BB_2 receptors, respectively; PD176252 is also an agonist of N-Formyl peptide receptor1/2 (FPR1/FPR2), with EC_{50}s of 0.31 and 0.66 μM in HL-60 cells.

IC_{50} & Target

Ki: 0.17 nM (Human BB_1 receptor), 0.66 nM (Rat BB_1 receptor), 1 nM (Human BB_2 receptor), 16 nM (Rat BB_2 receptor)[1]
EC50: 0.31 μM (FPR1), 0.66 μM (FPR2)[2]

In Vitro

PD176252 is a potent antagonist of neuromedin-B preferring (BB_1) and gastrin-releasing peptide-preferring (BB_2) receptor with K_is of 0.17 nM and 1 nM for human BB_1 and BB_2 receptors, and 0.66 nM, 16 nM for Rat BB_1 and BB_2 receptors, respectively. PD176252 inhibits acidification responses to neuromedin-B or neuromedin-C at the human BB_1 or BB_2

	receptors expressed in CHO cells, with the appK_Bs of 4.0 nM or 13 nM, and blocks bombesin-evoked increases in intracellular calcium levels in CHO cells stably expressing human BB_1 or BB_2 receptors, with appK_Bs of 2.3 nM and 36 nM, respectively. PD176252 is also an agonist of N-Formyl peptide receptor1/2 (FPR1/FPR2), with EC_{50}s of 0.31 and 0.66 μM in HL-60 cells. PD176252 activates Ca^{2+} mobilization in HL-60 cells transfected with human FPRs (EC_{50}, 0.72 ± 0.21 μM)[2]. PD176252 inhibits little specific ^{125}I-gastrin releasing peptide binding to NCI-H345 cells at 1 nM and suppresses almost all specific bindings at 1000 nM, with an IC_{50} of 30 nM. PD176252 (10, 30 μM) significantly inhibits the growth of NCI-H345 or H1299 cells, with IC_{50}s of 7 and 5 μM[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PD176252 (1, 10 μg, p.o.) potently inhibits the growth of the proliferation of NCI-H1299 xenografts in nude mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Growth studies in vitro are conducted using the MTT colorimetic assays. NCI-H1299 cells (10^4/well) are placed in SIT medium and various concentrations of PD176252 or PD168368 added. After 4 days, MTT is added. After 4 h, 150 μL of DMSO is added. After 16 h, the optical density at 570 nm is determined[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Female athymic Balb/c nude mice, 4-5 weeks old, are housed in a pathogen-free temperature controlled isolation room, with a diet consisting of autoclaved rodent chow and autoclaved water given ad libitum. NCI-H1299 cells (1×10^7) are injected into the right flank of each mouse by subcutaneous injection. Palpable tumors are observed in approximately 90% of the mice after 1 week. Polyethylene glycol (PEG, 100 μL) or PD176252 (10 or 1 μg in 100 μL of PEG 400) are injected daily by gavage. The tumor volume (height×width×depth) is determined weekly by calipers and recorded[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Ashwood V, et al. PD 176252--the first high affinity non-peptide gastrin-releasing peptide (BB2) receptor antagonist. Bioorg Med Chem Lett. 1998 Sep 22;8(18):2589-94.

[2]. Schepetkin IA, et al. Gastrin-releasing peptide/neuromedin B receptor antagonists PD176252, PD168368, and related analogs are potent agonists of human formyl-peptide receptors. Mol Pharmacol. 2011 Jan;79(1):77-90.

[3]. Moody TW, et al. Nonpeptide gastrin releasing peptide receptor antagonists inhibit the proliferation of lung cancer cells. Eur J Pharmacol. 2003 Aug 1;474(1):21-9.

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