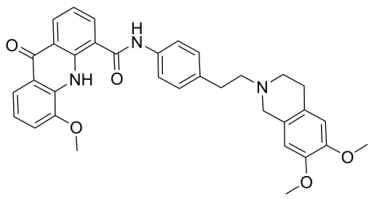
Data Sheet

Product Name:	Elacridar
Cat. No.:	CS-1112
CAS No.:	143664-11-3
Molecular Formula:	$C_{34}H_{33}N_3O_5$
Molecular Weight:	563.64
Target:	BCRP; P-glycoprotein
Pathway:	Membrane Transporter/Ion Channel
Solubility:	DMSO : 5 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

Elacridar is an orally active **P-glycoprotein (Pgp)** and **breast cancer resistance protein (BCRP)** inhibitor. Elacridar can be used to examine the influence of efflux transporters on drug distribution to brain and the research of cancer[1][2]. IC50 & Target: P-glycoprotein (Pgp), BCRP[1] ***In Vitro:*** Elacridar (0.001-1 μM; 2 h) inhibits cell viability of 786-O cells[2].
Elacridar (5 μM; 24 h) affects P-glycoprotein and ABCG2 protein expression levels in MCF-7 and 786-O cell lines[2].
Elacridar (5 μM; 24 h) affects ^{99m}Tc-MIBI intracellular accumulation in MCF-7 and 786-O cells[2]. ***In Vivo:*** Elacridar (100 mg/kg; i.p. once) shows different distribution in brain and plasma[1].
Plasma Pharmacokinetic Parameters of Elacridar in mice[1].

	Mice PO 100 mg/kg	Mice IP 100 mg/kg	Mice IV 2.5 mg/kg
CL/F (ml/min)	2.05	33.2	0.46
Vd/F (liter)	3.5	12.3	0.17
$t_{1/2}$ (h)	20	4.3	4.4
$AUC_{0\text{-}inf}$ (μg?min/ml)	1460	90.3	161.4
F	0.22	0.013	1

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [2]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.

Cell Assay: Elacridar is dissolved in 0.1% DMSO.[3]3.0×10^3 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].

Animal Administration: Elacridar hydrochloride is dissolved in dimethyl sulfoxide (106 mg/mL).[1]Mice are fasted for 3 hr before oral administration of either elacridar (100 mg/kg) or elacridar vehicle. Two hours later, PF-02341066 (5 mg/kg) is administered to mice orally. Blood and brains are isolated 4 hr after PF-02341066 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.

References:

[1]. Sane R, et al. Brain distribution and bioavailability of elacridar after different routes of administration in the mouse. Drug Metab Dispos. 2012 Aug;40(8):1612-9.

[2]. Sato H, et al. Elacridar enhances the cytotoxic effects of sunitinib and prevents multidrug resistance in renal carcinoma cells. Eur J Pharmacol. 2015 Jan 5;746:258-66.

CAIndexNames:

4-Acridinecarboxamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-9,10-dihydro-5-methoxy-9-oxo-

SMILES:

O=C1C2=CC=CC(C(NC(C=C3)=CC=C3CCN4CC(C=C(C(OC)=C5)OC)=C5CC4)=O)=C2NC6=C1C=CC=C6OC

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