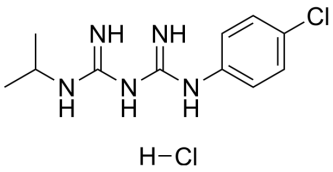
Proguanil hydrochloride

Cat. No.:	HY-B0806A
CAS No.:	637-32-1
Molecular Formula:	$C_{11}H_{17}Cl_2N_5$
Molecular Weight:	290.19
Target:	Parasite; Antifolate
Pathway:	Anti-infection; Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Proguanil hydrochloride, an antimalarial proagent, is metabolized to the active metabolite Cycloguanil (HY-12784). Proguanil hydrochloride is a dihydrofolate reductase (DHFR) inhibitor[1][2].
IC_{50} & Target	Plasmodium
In Vitro	Proguanil per se has only weak antimalarial activity in vitro (IC_{50}=2.4-19 μM), and its effectiveness depends on the active metabolite Cycloguanil (IC_{50}=0.5-2.5 nM). The Cycloguanil is a dihydrofolate reductase (DHFR) inhibitor. The combination of Atovaquone and Proguanil is synergistic in vitro. Both drugs also have activity against gametocytes and pre-erythrocytic (hepatic) stages of malaria parasites[1]. Proguanil acts as a biguanide rather than as its metabolite Cycloguanil (a parasite dihydrofolate reductase [DHFR] inhibitor) to enhance the Atovaquone effect. Proguanil-mediated enhancement is specific for Atovaquone, since the effects of other mitochondrial electron transport inhibitors, such as Myxothiazole and Antimycin, are not altered by inclusion of Proguanil[2]. $5\text{-}HT_3$ receptor responses are reversibly inhibited by Proguanil, the metabolite 4-chlorophenyl-1-biguanide (CPB) and the active metabolite Cycloguanil (CG), with an IC_{50} of 1.81, 1.48 and 4.36 μM, respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Proguanil (p.o.; 2.9 mg/kg body weight; daily for 5 days and 6 weeks respectively) shows mild degenerative changes for five days, while shows severe degenerative changes for six weeks in wistar strain albino rats[4]. Serum testosterone level is significantly decreased for proguanil treatment rats[4]. Administration of Malarone (Atovaquone and Proguanil) to experimentally B. gibsoni infected two dogs in chronic stage and three dogs in acute stage results in decrease in parasitemia, and clinical improvements are observed[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Pudney M, et al. Atovaquone and proguanil hydrochloride: a review of nonclinical studies. J Travel Med. 1999 May;6 Suppl 1:S8-12.

[2]. Srivastava IK, et al. A mechanism for the synergistic antimalarial action of atovaquone and proguanil. Antimicrob Agents Chemother. 1999 Jun;43(6):1334-9.

[3]. Lochner M, et al. The antimalarial drug proguanil is an antagonist at 5-HT3 receptors. J Pharmacol Exp Ther. 2014 Dec;351(3):674-84.

[4]. Stephen AO, et al. Prolonged administration of proguanil induces reproductive toxicity in male rats. J Toxicol Sci. 2011 Oct;36(5):587-99.

[5]. Iguchi A, et al. The in vitro interactions and in vivo efficacy of atovaquone and proguanil against Babesia gibsoni infection in dogs. Vet Parasitol. 2013 Nov 8;197(3-4):527-33.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA