

产品名称: **U-73122 hydrate**

产品别名: **U-73122**

生物活性:				
Description	U-73122 is a phospholipase C (PLC) and 5-LO (5-lipoxygenase) inhibitor with an IC ₅₀ of 1-2.1 μM for PLC.			
IC ₅₀ & Target	5-LOX			
In Vitro	U-73122 potently inhibits receptor-coupled activation of PLC in membranes isolated from PMNs[1]. U-73122 inhibits N-formyl-methionyl-leucyl-phenylalanine-induced aggregation of human polymorphonuclear neutrophils (PMN) and the associated production of IP ₃ and diacylglycerol[2]. U-73122 markedly inhibits inositol phosphate release elicited by either oxotremorine-M or guanosine-5'-O-(3-thiotriphosphate) than that induced by added Ca ²⁺ in digitonin-permeabilized cells[3].			
In Vivo	U73122 significantly attenuates TNF-α mRNA expression, has no effect on sham animals, but significantly increases heart work and rate of contraction and relaxation without affecting heart rate in endotoxemic mice[4]. U73122 (400 nM/μL) significantly reduces total lordosis durations, compared to vehicle infusions to the VTA, of oestradiol and progesterone-primed hamsters. VTA infusions of U73122 do not alter motor behaviour of hamsters in the activity monitor, but there is a significant effect of muscimol to decrease total number of beam breaks compared to hamsters administered SKF38393[5].			
Solvent&Solubility	In Vitro: DMSO : 12.5 mg/mL (26.90 mM; Need ultrasonic) H ₂ O : < 0.1 mg/mL (insoluble)			
		Solvent Concentration	Mass	
	Preparing	1 mM	1 mg	5 mg10 mg
	Stock Solutions	5 mM	2.1522 mL	10.7610 mL21.5220 mL
		10 mM	0.4304 mL	2.1522 mL4.3044 mL
			0.2152 mL	1.0761 mL2.1522 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 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: 1.25 mg/mL (2.69 mM); Suspended solution; Need ultrasonic
此方案可获得 1.25 mg/mL (2.69 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。
以 1 mL 工作液为例，取 100 μL 12.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀，向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)
Solubility: 1.25 mg/mL (2.69 mM); Suspended solution; Need ultrasonic
此方案可获得 1.25 mg/mL (2.69 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

	<p>以 1 mL 工作液为例，取 100 μL 12.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO \rightarrow90% corn oil Solubility: \geq 1.25 mg/mL (2.69 mM); Clear solution</p> <p>此方案可获得 \geq 1.25 mg/mL (2.69 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。</p> <p>以 1 mL 工作液为例，取 100 μL 12.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
References	<p>[1]. Smith RJ, et al. Receptor-coupled signal transduction in human polymorphonuclear neutrophils: effects of a novel inhibitor of phospholipase C-dependent processes on cell responsiveness. J Pharmacol Exp Ther. 1990 May;253(2):688-97.</p> <p>[2]. Bleasdale JE, et al. Selective inhibition of receptor-coupled phospholipase C-dependent processes in human platelets and polymorphonuclear neutrophils. J Pharmacol Exp Ther. 1990 Nov;255(2):756-68.</p> <p>[3]. Thompson AK, et al. The aminosteroid U-73122 inhibits muscarinic receptor sequestration and phosphoinositide hydrolysis in SK-N-SH neuroblastoma cells. A role for Gp in receptor compartmentation. J Biol Chem. 1991 Dec 15;266(35):23856-62.</p> <p>[4]. Peng T, et al. Disruption of phospholipase Cgamma1 signalling attenuates cardiac tumor necrosis factor-alpha expression and improves myocardial function during endotoxemia. Cardiovasc Res. 2008 Apr 1;78(1):90-7. Epub 2007 Dec 12.</p> <p>[5]. Frye CA, et al. In the ventral tegmental area, the membrane-mediated actions of progestins for lordosis of hormone-primed hamsters involve phospholipase C and protein kinase C. J Neuroendocrinol. 2007 Sep;19(9):717-24.</p> <p>[6]. Hörnig M, et al. Inhibition of 5-lipoxygenase by U73122 is due to covalent binding to cysteine 416. Biochim Biophys Acta. 2012 Feb;1821(2):279-86.</p> <p>[7]. Xie W, et al. 3Beta-hydroxy-6-aza-cholestane and related analogues as phosphatidylinositol specific phospholipase C (PI-PLC) inhibitors with antitumor activity. Bioorg Med Chem. 2000 Apr;8(4):699-706.</p>
实验参考：	
Cell Assay	<p>Agonist-induced production of IP₃ in PMN is measured by use of the competitive radiobinding assay. PMN (2 x 10⁶-10⁷) in 0.2 mL of phosphate-buffered saline, pH 7.4 [NaCl (138 mM), Na₂HPO₄ (8.1 mM), KH₂PO₄ (1.5 mM), KCl (2.7 mM), CaCl₂ (1.0 mM), MgCl₂ (1.0 mM) and glucose (0.1%, w/v)] are incubated in conical polypropylene tubes at 37°C in a shaking water bath. U-73122 or U-73343 is added (in 1 μL of DMSO) 3 min before the addition of agonist, FMLP (0.1 μM) plus cytochalasin B (5 μg/mL). FMLP and cytochalasin B are added in 1 μL each of DMSO and ethanol, respectively. Appropriate vehicle controls are included in each experiment. PMN incubation mixtures are quenched with the addition of 0.07 mL of ice-cold TCA (20%, w/v) and a portion (0.2 mL) of the TCA extract is processed for the measurement of IP₃ by competitive radiobinding as described above for platelets. [2]</p>
Animal Administration	<p>Hamsters are hormone-primed with 17β-oestradiol at h 0 and progesterone at h 45. At h 48, hamsters are pretested for motor behaviour, followed by sexual behaviour testing, and bilateral infusions of U73122 (400 nM/μL) or saline vehicle. Thirty minutes after infusions, hamsters are re-tested for sexual behaviour (post inhibitor infusion test) and, immediately after testing, infused bilaterally with SKF38393 (100 ng/μL), muscimol (100 ng/μL), or saline vehicle. Thirty minutes after</p>

