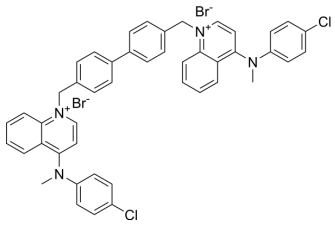
RSM-932A

Cat. No.:	HY-101144
CAS No.:	850807-63-5
Molecular Formula:	$C_{46}H_{38}Br_2Cl_2N_4$
Molecular Weight:	877.53
Target:	Others
Pathway:	Others
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (19.00 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1396 mL	5.6978 mL	11.3956 mL
	5 mM	0.2279 mL	1.1396 mL	2.2791 mL
	10 mM	0.1140 mL	0.5698 mL	1.1396 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (1.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RSM-932A (TCD-717) is a specific ChoKα inhibitor with IC_{50}s of 1 and 33 μM for human recombinant ChoKα and ChoKβ enzymes, respectively. RSM-932A acts as the “first in humans” compound targeting ChoKα. RSM-932A is potent in vitro anti-proliferative and in vivo anti-tumoral activity against human xenografts in mice, showing high efficacy with low toxicity profiles[1][2][3].

IC_{50} & Target

ChoKα[1]

In Vitro

RSM-932A has a potent anti-proliferative activity against most tumor-derived cell lines tested, including those derived from breast, lung, colon, bladder, liver, ovary, bone, cervix, kidney, pancreas, melanoma, and brain tumors, with IC_{50}s of 1.3-7.1 μM for 72 hours[1].

?RSM-932A (TCD-717; 2-4 μM; for 24 hours) promotes cell death of colon cancer cells[2].

?RSM-932A (2-10 μM) exhibits a dosage-dependent decrease in the levels of thymidylate synthase (TS) and thymidine kinase (TK1) proteins proteins[2].

?RSM-932A inhibits Streptococcus pneumoniae choline kinase (sChoK) with IC_{50} of 0.5 μM in LDH/PK and colorimetric enzymatic assays[3].
?The minimum inhibitory concentration (MIC) of RSM-932A for S. pneumoniae is 0.4 μM, and the minimum lethal concentration (MLC) is 1.6 μM[3].
?RSM-932A is a comparatively potent inhibitor with the IC_{50} of 1.75 μM in a steady-state reaction in which the concentration of Choline is equivalent to its K_m[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	DLD-1, HT29, SW620 and HCT116 CRC cell lines and the non-tumourigenic CCD-841 cell line
Concentration:	2, 3, 4 μM
Incubation Time:	24 hours
Result:	Triggered to cell death.

Western Blot Analysis[2]

Cell Line:	DLD-1, HT29 and SW620 cell lines
Concentration:	2, 4, 6, 8, 10 uM
Incubation Time:	24 hours
Result:	A dosage-dependent decrease in the levels of thymidylate synthase (TS) and thymidine kinase (TK1) proteins.

In Vivo

RSM-932A exhibits a potent in vivo anticancer activity, and lack of toxicity at the effective doses[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Athymic nu/nu mice, CD1 nude mice, and BALB/c nude (six-week-old) bearing human tumor xenografts (colon adenocarcinoma HT29, non-small cell lung cancer (NSCLC) H-460, breast adenocarcinoma MDA-MB-231)[3]
Dosage:	7.5 mg/kg, 6 mg/kg, 5 mg/kg, 3 mg/kg, 1 mg/kg, 0.3 mg/kg
Administration:	Administration routes (intraperitoneal or intravenous), treatment schedule (5 consecutive days, 3 days per week, 2 days per week, 1 day per week)
Result:	The LD_{50} was 10.9 mg/kg in mice. The effective dose used in the in vivo experiments was 7.5 mg/kg.

REFERENCES

[1]. Juan Carlos Lacal, et al. Preclinical characterization of RSM-932A, a novel anticancer drug targeting the human choline kinase alpha, an enzyme involved in increased lipid metabolism of cancer cells. Mol Cancer Ther. 2015 Jan;14(1):31-9.

[2]. Ana de la Cueva, et al. Combined 5-FU and ChoKα inhibitors as a new alternative therapy of colorectal cancer: evidence in human tumor-derived cell lines and mouse xenografts. PLoS One. 2013 Jun 10;8(6):e64961.

[3]. Tahl Zimmerman, et al. Identification and validation of novel and more effective choline kinase inhibitors against Streptococcus pneumonia. Sci Rep. 2020 Sep 22;10(1):15418.

[4]. Tahl Zimmerman, et al. Antiplasmodial activity and mechanism of action of RSM-932A, a promising synergistic inhibitor of Plasmodium falciparum choline kinase. Antimicrob Agents Chemother. 2013 Dec;57(12):5878-88.

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