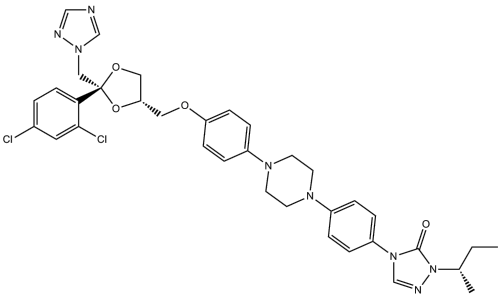
Product Data Sheet

Product Name: Itraconazole
Cat. No.: GC11056

Chemical Properties

Cas. No.	84625-61-6		
Chemical Name	2-butan-2-yl-4-[4-[4-[4-[[(2R,4S)-2-(2,4-dichlorophenyl)-2-(1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazin-1-yl]phenyl]-1,2,4-triazol-3-one		
SMILES	CCC(C)N1C(=O)N(C=N1)C2=CC=C(C=C2)N3CCN(CC3)C4=CC=C(C=C4)OCC5COC(O5)(CN6C=NC=N6)C7=C(C=C(C=C7)Cl)Cl		
Formula	C35H38Cl2N8O4	M.Wt	705.63
Solubility	≥ 8.83mg/mL in DMSO	Storage	4°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Protocol

Cell experiment [1]:

Cell lines SW-480 cells

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Preparation Method	SW-480 cells were cultured in RPMI 1640 medium supplemented with 10% fetal bovine serum, 100U/ml penicillin, and 100μg/ml streptomycin at 37°C with 5% CO_2 and 95% saturated atmospheric humidity. Cells were seeded into 96-well microplates at a density of 5×10^3 cells/ml for 24h. Various concentrations of Itraconazole (0, 2.5, 5, 10, 20, 40, 60, 80, and 100μM) were added to each well. At the end of the incubation period (48h at 37°C), cell viability was analyzed.
Reaction Conditions	0, 2.5, 5, 10, 20, 40, 60, 80, and 100μM; 48h
Applications	Itraconazole treatment significantly induced cell death of SW-480 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	BALB/c mice
Preparation Method	BALB/c mice (6 weeks old) were maintained under a 12h light and 12h dark cycle at a temperature of 25°C and humidity of 50%±10%, free with water and diet. 5×10^6 MKN45 cells were suspended in 100ml of PBS and injected subcutaneously into the right flank of male nude mice. When tumors reached a size measuring 40 to 70mm^3, calculated as $V = L \times W^2/2$(V = Tumor volume, L = Length, W = Width), mice were treated with hydroxypropyl-cyclodextrin (vehicle control), Itraconazole (75mg/kg; twice daily by oral administration). Tumors were measured three times per week for 2 weeks. Then mice were sacrificed, and the tumor tissues were isolated for analysis.
Dosage form	75mg/kg; twice daily for 2 weeks; p.o.
Applications	Itraconazole treatment inhibited tumor growth in mice with MKN45 xenografts.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:
[1] Deng H, Huang L, Liao Z, et al. Itraconazole inhibits the Hedgehog signaling pathway thereby inducing autophagy-mediated apoptosis of colon cancer cells[J]. Cell Death & Disease, 2020, 11(7): 539.
[2] Hu Q, Hou Y C, Huang J, et al. Itraconazole induces apoptosis and cell cycle arrest via inhibiting Hedgehog signaling in gastric cancer cells[J]. Journal of Experimental & Clinical Cancer Research, 2017, 36(1): 50.

Background

Itraconazole is an orally active antifungal drug that can strongly inhibit the Hedgehog (Hh) signaling pathway, with an IC_{50} value is 800nM [1]. Itraconazole inhibits the NaV channel in the heart (IC_{50}=4.2μM) and regulates the contractility of the left ventricle of the heart [2]. Itraconazole inhibits ergosterol synthesis by interacting with the substrate binding site of the fungal 14α-demethylase, increasing cell membrane permeability and disrupting cell membrane integrity[3]. Itraconazole has been widely used to inhibit the growth of various tumor cells and promote autophagy in cancer cells[4].

In vitro, Itraconazole treatment for 36 hours significantly inhibited the proliferation of human umbilical vein endothelial cells (HUVECs), with an IC_{50} value of 0.16μM[5]. Treatment of MCF-7 cells with 20μg/ml Itraconazole for 24 hours significantly induced cell death, accompanied by changes in mitochondrial membrane potential[6]. Treatment of SW-480 cells with 5μM Itraconazole for 48 hours significantly promoted cell apoptosis, induced G1 phase cell cycle arrest and significantly accumulated autophagosomes[7].

In vivo, Itraconazole treatment via intravenous administration at a dose of 20mg/kg/day for 4 days significantly reduced the fungal load in the lung tissues of mice with invasive pulmonary aspergillosis (IPA) and improved the survival rate of the mice[8]. Oral administration of 75mg/kg of Itraconazole twice daily for 2 weeks significantly inhibited tumor growth in a xenograft mouse model of MKN45 cells[9].

References:

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[1] Kim J, Tang J Y, Gong R, et al. Itraconazole, a commonly used antifungal that inhibits Hedgehog pathway activity and cancer growth[J]. Cancer cell, 2010, 17(4): 388-399.
[2] Qu Y, Fang M, Gao B X, et al. Itraconazole decreases left ventricular contractility in isolated rabbit heart: mechanism of action[J]. Toxicology and applied pharmacology, 2013, 268(2): 113-122.
[3] De Beule K, Van Gestel J. Pharmacology of itraconazole[J]. Drugs, 2001, 61(Suppl 1): 27-37.
[4] Wei X, Liu W, Wang J Q, et al. “Hedgehog pathway”: a potential target of itraconazole in the treatment of cancer[J]. Journal of cancer research and clinical oncology, 2020, 146(2): 297-304.
[5] Chong C R, Xu J, Lu J, et al. Inhibition of angiogenesis by the antifungal drug itraconazole[J]. ACS chemical biology, 2007, 2(4): 263-270.
[6] Wang X, Wei S, Zhao Y, et al. Anti-proliferation of breast cancer cells with itraconazole: Hedgehog pathway inhibition induces apoptosis and autophagic cell death[J]. Cancer letters, 2017, 385: 128-136.
[7] Deng H, Huang L, Liao Z, et al. Itraconazole inhibits the Hedgehog signaling pathway thereby inducing autophagy-mediated apoptosis of colon cancer cells[J]. Cell Death & Disease, 2020, 11(7): 539.
[8] Tansho S, Abe S, Ono Y, et al. Efficacy of intravenous itraconazole against invasive pulmonary aspergillosis in neutropenic mice[J]. Journal of infection and chemotherapy, 2006, 12(6): 355-362.
[9] Hu Q, Hou Y C, Huang J, et al. Itraconazole induces apoptosis and cell cycle arrest via inhibiting Hedgehog signaling in gastric cancer cells[J]. Journal of Experimental & Clinical Cancer Research, 2017, 36(1): 50.

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