Manogepix

Cat. No.: HY-18233

CAS No.: 936339-60-5

Molecular Formula: $C_{21}H_{18}N_4O_2$

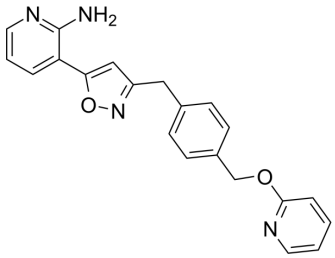
Molecular Weight: 358.39

Target: Fungal

Pathway: Anti-infection

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 : 100 mg/mL (279.03 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7903 mL	13.9513 mL	27.9026 mL
	5 mM	0.5581 mL	2.7903 mL	5.5805 mL
	10 mM	0.2790 mL	1.3951 mL	2.7903 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 (5.80 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.80 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.80 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Manogepix (E1210) is a first-in-class, broad-spectrum and orally active antifungal. Manogepix has a mechanism of action-inhibition of fungal glycosylphosphatidylinositol (GPI) biosynthesis[1][2].

IC_{50} & Target

Fungal[1][2]

In Vitro

Manogepix inhibits the inositol acylation activity of C. albicans Gwt1p and A. fumigatus Gwt1p with IC_{50}s of 0.3 to 0.6 μM but has no inhibitory activity against human Pig-Wp even at concentrations as high as 100 μM. To confirm the inhibition of

	fungal glycosylphosphatidylinositol (GPI) biosynthesis, expression of ALS1 protein, a GPI-anchored protein, on the surfaces of C. albicans cells treated with Manogepix is studied and shown to be significantly lower than that on untreated cells. Manogepix inhibits germ tube formation, adherence to polystyrene surfaces, and biofilm formation of C. albicans at concentrations above its MIC[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Manogepix (2.5 mg/kg, 5 mg/kg and 10 mg/kg; oral administration; twice daily; for 3 days; specific-pathogen-free female ICR mice) treatment reduces the number of viable C. albicans cells in the oral cavity in a dose-dependent manner[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Specific-pathogen-free female ICR mice (5 weeks; ~25 g) with C. albicans[2]
Dosage:	2.5 mg/kg, 5 mg/kg and 10 mg/kg
Administration:	Oral administration; twice daily; for 3 days
Result:	Reduced the number of viable C. albicans cells in the oral cavity in a dose-dependent manner.

REFERENCES

[1]. Watanabe NA, et al. E1210, a new broad-spectrum antifungal, suppresses Candida albicans hyphal growth through inhibition of glycosylphosphatidylinositol biosynthesis. Antimicrob Agents Chemother. 2012 Feb;56(2):960-71.

[2]. Hata K, et al. Efficacy of oral E1210, a new broad-spectrum antifungal with a novel mechanism of action, in murine models of candidiasis, aspergillosis, and fusariosis. Antimicrob Agents Chemother. 2011 Oct;55(10):4543-51.

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