	<p>the agonist or vehicle infusions, lordosis and motor behaviour of hamsters is reassessed (post agonist infusion test). All hamsters are assigned to one pretreatment condition, U73122 or vehicle, and are tested once a week for 3 weeks until all infusion conditions (SKF38393, muscimol or vehicle), are received. The order in which hamsters receive SKF38393, muscimol or vehicle infusions is counterbalanced across the group. [5]</p>
References	<p>[1]. <u>Smith RJ, et al. Receptor-coupled signal transduction in human polymorphonuclear neutrophils: effects of a novel inhibitor of phospholipase C-dependent processes on cell responsiveness. J Pharmacol Exp Ther. 1990 May;253(2):688-97.</u></p> <p>[2]. <u>Bleasdale JE, et al. Selective inhibition of receptor-coupled phospholipase C-dependent processes in human platelets and polymorphonuclear neutrophils. J Pharmacol Exp Ther. 1990 Nov;255(2):756-68.</u></p> <p>[3]. <u>Thompson AK, et al. The aminosteroid U-73122 inhibits muscarinic receptor sequestration and phosphoinositide hydrolysis in SK-N-SH neuroblastoma cells. A role for Gp in receptor compartmentation. J Biol Chem. 1991 Dec 15;266(35):23856-62.</u></p> <p>[4]. <u>Peng T, et al. Disruption of phospholipase Cgamma1 signalling attenuates cardiac tumor necrosis factor-alpha expression and improves myocardial function during endotoxemia. Cardiovasc Res. 2008 Apr 1;78(1):90-7. Epub 2007 Dec 12.</u></p> <p>[5]. <u>Frye CA, et al. In the ventral tegmental area, the membrane-mediated actions of progestins for lordosis of hormone-primed hamsters involve phospholipase C and protein kinase C. J Neuroendocrinol. 2007 Sep;19(9):717-24.</u></p> <p>[6]. <u>Hörnig M, et al. Inhibition of 5-lipoxygenase by U73122 is due to covalent binding to cysteine 416. Biochim Biophys Acta. 2012 Feb;1821(2):279-86.</u></p> <p>[7]. <u>Xie W, et al. 3Beta-hydroxy-6-aza-cholestane and related analogues as phosphatidylinositol specific phospholipase C (PI-PLC) inhibitors with antitumor activity. Bioorg Med Chem. 2000 Apr;8(4):699-706.</u></p>

源叶生物