IC261

Cat. No.: HY-12774

CAS No.: 186611-52-9

Molecular Formula: $C_{18}H_{17}NO_4$

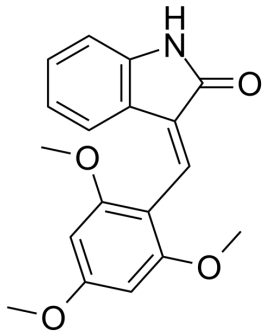
Molecular Weight: 311.33

Target: Casein Kinase; Apoptosis

Pathway: Cell Cycle/DNA Damage; Stem Cell/Wnt; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 33 mg/mL (106.00 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.2120 mL	16.0601 mL	32.1203 mL
5 mM	0.6424 mL	3.2120 mL	6.4241 mL
10 mM	0.3212 mL	1.6060 mL	3.2120 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: ≥ 2.5 mg/mL (8.03 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IC261 is a selective, ATP-competitive CK1 inhibitor, with IC_{50}s of 1 μM, 1 μM, 16 μM for Ckiδ, Ckiε and Ckiα1, respectively.

IC_{50} & Target

CKIδ	CkIα1
1 μM (IC_{50})	16 μM (IC_{50})

In Vitro

IC261 is a selective, ATP-competitive CK1 inhibitor, with IC_{50}s of 1 μM, 1 μM, 16 μM for Ckiδ, Ckiε and Ckiα1, respectively. IC261 is less active on PKA, $p34^{cdc2}$, and $p55^{fyn}$ (IC_{50}s > 100 μM)[1]. IC261 induces mitotic arrest, spindle defects and centrosome amplification in AC1-M88 cells. IC261 (1 μM) increases G2/M cells after 12 h, and causes cell death at 24 h in AC1-M88 cells. IC261 (1 μM) also induces apoptosis in the extravillous trophoblast hybrid cells[2]. IC261 (1.25 μM) suppresses the proliferation of several pancreatic tumour cell lines, including ASPC-1, BxPc3, Capan-1, Colo357, MiaPaCa-2, Panc1, Panc89, PancTu-1 and PancTu-2 cells. IC261 (1.25 μM) specifically enhances CD95-mediated apoptosis of pancreatic tumour cells[3].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	IC261 (20.5 mg/kg) inhibits tumor growth of PancTu-2 cells in SCID mice, downregulates several anti-apoptotic proteins, such as CK1δ/⊠, KRAS, and IL6 and upregulates p21, ATM, CHEK1 and STAT1 in mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Casein kinase activity is assayed at 37°C. The standard reaction (40 μL) contains 25 mM 2-(N-morpholino)ethanesulfonic acid, pH 6.5, 50 mM NaCl, 15 mM $MgCl_2$, 2 mg/mL casein, 2 mM EGTA, 100 μM [γ-^{32}P]ATP (100-400 cpm/pmol). Initial velocity measurements are carried out in duplicate with ATP as the varied substrate. Kinetic constants and their standard errors are calculated. For assay of inhibitor potency (IC_{50}), [γ -^{32}P]ATP is held constant (10 μM), whereas IC261 concentration is varied (0.1, 0.3, 1, 3, and 10 μM). To assess kinetic mechanism, inhibitors are held constant (IC261, 20 μM; IC3608, 100 μM), whereas [γ -^{32}P]ATP is varied as above. For screening small molecule libraries, CK1 isoforms (Ckiα1, δ, and ε) are assayed that casein is used at 10 mg/mL, [γ -^{32}P]ATP is held constant at 2 μM or 1 mM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Human extravillous trophoblast cells irreversibly leave the cell cycle and die when isolated from its natural extracellular matrix. The cell line AC1-M88 is employed in vitro experiments. This cell line is generated by fusion of extravillous trophoblasts with AC1-1. Cells are grown in DMEM (CV-1) or DMEM/F-12 (AC1-M88) medium supplemented with 10% fetal calf serum (FCS) at 37°C in a humidified 5% CO_2 atmosphere. Where indicated, cells are γ-irradiated with 5 Gy and harvested at the given time points for western blot analysis, treated with 1 μM IC261 or 0.4 μM nocodazole for 12 h and fixed for immunofluorescence analysis, or treated with 1 μM IC261 and fixed for flow cytometrical analysis or lysed for western blot analysis at the indicated time points. IC261 and nocodazole are dissolved in DMSO as stock solutions (25 and 10 mM, respectively), and control cells are treated with 0.004% DMSO. For immunocytochemistry, the cells are grown on coverslips and are treated with methanol (−20°C) for 5 min, followed by acetone (−20°C) for 20-30 s prior to being used for immunocytochemical detection[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Five million PancTu-1 cells resuspended in 100 μL of a solution containing 50% Matrigel and 50% DMEM/RPMI-1640 (1:1) are injected into the dorsolateral site of 6-week-old C.B-17/IcrHsd-scid-bg mice. After 17 days, mice are randomised to the control group (n = 5), the IC261 treatment group (n = 5), the gemcitabine group (n = 5) and to the IC261/gemcitabine group (n = 5). Injection of dimethylsulfoxide (DMSO; control group), IC261 (20.5 mg/kg), gemcitabine (0.6 mg/kg) alone or in combination (20.5 mg/kg IC261/0.6 mg/kg gemcitabine) (treatment groups) is performed daily for 8 days. Mice are sacrificed by asphyxiation with CO_2 the day after the last treatment. Tumours are measured before and during treatment. Finally, the tumours are excised, measured, weighed and fixed in formalin or shock frozen. Tumour volume is calculated according to the formula for a rotational ellipsoid (length × height × width × 0.5236)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Int J Biol Sci. 2020 Jan 17;16(5):882-892.
- Int J Biol Sci. 2020 Jan 17;16(5):882-892.
- Transl Stroke Res. 2022 Jul 23.
- Molecules. 2021 Feb 10;26(4):946.

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REFERENCES

[1]. Mashhoon N, et al. Crystal structure of a conformation-selective casein kinase-1 inhibitor. J Biol Chem. 2000 Jun 30;275(26):20052-60.

[2]. Stöter M, et al. Inhibition of casein kinase I delta alters mitotic spindle formation and induces apoptosis in trophoblast cells. Oncogene. 2005 Dec 1;24(54):7964-75.

[3]. Brockschmidt C, et al. Anti-apoptotic and growth-stimulatory functions of CK1 delta and epsilon in ductal adenocarcinoma of the pancreas are inhibited by IC261 in vitro and in vivo. Gut. 2008 Jun;57(6):799-806.

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