



上海源叶生物科技有限公司
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产品名称: Elacridar

产品别名: GF120918; GW0918; GG918; GW120918

生物活性:				
Description	Elacridar is a potent P-glycoprotein (Pgp) and BCRP inhibitor.			
IC ₅₀ & Target	P-glycoprotein (Pgp), BCRP ^[1]			
In Vitro	Elacridar inhibits P-glycoprotein (P-gp) labeling by [³ H]azidopine with a IC ₅₀ of 0.16 μM ^[2] . In Caki-1 and ACHN cells, elacridar (2.5 μM) significantly inhibits the cell growth. The P-glycoprotein activity is found to be inhibited by elacridar. The combination of elacridar and sunitinib lead to a significant reduction in ABC Sub-family B Member 2 (ABCG2) expression in 786-O cells ^[3] .			
In Vivo	Oral co-administration of elacridar (100 mg/kg, p.o.) and crizotinib increases the plasma and brain concentrations and brain-to-plasma ratios of crizotinib in wild-type mice, equaling the levels in Abcb1a/1b; Abcg2 ^{-/-} mice ^[1] . In friend leukemia virus stain B mice, the brain-to-plasma partition coefficient (Kp, brain) of elacridar is 0.82, 0.43, and 4.31 after intravenous (2.5 mg/kg), intraperitoneal (100 mg/kg), and oral (100 mg/kg) treatment, respectively ^[4] . In Mrp4 ^(-/-) mice, elacridar fully inhibits P-gp mediated transport of topotecan, without significant effects on Bcrp1-mediated transport ^[5] .			
Solvent&Solubility	In Vitro: DMSO : 5 mg/mL (8.87 mM; Need ultrasonic) H ₂ O : < 0.1 mg/mL (insoluble)			
		Solvent Mass Concentration	1 mg	5 mg
	Preparing	1 mM	1.7742 mL	8.8709 mL
	Stock Solutions	5 mM	0.3548 mL	1.7742 mL
		10 mM	---	---
*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℃，6 months；-20℃，1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。 In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 0.5 mg/mL (0.89 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (0.89 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 5.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil				



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	<p>Solubility: 0.5 mg/mL (0.89 mM); Precipitated solution; Need ultrasonic</p> <p>此方案可获得 0.5 mg/mL (0.89 mM)</p> <p>以 1 mL 工作液为例, 取 100 μL 5.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p>
References	<p>[1]. Tang SC, et al. Increased oral availability and brain accumulation of the ALK inhibitor crizotinib by coadministration of the P-glycoprotein (ABCB1) and breast cancer resistance protein (ABCG2) inhibitor elacridar. <i>Int J Cancer</i>. 2014 Mar 15;134(6):1484-94</p> <p>[2]. Hyafil F, et al. In vitro and in vivo reversal of multidrug resistance by GF120918, an acridonecarboxamide derivative. <i>Cancer Res</i>. 1993 Oct 1;53(19):4595-602.</p> <p>[3]. Sato H, et al. Elacridar enhances the cytotoxic effects of sunitinib and prevents multidrug resistance in renal carcinoma cells. <i>Eur J Pharmacol</i>. 2015 Jan 5;746:258-66.</p> <p>[4]. Sane R, et al. Brain distribution and bioavailability of elacridar after different routes of administration in the mouse. <i>Drug Metab Dispos</i>. 2012 Aug;40(8):1612-9.</p> <p>[5]. de Vries NA, et al. P-glycoprotein and breast cancer resistance protein: two dominant transporters working together in limiting the brain penetration of topotecan. <i>Clin Cancer Res</i>. 2007 Nov 1;13(21):6440-9.</p>
实验参考:	
Cell Assay	<p>3.0\times10³ cells per well are seeded in a 96-well plate. After 24 h incubation, an optimum concentration gradient of elacridar is added to each well. After culturing for 48 h, cell viability is assessed using the proliferation reagent, MTT. Control cells are treated with the vehicle only, 0.1% DMSO. After this final incubation, the medium is aspirated and precipitated formazan crystals are dissolved in DMSO (100 μL/well). The absorbance of each well is measured at 540 nm, and a reference wavelength of 650 nm is read with a multiskan JX microplate reader. Cell viability is calculated as percentage of the control value^[3].</p>
Animal Administration	<p>Mice are fasted for 3 hr before oral administration of either elacridar (100 mg/kg) or elacridar vehicle. Two hours later, crizotinib (5 mg/kg) is administered to mice orally. Blood and brains are isolated 4 hr after crizotinib oral administration, and processed as described above. The brain concentrations are corrected for the amount of drug in the brain vasculature. Elacridar hydrochloride is dissolved in dimethyl sulfoxide (106 mg/mL) in order to get 100 mg pure elacridar per 1 mL of dimethyl sulfoxide. The stock solution is further diluted with a mixture of Polysorbate 80, ethanol and water [20:13:67 (v/v/v)] to yield a concentration of 10 mg/mL pure elacridar. [1]</p>
Kinase Assay	<p>10 μL of unlabeled cell membrane suspension (at 0.4 mg of protein/mL) are aliquoted into each well in 96-well plates. 5 μL of GF120918 are then added to each well. The plate is incubated 25 min at 25°C in the dark. 5 μL of tritiated azidopine (1.8 TBq/mmol) (0.6 μM in HCl 0.2 mM) are added to each well. After 25 min of incubation at 25°C in the dark, samples are simultaneously irradiated for 2 min at 254 nm at 0°C with a thin layer chromatography-designed UV lamp directly in contact with the plate. Samples are solubilized in sodium dodecyl sulfate-polyacrylamide gel electrophoresis sample buffer but not heated. After separation on a 7.5% polyacrylamide gel, the gel is treated for fluorography with Amplify and exposed during 3 days onto a photosensitive film. The fluorography is analysed using a Camag thin layer chromatography Scanner II densitometer. [2]</p>
	<p>[1]. Tang SC, et al. Increased oral availability and brain accumulation of the ALK inhibitor crizotinib</p>



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