产品名称：**TAK-242**
产品别名：瑞沙托维 ； **Resatorvid**

生物活性：					
Description	Resatorvid (TAK-242) is a selective Toll-like receptor 4 (TLR4) inhibitor and plays pivotal role in various inflammatory diseases. Resatorvid inhibits NO, TNF-R and IL-6 production with IC50s of 1.8 nM, 1.9 nM and 1.3 nM, respectively. Resatorvid downregulates expression of TLR4 downstream signaling molecules MyD88 and TRIF[1][2].				
IC_{50} & Target	TLR4				
In Vitro	Resatorvid suppresses the production of NO, TNF-α, and IL-6 from LPS-stimulated human peripheral blood mononuclear cells (PBMCs) at IC50 values from 11 to 33 nM[1]. Resatorvid (1-100 nM; 4 hours) inhibits mRNA expression of IL-6 and TNF-α induced by LPS and IFN-γ in RAW264.7 cells[1]. Resatorvid (1-100 nM; 15 minutes; PBMCs cells) markedly inhibits the LPS-induced phosphorylation of extracellular signal-regulated kinase 1/2 (Erk1/2), p38, and JNK/SAPK as well as degradation of IκBβ at a concentration of 100 nM[1].				
	RT-PCR[1]				
	Cell Line:	RAW264.7 cells			
	Concentration:	1 nM, 10 nM, 100 nM			
	Incubation Time:	4 hours			
	Result:	TNF-α and IL-6 mRNA expression levels were clearly suppressed at concentrations of 10 to 100 nM.			
	Western Blot Analysis[1]				
	Cell Line:	PBMCs cells			
	Concentration:	1 nM, 10 nM, 100 nM			
	Incubation Time:	15 minutes			
	Result:	The phosphorylation of mitogen-activated protein kinases induced by LPS was also inhibited in a concentration-dependent manner.			
In Vivo	Resatorvid (0.3 mg/kg; intraperitoneal injection; twice a week; for 4 weeks; ApoE knockout and wild-type mice) treatment inhibites serum autoantibodies (ANA and anti-dsDNA), cytokines (IFN-γ, TNF-α, IL-1β), lung inflammation, and intima-media thickness in brachiocephalic artery[3].				
	Animal Model:	30 ApoE knockout and 30 wild-type mice on C57BL/6 background (female, 10 weeks old)[3]			
	Dosage:	0.3 mg/kg			
	Administration:	Intraperitoneal injection; twice a week; for 4 weeks			
	Result:	Inhibited serum autoantibodies (ANA and anti-dsDNA), cytokines (IFN-γ, TNF-α, IL-1β), lung inflammation, and intima-media thickness in brachiocephalic artery.			
	In Vitro: **DMSO : 100 mg/mL** (**276.38 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)				
	Preparing	**Solvent / Mass / Concentration**	**1 mg**	**5 mg**	**10 mg**
		1 mM	2.7638 mL	13.8190 mL	27.6381 mL

<table>
<tr><td rowspan="3">Solvent&Solubility</td><td rowspan="2">Stock Solutions</td><td>5 mM</td><td>0.5528 mL</td><td>2.7638 mL</td><td>5.5276 mL</td></tr>
<tr><td>10 mM</td><td>0.2764 mL</td><td>1.3819 mL</td><td>2.7638 mL</td></tr>
<tr><td colspan="5">*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 (7.60 mM); Clear solution
此方案可获得 ≥ 2.75 mg/mL (7.60 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 27.5 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: 2.75 mg/mL (7.60 mM); Suspended solution; Need ultrasonic
此方案可获得 2.75 mg/mL (7.60 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 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

3.请依序添加每种溶剂： 10% DMSO →90% corn oil
Solubility: ≥ 2.75 mg/mL (7.60 mM); Clear solution
此方案可获得 ≥ 2.75 mg/mL (7.60 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。</td></tr>
<tr><td>References</td><td colspan="5">[1]. Ii M, et al. A novel cyclohexene derivative, ethyl (6R)-6-[N-(2-Chloro-4-fluorophenyl)sulfamoyl]cyclohex-1-ene-1-carboxylate (TAK-242), selectively inhibits toll-like receptor 4-mediated cytokine production through suppression of intracellular signaling.
[2]. Yamada M, et al. Discovery of novel and potent small-molecule inhibitors of NO and cytokine production as antisepsis agents: synthesis and biological activity of alkyl 6-(N-substituted sulfamoyl)cyclohex-1-ene-1-carboxylate. J Med Chem. 2005 Nov 17;48(23):7457-67.
[3]. Ni JQ, et al. Role of toll-like receptor 4 on lupus lung injury and atherosclerosis in LPS-challenge ApoE$^{-/-}$ mice. Clin Dev Immunol. 2013;2013:476856.</td></tr>
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