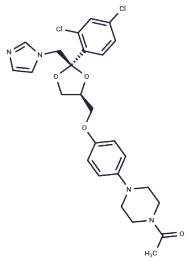
Data Sheet (Cat.No.T0679)

TargetMol

Ketoconazole

Chemical Properties



CAS No. : 65277-42-1

Formula: C26H28Cl2N4O4

Molecular Weight: 531.43

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Ketoconazole (R-41400) is an imidazole antifungal agent with broad-spectrum antifungal activity that primarily acts by inhibiting the biosynthesis of ergosterol in the fungal cell membrane. Ketoconazole inhibits the fungal cytochrome P450-dependent enzyme lanosterol 14α-demethylase (CYP51), thereby blocking the conversion of lanosterol to ergosterol. This leads to damage to the cell membrane structure and permeability, consequently inhibiting fungal growth and producing an antifungal effect. In addition, ketoconazole is a non-selective cytochrome P450 (CYP) inhibitor, specifically inhibiting drug-metabolizing enzymes such as human CYP3A4. In terms of endocrinology, ketoconazole also inhibits various enzymes involved in steroid synthesis (CYP17A1, CYP11A1).
Targets(IC50)	Antibacterial,Antifungal,Cytochromes P450,Hydroxylase,NADPH-oxidase,Ras
In vitro	**Methods**: Human liver microsomes were incubated at 37°C with ketoconazole (0.3, 1, 2, 3, 5, 10 μM) and CYP3A-specific substrates testosterone and midazolam. High-performance liquid chromatography (HPLC) was used to quantify the formation of metabolites (6β-hydroxy testosterone and 1'-hydroxy midazolam). **Results**: Ketoconazole inhibited CYP3A activity in a dose-dependent manner at all concentrations tested, reducing activity to below 3% (for testosterone) at 10 μM. [1] **Methods**: U87 glioma cells and patient-derived glioblastoma stem cells (GSCs) were treated with ketoconazole at concentrations ranging from 0.1 to 100 μM for 48–72 hours. Cell proliferation and apoptosis were assessed via Annexin V/PI staining. **Results**: Ketoconazole treatment reduced cell proliferation and increased apoptosis rates. [2]
In vivo	**Methods**: U87-luc cells or patient-derived GSC were implanted in situ into the brains of immunodeficient mice. After tumor formation, mice were randomly assigned to treatment groups. Daily intraperitoneal injections of Ketoconazole (50 mg/kg) or solvent control were administered for 4 consecutive weeks. Tumor growth was monitored via bioluminescence imaging, and mouse survival was recorded. **Results**: Tumor growth was significantly suppressed in the ketoconazole group, with markedly prolonged mouse survival. Histological analysis revealed reduced tumor cell proliferation, increased apoptosis, and decreased metabolic activity within tumors. [2] **Methods**: Wild-type mice received intraperitoneal injections of ketoconazole (50 mg/kg), followed approximately 30 minutes later by intravenous administration of a radiolabeled tracer ([^{11}C]lopipridil or [^{11}C]dLop). Mice were euthanized 30 minutes after

In vivo	tracer injection, and blood and whole brain samples were collected. **Results**: Ketoconazole (50 mg/kg, i.p.) partially inhibited the N-demethylation of [^{11}C] lopipridil in vivo, elevated its plasma concentration, and reduced the entry of polar metabolites into the brain. [3]
Kinase Assay	Whole Cell [3H]R1881 Binding Assay: Fibroblasts are grown to confluence in five or six 150 cm2 tissue culture flasks for routine assay. This usually requires 4-6 weeks from the time of the initial seeding of the cell line. All studies are performed between passages 3-20. Two days before assay, the medium is changed to one lacking fetal calf serum. This is repeated again 24 hours before assay. Competition assays are performed with 0.5-1.0 nM [3H]R1881 and increasing amounts of the nonradioactive compounds. Binding to low affinity sites is determined in the presence of 5 × 10-7 M R1881 and is subtracted from whole cell binding of [3H]R 1881 obtained in the absence of any inhibitor to assess binding to 5 high affinity site
Cell Research	HT29-S-B6 cells (5×105) are plated in 35-mm Petri dishes. The next day, the medium is changed and effectors are added in a small volume (10-20 µL). The incubation medium is renewed every day during the experiments. The same triplicate dishes are used for cell counts, [3H]thymidine incorporation, and flow cytometry. [3H]Thymidine (0.5 µCi) is allowed to incorporate for 24 hours; at the end of incubation, cells are rinsed with 1 mL of medium, detached with 1 mL of trypsin-EDTA, and diluted (1:3) with the culture medium. An aliquot (0.5-1 mL) is used for cell count with a Coulter Counter.(Only for Reference)

Solubility Information

Solubility	DMSO: 25 mg/mL (47.04 mM),Sonication and heating are recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 0.53 mg/mL (1 mM),Solution. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8817 mL	9.4086 mL	18.8172 mL
5 mM	0.3763 mL	1.8817 mL	3.7634 mL
10 mM	0.1882 mL	0.9409 mL	1.8817 mL
50 mM	0.0376 mL	0.1882 mL	0.3763 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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