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产品名称: JW74
产品别名: JW74

生物活性:				
Description	JW74 antagonizes LiCl-induced activation of the canonical Wnt signaling with an IC ₅₀ of 420 nM.			
IC ₅₀ & Target	IC ₅₀ : 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 μ M 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 μ M JW74. Ki-67 expression is reduced from 97.5% in DMSO-treated cells to 86.7% in JW74-treated cells[2].			
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 μ mol/kg for JW74 150 mg/kg, 1.9 to 11.1 μ mol/kg for JW74 300 mg/kg, and 2.8 μ M in plasma for both doses[1].			
Solvent&Solubility	In Vitro: DMSO : ≥ 50 mg/mL (109.52 mM) H ₂ O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.			
		Solvent Mass Concentration	1 mg	5 mg
	Preparing	1 mM	2.1905 mL	10.9524 mL
	Stock Solutions	5 mM	0.4381 mL	2.1905 mL
		10 mM	0.2190 mL	1.0952 mL
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液; 一旦配成溶液, 请分装保存, 避免反复冻融造成的产品失效。 储备液的保存方式和期限: -80°C, 6 months; -20°C, 1 month。 -80°C 储存时, 请在 6 个月内使用, -20°C 储存时, 请在 1 个月内使用。 In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液, 再依次添加助溶剂: ——为保证实验结果的可靠性, 澄清的储备液可以根据储存条件, 适当保存; 体内实验的工作液, 建议您现用现配, 当天使用; 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比; 如在配制过程中出现沉淀、析出现象, 可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.75 mg/mL (6.02 mM); Clear solution 此方案可获得 ≥ 2.75 mg/mL (6.02 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μ L 27.5 mg/mL 的澄清 DMSO 储备液加到 400 μ L PEG300 中, 混合均匀			



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	向上述体系中加入 50 μL Tween-80, 混合均匀; 然后继续加入 450 μL 生理盐水平定容至 1 mL。 2.请依序添加每种溶剂: 10% DMSO $\rightarrow$90% corn oil Solubility: $\geq$ 2.75 mg/mL (6.02 mM); Clear solution 此方案可获得 $\geq$ 2.75 mg/mL (6.02 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例, 取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。
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.
实验参考:	
Cell Assay	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].
Animal Administration	Mice[1] 40 female C.B-Igh-1b/IcrTac-Prkdcscid mice are injected subcutaneously (s.c.) at the right posterior flank with 10^7SW480 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$\times$0.3 mm column is used for separation, and a Knauer K-2600 UV detector is used as a complimentary detector.
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.