

Product Data Sheet

Product Name: ARN-3236

Cat. No.: GC33070

Chemical Properties

Cas. No. 1613710-01-2

SMILES COC1=CC=C(C2=CNC3=NC=CC(C4=CSC=C4)=C32)C(OC)=C1

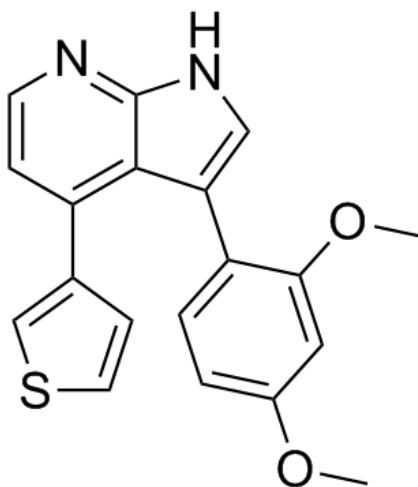
Formula $C_{19}H_{16}N_2O_2S$ M.Wt 336.41

Solubility DMSO : 130 mg/mL (386.43 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

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

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Cell experiment [1]:

Cell lines SKOV3, OVCAR8, A2780, HEY, OVCAR3, OVCAR5, OC316, ES-2, IGROV1, UPN251 (human ovarian cancer cell lines)

Preparation Method Cells were seeded in 96-well plates and incubated for 16 hours. Cells were then pretreated with DMSO or ARN-3236 for 24 hours, followed by an additional 72 hours incubation with paclitaxel (PTX) at indicated concentrations. Cell viability was measured using the sulforhodamine B (SRB) assay. For mechanistic studies, cells were treated with ARN-3236 (0.6–2 μ M) alone, and then processed for immunostaining, cell cycle, apoptosis, or western blot analysis.

Reaction Conditions 0.6–2 μ M; 24-72h.

Applications ARN-3236 inhibited ovarian cancer cell growth and synergistically enhanced sensitivity to paclitaxel in 8 out of 10 cell lines. ARN-3236 induced nuclear-centrosome uncoupling in interphase, blocked centrosome separation in mitosis, caused prometaphase arrest, and led to G2/M cell cycle arrest, apoptosis, and tetraploidy. ARN-3236 also inhibited AKT phosphorylation (at Ser473 and Thr308) and attenuated survivin expression.

Animal experiment [2]:

Animal models BALB/C male mice

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Preparation Method	A pulmonary fibrosis model was established by intratracheal instillation of bleomycin (BLM, 5mg/kg in 100 μ L PBS) on day 0. Mice were then intraperitoneally (i.p.) administered ARN-3236 (10mg/kg and 30mg/kg) or vehicle once daily, starting from the day of BLM instillation. Lung tissues were harvested 28 days after BLM instillation for histological analysis, hydroxyproline assay, and molecular analysis.
Dosage form	10mg/kg and 30mg/kg; i.p.; Once daily for 28 days.
Applications	ARN-3236 treatment dose-dependently attenuated bleomycin-induced pulmonary fibrosis in mice. ARN-3236 partly reversed BLM-induced body weight loss and increased lung coefficient, reduced hydroxyproline content in lung tissues, decreased fibrotic scarring and collagen deposition, and suppressed the expression of fibrotic markers α -SMA and COL1A.

References:

- [1] Zhou J, Alfraidi A, Zhang S, et al. A Novel Compound ARN-3236 Inhibits Salt-Inducible Kinase 2 and Sensitizes Ovarian Cancer Cell Lines and Xenografts to Paclitaxel. Clin Cancer Res. 2017 Apr 15;23(8):1945-1954.
- [2] Zou L, Hong D, Li K, et al. Salt-inducible kinase 2 (SIK2) inhibitor ARN-3236 attenuates bleomycin-induced pulmonary fibrosis in mice. BMC Pulm Med. 2022 Apr 11;22(1):140.

Background

ARN-3236 is a selective salt-inducible kinase 2 (SIK2) inhibitor with an IC₅₀ of less than 1nM. ARN-3236 also inhibits the activity of SIK1 (IC₅₀<21.63nM) and SIK3 (IC₅₀<6.63nM)^[1-2]. By inhibiting SIK2 activity, ARN-3236 blocks centrosome separation, induces cell cycle arrest and apoptosis. ARN-3236 is used in research related to cancer and neuroprotection^[3-4].

