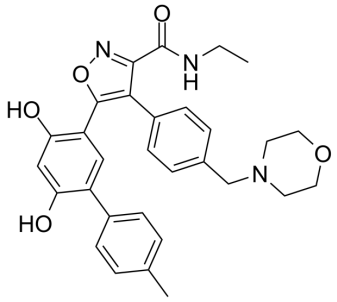
HSP90-IN-9

Cat. No.:	HY-145814
CAS No.:	2765247-36-5
Molecular Formula:	$C_{30}H_{31}N_3O_5$
Molecular Weight:	513.58
Target:	HSP; Fungal
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	HSP90-IN-9 is a potent and selective HSP90 inhibitor. HSP90-IN-9 displays a fungicidal effect in a dose-dependent manner. HSP90-IN-9 inhibits fungal biofilm formation and fungal morphological changes after being combined with FLC. HSP90-IN-9 recovers FLC resistance by down-regulating the expression of related genes (ERG11, CDR1 and CDR2)[1].
IC_{50} & Target	HSP90

In Vitro

HSP90-IN-9 (compound A17) (combined with FLC (2 μg/mL)) shows antifungal activities against the six FLC-resistant Candida albicans (C. albicans) strains (MIC_{80}s of 0.125 μg/mL in strain 901, strain 632, strain 100; MIC_{80}s of 0.25 μg/mL in strain 904, strain 103,strain311, respectively)[1].

HSP90-IN-9 (24 h) shows low toxic to human cancer cells, human normal cells and the macrophage lineage (IC_{50}s is 13.12, 34.09, 17.45, 7.15, >50, 21.33, 17.05, 10.34 μM in A549, MCF-7, HEPG2, THLE-2, BEAS-2B, NIH-3T3, Raw264.7, BV-2 cells, respectively)[1].

HSP90-IN-9 (32 μg/mL (combined with FLC (32 μg/mL)), 24 h) inhibits fungal biofilm formation and fungal morphological changes after being combined with FLC[1].

HSP90-IN-9 (C. albicans (strain 904), 48 h) displays a fungicidal effect in a dose-dependent manner[1].

HSP90-IN-9 (FLC + compound A17 (32 + 32 μg/mL)) recovers azole sensitivity in resistant C.albicans by down-regulating the expression of CYP51 (ERG11) efflux pump-related genes (CDR1 and CDR2)[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	A549, MCF-7, HEPG2, THLE-2, BEAS-2B, NIH-3T3, Raw264.7, BV-2 cells
Concentration:	
Incubation Time:	24 h
Result:	Showed low toxic to human cancer cells, human normal cells and the macrophage lineage (IC_{50}s of 13.12, 34.09, 17.45, 7.15, >50, 21.33, 17.05, 10.34 μM in A549, MCF-7, HEPG2, THLE-2, BEAS-2B, NIH-3T3, Raw264.7, BV-2 cells, respectively).

RT-PCR[1]

Cell Line:	Azole-resistant strain 904

Concentration:	32 μg/mL (combined with FLC (32 μg/mL))
Incubation Time:	24 h
Result:	Inhibited fungal biofilm formation and fungal morphological changes after being combined with FLC.

In Vivo

HSP90-IN-9 (10 mg/kg; i.v.) exhibits moderate pharmacokinetic properties in SD rats[1].

HSP90-IN-9 (A17 (10 mg/kg)+FLC (1 mg/kg); i.p.; once a day for 5 days) exhibits potent in vivo antifungal efficacy by reducing the colonization and dissemination of fungi in tissue[1].

Pharmacokinetic Parameters of HSP90-IN-9 in male Sprague-Dawley (SD) rats[1].

dose (mg/kg)	$T_{1/2}$ (h)	C_0 (ng/mL)	$AUC_{(0-t)}$ (h*ng/mL)	$AUC_{(0-\infty)}$ (h*ng/mL)	V_z (L/kg)	Cl (mL/min/kg)	$MRT_{(0-\infty)}$ (h)
10 mg/kg	1.26±0.31	4752.50±44.54	3005.15±35.59	3028.95±54.14	11.25±3.69	101.77±1.96	1.12±0.07

male Sprague-Dawley (SD) rats; 10 mg/kg; i.v.[1]

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

Animal Model:	male Sprague-Dawley (SD) rats[1]
Dosage:	10 mg/kg
Administration:	i.v.
Result:	Exhibited moderate pharmacokinetic properties in SD rats.

Animal Model:	female SD rats, 160-180 g (IFI rat model)[1]
Dosage:	10 mg/kg, A17 (10 mg/kg)+FLC (1 mg/kg)
Administration:	i.p., once a day, 5 days
Result:	Exhibited potent in vivo antifungal efficacy by reducing the colonization and dissemination of fungi in tissue.

REFERENCES

[1]. Yin W, et al. Species-Selective Targeting of Fungal Hsp90: Design, Synthesis, and Evaluation of Novel 4,5-Diarylisoxazole Derivatives for the Combination Treatment of Azole-Resistant Candidiasis. J Med Chem. 2022, 65(7):5539-5564.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA