SID 26681509

Cat. No.: HY-103353

CAS No.: 958772-66-2

Molecular Formula: $C_{27}H_{33}N_5O_5S$

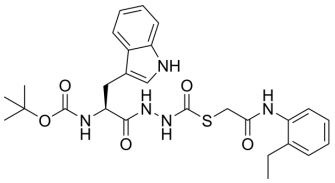
Molecular Weight: 539.65

Target: Cathepsin; Parasite

Pathway: Metabolic Enzyme/Protease; Anti-infection

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (92.65 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8531 mL	9.2653 mL	18.5305 mL
	5 mM	0.3706 mL	1.8531 mL	3.7061 mL
	10 mM	0.1853 mL	0.9265 mL	1.8531 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: ≥ 1.25 mg/mL (2.32 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.32 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.32 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SID 26681509 is a potent, reversible, competitive, and selective inhibitor of human cathepsin L with an IC_{50} of 56 nM. SID 26681509 inhibits in vitro propagation of malaria parasite ***Plasmodium falciparum*** and inhibits ***Leishmania major*** with IC_{50}s of 15.4 μM and 12.5 μM, respectively. SID 26681509 shows no inhibitory activity against cathepsin G[1].

IC_{50} & Target	cathepsin L	Plasmodium	Leishmania

In Vitro

After a 4 hr preincubation with cathepsin L, SID 26681509 becomes more potent, demonstrating an IC_{50} of 1.0 nM. SID 26681509 is determined to be a slow-binding and slowly reversible competitive inhibitor. Through a transient kinetic

	analysis for single-step reversibility, inhibition rate constants are kon = 24,000 $M^{-1}s^{-1}$ and koff = 2.2 × 10^{-5} s^{-1} (K_i = 0.89 nM). Molecular docking studies are undertaken using the experimentally-derived X-ray crystal structure of papain/CLIK-148[1]. SID 26681509 inhibits papain and cathepsins B, K, S, and V with IC_{50} values determined after one hour ranging from 618 nM to 8.442 μM. SID 26681509 shows no inhibitory activity against the serine protease cathepsin G[1]. SID 26681509 inhibits cathepsin V activity with an IC_{50} value of 0.5 μM. SID 26681509 (1-30 μM) blocks high-mobility group box 1 (HMGB1)-induced TNF-α production dose dependently without altering cell viability[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SID 26681509 treatment significantly improves survival in murine models of sepsis and reduces liver damage following warm liver ischemia/reperfusion (I/R) models[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2021 Mar 27;6(1):134.
- Nat Commun. 2022 May 26;13(1):2935.
- Nat Commun. 2020 Mar 27;11(1):1620.

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REFERENCES

[1]. Shah PP, et al. Kinetic characterization and molecular docking of a novel, potent, and selective slow-binding inhibitor of human cathepsin L. Mol Pharmacol. 2008 Jul;74(1):34-41.

[2]. Pribis JP, et al. The HIV Protease Inhibitor Saquinavir Inhibits HMGB1-Driven Inflammation by Targeting the Interaction of Cathepsin V with TLR4/MyD88. Mol Med. 2015 Dec;21(1):749-757.

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