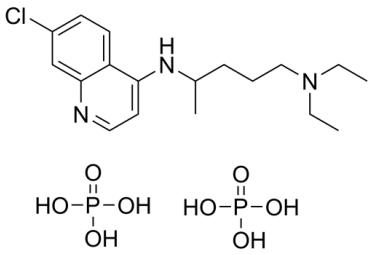
Data Sheet

Product Name:	Chloroquine (phosphate)
Cat. No.:	CS-3811
CAS No.:	50-63-5
Molecular Formula:	$C_{18}H_{32}ClN_3O_8P_2$
Molecular Weight:	515.86
Target:	Antibiotic; Autophagy; HIV; Parasite; SARS-CoV; Toll-like Receptor (TLR)
Pathway:	Anti-infection; Autophagy; Immunology/Inflammation
Solubility:	H_2O : ≥ 33 mg/mL;DMSO : < 1 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

Chloroquine phosphate is an **antimalarial** and anti-inflammatory agent widely used to treat malaria and rheumatoid arthritis. Chloroquine phosphate is an **autophagy** and **toll-like receptors (TLRs)** inhibitor. Chloroquine phosphate is highly effective in the control of **SARS-CoV-2 (COVID-19)** infection in vitro ($\mathbf{EC_{50}}$=1.13 μM)[1][2][3][4]. IC50 & Target:Parasite, Autophagy, SARS-COV-2, TLRs, HIV[1][2][3][4] ***In Vitro:*** Chloroquine (CHQ, 20 μM) inhibits IL-12p70 release and reduces Th1-priming capacity of activated human monocyte-derived Langerhans-like cells (MoLC). Chloroquine (CHQ, 20 μM) enhances IL-1–induced IL-23 secretion in MoLC and subsequently increases IL-17A release by primed $CD4^+$ T cells[1]. Chloroquine (25 μM) suppresses MMP-9 mRNA expression in normoxia and hypoxia in parental MDA-MB-231 cells. Chloroquine has cell-, dose- and hypoxia-dependent effects on MMP-2, MMP-9 and MMP-13 mRNA expression[2]. TLR7 and TLR9 inhibition using IRS-954 or chloroquine significantly reduces HuH7 cell proliferation in vitro[3].

Chloroquine (0.01-100 μM; 48 hours) potently blocks virus infection (vero E6 cells infected with SARS-CoV-2) at low-micromolar concentration (EC_{50}= 1.13 μM). Chloroquine blocks virus infection by increasing endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV[4]. ***In Vivo:*** Chloroquine (80 mg/kg, i.p.) does not prevent the growth of the triple-negative MDA-MB-231 cells with high or low TLR9 expression levels in the orthotopic mouse model[2]. TLR7 and TLR9 inhibition using IRS-954 or chloroquine significantly inhibits tumour growth in the mouse xenograft model. HCC development in the DEN/NMOR rat model is also significantly inhibited by chloroquine[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]The cells are cultured in 6-well plates with normal culture medium in the presence of vehicle or 25 or 50 μM chloroquine, until near confluency, after which they are rinsed with sterile phosphate-buffered saline (PBS) and cultured further for the indicated times in serum-free culture medium. At the desired time-points, the culture medium is discarded and the cells are quickly harvested in lysis buffer and clarified by centrifugation. Subsequent to boiling the supernatants in reducing sodium dodecyl sulphate (SDS) sample buffer, equal amounts of protein (100 μg) are loaded per lane and the samples are electrophoresed into 10 or 4-20% gradient polyacrylamide SDS gels, then transferred to a nitrocellulose membrane. To detect TLR9, the blots are incubated overnight at 4°C with anti-TLR9 antibodies, diluted 1:500 in Tris-buffered saline with 0.1% (v/v) Tween-20 (TBST). Equal loading is confirmed with polyclonal rabbit anti-actin. Secondary detection is performed with horseradish peroxidase-linked secondary antibodies. The protein bands are visualized by chemiluminescence using an ECL kit. **Animal Administration:** [2]Control and TLR9 siRNA MDA-MB-231 cells (5×10^5 cells in 100 μL) are inoculated into the mammary fat pads of four-week-old, immune-deficient mice (athymic nude/nu Foxn1). Treatments are started seven days after tumor cell inoculation. The mice are treated daily either with intraperitoneal (i.p.) chloroquine (80 mg/kg) or vehicle (PBS). The animals are monitored daily for clinical signs. Tumor measurements are performed

twice a week and tumor volume is calculated according to the formula $V=(\pi/6)\ (d1\times d2)^{3/2}$, where d1 and d2 are perpendicular tumor diameters. The tumors are allowed to grow for 22 days, at which point the mice are sacrificed and the tumors are dissected for a final measurement. Throughout the experiments, the animals are maintained under controlled pathogen-free environmental conditions (20-21°C, 30-60% relative humidity and a 12-h lighting cycle). The mice are fed with small-animal food pellets and supplied with sterile water ad libitum.

References:

[1]. Said A, et al. Chloroquine promotes IL-17 production by CD4+ T cells via p38-dependent IL-23 release by monocyte-derived Langerhans-like cells. J Immunol. 2014 Dec 15;193(12):6135-43.

[2]. Tuomela J, et al. Chloroquine has tumor-inhibitory and tumor-promoting effects in triple-negative breast cancer. Oncol Lett. 2013 Dec;6(6):1665-1672.

[3]. Mohamed FE, et al. Effect of toll-like receptor 7 and 9 targeted therapy to prevent the development of hepatocellular carcinoma. Liver Int. 2014 Jul 2. doi: 10.1111/liv.12626.

[4]. Wang M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 2020 Mar;30(3):269-271.

[5]. Colson P, et al. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. Int J Antimicrob Agents. 2020;55(4):105932.

[6]. Savarino A, et al. The anti-HIV-1 activity of chloroquine. J Clin Virol. 2001;20(3):131-135.

CAIndexNames:

1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl-, phosphate (1:2)

SMILES:

O=P(O)(O)O.O=P(O)(O)O.CC(NC1=CC=NC2=CC(Cl)=CC=C12)CCCN(CC)CC

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