GSK369796 Dihydrochloride

Cat. No.: HY-12082A

CAS No.: 1010411-21-8

Molecular Formula: $C_{20}H_{24}Cl_3N_3O$

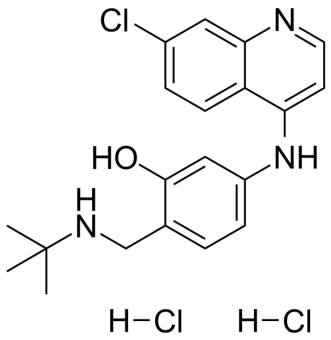
Molecular Weight: 428.78

Target: Potassium Channel; Parasite

Pathway: Membrane Transporter/Ion Channel; Anti-infection

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (233.22 mM; Need ultrasonic)

H_2O : 50 mg/mL (116.61 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.3322 mL	11.6610 mL	23.3220 mL
5 mM	0.4664 mL	2.3322 mL	4.6644 mL
10 mM	0.2332 mL	1.1661 mL	2.3322 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 (5.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK369796 Dihydrochloride is an affordable and effective antimalarial and inhibits hERG potassium ion channel repolarization with an IC_{50} of 7.5 μM.

IC_{50} & Target

IC50: 7.5 μM (hERG potassium ion channel)[1]

In Vitro

In vitro, GSK369796 Dihydrochloride can inhibit the growth of Plasmodium falciparum strains 3D7c, HB3c and K1d, with IC_{50} s of 11.2±2.2, 12.6±5.3 and 13.2±3.2 nM, respectively. Protein binding is higher for GSK369796 Dihydrochloride (compound 4) compare to desethyl amodiaquine in the mouse (93 vs 74%) but similar in human (88 vs 86%). GSK369796 Dihydrochloride can also inhibit hERG potassium ion channel repolarization with an IC_{50} of 7.5±0.8 μM[1].

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

In Vivo	In vivo, GSK369796 Dihydrochloride can inhibit the growth of Plasmodium berghei ANKA with ED_{50} and ED_{90} of 2.8 and 4.7 mg/kg, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Assays are performed in sterile 96-well microtiter plates, each plate contains 200 mL of parasite culture (2% parasitemia, 0.5% hematocrit) with or without 10 mL drug dilutions (including GSK369796 Dihydrochloride). Each drug is tested in triplicate and parasite growth is compared to control wells (which constitutes 100% parasite growth). Cultures are incubated for a further 24 h before they are harvested onto filter mats, dried for 1 h at 55 °C, and counted. IC_{50} values are calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	The efficacy of selected 4-aminoquinolines (including GSK369796 Dihydrochloride) is measured against P. yoelii or P. berghei in a 4-day test. 28 Cohorts of age-matched female mice are infected iv with 6.4×10^6 or 10.0×10^6 parasites obtained from infected donors, and the mice are randomly distributed in groups of n=5 mice/group (day 0). Treatments are administered from day 0 (one hour after infection) until day 3. The therapeutic efficacy of compounds (including GSK369796 Dihydrochloride) is expressed as the effective dose that reduces parasitemia by 50% (ED_{50}) and 90% (ED_{90}) with respect to vehicle treated groups (ED_{90}) and the dose that achieved eradication of parasitemia until day 23 after infection (NRL). All compounds (including GSK369796 Dihydrochloride) and corresponding vehicles are administered orally at 20 mg/kg or subcutaneously at 10 mg/kg, as appropriate[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. O'Neill PM, et al. Candidate selection and preclinical evaluation of N-tert-butyl isoquine (GSK369796), an affordable and effective 4-aminoquinoline antimalarial for the 21st century. J Med Chem. 2009 Mar 12;52(5):1408-15.

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