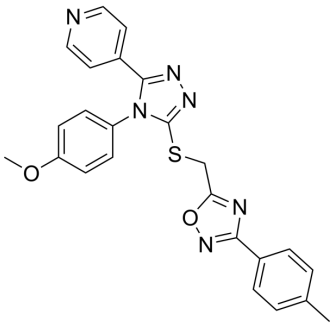
JW74



Cat. No.:	HY-19739
CAS No.:	863405-60-1
Molecular Formula:	$C_{24}H_{20}N_6O_2S$
Molecular Weight:	456.52
Target:	Wnt
Pathway:	Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (109.52 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1905 mL	10.9524 mL	21.9048 mL
	5 mM	0.4381 mL	2.1905 mL	4.3810 mL
	10 mM	0.2190 mL	1.0952 mL	2.1905 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.75 mg/mL (6.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (6.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JW74 antagonizes LiCl-induced activation of the canonical Wnt signaling with an IC_{50} of 420 nM.

IC_{50} & Target

IC50: 420 nM (Wnt)[1]

In Vitro

JW74 shows a reduction of canonical Wnt signaling in the ST-Luc assay with an IC_{50} of 790 nM[1]. The effect of tankyrase inhibition on cellular viability is tested by performing an MTS assay. The cellular viability of U2OS cells treated for 72 h treatment with 10 μM JW74 is reduced to 80%, relative to DMSO-treated cells. Flow cytometry is also performed to determine the expression marker Ki-67 in U2OS following 48 h treatment with DMSO or 10 uM JW74. Ki-67 expression is reduced from 97.5% in DMSO-treated cells to 86.7% in JW74-treated cells[2].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The in vivo efficacy of JW74 is tested using SW480 cell xenografts. A relatively high dose of JW74 (150 or 300 mg/kg) is used because of a rapid compound degradation in the organism as indicated in the human liver microsome analysis ($t_{1/2}$=2.5 minutes) and in pharmacokinetic analyses (after per oral injections: $t_{1/2}$=30 minutes and intravenous injections: $t_{1/2}$=15 minutes). The presence of JW74 in tumors and plasma is identified by mass spectrometry. JW74 concentration in tumors is in the range 4.2 to 72.1 µmol/kg for JW74 150 mg/kg, 1.9 to 11.1 µmol/kg for JW74 300 mg/kg, and 2.8 µM in plasma for both doses[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The cell lines U2OS, SaOS-2, and KPD are cultured in RPMI-1640. Two to three thousand cells attached overnight in 96-well plates are treated with culturing medium containing 0.1% DMSO (control) or JW74 (10-0.1 µM). Proliferation rates based on cell confluence are determined by live cell imaging. Cellular viability is also determined by MTS assay. Expression of the proliferation marker Ki-67 is performed by staining cells with PE-mouse anti-human Ki-67 and by analyzing the expression by flow cytometry[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] 40 female C.B-Igh-1b/IcrTac-Prkdcscid mice are injected subcutaneously (s.c.) at the right posterior flank with 10^7 SW480 cells diluted in 100 µL PBS. Injections are initiated when tumor formation is visible in 50 % of the animals (7 days). Mice are randomized and divided into three treatment groups: JW74 150 mg/kg, JW74 300 mg/kg and vehicle control, 1 % Tween 80. Daily intra peritoneal (i.p.) injections (200 µL) with two day injection intermissions after every fifth injection day are performed until the experiment end (29 days). At the termination day, 24 hours after the last injection, blood is collected after cardiac puncture and tumors are dissected and weighed. The compound concentration in tumors and blood are determined using on-line and off-line Solid Phase Extraction-Capillary Liquid Chromatography (SPE-CapLC) instrumentation coupled to a Time of Flight (TOF) mass spectrometer. A Zorbax SB C18 5 µm 150×0.3 mm column is used for separation, and a Knauer K-2600 UV detector is used as a complimentary detector. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Cell Mol Med. 2020 Apr;24(8):4439-4451.
- Sci Rep. 2018 Sep 24;8(1):14268.
- Journal of Traditional and Complementary Medicine. 2024 Mar 7.

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REFERENCES

[1]. Waaler J, et al. Novel synthetic antagonists of canonical Wnt signaling inhibit colorectal cancer cell growth. Cancer Res. 2011 Jan 1;71(1):197-205.

[2]. Stratford EW, et al. The tankyrase-specific inhibitor JW74 affects cell cycle progression and induces apoptosis and differentiation in osteosarcoma cell lines. Cancer Med. 2014 Feb;3(1):36-46.

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

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