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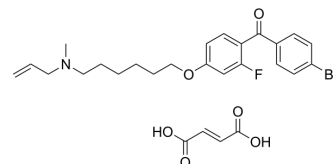
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Ro 48-8071 fumarate

Cat. No.:	HY-18630A
CAS No.:	189197-69-1
Molecular Formula:	C ₂₇ H ₃₁ BrFNO ₆
Molecular Weight:	564
Target:	Others
Pathway:	Others
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

H₂O : 100 mg/mL (177.30 mM; Need ultrasonic)
DMSO : ≥ 55 mg/mL (97.52 mM)
* "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		1.7730 mL	8.8652 mL	17.7305 mL
	5 mM		0.3546 mL	1.7730 mL	3.5461 mL
	10 mM		0.1773 mL	0.8865 mL	1.7730 mL

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

In Vivo

1. Add each solvent one by one: PBS
Solubility: 12.5 mg/mL (22.16 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Ro 48-8071 fumarate is an inhibitor of OSC (Oxidosqualene cyclase) with IC ₅₀ of appr 6.5 nM.
IC ₅₀ & Target	IC ₅₀ : appr 6.5 nM (Oxidosqualene cyclase) ^[1]
In Vitro	In HepG2 cells, Ro 48-8071 reduces cholesterol synthesis dose dependently with an IC ₅₀ value of appr 1.5 nM ^[1] . Ro 48-8071

(10 μ M) significantly reduces the viability of PC-3 prostate cancer cells, but not normal prostate cells. Ro 48-8071 (10-30 μ M) induces apoptosis of both LNCaP and C4-2 cell lines in a dose-dependent manner. And castration-resistant PC-3 and DU145 cells also demonstrate significant levels of apoptosis following 24-hour treatment with Ro 48-8071. Ro 48-8071 (10-25 μ M) reduces AR protein expression in a dose-dependent manner. Ro 48-8071 (0.1-1 μ M) increases ER β protein expression dose-dependently in both hormone-dependent LNCaP and castration-resistant PC-3 cells^[2]. Using mammalian cells engineered to express human ER α or ER β protein, together with an ER-responsive luciferase promoter, Ro 48-8071 dose-dependently inhibits 17 β -estradiol (E2)-induced ER α responsive luciferase activity (IC₅₀, appr 10 μ M), under conditions that are non-toxic to the cells^[3].

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

In Vivo

Ro 48-8071 lowers LDL-C maximally appr 60% at 150 μ mol/kg per day, with no further reduction up to 300 μ mol/kg per day, leaving HDL-C unchanged at all doses in hamsters. Ro 48-8071 (\geq 100 μ mol/kg per day) increases the amount of MOS in liver of hamsters. Ro 48-8071 (300 μ mol/kg per day) remarkably and significantly reduces VLDL secretion of hamsters^[1]. Ro 48-8071 (5 or 20 mg/kg) significantly reduces in vivo tumor growth in mice, without weight loss of the mice. Furthermore, Ro 48-8071 at a concentration of 20 mg/kg, completely eradicates two of the 12 tumors being monitored in the mice in the timeframe tested^[2]. Ro 48-8071 (20 mg/day/kg body weight) leads to a rapid and sustained inhibition (>50%) of cholesterol synthesis in the whole small intestine of BALB/c mice. Sterol synthesis is also reduced in the large intestine and stomach^[4].

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

PROTOCOL

Animal Administration ^[2]

Six-week-old male athymic nude mice (nu/nu) weighing 20-22 g are used in the assay. Castration-resistant PC-3 cells (5×10^6 in 0.15 mL solution) are mixed with matrigel and RPMI-1640 medium (1/1, v/v) and injected subcutaneously into both flanks of each mouse (n=6 animals/group) and tumors allowed to develop. The tumors are measured twice per week with a digital caliper. Tumor volumes are calculated by the formula $(L \times W \times H) \times \pi/6$. Drug treatment is started when tumor volumes reach appr 100 mm³. Mice are given daily tail vein injections of 0.1 mL solution of either 5 or 20 mg/kg Ro 48-8071 for 5 days. This is followed by an injection every other day for six additional treatments and then a final injection 2 hours prior to sacrifice. Control mice receive the same volume of phosphate-buffered saline on the same schedule. The animals are weighed and tumor volumes are measured twice weekly throughout the drug treatment period.

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

CUSTOMER VALIDATION

- Cancer Cell. 2023 May 23;S1535-6108(23)00142-3.
- Nat Commun. 2023 Jul 17;14(1):4267.
- Mol Cell. 2021 Jul 1;81(13):2736-2751.e8.
- Sci China Life Sci. 2021 May 27;1-21.
- Cell Death Dis. 2021 May 13;12(5):482.

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REFERENCES

[1]. Morand OH, et al. Ro 48-8071, a new 2,3-oxidosqualene:lanosterol cyclase inhibitor lowering plasma cholesterol in hamsters, squirrel monkeys, and minipigs: comparison to simvastatin. J Lipid Res. 1997 Feb;38(2):373-90.

[2]. Liang Y, et al. Cholesterol biosynthesis inhibitor RO 48-8071 suppresses growth of hormone-dependent and castration-resistant prostate cancer cells. Onco Targets Ther. 2016 May 30;9:3223-32

[3]. Liang Y, et al. Cholesterol biosynthesis inhibitors as potent novel anti-cancer agents: suppression of hormone-dependent breast cancer by the oxidosqualene cyclase inhibitor RO 48-8071. *Breast Cancer Res Treat.* 2014 Jul;146(1):51-62.

[4]. Chuang JC, et al. Sustained and selective suppression of intestinal cholesterol synthesis by Ro 48-8071, an inhibitor of 2,3-oxidosqualene:lanosterol cyclase, in the BALB/c mouse. *Biochem Pharmacol.* 2014 Apr 1;88(3):351-63.

Caution: Product has not been fully validated for medical applications. For research use only.

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