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产品名称：氯胍
产品别名：Proguanil

生物活性：

Description	Proguanil is an antimalarial prodrug that is metabolized to the active metabolite cycloguanil, a dihydrofolate reductase (DHFR) inhibitor.
In Vitro	Proguanil per se has only weak antimalarial activity in vitro (IC50=2.4-19 μM), and its effectiveness depends on the active metabolite cycloguanil (IC50=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-HT_3 receptor responses are reversibly inhibited by proguanil, the metabolite 4-chlorophenyl-1-biguanide (CPB) and the active metabolite cycloguanil (CG), with an IC50 of 1.81, 1.48 and 4.36 μM, respectively[3].
In Vivo	Proguanil could induce infertility in rats which may act by distorting the blood-testis barrier formed by the Sertoli cells. Duration dependent significant decrease in body and organ weights and also in sperm parameters is observed. 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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 33 mg/mL (130.06 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.9412 mL	19.7060 mL	39.4120 mL
5 mM	0.7882 mL	3.9412 mL	7.8824 mL
10 mM	0.3941 mL	1.9706 mL	3.9412 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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.

实验参考：

Cell Assay	Sertoli cells obtained from sixteen to eighteen day-old-rats are cultured and treated with 0.3 μM to 10 μM of proguanil for 5 days after which Sertoli cell viability and nuclei integrity are determined. Also, the genetic expressions of transferrin and Glial cell line-derived neurotrophic factor are assessed[4].
Animal Administration	Rats: Groups of ten to twelve-week-old rats are administered proguanil (2.9 mg/kg body weight) daily for 5 days and 6 weeks respectively. Thereafter, body and reproductive organ weights are taken, sperm parameters are analyzed, while the histology of the testis and epididymis are carried out. Also, serum levels of testosterone, luteinizing hormone and follicle stimulating hormone are determined[4].
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.