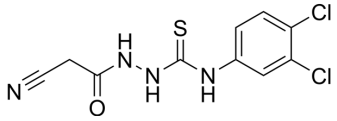
iKIX1

Cat. No.:	HY-124952
CAS No.:	656222-54-7
Molecular Formula:	$C_{10}H_8Cl_2N_4OS$
Molecular Weight:	303.17
Target:	Fungal
Pathway:	Anti-infection
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.33 mg/mL (274.86 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.2985 mL	16.4924 mL	32.9848 mL
	5 mM	0.6597 mL	3.2985 mL	6.5970 mL
	10 mM	0.3298 mL	1.6492 mL	3.2985 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: 2.08 mg/mL (6.86 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.86 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.86 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

iKIX1 is an antifungal agent and resensitizes drug-resistant C. glabrata to azole antifungals in vitro. iKIX1 inhibits the interaction between the KIX domain of the mediator subunit CgGal11A and the activation domain of CgPdr1, the IC_{50} and K_i values are 190.2 μM and 18 μM, respectively. iKIX1 is used for the study of multidrug resistance and C. glabrata infection[1].

IC_{50} & Target

IC50: 190.2 μM (interaction between CgGal11A and CgPdr1)
Ki: 18 μM (interaction between CgGal11A and CgPdr1)[1]

In Vitro

iKIX1 (10-20 μg/ml) inhibits cell growth in a concentration-dependent manner in the presence of 5 μM ketoconazole (KET) in

HepG2 cells[1].

FP titration curve showing the interaction of CgGal11A KIX domain with CgPdr1 AD30 fitted to a K_d of 319.7 nM. iKIX1 competes out CgPdr1 AD30 with an IC_{50} of 190.2 μM . In vitro binding studies, iKIX1 reveals that the K_d of the Cg Pdr1 activation domain (AD) for the CgGal11A KIX domain is 0.32 μM and the apparent K_i for iKIX1 is 18 μM[1].

iKIX1 (0-50 μM) inhibits Ketoconazole (KET)-induced upregulation of luciferase activity in a dose-responsive manner in a Sc pdr1Δpdr3Δ strain containing plasmid-borne CgPDR1 and 3XPDRE-luciferase[1].

A chromatin immunoprecipitation (ChIP) assay is used to examine Gal11/Med15 recruitment to Pdr1-regulated target genes in S. cerevisiae. Ketoconazole induces Gal11/Med15 rapidly recruited to the promoters of the Pdr1 target genes PDR5 and SNQ2. iKIX1 abrogates Ketoconazole-induced recruitment of Gal11/Med15 and strongly inhibits azole-induced transcription of ScPdr1 target genes[1].

iKIX1 (20 μM) has an effect on the transcription of C. glabrata Pdr1-regulated genes involved in drug efflux and MDR (CgCDR1, CgCDR2 and CgYOR1). iKIX1 alone does not significantly affect Pdr1-target gene induction. But pre-treatment with iKIX1 reduces ketoconazole-induced CgPdr1 up-regulation in a durable and concentration-dependent manner[1].

In RNA sequencing (RNA-Seq) assay of a C. glabrata SFY114 (PDR1 wild-type) strain. Azole up-regulates Pdr1-dependent genes in both yeasts, such as the drug efflux pumps ScPDR5 and CgCDR1i. KIX1 combines azole strongly blunts expression of many azole-activated and Pdr1-dependent genes in both S.cerevisiae and C. glabrata, but iKIX1 alone affects very different sets of genes in S.cerevisiae and C. glabrata. And then iKIX1 does not significantly alter the expression of PDR1 or GAL11/MED15 affects very different sets of genes in S.cerevisiae and C. glabrata[1]. iKIX1 (0-150 μM) restores the efficacy of azoles towards CgPDR1 gain-of-function mutants. It restores azole-sensitivity to PDR1 gain-of-function mutant strains in a concentration-dependent manner[1].

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

REFERENCES

[1]. Joy L Nishikawa, et al.Inhibiting fungal multidrug resistance by disrupting an activator-Mediator interaction. Nature. 2016 Feb 25;530(7591):485-9.

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