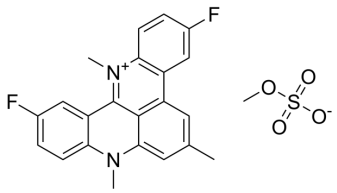
RHPS4

Cat. No.:	HY-101089
CAS No.:	390362-78-4
Molecular Formula:	$C_{23}H_{20}F_2N_2O_4S$
Molecular Weight:	458.48
Target:	Telomerase; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 1 mg/mL (2.18 mM; ultrasonic and warming and heat to 60°C)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1811 mL	10.9056 mL	21.8112 mL
5 mM	---	---	---
10 mM	---	---	---

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

RHPS4 is a potent telomerase inhibitor (IC_{50} = 0.33 μM). RHPS4 is a DNA damage inducer[1][2].

IC_{50} & Target

IC50: 0.33 μM (telomerase in the TRAP assay)[1].

In Vitro

RHPS4 could sensitize tumor cells to anticancer agents that act via disparate mechanisms[1].

RHPS4 (0.5-1 μM, 15 days) induces a senescent-like growth arrest in MCF-7 cells[1].

RHPS4 (1 μM, 4 days) induces phosphorylation of H2AX in transformed and tumor cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	MCF-7, MCF-7 vector control, and MCF-7 c81 cells.
Concentration:	0, 0.2, 0.5, or 1 μM.
Incubation Time:	7 days.

Result:	Inhibited cell proliferation.

In Vivo

RHPS4 (15 mg/kg, iv, 15 days) treatment produces a marked inhibition of tumor weight (tumor weight inhibition [TWI] about 80%; $P < 0.001$) in a very short time, and this effect persists for at least 30 days. A complete tumor response is observed in 80% of mice, and 40% are cured[2].

In all the other tumor xenografts, RHPS4 treatment produces about 50% ($P < 0.001$) TWI at the nadir of the effect and, more important, results in a delay of tumor growth of about 15 (M14 and PC3) and 10 (HT29 and H460) days[2].

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Animal Model:	CD-1 male nude (nu/nu) mice, 6–8 weeks old and weighing 22-24 g (H460, CG5 and HT29, PC3 and M14 cancer models)[2].
Dosage:	15 mg/kg.
Administration:	IV, daily for 15 consecutive days.
Result:	Active as a single agent on all the tumors analyzed. CG5 breast xenografts resulted in the most sensitive tumor.

REFERENCES

[1]. Jennifer C Cookson, et al. Pharmacodynamics of the G-quadruplex-stabilizing telomerase inhibitor 3,11-difluoro-6,8,13-trimethyl-8H-quino[4,3,2-kl]acridinium methosulfate (RHPS4) in vitro: activity in human tumor cells correlates with telomere length and can be enhanced, or antagonized, with cytotoxic agents. Mol Pharmacol. 2005 Dec;68(6):1551-8.

[2]. Erica Salvati, et al. Telomere damage induced by the G-quadruplex ligand RHPS4 has an antitumor effect. J Clin Invest. 2007 Nov;117(11):3236-47.

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