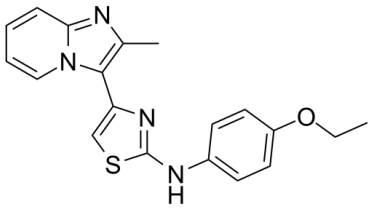
Data Sheet

Product Name:	JK184
Cat. No.:	CS-6080
CAS No.:	315703-52-7
Molecular Formula:	C19H18N4OS
Molecular Weight:	350.44
Target:	Hedgehog
Pathway:	Stem Cell/Wnt
Solubility:	DMSO : ≥ 50 mg/mL (142.68 mM)



BIOLOGICAL ACTIVITY:

JK184 is a potent **Hedgehog (Hh)** pathway inhibitor with **IC_{50}** of 30 nM in mammalian cells. IC50 & Target: IC50: 30 nM (Hedgehog)[1] **In Vitro:** JK184 is designed to antagonize Hh signaling by inhibiting glioma (Gli)-dependent transcriptional activity in a dose dependent manner. JK184 significantly inhibitts proliferation of HUVECs with IC_{50} of 6.3 μg/mL after three days incubation. To evaluate anti-tumor effect of JK184, MTT assay is conducted in Panc-1 and BxPC-3 cells after administration with indicated concentrations of compounds, half maximal inhibitory concentration (IC_{50}) of JK184 (23.7 ng/mL in anc-1 and 34.3 ng/mL in BxPC-3)[1] . Claudin-low cell lines are more sensitive to JK184 treatment than are MCF10a, MTSV1-7, or HMLE-shGFP and HMLE-pBP cells, and JK184 induced a dose-dependent decrease in glioma-associated oncogene homolog 1 (GLI1) transcript and protein levels in these cells. Treatment with the IC_{50} dose of JK184 enhances the proportion of HMLE-shEcad cells that stained with Annexin-V, but are negative for propidium iodide (PI) ($P<0.0001$, t test)[2]. **In Vivo:** JK184 (5 mg/kg, injected intravenously) exhibits good anti-proliferative activity in subcutaneous Panc-1 and BxPC-3 tumor models, and is a good candidate as antitumor drug targeted Hh signaling. However, JK184 has a poor pharmacokinetic profile and bioavailability[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: JK184 is dissolved in DMSO and stored, and then diluted with appropriate medium before use[1]. [1]The Shh-LIGHT2 cells are seeded in 96-well plates and grown to confluency. The Shh-LIGHT2 cells are treated with various concentrations of JK184 micelles or free JK184 or micelles in DMEM containing 0.5% CS, 0.1 mg/mL streptomycin, 100 U/mL penicillin, 5% Shh-N conditioned medium obtained from Shh-N-producing HEK293 cells. The treated cells are cultured further for 60 h, and firefly and Renilla luciferase activities are measured using a dual luciferase kit. Proliferation assay or apoptosis evaluation of HUVECs is measured using MTT method or FCM analysis, respectively. HUVECs are treated with a series concentration of free JK184, JK184 micelles, or blank MPEG-PCL micelles for 48 h, respectively. The mean percentage of cell inhibition or apoptosis is calculated[1]. **Animal Administration:** JK184 is dissolved in DMSO and then diluted with PBS or saline[1].[1]Mice[1]

Five-week-old female athymic (nu/nu) mice are used. BxPC-3 and Panc-1 tumors are established by s.c. injection of 1×10^7 cells. Mice bearing tumors around 100 mm^3 are selected and randomized into treatment groups (5 mice per group). Mice are injected intravenously every day for 30 days with 100 μL of NS (control), blank micelles, free JK184 (5 mg/kg body weight), or JK184 micelles (5 mg/kg body weight), respectively. Tumor length and width are determined every 3 days and tumor volume (TV) is calculated using the following formula: $TV=0.5\times length\times width^2$. At the end of experiment, mice are sacrificed. Solid tumors are removed and processed for immunohistochemical analysis and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay.

References:

[1]. Zhang N, et al. Biodegradable polymeric micelles encapsulated JK184 suppress tumor growth through inhibiting Hedgehog signaling pathway. Nanoscale. 2015 Feb 14;7(6):2609-24.

[2]. Colavito SA, et al. Significance of glioma-associated oncogene homolog 1 (GLI1) expression in claudin-low breast cancer and crosstalk with the nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) pathway. Breast Cancer Res. 2014 Sep 25;16(5):444.

CAIndexNames:

2-Thiazolamine, N-(4-ethoxyphenyl)-4-(2-methylimidazo[1,2-a]pyridin-3-yl)-

SMILES:

CC1=C(C2=CSC(NC3=CC=C(OCC)C=C3)=N2)N4C=CC=CC4=N1

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