SQ109

Cat. No.: HY-14989

CAS No.: 502487-67-4

Molecular Formula: $C_{22}H_{38}N_2$

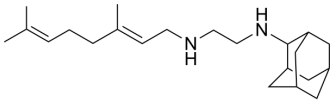
Molecular Weight: 330.55

Target: Parasite; Bacterial; Antibiotic

Pathway: Anti-infection

Storage:

Pure form	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 25 mg/mL (75.63 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0253 mL	15.1263 mL	30.2526 mL
5 mM	0.6051 mL	3.0253 mL	6.0505 mL
10 mM	0.3025 mL	1.5126 mL	3.0253 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: ≥ 2.5 mg/mL (7.56 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.56 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SQ109 is a potent inhibitor of the trypomastigote form of the parasite, with IC_{50} for cell killing of 50±8 nM. SQ109, targets MmpL3, is an antitubercular agent.

IC_{50} & Target

Trypanosoma

In Vitro

SQ109 also inhibits extracellular epimastigotes (IC_{50}, 4.6±1 μM) and the clinically relevant intracellular amastigotes (IC_{50},

	~0.5 to 1 μM), with a selectivity index of ~10 to 20. SQ109 has little effect (EC_{50}, ~80 μM) in a red blood cell hemolysis assay. Besides, SQ109 causes major ultrastructural changes in all three life cycle forms, as observed by light microscopy, scanning electron microscopy (SEM), and transmission electron microscopy (TEM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral administration of SQ109 (0.1-25 mg/kg per day) to the mice for 28 days results in dose-dependent reductions of mycobacterial load in both spleen and lung comparable to that of EMB administered at 100 mg/kg per day, but is less potent than isoniazid (INH) at 25 mg/kg per day. Pharmacokinetic profiles of SQ109 in mice following a single administration showed its C_{max} as 1038 (intravenous (i.v.)) and 135 ng/mL (p.o.), with an oral T_{max} of 0.31 h. The elimination $t_{1/2}$ of SQ109 is 3.5 (i.v.) and 5.2 h (p.o.). The oral bioavailability is 4%[2]. The terminal half-life ($t_{1/2}$) of SQ109 in dogs (12-29 h, mean 29.3 h) is longer than in rats (7-8 h, mean 7.4 h), as reflected by the significantly larger volume of distribution of SQ109 in dogs. The oral bioavailability of SQ109 in rats and dogs is determined to be 12% and 5%, respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The LLC-MK_2 cells are treated with SQ109 (2.5 to 20 μM) and incubated for 96 h at 37°C. Fresh RPMI 1640 medium containing only 10% FBS is added to the untreated samples as a control. To determine toxicity, the MTS/PMS assay is performed. The selectivity index of SQ109 is determined based on its activities against the trypomastigote and intracellular amastigote forms of T.cruzi, calculated as the ratio of the 50% cytotoxic concentration (CC_{50}) of mammalian cells to the IC_{50} or 50% lysing concentration (LC_{50}) of T.cruzi. All experiments are performed in duplicate. The means are determined from ≥3 experiments[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2][3]	Mice[2] Female C57BL/6 mice (8 weeks old) are used. Oral treatment of mice with INH (25 mg/kg), ethambutol (EMB) (100 mg/kg) and SQ109 (0.1, 10 and 25 mg/kg) is initiated 20 days after inoculation. Control groups of infected but untreated mice are killed at the initiation of therapy (early controls) or at the end of the treatment period. There are six mice per group. Chemotherapy is given daily for 5 days per week until the mice are killed, 4 weeks after initiation of treatment. The spleen and lungs are aseptically removed and weighed. The organs are homogenized in 2 ml of sterile PBS containing 0.05% Tween-80. Homogenate samples from individual tissues are diluted 10-fold in PBS and plated on 7H10 agar dishes. Inoculated dishes are incubated at 37°C in ambient air for 3 weeks prior to calculation of CFU. Viable counts are converted to a logarithmic scale; readings are corrected to represent whole organ totals. The severity of infection and the effectiveness of the treatments are assessed by the survival rate, and the mean number of CFU in mouse organs. Rats and Dogs[3] Male Fischer rats (271-289 g) and beagle dogs (7.5-8.9 kg, two males and two females per dose group) are used. Rats are given either a single intravenous (i.v.) bolus dose of 1.5 mg/kg (9 mg/m^2) or an oral dose of 13 mg/kg (78 mg/m^2) of SQ109 (n=8 per dose group); rats are divided into subgroups consisting of four rats per subgroup. Rat blood (0.7 mL) is withdrawn from the jugular vein catheter at alternating time points from individual rats in each subgroup. Blood samples are collected at 2, 5, 10, 15 and 30 min and 1, 3, 6, 10 and 24 h after a single i.v. administration, or 5, 15 and 30 min and 1, 2, 4, 6, 10 and 24 h after a single oral administration. Each blood sample is centrifuged to separate plasma, which is then stored at −70°C until analysis. Beagle dogs are dosed by gavage at either 3.75 or 15 mg/kg (75 or 300 mg/m^2), or intravenously at either 0.45 or 4.5 mg/kg (9 and 90 mg/m^2). Dog blood (0.7 mL) is withdrawn from the jugular vein at 2, 5, 10, 20 and 30 min and 1, 2, 4, 8, 12, 18 and 24 h after a single i.v. administration, or 10, 20 and 30 min and 1, 2, 4, 8, 12, 18 and 24 h after a single oral administration. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- ACS Infect Dis. 2016 Jul 8;2(7):500-8.
- Dis Model Mech. 2021 Oct 13;dmm.049145.
- Advanced Biochemistry, University of Madras, American.2019, Jan

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REFERENCES

[1]. Veiga-Santos P, et al. SQ109, a new drug lead for Chagas disease. Antimicrob Agents Chemother. 2015 Apr;59(4):1950-61.

[2]. Jia L, et al. Pharmacodynamics and pharmacokinetics of SQ109, a new diamine-based antitubercular drug. Br J Pharmacol. 2005 Jan;144(1):80-7

[3]. Jia L, et al. Interspecies pharmacokinetics and in vitro metabolism of SQ109. Br J Pharmacol. 2006 Mar;147(5):476-85.

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