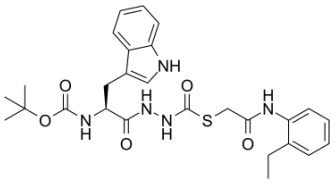
SID 26681509

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



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	IC50: 56 nM (Human cathepsin L), 0.5 μM (Cathepsin V), 15.4 μM (Plasmodium falciparum), 12.5 μM (Leishmania major)[1]
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

- 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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