In vitro, colorectal cancer cells were pretreated with ARN-3236 (5–10 μ M) for 24 hours and

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subsequently irradiated with X-rays (2–6Gy). ARN-3236 significantly enhanced cellular radiosensitivity and increased radiation-induced growth inhibition and apoptosis. ARN-3236 dose-dependently reduced the efficiency of homologous recombination repair by inhibiting SIK2 kinase activity^[5]. SKOV3, OVCAR8, and other ovarian cancer cells were pretreated with ARN-3236 (0.6–2μM) for 24 hours, followed by treatment with paclitaxel (0–25μM) for 72 hours. By inhibiting SIK2 kinase activity, ARN-3236 blocked centrosome separation and attenuated the AKT/survivin signaling pathway, thereby significantly enhancing the cytotoxicity of paclitaxel while inducing G2/M phase arrest and apoptosis^[6].

In vivo, a pulmonary fibrosis model was established in BALB/C mice via intratracheal instillation of bleomycin (5 mg/kg). Starting on the day of modeling, the mice received a daily intraperitoneal injection of ARN-3236 (10–3mg/kg) for 28 days. ARN-3236 dose-dependently alleviated bleomycin-induced body weight loss and increased lung coefficient. ARN-3236 reduced hydroxyproline content, collagen deposition, and the expression of α-smooth muscle actin (α-SMA) and type I collagen (COL1A) in lung tissue, thereby significantly mitigating bleomycin-induced pulmonary fibrosis^[7]. A depression model was induced in C57BL/6J mice using chronic social defeat stress (CSDS) or chronic unpredictable mild stress (CUMS). Starting at the end of the stress induction, the mice received a daily intraperitoneal injection of ARN-3236 (10–60mg/kg) for 2 weeks. ARN-3236 ameliorated CSDS-induced social avoidance behavior and produced significant antidepressant-like effects^[8].

References:

- [1] Lombardi MS, Gilliéron C, Dietrich D, et al. SIK inhibition in human myeloid cells modulates TLR and IL-1R signaling and induces an anti-inflammatory phenotype. *J Leukoc Biol.* 2016 May;99(5):711-21.
- [2] Bon H, Wadhwa K, Schreiner A, et al. Salt-inducible kinase 2 regulates mitotic progression and transcription in prostate cancer. *Mol Cancer Res.* 2015 Apr;13(4):620-635.
- [3] Rong Z, Zhang L, Li Z, et al. SIK2 maintains breast cancer stemness by phosphorylating LRP6 and activating Wnt/β-catenin signaling. *Oncogene.* 2022 Apr;41(16):2390-2403.
- [4] Fang N, Wang Y, Chen Y, et al. SIK2 mediated mitochondrial homeostasis in spinal cord injury: modulating oxidative stress and the AIM2 inflammasome via CRTC1/CREB signaling. *J Neuroinflammation.* 2025 Dec 3;22(1):283.
- [5] Meng Y, Li S, Lu DS, et al. Salt-inducible kinase 2 confers radioresistance in colorectal cancer by facilitating homologous recombination repair. *MedComm (2020).* 2025 Jan 28;6(2):e70083.

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- [6] Zhou J, Alfraidi A, Zhang S, et al. A Novel Compound ARN-3236 Inhibits Salt-Inducible Kinase 2 and Sensitizes Ovarian Cancer Cell Lines and Xenografts to Paclitaxel. Clin Cancer Res. 2017 Apr 15;23(8):1945-1954.
- [7] Zou L, Hong D, Li K, et al. Salt-inducible kinase 2 (SIK2) inhibitor ARN-3236 attenuates bleomycin-induced pulmonary fibrosis in mice. BMC Pulm Med. 2022 Apr 11;22(1):140.
- [8] Liu Y, Tang W, Ji C, et al, The Selective SIK2 Inhibitor ARN-3236 Produces Strong Antidepressant-Like Efficacy in Mice via the Hippocampal CRTIC1-CREB-BDNF Pathway. Front Pharmacol. 2021 Jan 14;11:624429.

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