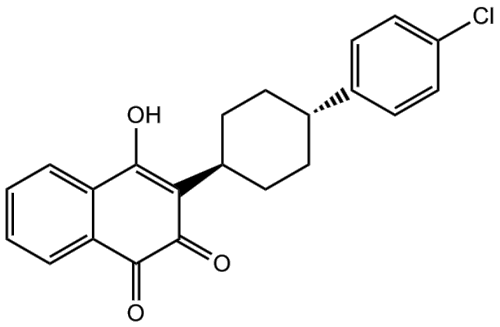
Product Data Sheet

Product Name: Atovaquone
Cat. No.: GC17903

Chemical Properties

Cas. No.	95233-18-4		
Chemical Name	3-(4-(4-chlorophenyl)cyclohexyl)-4-hydroxynaphthalene-1,2-dione		
SMILES	ClC1=C([H])C([H])=C(C([H])=C1[H])C2([H])C([H])([H])C([H])([H])C(C(C3=O)=C(C4=C([H])C([H])=C([H])C([H])=C4C3=O)O[H])([H])C([H])([H])C2([H])[H]		
Formula	$C_{22}H_{19}ClO_3$	M.Wt	366.84
Solubility	≥ 17.03mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines	MCF7 breast cancer cells
Preparation Method	MCF7 cells were treated with Atovaquone (5μM and 10μM) for 48 hours. Vehicle alone (DMSO) control cells were processed in parallel.

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Reaction Conditions	5μM and 10μM; 48h
Applications	Atovaquone treatment markedly inhibited the mitochondrial respiration, with significant reductions in basal respiration, maximal respiration, and ATP levels. Atovaquone treatment increased aerobic glycolysis, glycolytic reserve, and glycolytic reserve capacity. Atovaquone treatment decreased mitochondrial mass and membrane potential, with an increase in ROS levels.

Animal experiment [2]:

Animal models	BALB/c nude female mice subcutaneously injected with FaDu or HCT116 cells
Preparation Method	Mice bearing FaDu and HCT116 xenografts were treated with 50mg/kg Atovaquone for 7 days to investigate the effect on tumour hypoxia. Tumours were harvested after i.p. administration of 0.01ml/g of 10mM EF5 and measured with calipers after 7 days treatment.
Dosage form	50mg/kg/d; 7d; p.o.
Applications	The tumour volume was not significantly altered and EF5 staining confirmed that tumour hypoxia was virtually abolished in both the FaDu and HCT116 xenografts.

References:

[1] Fiorillo M, Lamb R, Tanowitz HB, et al. Repurposing atovaquone: targeting mitochondrial complex III and OXPHOS to eradicate cancer stem cells. *Oncotarget*. 2016;7(23):34084-34099.
[2] Ashton TM, Fokas E, Kunz-Schughart LA, et al. The anti-malarial atovaquone increases radiosensitivity by alleviating tumour hypoxia. *Nat Commun*. 2016;7:12308.

Background

Atovaquone is a hydroxy-1,4-naphthoquinone analogue of ubiquinone, also known as Co-enzyme

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Q10 (CoQ10)[1]. Atovaquone is thought to act as a potent and selective OXPHOS inhibitor, by targeting the CoQ10-dependence of mitochondrial complex III[1]. Atovaquone also has anti-cancer activity, directed against Cancer Stem-like Cells (CSCs)[1]. Atovaquone is an FDA-approved antimalarial drug, currently primarily used clinically to treat Pneumocystis pneumonia (PCP) and toxoplasmosis in immunocompromised patients[1].

In vitro, 5-10μM Atovaquone treatment of MCF7 breast cancer cells for 48h inhibits oxygen-consumption and metabolically induced aerobic glycolysis (the Warburg effect), as well as oxidative stress[1]. Atovaquone potently inhibited the propagation of MCF7-derived CSCs, with an IC_{50} of 1μM[1]. A 24h treatment with Atovaquone alleviated hypoxia in FaDu spheroids at 30μM and in HCT116 and H1299 spheroids at 20μM[2].

In vivo, oral administration of Atovaquone (50mg/kg/d) to FaDu and HCT116 xenograft mice for 7 days did not alter tumor volume but almost completely eliminated tumor hypoxia[2]. Treatment with Atovaquone (17-25mg/kg, p.o.) plus proguanil reduced parasitemia in dogs infected with *Babesia gibsoni*, although relapse of parasitic infection was observed [3].

References:
[1] Fiorillo M, Lamb R, Tanowitz HB, et al. Repurposing atovaquone: targeting mitochondrial complex III and OXPHOS to eradicate cancer stem cells. *Oncotarget*. 2016;7(23):34084-34099.
[2] Ashton TM, Fokas E, Kunz-Schughart LA, et al. The anti-malarial atovaquone increases radiosensitivity by alleviating tumour hypoxia. *Nat Commun*. 2016;7:12308.
[3] Iguchi A, Matsuu A, Fujii Y, Ikadai H, Hikasa Y. The in vitro interactions and in vivo efficacy of atovaquone and proguanil against Babesia gibsoni infection in dogs. *Vet Parasitol*. 2013;197(3-4):527-533.

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