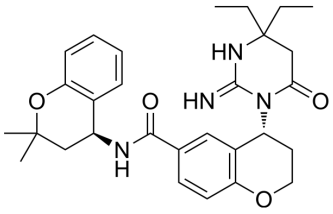
WM382

Cat. No.:	HY-151561
CAS No.:	2606990-92-3
Molecular Formula:	$C_{29}H_{36}N_4O_4$
Molecular Weight:	504.62
Target:	Parasite
Pathway:	Anti-infection
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 5 mg/mL (9.91 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9817 mL	9.9084 mL	19.8169 mL
	5 mM	0.3963 mL	1.9817 mL	3.9634 mL
	10 mM	---	---	---

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

WM382 is an orally active and potent dual plasmepsin IX/X (PMIX/X) inhibitor with IC_{50} values of 1.4 nM and 0.03 nM, respectively. WM382 has robust in vivo efficacy at multiple stages of the malaria parasite life cycle and an excellent resistance profile[1][2][3].

IC_{50} & Target

Plasmodium

In Vitro

WM382 shows moderate cytotoxicity against HepG2 cells (IC_{50}=24.8 μM), and inhibits Plasmodium falciparum and P. vivax with an IC_{50} value of 0.6 nM (P. falciparum)[2][3].
WM382 selectively binds PMV and PMX with K_i values of 13.4 μM and 0.035 nM, respectively[3].
WM382 (1 nM and 100 nM) reminds the time to patent blood infection following injection of 65 h in P. berghei-infected HepG2 in vitro cultures[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

WM382 (20 mg/kg twice daily or 1-30 mg/kg once daily; p.o.; for 4 d) can clear mouse models of P. berghei and P. falciparum parasites. WM382 is also efficacious against P. falciparum asexual infection in humanized mice and prevents transmission to mosquitoes[3].

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

Animal Model:	Mice infected with P. berghei[3]
Dosage:	20 mg/kg
Administration:	Oral gavage; twice daily for 4 days; monitored for 30 days
Result:	Cured mice of P. berghei and prevents blood infection from the liver.

Animal Model:	Humanized nonobese diabetic-severe combined immunodeficiency (NOD-scid) IL2Rg^{null} mouse model (NSG)[3]
Dosage:	1, 3, 10, 30 mg/kg
Administration:	Oral gavage; once daily for 4 days; monitored for 7 days
Result:	Cleared of parasitemia by day 6 at 30 mg/kg or day 7 at 3 and 10 ma/kg.

REFERENCES

[1]. Manuel de LR, et al. The Invention of WM382, a Highly Potent PMIX/X Dual Inhibitor toward the Treatment of Malaria. ACS Med Chem Lett. 2022 Oct 12.

[2]. Hodder AN, et al. Basis for drug selectivity of plasmepsin IX and X inhibition in Plasmodium falciparum and vivax. Structure. 2022 Jul 7;30(7):947-961.e6.

[3]. Favuzza P, et al. Dual Plasmepsin-Targeting Antimalarial Agents Disrupt Multiple Stages of the Malaria Parasite Life Cycle. Cell Host Microbe. 2020 Apr 8;27(4):642-658.e12.

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